(1)

CMAT Control #
1997206-0000-036

[DECLASSIFIED 19 OCT 95]

THE JOINT STAFF
WASHINGTON, DC

Reply ZIP Code:
20318-4000

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE HEALTH AFFAIRS

Subject: Vaccination and Immunization Against Biological Warfare (BW) Agents.

1. The Joint Staff concurs in your recommendation* to vaccinate personnel deployed in support of Operation DESERT SHIELD against Biological Warfare (BW) agents of Anthrax and Botulinum Toxin.

2. Ongoing cooperative efforts involving the Food and Drug Administration and your office are encouraging. Capability to meet all mobilization requirements associated with vaccination against such threats must be adequate. Additionally, we are concerned that dissemination of this policy below the command level be carefully considered in light of the potential negative psychological impact such information will likely generate. Appropriate public affairs and military leadership guidelines will be necessary for successful implementation.

3. The Joint Staff will continue to monitor this military-unique contingency policy.

Reference:
* ASD(HA) Memorandum, 4 Sep 90, SAB

CLASSIFIED BY: J4/MRD
DECLASSIFY ON: OADR

[DECLASSIFIED 19 OCT 95]

JOINT STAFF ACTION PROCESSING FORM

TO DJS	CLASSIFICATION	ACTION NUMBER	ORIG SUSPENSE
		SJS 1865-156-00	6 SEP 90
THRU J-3		ACTION	CJCS SUSPENSE
		X APPROVAL	
		X SIGNATURE	SJS SUSPENSE
		INFORMATION	
			J SUSPENSE
			5 SEP 90

SUBJECT Vaccination and Immunization Against Biological Warfare (BW) Agents

ACTION SUMMARY

1. (U) Purpose: To obtain approval and release of the letter at TAB A.

2. Background: The Assistant Secretary of Defense (Health Affairs) requested* comments concerning vaccination against the BW agent Anthrax and vaccination against the BW agent Botulinum Toxin.

3. Discussion: Current intelligence suggests that Iraq has developed and weaponized two BW agents: Anthrax and Botulinum Toxin.

[

EXEMPTION 1.3 (A)(2)

]

Fatalities in unvaccinated service members is greater than 90% .

Limited quantities of vaccine is only produced by one US vendor, the Michigan Department of Public Health.

Vaccine has negative side effects. 13,623 immunizations produced mild reaction in 7.6%, moderate reactions in 0.8%, and severe reactions in 0.1% of cases.

Severe reactions are not life threatening. Severe reactions could cause limited physical activity for 48 - 72 hrs.

[DECLASSIFIED 19 OCT 95]

[

EXEMPTION 1.3 (A)(2)

]

Fatalities in unvaccinated service members is high. Protection afforded by vaccine is unknown among human subjects; animal studies indicate that immunization would only provide limited protection.

ACTION OFFICER/DIV/PHONE [EXEMPTION (b)(1)]

DATE PREPARED 5 SEP 90 CLASSIFICATION Classified by Declassify on OADR

JS FORM 136L FEB 90 Internal Staff Paper, Release Covered by MOP 39

PREVIOUS EDITIONS OF THIS FORM ARE OBSOLET

Limited quantities of vaccine is only produced by one US vendor, the Michigan Department of Public Health.

Vaccine produces moderate to severe side affects in 1.3%to 10.8% of those receiving the second immunization.

Reaction could limit physical activity for 5 - 10 days.

Constraints: Both vaccines are only produced by one vendor.

ASD(HA) recommended position is: for Anthrax, begin vaccination of troops as soon as sufficient quantity of vaccine is available; for Botulinum Toxin, begin vaccination of selected units and personnel having high probability of exposure.

Joint Staff position is to concur with the recommendation to immunize service members against known BW threats with specific attention paid to the issuance of clear public affairs and leadership guidelines associated with this sensitive issue.

[DECLASSIFIED 19 OCT 1995]

4. Recommendation: Recommend the DJS approve and sign the attached memorandum at TAB A.

Reference:
* ASD(HA) Memorandum, 4 Sep 90, SAB

[DECLASSIFIED 19 OCT 95]

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS 4 SEP 95

MEMORANDUM FOR THE CHAIRMAN OF THE JOINT CHIEFS OF STAFF
UNDER SECRETARY OF DEFENSE FOR ACQUISITION
UNDER SECRETARY OF DEFENSE FOR POLICY

SUBJECT: Vaccination and Immunization Against Biological Warfare (BW) Agents

Current intelligence suggests that Iraq has developed and weaponized two BW agents, Botulinum Toxin and Anthrax. The medical community has reviewed these issues and formulated a medical recommendation for each (attachments 1 and 2). The non-medical concerns surrounding these issues were not considered. I request that you review the attached decision papers and provide any comments you may have by COB September 6, 1990.

[EXEMPTION (b)(6)]

Attachments:
As Stated

[DECLASSIFIED 19 OCT 95]

ATTACHMENT 1

EXECUTIVE SUMMARY/COVER BRIEF

MEMORANDUM FOR THE SECRETARY OF DEFENSE

THROUGH: DEPUTY SECRETARY OF DEFENSE
FROM: ASSISTANT SECRETARY OF DEFENSE FOR HEALTH AFFAIRS
SUBJECT: Vaccination Against The Biological Warfare (BW) Agent - Anthrax

PURPOSE: ACTION--Approve the administration of the anthrax vaccine to troops involved in operation DESERT SHIELD.

DISCUSSION:

1. Iraqi BW capabilities:

a) Intelligence suggests that Anthrax is one of the two BW agents developed and weaponized by the Iraqi military.

2. Effects of Anthrax BW agent:

a) It takes from 1 to 6 days for the symptoms to appear following inhalation. Fatality for symptomatic pulmonary anthrax in unvaccinated service members is greater than 90 percent.

3. Preventive capabilities:

a) [

EXEMPTION 1.3 (A)(2)

].

b) A vaccine against Anthrax is also available and provides antibody protection.

c) Vaccination is administered by syringe injections. Following the initial vaccination a booster shot is given two weeks later. A second booster shot will be administered

no sooner than two weeks following the first booster shot. The timing of the second booster will be dependent on the availability of vaccine. Vaccination by multi-dose injection guns is not possible.

d) The vaccination protection afforded against high levels of pulmonary inhalation exposure possible in BW weapons is unknown among human subjects. However, there have been positive results using animal research models.

4. Negative side effects of vaccine:

a) Immunization of 13,623 cases produced mild reaction in 7.6%, moderate reactions in 0.8%, and severe reactions in 0.1% of the cases. Severe reactions are not life threatening and are easily treated. Only severe reactions would cause limited physical activity for an estimated 48 to 72 hours.

b) Those who have had a prior Anthrax infection are advised against vaccination.

5. Constraints:

a) The vaccine is only produced by one vendor, the Michigan Department of Public Health, in limited quantities.

b) Cooperative efforts involving the U.S. Army Medical Research and Development Command and the Food and Drug Administration, which approves release of each vaccine batch, will allow for sufficient quantities to be available shortly.

RECOMMENDATION

Begin the vaccination of troops participating in operation DESERT SHIELD as soon as a sufficient quantity of vaccine is available. The vaccination priority of troops would be established by CINCCENT.

In addition to the coordinations below, this recommendation also represents the consensus of the three Surgeons General and the Armed Forces Epidemiological Board.

Coordination:

JCS
USDA

USDP

SECDEF DECISION

Approved

Disapproved

Other:

[DECLASSIFIED 19 OCT 95]

ATTACHMENT 2

EXECUTIVE SUMMARY/COVER BRIEF

MEMORANDUM FOR THE SECRETARY OF DEFENSE

FROM: ASSISTANT SECRETARY OF DEFENSE FOR HEALTH AFFAIRS

SUBJECT: Immunization Against the Biological Warfare (BW) Agent - Botulinum Toxin (BT)

PURPOSE: ACTION -- Approve the botulinum toxin immunization for a limited number of troops involved in Operation DESERT SHIELD.

DISCUSSION:

1. Iraqi Capabilities:

a) [EXEMPTION (b)(1)]

2. Effects of BW agent - Botulinum Toxin:

a) BT is a toxic product of a bacterium and is therefore categorized as a BW agent. Its effcts are those of a neuro-toxin and not that of a live organism.

b) The effects of inhaled BT exposure occur in 3-48 hours producing a neuromuscular paralysis with a high fatality rate from respiratory arrest.

3. Preventive capabilities:

a) The use of Mission-Oriented Protective Posture (MOPP) gear is required. [EXEMPTION (b)(1)] Skin absorption of this agent, unlike chemical agents, is not a factor.

b) An investigational vaccine being developed by the Center for Disease Control against BT is available but provides a relatively poor antibody response.

c) Vaccination is administered by syringe injections. Following the initial vaccination a booster

[DECLASSIFIED 19 OCT 1995]

shot is administered ten weeks following the first booster shot.

d) Two Antisera are available, horse and human, to provide passive immunization.

e) The protection afforded by both the vaccine and antisera against high levels of pulmonary inhalation exposure possible in BW weapons is unknown among human subjects. Limited animal studies and an understanding of BT's physiological affects makes it likely that immunization would only provide limited protection.

4. Negative side affects of vaccine:

a) The vaccine produces moderate to severe side affects in 1.3% to 10.8% of those receiving the second immunization. The reaction could limit physical activity for 5 to 10 days.

5. Constraints

a) Production of the vaccine is by one vendor, the Michigan Department of Public Health, in limited quantities.

b) Cooperative efforts involving the U.S. Army Medical Research and Development Command and the Food and Drug Administration, which has oversight of investigational drugs and vaccines, will allow for sufficient quantities to be available shortly.

c) The vaccine available only covers 5 of the 7 different types (serotype) of botulinum toxins known to exist. [exemption 1.3 (A)(2)]

d) Passive immunization by horse antisera contains all 7 of the serotypes. The antisera has a half life of approximately 10-14 days therefore, the protection afforded by this immunization is short lived.

e) Passive immunization by human antisera only contains five of the seven serotypes and the quantities available are limited by the number of human donors.

[DECLASSIFIED 19 OCT 1995]

RECOMMENDATION

Begin the vaccination of selected Operation Desert Shield units and personnel that have a high probability of exposure.

In addition to the coordinations below, this recommendation also represents the consensus of the three Surgeons General and the Armed Forces Epidemiological Board.

Coordination:

JCS
USDA
USDP

SECDEF DECISION

Approved

Disapproved

Other:

~~SECRET~~

(2)

THE CHAIRMAN, JOINT CHIEFS OF STAFF

WASHINGTON, D.C. 20318

CM 576-90
2 October 1990

Reply ZIP Code:
20318-0300

MEMORANDUM FOR THE SECRETARY OF DEFENSE

SUBJECT: (S) Expansion of Industrial Base for Biological Vaccine Production

1. (S) This memorandum outlines the main points concerning US ability to produce BW vaccines and recommends you designate the Assistant Secretary of Defense (Health Affairs) as the focal point to express alternatives to increase production.

2. (S) Based on the judgment to delay vaccination against anthrax and botulinum toxin until sufficient inventories of vaccines exist, present stocks should be increased as rapidly as possible while exploring alternative sources for production.

a. (S) Both anthrax and botulinum toxin vaccines are available in limited stocks. Each is produced by only one (and the same) manufacturer. Only one vaccine can be produced at a given time in the same laboratory.

b. (S) Primary options for increasing production are to accelerate production efforts at the one existing facility, obtain other sources of production, and/or construct a new facility.

-- (S) Estimated time to initial delivery of anthrax vaccine from a new facility is 18-24 months with an estimated time to deliver 1M doses more than three years.

-- (S) For botulinum toxin, there is no realistic expectation for additional production capability in the near future to meet the current emergency.

c. (S) In the past, production of vaccines at other US facilities has not been feasible due to long lead times to adapt existing production capabilities to this product and the regulatory requirements of the Food and Drug Administration (FDA).

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3. (S) In order to ensure success in increasing our stocks of vaccines in the shortest possible time, I recommend the following actions be taken:

a. (U) The Assistant Secretary of Defense (Health Affairs) (ASD(HA)) should charter a Task Force under the direction of the US Army Surgeon General with Tri-Service participation. Oversight will be by the Deputy Assistant Secretary of Defense (Medical Readiness) (DASD(MR)). This Task Force should survey the capability of the pharmaceutical industry to support expanded production of BW vaccines, to include whether or not new facilities need to be constructed.

b. (S) The executive agent should ensure every effort is taken to increase production at the existing facility, to include enhancements to existing production.

c. (U) Direct fiscal support should be borne by OSD for this unprogrammed requirement.

d. (U) The following are suggested milestones for improved capability:

--(U) The US Army Surgeon General - Under oversight by the ASD(HA), establish executive management authority no later than Day + 1.

--(U) ASD(HA) - Charter Tri-Service Task Force to develop all options no later than Day + 3. The Task Force should be prepared to respond to the direction of the DASD(MR).

--(U) Executive agent - Complete a market investigation of industrial base capability no later than Day + 30.

--(S) Executive agent - Present options and recommendations for short term solutions to immediately increase vaccine production no later than Day + 45.

--(S) Executive agent - Present long range plan to meet increased need for vaccine production no later than Day + 60.

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4. (S) If you agree with this approach, a draft memorandum requesting the Assistant Secretary of Defense (Health Affairs) acquire a second source for production of biological vaccines is attached for approval.

DAVID E. JEREMIAH
VICE CHAIRMAN
JOINT CHIEFS OF STAFF

Enclosure

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3 of 3

THE SECRETARY OF DEFENSE
WASHINGTON, DC 20301

3 October 1990

Reply ZIP Code:
20301-1000

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFF

SUBJECT: Expansion of Industrial Base for Biological Vaccine Production ~~(S)~~

~~(S)~~ As a matter of priority, please take necessary actior acquire a second source to produce biological vaccines to prot against known Iraqui biological capability: anthrax and botul toxin. Please keep USDP and the Joint Staff informed.

(U) Suggested milestones are attached.

Enclosure

V

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THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

MEMORANDUM FOR SECRETARY OF THE ARMY

SUBJECT: Expansion of Industrial Base for Biological Vaccine Production ~~(S)~~

~~(S)~~ On October 3, 1990, the Secretary of Defense directed that I take the necessary actions, on a priority basis, to acquire second sources to produce biological vaccines to prote against anthrax and botulinum toxin (Enclosure 1). To accompl this in an accelerated timeframe, on October 5, 1990, I charte a Tri-Service Task Force to develop short-term options and recommendations for increasing vaccine production (Enclosure 2

~~(S)~~ Enclosure 3 is a copy of the Tri-Service Task Force's report on the Short Term Production of Anthrax Vaccine. Enclosure 4 is a copy of the Tri-Service Task Force's report o Short Term Production of Botulinum Toxoid.

~~(S)~~ Currently, the Army has a contract with the Michigan Department of Public Health in Lansing, Michigan, to produce anthrax vaccine and another contract with them to blend availa botulinum toxoid serotypes into pentavalent botulinum toxoid vaccine doses. In addition, Porton International, Inc., of Porton Down, United Kingdom, is under contract to the Army to produce a serotype F botulinum toxoid; however, human safety testing of serotype F has not been initiated.

~~(S)~~ After carefully reviewing both of the reports, I requ that you take the necessary steps, on a priority basis, to car [illegible]

out the following actions:

1. Closely monitor the ongoing efforts to increase production capability of the current contractor, Michigan Department of Public Health in Lansing, Michigan. Provide any support that may be necessary to ensure that production is increased by February 20, 1991.

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2. Contract with Lederle-Praxis Biologicals of Pearl River, New York, to begin production of [redacted] anthrax vaccine by February 15, 1991.

3. Establish the appropriate inter-governmental arrangements with the National Cancer Institute - Frederick Cancer Research Facility at Fort Detrick, Maryland, to begin production of [redacted] anthrax vaccine by February 15 1991.

4. Modify the contract with [redacted] Inc., to produce serotype E and C botulinum toxoid with [redacted] doses of serotype E production to be completed by May 15, 1991. Upon completion of the serotype E, production of [redacted] serotype C is to commence.

5. Modify the contract with the Michigan Department Public Health to renovate their facility to allow for the simultaneous production of multiple serotypes of botulinum toxo by September 1, 1991.

6. The U.S. Army Surgeon General's Office is to evaluate by December 15, 1990, the mission priorities of the U. Army Medical Research Institute of Infectious Diseases (USAMRII at Ft. Detrick, Maryland, to determine if their effort should b directed into production of botulinum toxoid. While this evaluation is ongoing begin the required renovations, purchase equipment and vaccination of personnel at USAMRIID necessary t qualify the facility for production of botulinum toxoid.

~~(S)~~ In addition, I request that you task the U.S. Army Surgeon General to establish and be the executive manager of an Implementation Working Group to expedite these actions. The Implementation Working Group should be led by a flag officer. The Implementation Working Group should be provided with the highest priority in funding, contractual, acquisition, and procurement matters.

Enrique Mendez, Jr., M.D.

Attachments:
As stated

cc:
U.S. Army Surgeon General

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RATIONALE FOR ANTIBIOTICS IN PROPHYLAXIS AGAINST INHALATION ANTHRAX

Inhalation anthrax is an almost uniformly fatal disea Experience with this syndrome in humans is limited; what information is available indicates that once clearcut symp and signs emerge, even massive doses of antibiotics are fu There is no question that the best approach to the threat inhalation anthrax is active immunization prior to exposur possibly coupled with use of antibiotics after exposure. absence of widely available vaccine, however, administrati appropiate antibiotics prior to exposure, or in the immedi post-exposure period, offers a secondary option which coul improve survival, particularly if antibiotic use is combin immunization in the post-exposure period. Rationale for t position is based on the following facts: a) the in vitro sensitivity of Bacillus anthracis to certain antibiotics; demonstrated utility of antibiotics in treatment of cutane anthrax; and (probably most importantly) c) results of experiments in non-human primates which indicate clearly t

antibiotics administered after exposure to lethal challeng
anthrax spores will prevent disease while they are being g
(and may reduce mortality if continued for a sufficient pe
time).

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ON: 31 OCT 96
BY: SEC ARMY (DAMH) UNDER SEC 3.

A: In vitro sensitivity:

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The vast majority of anthrax strains are sensitive in to penicillin. Historically, this drug has been considered "treatment of choice" for all forms of anthrax; tetracyclir erythromycin, and chloramphenicol have been recommended in penicillin-allergic patients. Rare penicillin-resistant st exist naturally, however, and one has been recovered from a human case. In addition, it is not difficult to induce resistance to both penicillin and tetracycline through lab manipulation of anthrax bacilli. Ciprofloxacin is a relati new antibiotic with a novel mechanism of action (DNA gyras inhibitor). To date, all strains of anthrax tested have p quite sensitive (1,2). Because this is a relatively new d and because of its unusual mechanism of action, it is unli that resistance has been "engineered" at this time. There ciprofloxacin, a drug with few recognized side effects, a convenient oral dosing schedule (twice daily), and excelle activity both in vitro and in vivo offers a good option fo antibiotic use in countering possible infection with this organism. Many of these same arguments can be made for doxycycline as well; however, the methods for "engineering

resistance to tetracyclines are simple and readily availab: the open literature. This combined with recognized photosensitivity make doxycycline a secondary option.

B: Utility of antibiotics in cutaneous anthrax

Published series confirm that cutaneous anthrax is ra:

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cured with appropriate antibiotic therapy, particularly if recognized early and treated early in the disease course (3) variety of antibiotics have been used with success, but penicillin generally provides the most rapid sterilization resolution of the lesion.

C: Non-human primate experiments

The effect of antibiotics on the course of inhalation anthrax has been most extensively examined in non-human pri models of the disease. Several studies conducted in the 19 and 1960s demonstrated that the course of inhalation anthra could be modified through antibiotic use after exposure to doses of spores by inhalation (4,5,6). These experiments a notable for the following points: 1. antibiotic therapy a seems capable of prolonging the time to death. Animals see survive as long as the drug is being actively administered, die at varying intervals after its discontinuation. 2. antibiotics combined with some form of immunological intervention--active (i.e., vaccination) or passive (i.e., serum)--in the post-exposure period offered the best chance

success.

A recent experiment conducted at USAMRIID seems to con
these previous observations (7). This study indicated that:
Under the conditions of the study, penicillin, doxycycline,
ciprofloxacin given for a 30 day period improved survival o
antibiotic treatment, 2. Deaths occurred, as predicted, aft

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antibotics were discontinued, 3. Doxycycline and ciproflo: may have offered some advantage over penicillin in this (inhalation anthrax) setting, and 4. Combined antibiotics vaccination in the post-exposure period resulted in the ba survival.

A simplified review of pathogenesis coupled with speci about machanism of antibiotic activity might shed light on observed findings. Anthrax organisms are most effectively delivered by inhalation in the form of spores. Inhalation these spores results in seeding of terminal respiratory bronchioles. Spores then are phagocytosed by alveolar macrophages and transported to lymphatic organs in the che (pulmonary and mediastinal lymph nodes) and elsewhere. Th the spores germinate, becoming "vegetative" organisms whi release toxins and exert adverse physiologic effects. Wit continued replication of these "vegetative" bacilli, incre larger numbers of organisms and their toxins circulate. Fi the host is overwhelmed and death ensues. With administrat appropriate antibiotics, vegetative forms (not spores) are

killed. In some cases, this may be adequate for a "cure." many others, however, additional spores probably remain dor until antibiotics are discontinued. In these individuals, residual spores then germinate, and the replicative process begins anew. Theoretically, these persons could remain on antibiotics for prolonged periods, and survive. In practic

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however, such a strategy is fraught with additional problems (e.g., how long is long enough, antibiotic-related toxicities etc.), and is therefore not feasible. It then is necessary supplement the suppressive effect of antibiotics with an ac immune response which would serve to "mop up" the late-germinating vegetative forms from these spores. Consequent the presence of an active immune response, generated prior exposure, offers the highest probability of survival. Fail that, initiation of vaccination in concert with antibiotics exposure should enable an infected individual to generate a immune response that could react in a similar way, albeit w somewhat less certainty. In the primate experiments summar above, this strategy proved effective.

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TREATMENT OF MONKEYS EXPOSED TO ANTHRAX SPORES

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POST EXPOSURE TREATMENT OF MONKEYS AEROSOL CHALLENGED WITH ANTHRAX SPORES

TREATMENT*	DURATION	SUBJECTS	SURVIVAL	DAY OF D
PLACEBO	30 DAYS	10	10%	3-8
VACCINATION	DAYS 1&14	10	20%	5-10
ANTIBIOTIC (P)	30 DAYS	10	70%	39,42
ANTIBIOTIC (C)	30 DAYS	9	89%	36
ANTIBIOTIC (D)	30 DAYS	10	90%	36
VACCINATION + ANTIBIOTIC (D)	DAYS 1&14 30 DAYS	9	100%	NONE

* ALL TREATMENTS BEGAN WITHIN 1 DAY OF EXPOSURE
P: PENICILLIN C: CIPROFLOXACIN D: DOXYCYCLINE

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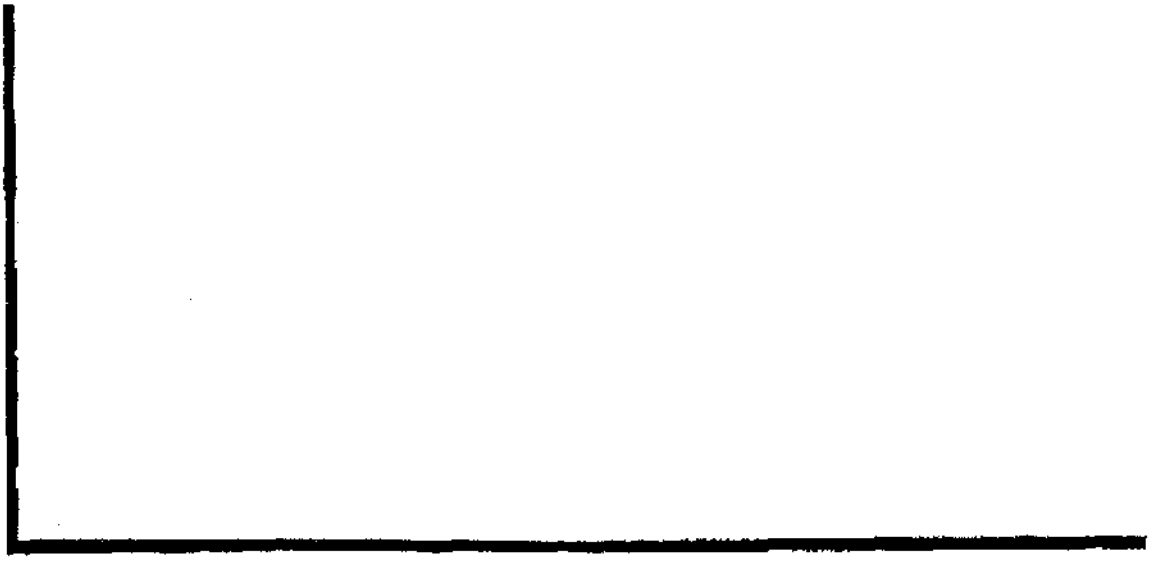
REMARKS:

Information paper per our conversation.



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DOD Response to Anthrax Program Congressional Request May 16, 2000

On May 12, 2000, Congressman Jack Metcalf (R-Wash.) and 34 of his colleagues sent a letter to the Secretary of Defense requesting that the DOD halt its Anthrax Vaccine Immunization Program. The following is DOD's response to the request.

The Department of Defense respectfully cannot agree to such a request. To suspend the program would place thousands of our fine men and women in a vulnerable position where they would go to work every day in areas of the world where potential adversaries possess the ability to deliver deadly weaponized aerosolized anthrax at any moment.

Anthrax is a deadly biological warfare agent that at least ten nations, including North Korea and Iraq, are known to possess or have in development. If an individual inhales aerosolized anthrax, there is little chance of survival from this devastating disease. Antibiotics exist, but they must be taken before symptoms develop. However, the chance of that is minimal since aerosolized anthrax is colorless, odorless, tasteless and very difficult to detect. By the time we determine an attack has occurred, it would most likely be too late.

Suspension of the program would recklessly jeopardize the safety of the very people for whom we are most concerned. Knowing that the threat exists and that we have a safe and effective FDA-approved vaccine available, the Defense Department would be irresponsible if it suspended the program. This FDA-approved vaccine has also been validated by the Centers for Disease Control and the National Institutes of Health. The threat is so serious that our Commanders-in-Chief in Korea and Southwest Asia are adamant in their insistence that all of their forward-deployed forces and all inbound personnel be vaccinated. This is a force protection matter that we take very seriously. We would not want to endanger any person by sending them in harms way without protection from this deadly disease.

There are a lot of erroneous data being presented by individuals and groups opposed to the Department's inoculation program. We also know that sensational stories have been told about anthrax reactions, the overwhelming majority of which are not true. When you administer over 1.7 million doses of vaccine to over 440,000 people, some will get sick, for some reason, inevitably, at some point in time. Although opponents of the inoculation program would have you believe otherwise, most of these illnesses are not related to anthrax vaccine. We work to provide the best medical care for all of our sick servicemen and women and we try to determine the cause of every illness. Many illnesses reported by opponents as anthrax reactions have in fact been traced, by both military and civilian hospitals, to be due to other causes. This includes a case in which a serviceman's picture was projected on the wall during a congressional hearing on anthrax and portrayed as an "anthrax vaccine reaction" victim. In fact, the picture depicted a skin condition completely unrelated to the anthrax vaccine.

In 1898, the British were preparing to fight the Boer War. Their senior leadership considered giving all their troops the recently approved Typhoid Vaccine. Opposition arose, some protests were held, some in Parliament objected, and the vaccine was made voluntary. Fourteen thousand troops elected to take the shot. The troops went to war and 59,000 came down with typhoid. Nine thousand of them died while a perfectly safe and effective vaccine remained on the shelf - unused! We cannot allow the last chapter of the anthrax story to be a Boer War analogy.

Anthrax Vaccination Program

- First Point – "The Institutes of Medicine says there is insufficient evidence to determine the long term safety of the vaccine."

  Comment– The same IOM report also states in adjacent paragraphs:

  a. "... few vaccines for any disease have been actively monitored for adverse effects over long periods of time."

     and

  b. "To date, published studies have reported no significant adverse effects of the vaccine."

     and

  c. FDA has stated that "the reports on the anthrax vaccine received thus far do not raise any specific concerns about the vaccine."

- Second Point – "Two Air Force Reserve Judge Advocates say that anthrax vaccination are illegal."

  Comment – The two lawyers quoted were assigned as defense attorneys for an Air Force client charged with violating a lawful order to take the vaccine. As such, the lawyers were required to assert a defense. To do this, they prepared these comments as part of their planned defense tactic. The FDA has continually stated that the vaccine is approved and has been since 1970, as such, is not an investigational drug. Any suggestion that these lawyers' work-product is the opinion of the Air Force or the Department of Defense is absolutely incorrect

- Third Point – "The Inspector General, Department of Defense has documented the troubling financial management practices and multiple deficiencies cited by FDA that continue to compromise the AVIP program."

  Comment – The Inspector General did, as it usually does, find areas that needed improvement. They also found, however, that the contractual relief was provided within Federal Acquisition Regulation guidelines. All vaccine being used has been FDA certified for its safety and efficacy.

- Fourth Point – "The House Subcommittee on National Security Veterans Affairs and International Relations recommends that AVIP should be suspended until the DOD obtains approval of an Improved vaccine."

  Comment – The current vaccine was approved in 1970, and reevaluated and re-certified by FDA in 1985. DOD has given over 1,700,000 shots to over 440,000 personnel. Only .00008 percent have resulted in loss of duty. Only .00001% or 31people have required hospitalization. Of these 31, only 6 have been determined to, more probably than not, have illnesses which have resulted from anthrax vaccination. These personnel have been granted waivers to not receive future vaccinations. These determinations were made by an independent panel of experts convened by the U.S. Department of health and Human Services.

- Fifth Point – "The American Public Health Association Governing Council urges

the DOD to delay any further immunization against anthrax using the current vaccine or at least to make immunization voluntary."

Comment – A reading of that association's 17th Edition of the American Public Health Association's Control of Communicable Diseases Manual (James Chin, MD, MPH editor) specifies a preventive measure for exposure to anthrax is to "immunize high risk persons with a cell-free vaccine prepared from a culture filtrate containing the protective antigen. Evidence indicates that this vaccine is effective in preventing cutaneous and inhalational anthrax; it is recommended for laboratory workers who routinely work with B anthrax and workers who handle potentially contaminated industrial raw materials. It may also be used to protect military personnel against potential exposure to anthrax used as a biological warfare agent. Annual booster injections are recommended if the risk of exposure continues."

- Sixth Point – "The General Accounting has stated that the DOD data indicates that women have had a higher rate of negative reactions to the anthrax vaccine."

Comment – While the rate of adverse reactions is higher for women than men, when scientists of the USAMRIID Ft. Detrick, MD, studied the adverse events of 1,255 men and 335 women, 2% to 4% of men reported events compared to 4% to 7% of women.

Another study conducted by the Preventive Medicine Division at Tripler Army Medical Center reports overall events or effects by gender as between 4% and 14% for women compared to 2% to 5% men.

A third study conducted by the Department of Preventive Medicine 121st Evacuation Hospital, Seoul Korea showed an overall rate of events or effects by gender to be 72% to 74% of women and 42% to 44% of men.

7

Search Criteria: SEARCH-IN = '0', DOCNUM = '42479'

Doc #	Name
42479	Concerning Son Receiving Anthrax Shot

SECRETARY OF DEFENSE **CORRESPONDENCE ACTION** REPORT

This form must be completed and forwarded to the Correspondence Control Division (CCD), WHS Room 3A948 Suspense Desk (b)(6) FAX Number (b)(6) (b)(6) Email (b)(6) @osd pentagon mil

Action Agency: SN

Suspense Date: 12/03/2002

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- [ ] a ACTION HAS BEEN COMPLETED (Copy attached)
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- [ ] c INTERIM REPLY HAS BEEN SENT (Copy attached) EXTEND **SUSPENSE** TO _____ *(Justify* below)
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2. JUSTIFICATION

3. REPORTING **AGENCY**

a **ACTION** 4GENCY: SN

b NAME OF ACTION OFFICER

c TELEPHONE NO

d DATE

e APPROVING AUTHORITY
(Service Secretary/Under Secretary/ASD/Military/Executive Assistant Level)

Signature | Date Signed

5. ACTION TAKEN (For EXSEC/ Correspondence Control Division Use Only)

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c OTHER (Specify)

Signature | Date Signed

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SECRETARY OF DEFENSE CORRESPONDENCE ROUTING SLIP

Action Agency SECRETARY OF THE NAVY
Action Required REPLY DIRECT (Forward copy of reply to **CCD,** Room **3A948)**
Coordinate With **LA**

Remarks

Special Instructions

Suspense Date **December/3/2002**	Routing Date **October/26/2002**	OSD CONTROL **#U17539-02**

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(b)(6)

Republican Walter Jones
1105-C Corporate Drive
Greenville, NC 278584211

The Honorable Barbara Mikulski
Suite 709, Hart Senate Building
Washington, DC 20510

October 21, 2002

Attn Congressman Jones and Tony Joyner
Attn: Barbara Mikulski and Evelina Erickson

During the week of October 7, 2002, I contacted your office to solicit your help. My family was, and is now, experiencing an emergency related to the government's anthrax vaccine program My son is a marine stationed at Camp Lejeune, NC and is scheduled to go overseas early next year With no pnar warning or education about anthrax vaccine, our son, along with other marines, was *forced* to accept the anthrax vaccine You may recall my story. He initially refused the vaccine. But after intense threats of jail and court martial, he relented He even went to Q chaplain to obtain help, who by the way, was of no support and only criticized my son As parents, my husband and I called everyone we could think of, *including your office* fur *intervention* But, to no avail. No one really wants to get involved to any great level

I would like to be clear that I am not against vaccine in general, and I am a very patriotic individual However. there is enough information to prove that the current anthrax vaccine is uneafe. Also, the manufacturer, BioPort Corporation has been criticized for its business practices and they have failed multiple FDA inspections Their current FDA approval is only related to cutaneous exposure, not inhalation. While our government is busily trying to disprove symptoms brought on because of the vaccine, I am hearing daily accounts of individuals who are reacting to it. Some of the account8 are staggering and very scary. My son, who is currently on a ship, knows of several who have reacted. One individual's neck has swollen up to the size of a baseball. But, we continue to dismiss these anthrax vaccine symptoms-we call them something else, because no one wants to be accountable I understand we are an the eve of war, and there are certain safety measures that must be accomplished One would think the vaccine would be one of the safe measures One would also thrnk we would safely send our men and women to attend to this war. Instead, they are getting the vaccine and are ending up sick once they arrive to the destination So, we not only expect them to fight this war, but we dorif care if they are ill while they are doing it My comments are not mythology-these events are happening every day Also, how many long-term affects Of using the drug are we to fear If you review the countless articles and visit the websites that reveal the truth, you would see we have a very serious problem There are accounts of how the multiple injections *ore* what cause the problem Here's one of many sites. www anthraxvaccine org

Nat only do I grieve over this issue becauac Of my awn sun, but there *is* the larger picture which includes everyone else's son or daughter I work In a healthcare environment which requires a plan to handle this issue as well

Debate continues among our government officials as to whether or not we should be going to war We may not be able lo change that final outcome However, we certainly *can change* the way this vaccine is being administered and deal with the safety issue New vaccine is on Its way, but why are we using our service members as guinea pigs with unsafe vaccine until it arrives If we look at history and what our Gulf War veterans are going through, why arent we taking action. Military authority denies that the symptoms are related to anthrax vaccine So, now we aond new veterans who will return with same issues. Certainly data speaks when reporting However, if we dont recognize the symptoms to report-the data la never generated or accurate

My *son was* not *given due process-not even when* it came *to religion* He was not allowed to ask questions about the safety of this "investigational" drug. Instead he was scoffed at and berated for his questions When we attempted to submit data proving our medical history as a potential risk for his health, it was discarded as a joke As far as I know, we still have a "voluntary" military, and my son voluntarily signed up to serve While military law is different from civilian *law--does* this mean we are now Inhumane to our service members? We certainly don't pay them well, but now we dont treat them like humans either. The service members can not facilitate advocacy, which is why I have taken *this stand* an *behalf of my son.*

My request is that members of the Congress and the Senate *take a look at this crucial* issue and make legislation recommendations far change immediately. The lives Of our service members are at stake. They can only do the job if they are healthy Please investigate the current cases involving those who have refused and faced maximum punishment. I realize the complexity of this issue and how many people and organizations will be held accountable for the thousands they have Ignored in past years However, It is time to atop this whirlwind of deception to protect our future What we compromise to keep In deception, we will ultimately lose

Sincerely

(b)(6)

Copies to Sen Richard Colbourn
Copies to Del Addie Eckardt

BARBARA A MIKULSKI
MARYLAND

COMMITTEES:
APPROPRIATIONS
HEALTH, EDUCATION, LABOR, AND PENSIONS

United States Senate
WASHINGTON, DC 20510-2003

IN REPLY PLEASE REFER TO OFFICE INDICATED

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(410) 546-77[illegible]

October 24, 2002

The Honorable Powell A. Moore
Assistant Secretary of Defense for Legislative Affairs
U.S. Department of Defense
1300 Defense Pentagon
Washington, D.C. 20301-1300

Via Fax

Dear Mr. Moore:

I would appreciate it if you would review the enclosed correspondence and would contact my office as soon as possible with the appropriate information to respond to my constituent.

Please send your response in duplicate form to the attention of *my* assistant, Evelina Erickson, in *my* office at 60 West Street, Suite 202, Annapolis, Maryland 21401.

Thank you for your consideration of this matter.

Sincerely,

Barbara A. Mikulski
United States Senator

BAM:ee

Enclosure

U17539-02

SECFILES FULL RECORD DETAIL

Pnnt Date **10/25/2002**

OSD CONTROL **U17539-02** DOC **10/24/2002** DOR **10/26/2002** SIGNATURE CASE
FROM USS **MIKULSKI, B** TO L A
SUBJECT CONCERNING SON RECEIVING ANTHRAX SHOT
KEYWORDS
COMMENTS
FN **UNKNOWN** SEC **U** OCN RDD

STATUS CODE DECISION **DECISION** DATE PRIORITY ACTION REPORT
AGENCY SN ACTION ASSIGNED RD SUSPENSE
SUSPENSE **COMPLETE** ACD COORDINATION LA
SUSPENSE STATUS

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OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

November 14, 2002, 4:00 PM

FOR: ELLEN P. EMBREY, DASD, (FHP & R)

FROM: Michael E. Kilpatrick, Deputy Director, DHSD

SUBJECT: Reply to Correspondence from Senator Barbara Mikulski

- Senator Mikulski wrote on behalf of her constituent (b)(6) (TAB B). (b)(6) expressed some concerns about the military's anthrax vaccination program. Her son, an active duty Marine, initially refused the vaccine, but took it despite his and his mother's concerns.

- This response explains the DoD AVIP program and provides Senator Mikulski with the correct information regarding the safety and effectiveness of the anthrax vaccine.

RECOMMENDATION: Sign the proposed response to Senator Mikulski (TAB A)

COORDINATION: TAB C

See edits. Ellen

Prepared by: (b)(6), DHSD, (b)(6) PCDOCS #42479, 43448

SUBJECT: Reply to Correspondence from Senator Barbara Mikulski

COORDINATION

PI (HA)	LTC (b)(6)	Concur 11/18/02
AVIP Office	COL Randolph	11/19/02 Concur w/ve commented changes

SUBJECT: Reply to Correspondence from Senator Barbara Mikulski

COORDINATION

PI (HA)

LTC (b)(6)

(b)(6)

SUBJECT: Reply to Correspondence from Senator Barbara Mikulski

COORDINATION

PI (HA)	LTC (b)(6)	Concur 11 /18/02
AVIP Office	COL Randolph	Concur 1 1/20/02

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

NOV 2 7 2002

The Honorable Barbara Mikulski
United States Senator
Attention: Evelina Erickson
60 West Street, Suite 202
Annapolis, Maryland 2 140 1

Dear Senator Mikulski:

This is in reply to your letter to the Assistant Secretary of Defense (Legislative Affairs), on behalf of your constituent, (b)(6). (b)(6) has some concerns regarding the military's anthrax vaccination program. Your letter was forwarded to our office for response because we are the Department of Defense office that is working on deployment health issues.

(b)(6) wrote about her son, an active duty Marine, and his attempts to refuse the anthrax vaccine. She claimed he was not provided any educational materials or prior warning before being offered the vaccine. Although we cannot comment on this specific case, it is DoD policy that commanders and health care professionals provide anthrax vaccine recipients information about the vaccine. Information has also been provided to military personnel through command channels and Web sites, military newspapers, television, and radio. The primary source of information about the military anthrax vaccination program is available to the public on the Internet at http://www.anthrax.mil.

The anthrax vaccine is mandatory for all personnel in areas of higher threat for more than 15 days and whose duties are essential to mission critical capabilities. The only exceptions are those provided under applicable medical and administrative exemption policies. (b)(6) wrote that her son met with a chaplain to obtain a religious waiver. Religious waivers are granted only in the case of legitimate religious objections to immunization, and can be revoked to ensure accomplishment of the military mission. Waivers from private physicians based on personal or philosophical beliefs or attitudes are not authorized. The authority to grant temporary waivers in the Navy and Marine Corps is delegated to the Chief, Bureau of Medicine and Surgery.

When a servicemember refuses the vaccine, it is DoD policy to begin with the assumption that they may be uninformed about the facts related to the deadly effects of exposure to the anthrax agent and the protection afforded by the vaccine. Our first action with those who might refuse the vaccine is to determine their concern and provide information.

If a servicemember continues to refuse the vaccine, then a commander will manage the situation as he or she would for any failure to obey a lawful order. We expect servicemembers to comply with administration of this vaccine as for any other mandatory vaccination. It is comparable to an order to wear body armor during armed engagement, or to don a protective mask in a suspected chemically or biologically contaminated environment. Any servicemember who does not comply with these measures endangers his or her own health, and places both their

unit and mission accomplishment at risk. Military and civilian judges uniformly have found orders for members to be vaccinated to be lawful orders.

The Department of Defense's use of the anthrax vaccine in the Anthrax Vaccine Immunization Program for pre-exposure prevention is consistent with the Food and Drug Administration-licensed use of the vaccine. It is not an "investigational" drug. Contrary to what (b)(6) has read, the anthrax vaccine is FDA-approved for all types and strains of anthrax. While no vaccine is 100 percent effective, this vaccine greatly reduces the risk of contracting anthrax, regardless of route of exposure. Based on human and animal data the National Academy of Sciences' Institute of Medicine concluded in March 2002 that anthrax vaccine is "an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by all known or plausible engineered strains of Bacillus anthracis." The first Institute of Medicine report can be reach at **www.nap.edu/catalog/103 1 0.html.**

(b)(6) also believes that the anthrax vaccine may be a cause for the illnesses some Gulf War veterans are experiencing, and is concerned by her son's accounts of adverse reactions he has seen. There are no established connections between the anthrax vaccine and the persistent and unexplained illnesses reported by some Gulf War veterans, although research continues on this issue. The National Academy of Science's Institute of Medicine report concluded that, while data are limited, no convincing evidence shows that personnel who received the vaccine have elevated risks of later on-set health effects.

Based on more than 30 years of anthrax vaccine use, we know that transient injection site reactions do occur. It is known that from 30 to 60 percent of those who receive anthrax vaccine will develop an injection site reaction (less than one inch). About one in a hundred will develop a reaction five inches in diameter or larger. The rate of side effects away from the injection site (headaches, muscle aches, tiredness) is about the same as for other vaccines: from five to 35 percent, with these effects disappearing within a few days. As the National Academy of Sciences noted in their March 2002 report, these rates are similar to other vaccines.

If a health problem occurs following injection of any vaccine, affected personnel have been counseled to seek medical care to resolve their immediate health problem. If the symptoms persist, they have been advised they may also wish to contact the Walter Reed Vaccine Healthcare Center at (202) 782-0411. The Department of Defense is committed to giving our forces the best individualized care, no matter what caused the problem.

Personnel covered by this vaccination policy have also been informed at the time of each vaccination that anyone experiencing adverse health effects may also report them to the Vaccine Adverse Event Reporting System(**VAERS**). The forms are available at **http://www.vaers.org** or by calling (800) 822-7967. Health care workers and vaccine recipients are encouraged to report via the VAERS system any severe reactions that might occur within 30 days of vaccine injection that require medical treatment and/or interfere with work or recreation. Within DoD, VAERS reporting is required for any reactions that cause hospitalization or loss of work for 24 hours or more.

Anthrax is an attractive weapon of mass destruction for our enemies. It is highly lethal, easily produced in large quantities, easily developed as a weapon, can be stored and remain dangerous for a long time. For this reason, anthrax may represent the most likely biological warfare threat facing U.S. forces. The Intelligence Community believes several countries

currently have or are developing an offensive biological warfare capability using anthrax. U.S. forces may have little or no warning before an anthrax attack, which could be delivered by unconventional means. U.S. military forces around the world face a very real threat of a surprise anthrax attack. The threat is real and the consequences are grave. Former Director of the CIA James Woolsey referred to it as the single most dangerous threat to our national security in the foreseeable future. We have a responsibility to use this vaccine to protect our forces against this threat. Vaccination is the best way to protect our forces from an unknown on covert anthrax attack.

Thank you for the opportunity to assist your constituent, (b)(6) . If we can provide any additional information please contact us again.

Sincerely,

Ellen P. Embrey
Deputy Assistant Secretary of Defense
Force Health Protection & Readiness

(8)

Written Testimony of Maj. Dingle and Capt. Rempfer, CT ANG

- **Spring 1998**: Flight Surgeon briefed the AVIP. He said that it was a six shot series and very expensive, and that the ANG would have very low priority, so we wouldn't be seeing it at our base for a long time.
- **Spring and Summer 1998**: Research by officers began from Internet sites, and government documents. Officers remained skeptical of reports or stories that did not cite references. We obtained a copy of Senate Report 103-97 (Is Military Research Hazardous to Veterans' Health?; Lessons Spanning Half a Century). It was an official government document that said the vaccine should be considered investigational, and that the government could not rule out the vaccine as a causal factor in Gulf War Syndrome.
- **Late Summer 1998**: We began to develop a roster of pilots to deploy to the Gulf. The DOD guidelines were that you don't require the vaccine unless you're spending more than thirty days in the theater. Most pilots would be going for less than three weeks, so we wouldn't be getting the shots. It became apparent that several officers would not be taking the shot under any circumstances when they did become a requirement, and this word made its way to the command structure.
- **September UTA, 1998**: The wing commander announced a policy regarding anthrax: all officers regardless of mobility status would begin the anthrax shot series in October whether they were deploying to the Gulf or not. Considerable resistance surfaced, so a meeting was held on September 27, 1998. At this meeting the wing commander assured us that those who chose not to get the shot would be treated equally, i.e. a pilot would receive the same punishment as a supply officer, and flying status would not be used as a punishment tool for pilots. We were supplied with basic Xeroxed information regarding the vaccine (Exh. A, B, C)
- **Early October 1998**: Tiger Teams were formed, and for a short time the shots became optional, unless you were scheduled to be in the Gulf for more than 30-days. Maj. Dingle announced his intention to leave the unit at this time, but only after completing his performance report duties, and serving on Tiger Team Alpha. Tiger Team Alpha would research the anthrax vaccine and develop a list of questions for the commander to send to higher HQs. Tiger Team Bravo would research the legal aspects, avenues, and options for guardsman that chose not to take the shot. Maj. Dingle and Capt. Rempfer were the two pilot participants in Tiger Team Alpha. Maj. Dingle performed the bulk of the research and worked very hard to ensure the information presented was factual. Only material including government documents or established publications

were used. The team member's initial list of questions (Exh. D, E) ultimately evolved into the dictated document that was to be no more than two pages (Exh. F). We presented 15 questions with supporting information to the commander. Examples of our documents include the FDA report (Exh. G) showing microbial contamination in the sublots our unit's lot was derived from (FAV 030). (Note: not all our sources were obtained for the original Tiger Team report – yet many additional references are obtained through our research paper at the end of this summary chronologically listing the attachments). I.e. We've included the Dr. Burrow's letter (Exh. H), stating in Enclosure point #2 that the FDA inspection drove supplemental testing. As well, and in contrast, a letter to the editor by Dep. Sec. Of Def. Hamre (Exh. I) contradicts the Dr. Burrows letter by saying the exact opposite. Finally, we asked our wing commander for the supplemental testing results of our lot FAV 030. We were only provided with the '96 paperwork for the original production testing (Exh. K). We pressed for the supplemental testing results and they were never provided.

- **October 1998**: The wing commander subsequently forwarded Tiger Team Alpha's questions to Major General Weaver (Exh. K). We are still waiting for answers. According to the wing commander, the shots were to be delayed until the answers came back, and they would be optional unless you were scheduled to be in the Gulf from more than the thirty days IAW HQs guidance. The wing commander later informed us he actually forwarded a letter up the chain of command to summarize our inputs (Exh. L). His letter reduced our questions to 4, and in the 5th note of the attachment he refers to us as "hard liners", and maintains the unit will be better off when we are gone. At this point we were not very confident answers would be forthcoming.

- **November 1998**: Unit leadership arranged Dr. Huxsoll, Dean of Veterinarian Medicine at LSU to appear at the unit to dispel our concerns. Upon the night of the event all unit members were provided with a guidance sheet of what they could and could not ask (Exh. N). Contrary to the flyer, Dr. Nass was not invited until 8pm the night prior, via a phone message on answering machine to one of the unit members. Maj. Dingle attended the event and wrote a summation of the evening (Exh. O). As well, it was video taped and the video can be obtained from the NGB in DC. Although the NGB taped it and provided it to other ANG units on closed circuit TV, they did not edit it, and ANG members who have watched it have become very concerned with it's content.

- **November UTA 1998**: It became apparent that the answers to the Tiger Team inquiries were not forthcoming, and we were told that the anthrax debate was over, that our questions could not be answered, and that the shots would begin. As well, following our wing commanders' inquiries up the chain of command

as to the rational for the 30-day in country requirement, that requirement was changed to one-day. As a result, 16 vacancies appeared on the deployment list.

- **December UTA 1998**: As a result of the sudden vacancies, and the deployment roster being half full, the unit leadership announced another policy change. All pilots will either take the shots or leave the unit. We were encouraged to leave ASAP, or our fate might be out of our commander's hands. We were also relayed the message by our commanders from our State's TAG, MG Gay, that anyone refusing the vaccine and trying to leave over it, would never work in the military again in any capacity. The policy letter (Exh. P) designates a deadline of the Jan. UTA, and grounds all pilots not in compliance, despite earlier assurances that flying status would not be used as a punishment for refusal. Capt. Rempfer announced his intention to transfer to another military capacity at this time.
- **December 1998**: We gained access to two ANG messages. The first was the ANG message on Force Health Protection Guidelines (Exh. Q). This document prescribes the use of P-tabs for forces, despite our commander's insistence that he'd never make us take them. We felt this was a severe contrast to the way the Anthrax Vaccine Immunization Program (AVIP) was being conducted. As well, we received the ANG message on the AVIP (Exh. R). It specifically stated three phases, where with the most liberal interpretation we would be classified as Phase II. So why the rush to take the vaccine with a Jan. 2000 deadline? We were told it was to get rid of those who could not be relied upon. As a result Capt. Rempfer filed an IG complaint (Exh. S) with the NGB (subsequently he was informed it would not be investigated since it related to DOD policy):
    - I. If you go to a High Threat Area (HTA) for any amount of time, you require the Anthrax vaccination.
    - II. Early deployers have to get the shot by Jan. 2000.
    - III. All others by 2003.
- **Fall of 1998**: We contacted are elected representatives (Exh. T-1, to T-9). We are still waiting for responses from most, and the only initial letters we received maintained they would contact the DOD, or repeated information off the DOD website.
- **January UTA**: Nine pilots decided to not take the vaccine. One had decided in Oct. to transfer to another non-flying position, so he was not included in the numbers. The squadron commander issued a letter confirming the 8 losses (Exh. U). Subsequent to that he reported different numbers to the chain of command, which showed only 2 pilots departed due to the anthrax issue. All

the involved pilots were upset at the misrepresentation and signed, a letter confirming it was the anthrax policy that forced them out of the cockpit (Exh. V). The TAG reported these inaccurate numbers to a congressional interviewer, and Mr. Kevin Bacon reported it in a Pentagon newsbrief.

- **January 1999**: We evolved our original Tiger Team paper into an 11-page research document over time analyzing the myriad of issues of the AVIP (Exh. W). We pressed our concerns again up the chain of command and also posted them on the Internet.
- **February 1999**: As a result, we did obtain 17 detailed answers to our questions from sources outside our chain of command (Exh. X), but were later informed they were merely a draft prepared to answer the questions the Surgeon Generals might face by the 20/20 ABC news representatives. We are adding the answers to the website, despite the fact that they are still in draft form, to try to get the full set of information out to the public. Also, the NGAUS Magazine did an article (Exh. Y) in March dispelling the DOD's myth that the military members that are concerned with the vaccine are simply "misinformed." It specifically says the DOD didn't know our research was conducted professionally and thoroughly, and was well cited.
- **March 1999**: Capt. Rempfer published an Op Ed. in the Baltimore Sun to try to expand the debate on the AVIP. The goal is to help servicemember's, legislators, and Americans understand that the issues with respect to the AVIP are much more complicated than soldiers being scared of a vaccine.

Summary:

1. We feel the DOD's claims of widespread use of the anthrax vaccine are an exaggeration.
2. We feel the DOD's claim of safety and effectiveness is unsubstantiated exaggeration.
3. We feel the DOD is discrediting honest service members that are concerned about a very important force protection issue.
4. We feel the DOD is misrepresenting the numbers to Congress on the losses the AVIP is costing our country.
5. We feel the AVIP needs to be reviewed, and we know that almost every service member who we know feels the same way, even if they've taken the shot.

Good morning. I want to begin by thanking the Congress for all you do to insure America has the best trained, equipped, supported, and protected military in the world.

.herefore, I thank the members of this Committee for their willingness to thoroughly review the DOD Anthrax Vaccine Immunization Program. Given the rapid rate at which this costly program is progressing, I believe timely action by Congress is critical to insuring that the vaccination policy is truly in the best interests of servicemember's force protection, and therefore, our nation's defense.

At this point, I request permission to insert into the public record written testimony detailing Major Dingle's and my experience with the anthrax program.

(Pause)

There is an important common bond behind why we are all present today. It's because we all care about our armed forces. We simply disagree on what form of force protection is best for our troops. Do we achieve it through mandatory vaccines, or through other means? The answer to this question is important, because it is forcing servicemembers to make serious, principled choices about the future of their military careers.

Out of respect for the military and my chain of command, I am not here today in uniform. My ~rofessional dissent on this policy brings me to Congress only after attempting to resolve my ~oncerns through my chain of command. I believe it is my duty to continue to speak out against the dangerous doctrinal precedents and questionable effectiveness of the Anthrax Vaccine Immunization Program.

As an Air Force Officer, I have obeyed orders for nearly 16 years while serving as a fighter pilot in the Middle East, Bosnia, Korea, and Central America. However, as an American soldier I have also been trained to question orders if they are objectionable. I learned this at the Air Force Academy from instructors who fought in the Vietnam War.

In this case, it is not the legitimacy of the orders that I question, or the officers enforcing this Department of Defense Directive. Instead, I question the assumptions on which the policy is based, and feel that by implying our troops are protected, we actually place them in greater danger than if they were not vaccinated at all.

The Defense Department acknowledges that they did not anticipate the level of resistance the anthrax vaccination policy has encountered. Resistance to the policy is based partly on the cursory nature of the review that occurred prior to implementation of this program. Therefore, I believe a Congressionally directed, comprehensive review should also answer the following ~uestions:

1. What suddenly mandates the use of this outdated vaccine? Both the capability to weaponize anthrax and the FDA approval for the vaccine have existed for decades. The troops are asking, why now?

2. Why force us to take a vaccine that was not intended to combat inhalation exposure to anthrax, and that will be defeated with mutated strains of anthrax, or simply a different pathogen?

3. Why abandon the time-tested deterrence doctrine of massive retaliation that was successful in the Gulf War by mandating a force protection measure that may create a façade of force protection, endangering our soldiers.

4. Is it dangerous to erroneously imply to our top military and civilian leaders that we can withstand a biological weapons attack through defensive posturing? Why has this been prudently avoided for the preceding three decades?

After answering these questions, I believe you will conclude that we can do better than an outdated, marginally effective vaccine against only one of many potential biological pathogens. Hopefully, Congress will mandate a program that offers real force protection based on four logical foundations of intelligence, detection, external protection, and medical treatment.

These foundations of force protection rely upon a credible willingness to use force. The old phrase, "The best defense is a good offense," was the philosophy that successfully deterred our adversaries during the Cold War. The defensive anthrax vaccination policy may abandon this time-tested doctrine and inadvertently legitimizing biological warfare.

A monument in Washington honors America's soldiers by saying, "First in war, first in peace, and first in the hearts of our countrymen." Just as that quote impressed me, I am equally encouraged by your committee's decision to keep servicemembers interests "First" by reviewing the anthrax vaccination policy.

These issues weigh heavily on my mind, but your actions can turn the corner on this debate. You can perform a vital service to this nation by halting this doctrinal shift. You can insure our armed force's readiness by stopping personnel losses due to this program. And you can help make the armed forces an attractive service option for young Americans.

It is my ardent hope that this review will stop any further mandatory vaccinations until a thorough, unbiased, and scientific review is conducted. This review may find that the costs of the anthrax vaccination policy far outweigh its limited force protection benefits.

I sincerely thank you for the opportunity to testify today.

Subj: **verbal drivel from me!**
3/23/99 1:59:56 AM Eastern Standard Time
From: redingle@ziplink.net (Russell Dingle)
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If you guys don't have enough to read, here's my next and hopefully final whack at doing the testimony thing. Good night and see ya Tuesday. Russ D.

Thank you for the opportunity to appear today. I am Russell Dingle, a citizen soldier, a Major and a former Flight Commander in the CTANG. I have just completed my tenth year flying A-10's for CT. I will not see an eleventh. I have declined the opportunity to receive the anthrax vaccine and am resigning on April 3rd of this year.

Last September my unit announced an anthrax vaccination policy that many officers objected to. In response, the wing commander delayed the shot schedule and formed a team to research the vaccine. I was a key member of that team. In little more than a week the information I gathered presented a compelling argument, against the DoD and its claims of safety and effectiveness.

The team presented 15 questions to the commander on October 14th. He forwarded these questions to his superiors. By the end of October, and with no answers forthcoming, we were told the anthrax conversation was over and that the shots would commence as scheduled.

CT's AVIP began on November 7th. Our unit was using lot FAV030, a lot specifically identified by the FDA as being contaminated in their 1998 inspection of the Michigan production facility.

It was becoming apparent that our use of the chain of command to affect a difference was not working, nor were our attempts at our elected officials involved. We felt that public involvement was our last opportunity to get this program reviewed and perhaps halted.

This has brought me before you today. I have been a reluctant participant in this ongoing tragedy. As a guardsman I am in a unique position. I have the option to resign when I don't agree with an order. While it would be easy to just walk away and leave this mess for others to deal with, I cannot in good conscience allow this program to go unchallenged.

I am here today to try to highlight the fallacies of the DoD claims of safety and efficacy, and the uncertainty that traditional guardsmen and reservists face. The questions we raised have been distributed to our commander, the news media, all of you, and others.

Have our military leaders sought to answer these questions?

Have they developed patent answers just in case you ask them?

I cannot begin to argue complex medical issues with these experts, yet the literature contains clear, unambiguous statements that don't agree with the DoD position. For instance:

If the vaccine has been FDA approved and licensed since 1970, why did a former USAMRIID commander define the vaccine as experimental in a 1990 article?

If the vaccine is absolutely safe and effective, why did a USAMRIID commander conclude that the vaccine was unsatisfactory in a 1994 edition of the medical textbook Vaccines?

If the vaccine is so widely used, why isn't it in the latest PDR?

While it appears that the DoD is devoting vast amounts of time, money, and manpower educating its members about how safe this program is, it is falling short in some key areas.

Why isn't the DoD telling members of the military what side effects to be aware of or report?

Why are they discounting those who do report side effects and then not report those incidents to higher headquarters?

Why isn't the VAERS form available or made known to members?

As citizen soldiers, part-timers, we all face the uncertainty of medical care should our health be affected while in some sort of military status. We may be soldiers on the weekend, but when Monday roles around we are civilians.

What happens when a guardsman reacts to this vaccine on Tuesday, or next week, or two years after she retires?
Will the state be forced to pay for the medical care of affected unit members?
Will their civilian insurance companies pick up the tab?
Will the federal government pay?
Or will the member face a revolving door of denials and blame games between the VA, the state, and the insurance companies?
A threat to our personal health, perceived or real, is a critical factor in whether or not we choose to "volunteer" our bodies in service to our country. How will this threat affect my civilian job? Should I risk both my military job and my civilian career? These are real and serious questions that many volunteers are asking themselves. This threat and the uncertainty of care needs to be addressed.

And finally, the number games the DoD plays needs to be challenged. There does not seem to be one set of numbers that the DoD is using for public relations. One DoD spokesman says they don't know how many shots were given in Desert Storm, the next spokesman has an exact number, including how many suffered adverse reactions. Another DoD spokesman reports one number of pilots resigning and, having first hand knowledge, I know this number is incorrect. The lack of consistent data is troublesome.

Last year I spent several anxious days contemplating how I should proceed with respect to the anthrax issue. What am I missing, should I risk my health and play the odds, am I letting my country down by quitting; I've never refused an order, now what?

This controversy is not about the CTANG, the people seated with me, or myself. It is about what is right, not who is right. And this is wrong. I urge this committee to ask the tough questions, to demand forthright answers based on documented evidence, to hold the military accountable for its actions and decisions that effect the health of all its members, including its' citizen soldiers.

Thank you.

———— Headers ————
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Received: from rly-zc03.mx.aol.com (rly-zc03.mail.aol.com [172.31.33.3]) by air-zc05.mail.aol.com (v68.13) with SMTP; Tue, 23 Mar 1999 01:59:48 -0500
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	EXECUTIVE SECRETARY		X				
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	Director, Defense Research & Engineering				Director, Joint Staff		
	UNDER SECRETARY FOR POLICY						
	ASD (International Security Affairs)				BALLISTIC MISSILE DEFENSE ORGANIZATION		
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	ASD (Strategy &Threat Reduction)				DEFENSE COMMISSARY AGENCY		
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1	UNDER SEC FOR PERSONNEL & READINESS	X			DEFENSE INFORMATION SYSTEMS AGENCY		
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	DIR, OPERATIONAL TEST & EVALUATION						
	DIR, ADMINISTRATION & MANAGEMENT						
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					GWI		X

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Remarks:

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BENJAMIN A. GILMAN
20th District, New York

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Congress of the United States
House of Representatives
Washington, DC 20515–3220

OSAGWI

July 20, 1999

JUL 26 1999

The Honorable William Cohen
Secretary of Defense
1000 Defense Pentagon
Washington D.C. 20301

Dear Mr. Secretary:

We are writing to you to express our concerns with the Anthrax vaccination program currently being implemented by the Department of Defense. As you know, the House Subcommittee on National Security, Veterans Affairs, and International Relations has held three hearings on this subject and is expected to hold at least two more during the second half of this year.

The hearings held in March, April, and June have raised a number of concerns about the vaccination program including its purpose, its value, the manner in which it is being carried out, and its effects on those who serve in uniform. These concerns have been heightened by recent media reports and information circulating among those affected by the vaccine. Subsequently, our offices are receiving an increasing number of contacts from concerned constituents, both members of the Armed Forces, as well as their distraught parents or relatives.

Mr. Secretary, you had set four specific conditions that had to be met before the vaccination program could start: 1) supplemental testing to assure sterility, safety, potency and purity of the vaccine stockpile; 2) implementation of a system for fully tracking anthrax immunizations; 3) approval of operational plans to administer the vaccine and communications plans to inform military personnel; and 4) review of medical aspects of the program by an independent expert.

According to the hearing testimony before the Subcommittee, none of these conditions was satisfactorily addressed before the vaccine program was implemented. While we do not want to duplicate the efforts of our colleagues who are pursuing their own investigations, we would request that you direct your attention to the following issues.

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The first of these relates to the overall effectiveness of the vaccine. The FDA approval cited by the Defense Department was for a vaccine that was designed to protect workers in the woolen industry from cutaneous contact with anthrax spores. Conversely, the primary anthrax threat facing military personnel is not cutaneous, but weaponized versions of the bacteria, which are inhaled by their victims. There has been little or no testing of the vaccine's effectiveness in humans against this form of anthrax for obvious reasons. Testing results on animals has had mixed results, with the most promising returns coming from laboratory monkeys. However, to assume a drug that has achieved successful results in primates will have a similar response with humans is only the start of basic research.

Additionally, we have yet to see any evidence from the Defense Department that this vaccine would be effective against altered or multiple anthrax strains. Given that the Soviet Union placed a high priority on the development of the deliverable multiple anthrax strains, this is a legitimate concern. Analysis of tissue samples from Russians killed in an accidental anthrax release from a production facility in the 1970s have indicated infection from a combination of individual strains. In fact, the Russian biowarfare expert, Ken Alibek, has even been quoted as saying vaccines aren't the answer. Given the extremely poor performance of the vaccine against even individual multiple strains in the Ft Detrick guinea pig studies, does the Defense Department have any evidence that the vaccine currently being issued is effective against a combination of multiple anthrax strains?

We are also concerned about the value of supplemental testing and whether such testing can really determine the sterility, potency, purity, and safety of the vaccine. Written GAO testimony from the April 29 hearing left this issue unresolved. They wrote, ". . . quality cannot be guaranteed for final tests on random samples but only from a combination of in-process tests, end-product tests, and strict controls of the entire manufacturing process." The FDA inspection results from February 1998 already indicate a significant lack of quality controls during manufacturing. It would seem that any damage done could not really be reversed at this point. Can you provide specific details of just how the supplemental testing process is able to overcome problems already present in the final vaccine product without remanufacturing the lots?

The second concern relates to the overall safety of the vaccine. As with any drug, there are concerns about harmful side effects. Since 1970, the primary recipients of the vaccine have been several thousand mill workers and mostly DOD researchers. This limited civilian usage of the drug has resulted in limited evidence of adverse reactions. The one exception to this was the inoculation of approximately 150,000 Gulf War troops. However, the Defense Department's poor record keeping after the Gulf War has made gleaning any useful information about the vaccine's effectiveness or harmful side effects impossible.

Once again, it may be premature to conclude that a drug used on several thousand individuals with a small incidence of adverse effects is safe to administer to 2.5 million military personnel. A simple overall 2% rate would yield 50,000 adverse reactions each and every year. This is an unacceptably high rate (more on the DOD reported reaction rate later). It is also completely unknown what will be the effect of cumulative annual boosters, let alone the combined effects from 15 or so other biological warfare vaccines under development. What other force protection program has, as a built-in component, such a high casualty rate and unknown level of future risk?

Another source of safety concerns comes from the vaccine plant. It is well known that the original manufacturer of the vaccine, Michigan Biologics Products Institute (MBPI), "voluntarily" closed down in March 1998 in order to make $1.8 million in renovations and a $15 million expansion which was funded by the Defense Department. Prior to this, MBPI had been cited repeatedly by the FDA for quality control problems and manufacturing violations dating back to 1990. Will you inform us as to what steps the new owner of the manufacturing site, Bioport Corporation, is taking to improve the production and testing process for the safety of the vaccine?

The Subcommittee briefing from the April 29 hearing, stated that the vaccine "is dangerous enough the manufacturer demanded, and received, indemnification from the Army against the possibility that persons vaccinated may develop anaphylaxis or some unforseen reaction of serious consequences, including death. Private indemnity insurance was considered too costly." If the manufacturer was highly concerned about potential civil litigation, why was the Defense Department so quick to convey the message that the vaccine was safe for general use?

The third concern relates to the tracking system being implemented with this vaccine. The Gulf War experience illustrated the need for a comprehensive tracing system to measure the potential side effects of the multiple vaccinations often administered to soldiers being deployed overseas. While we understand that such a tracking system has been developed for this program, there have been several reports of individuals being inoculated with expired lots of the vaccine, to the significant detriment of their health as recorded in testimony and the media. What steps are being taken to improve upon this Gulf War experience and what is being done to avoid further health impacts with expired lots in this program?

Moreover, it appears that adverse exclusionary categories, such as respiratory conditions, previous reactions, chills and fever, and pregnancy are not being adequately reviewed by the personnel in charge of administering the shots. Rather, the subcommittee has received reports that many of those administering the vaccine are simply glossing over communicating the exclusionary requirements in an effort to inoculate as many individuals as rapidly as possible. Likewise, we are also concerned that the reporting of adverse reactions among troops who have received the vaccine, is being discouraged, so as not to cause undue alarm in those units which have not received their first round of shots.

In that same regard, the official Defense department's reported reaction rates of between .0002% and .007% this year is not reassuring for several reasons. We have received reports that VAERS forms are not available to service members, not filled out, or not forwarded. FDA and JAMA sources indicate extremely low percentages of reactions are ever reported anyway, and the military's record of reaction reports with the 1970s swine flu vaccine is far below that of civilian rates. Given these qualifiers, why are the DOD reported reaction rates not accompanied by reasonable disclaimers?

The fourth area of concern deals with the operational plans to administer the vaccine. There appears to be some confusion deadlines as some units begin their shots and frequent deadline adjustments for unit personnel to receive their shots. Some of those deadline adjustments appear due to commander fear of excessive personnel losses because of the vaccine. Additionally, as reserve component personnel express an interest in transferring or terminating their participation because of the vaccine, we are hearing they are met with delays, instructions to not list the vaccine as a reason, and even threats of poor evaluation reports. Last we heard, this is still a voluntary force. If members are convinced after careful research that a policy truly threatens their civilian livelihood, they should be allowed to communicate the truth about their perspective. What assurances can you provide that these repressions will not occur in the future?

Furthermore, the Reserve Officers Association has recommended that all National Guard and Reserve units should receive shots from lots of newly made vaccine. The ROA is chartered by Congress to review defense policies to ensure their adequacy. Since they represent 80,000 current, experienced, and retired reservists, their opinion should be considered carefully. Given that Bioport Corporation is not due to begin production of new vaccine until next year, and we know Guard and Reserve units are being vaccinated, why has this recommendation for new lots been ignored?

We would also appreciate data the DOD collected, if any, regarding how many and what percent of service members were inoculated to be protected prior to deploying to the Allied Force operation in Kosovo. Also, what percent of members deployed without the vaccine's protection? Given Russian support for Serbia, we assume DOD took into account the possible anthrax supply provided to the enemy for use against our forces or the Kosovars.

Finally, we have serious concerns about the independent review of the medical aspects of the vaccination program. The reviewer in question, Dr. Gerald N. Burrow, has been cited by the Defense Department as approving of the safety and effectiveness of the vaccine. Yet in a letter to the Subcommittee dated April 26, 1999, Dr. Burrow Stated: "the Defense Department was looking for someone to review the program in general and make suggestions, and I accepted out of patriotism. I was very clear that I had no expertise in Anthrax and they were very clear they were looking for a general oversight of the vaccination program. . . I had no access to classified information. The suggestions I made were to utilize focus groups to be sure the message they wanted to send to force personnel was being heard, and to use the vaccination tracking system as a reminder for subsequent vaccinations. I had no further contact after delivering my report and do not know whether my suggestions were implemented."

Given that the independent reviewer was admittedly not an expert in the field of anthrax, how can the Defense Department stand by his earlier claims that the vaccine was safe for distribution and the "best protection against wild-type anthrax?" Given past poor credibility in these issues, the history with Gulf War Illnesses, and the enormous potential risk to our entire population of uniformed defenders, why was this individual, and not someone with a background in large vaccination programs or biological agents like anthrax, selected for the independent review?

One more specific concern we have relates to the approach of our allies to the biowarfare issue. We know Britain has a voluntary vaccine policy which yields only 30% cooperation. We know the French didn't force their troops the to take anthrax or other vaccines in the Gulf War and don't have the illnesses our service members complain about. We know the Canadians have faced the same controversies and even more severe logistics problems with the vaccine and are not currently administering it to their troops. We know Israel, which is conceivably at the greatest risk in the Middle East and has received SCUDs attacks, does not rely on vaccines, but antibiotics. And the State Department, which arguably has more personnel risk because embassies are less well protected than military units, has only a voluntary policy. It is almost inescapable that this policy appears as a captive research market. Why in light of everyone else's lack of forced inoculations is it necessary to put U. S. service member trust on the line when two surveys have indicated that 80% of the civilian and military respondents oppose the program?

Above and beyond the specific concerns mentioned here, we are concerned about the public perception of the anthrax vaccination program and its impacts on service member morale. We must ensure that this single force protection measure which addresses only one of a myriad of biological threats is not itself a more real threat to our citizens in uniform.

We welcome your review of this issue, and look forward to hearing your response to our specific concerns.

Sincerely,

BENJAMIN A. GILMAN
Member of Congress

CHRISTOPHER SHAYS
Member of Congress

SUE KELLY
Member of Congress

MARK SOUDER
Member of Congress

DOUG OSE
Member of Congress

JAMES TALENT
Member of Congress

Congressman Ben Gilman

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To: SECRETARY COHEN Fax#: (b)(6)

From: BENJAMIN GILMAN

Number of pages (including cover sheet): 6 Date: Time:

Comments:

THE SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1000

SEP 3 0 1999

Honorable Benjamin A. Gilman
House of Representatives
Washington, DC 20515-3220

720

Dear Ben:

Thank you for your letter regarding the Department of Defense's Anthrax Vaccine Immunization Program. With over one million anthrax immunizations given, I believe our experience with the program fully reinforces my approval last year of the recommendations of the Chairman and the Joint Chiefs of Staff to implement the Total Force Anthrax Vaccine Immunization Program.

All four of the conditions that I set as prerequisites for program implementation were successfully met before I approved the Total Force Anthrax Vaccine Immunization Program and, therefore, the order to implement was not conditional. The supplemental testing program to test for potency, purity, sterility, and general safety of the vaccine stockpile previously approved for release by the FDA has affirmed that proper lot release standards were met on all vaccine used. Service implementation plans are being effectively carried out, delivering nearly one million vaccinations with very few instances of noncompliance or serious adverse events. The immunization tracking systems are performing very well, showing the record keeping problems experienced during the Gulf War have been addressed. The independent review of the health and medical aspects of the program completed by Dr. Gerard N. Burrow, the Special Advisor for Health Affairs for the President of Yale University, stands with other independent medical judgment expressing confidence in the use of the vaccine, including that of the Centers for Disease Control and Prevention, the World Health Organization, the Institute of Medicine, and other health organizations.

Anthrax poses a clear and present danger to our armed forces. It is the weapon of choice for germ warfare because it is easy to weaponize and is as lethal as the Ebola virus. At least seven potential adversaries have worked to develop the offensive use of anthrax. We have an FDA-licensed vaccine which has been used for nearly 30 years and has an excellent safety record. It would be unconscionable not to protect our entire force with a safe and effective FDA-licensed vaccine.

As we implement this vital program, we are reinforcing our adverse event reporting and tracking system to further assure expert review of any adverse events possibly related to vaccinations. We are working with the vaccine manufacturer as it transitions from State ownership to an excellent, state-of-the-art private facility. Furthermore, we are addressing the misinformation that is circulating on the Internet and elsewhere by educating Service

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members in both the active and reserve components with the facts: anthrax kills and anthrax vaccination protects.

Enclosed are responses to the questions and concerns in your letter. Representatives Shays, Kelly, Souder, Ose, and Talent have also received a similar reply.

Sincerely,

Enclosure:
As Stated

Responses to Anthrax Vaccine Immunization Program (AVIP) Questions
Congressional Letter, July 20, 1999

Question #1:

The first of these relates to the overall effectiveness of the vaccine. The FDA approval cited by the Defense Department was for a vaccine that was designed to protect workers in the woolen industry from cutaneous contact with anthrax spores. Conversely, the primary anthrax threat facing military personnel is not cutaneous, but weaponized versions of the bacteria, which are inhaled by their victims. There has been little or no testing of the vaccine's effectiveness in humans against this form of anthrax for obvious reasons. Testing results on animals has had mixed results, with the most promising returns coming from laboratory monkeys. However, to assume a drug that has achieved successful results in primates will have a similar response with humans is only the start of basic research.

Additionally, we have yet to see any evidence from the Defense Department that this vaccine would be effective against altered or multiple anthrax strains. Given that the Soviet Union placed a high priority on the development of the deliverable multiple anthrax strains, this is a legitimate concern. Analysis of tissue samples from Russians killed in an accidental anthrax release from a production facility in the 1970s have indicated infection from a combination of individual strains. In fact, the Russian biowarfare expert, Ken Alibek, has even been quoted as saying vaccines aren't the answer. Given the extremely poor performance of the vaccine against even individual multiple strains in the Ft Detrick guinea pig studies, does the Defense Department have any evidence that the vaccine currently being issued is effective against a combination of multiple anthrax strains?

Answer #1:

The evidence of efficacy of the FDA-licensed anthrax vaccine is based upon data from both humans and animal models. The protective component of the licensed vaccine is a protein called protective antigen. The only clinical study conducted in humans [Brachman et al. Amer. J. Pub. Health 52:632 (1962)] to evaluate efficacy used a vaccine similar but not identical to the current licensed anthrax vaccine. The vaccine used was a precursor in the development of the licensed vaccine. However, both vaccines, the vaccine used in the Brachman study and the current licensed vaccine, were based on the immunity induced by the protective antigen.

Several experimental animal models, including guinea pigs, rabbits, and non-human primates, have been used to evaluate the efficacy of anthrax vaccines. In the guinea pig model, the FDA-licensed anthrax vaccine can confer varying protection against an intramuscular challenge with the Ames strain, with 13-90% of animals surviving in various experiments [Turnbull et al. Infect. & Immun. 52:356 (1986); Ivins et al. Vaccine 12:872 (1994); Fellows et al. However, the anthrax vaccine has been unable to provide good protection in the guinea pig against an aerosol challenge, where only 20-26% of the animals survived [Ivins et al. Vaccine 13:1779 (1995)].

In more recent studies, the rabbit has also been used to evaluate the anthrax vaccine. In an initial unpublished study, 9 of 10 rabbits immunized with 2 doses of FDA-licensed anthrax vaccine survived lethal aerosol challenge. In a subsequent study, a total of 48 rabbits immunized with 2 doses of vaccine (28 were given a full dose of vaccine and 20 were given a 1 to 4 dilution of the vaccine) all survived aerosol challenge [Pitt et al. Presented at 3rd International Conference on Anthrax, 1998, abstract in press]. Thus, in various experiments, 57 of 58 rabbits (98%) immunized with anthrax vaccine survived lethal aerosol challenge. In these studies, none of a total of 28 unvaccinated control animals survived the challenge. The rabbit, therefore, is like the non-human primate in that immunization with anthrax vaccine confers excellent protection against aerosol challenge. This contrasts dramatically with the guinea pig model where immunization with anthrax vaccine gives poor protection. Because the response of the rabbit to immunization is similar to that of the non-human primate and because the pathologic lesion caused by Bacillus anthracis is closer in rabbits than in guinea pigs to that seen in humans, the rabbit is considered to be better than the guinea pig as a small animal model for evaluating anthrax vaccine efficacy.

In the non-human primate, the model that best approximates inhalation anthrax in humans, the FDA-licensed anthrax vaccine is able to provide close to 100% protection against an aerosol challenge with the Ames strain. In one study, 20/21 animals immunized at 0 and 2 weeks survived [Ivins et al. Salisbury Med. Bulletin 87:125 (1996)]. In a second study 9 of 9 animals immunized at 0 and 4 weeks survived [Pitt et al. Salisbury Med. Bulletin 87:130 (1996)]. As part of another unpublished study conducted at USAMRIID, 5 animals immunized at 0 and 4 weeks all survived lethal aerosol challenge. Overall, 34 of 35 animals given 2 doses of anthrax vaccine were protected against a lethal aerosol challenge using a strain that killed approximately 80% of vaccinated guinea pigs challenged by the aerosol route. An additional study in non-human primates showed that a single dose of anthrax vaccine protected 10 of 10 animals from lethal challenge at 6 weeks [Ivins et al. Vaccine 16:1141 (1998)]. Thus, a total of 44 of 45 [98%] non-human primates vaccinated with the licensed anthrax vaccine survived a lethal aerosol challenge. In the various studies with non-human primates, a total of 14 controls (unvaccinated animals) were challenged and none survived.

With respect to questions regarding the effectiveness of the anthrax vaccine against altered or multiple anthrax strains, a press conference on February 3, 1998 from the Los Alamos National Laboratory suggested that the FDA-licensed anthrax vaccine might be ineffective against a mixture of strains of *Bacillus anthracis*. Other recent news releases have questioned its effectiveness against strains possibly developed by Russian scientists.

Russian scientists have reported the creation of an antibiotic resistant strain of anthrax. They also described, in a 1997 publication, a study to improve their own anthrax vaccine. As part of that study, they genetically engineered a strain of anthrax to contain two foreign genes. That strain was resistant to the Russian anthrax vaccine unless the vaccine was modified to contain the same genes. This genetically engineered strain likely causes disease in humans (if it

indeed does so) by a different mechanism than that used by naturally occurring anthrax strains. We do not have confirmation of the Russian claims.

Scientists from Los Alamos National Laboratory have described identification, using gene probes, of multiple strains of anthrax in tissue specimens obtained from victims of the 1979 Sverdlovsk anthrax incident. The laboratory press release implied that mixtures of anthrax strains might overcome the protection afforded by anthrax vaccine. After discussions with the US Army Medical Research and Materiel Command officials, the author of the press release, Dr. Walt Kirchner, DoD Programs Office, Los Alamos National Laboratory, agreed to correct the press release to make it more accurate. The modification stated, in part, "...there is no experimental data or evidence to suggest that such a mixture is resistant to the FDA-licensed anthrax vaccine used by the US military."

The current US-licensed anthrax vaccine is considered to be highly effective against naturally occurring strains of anthrax, including antibiotic resistant strains. The development of genetically engineered new organisms using anthrax or any other biological warfare agent is a potential threat that must be evaluated carefully. We are not aware, however, of any information to suggest that these modified strains have been used in any context other than the research laboratory.

Question # 2:

We are also concerned about the value of supplemental testing and whether such testing can really determine the sterility, potency, purity, and safety of the vaccine. Written GAO testimony from the April 29 hearing left this issue unresolved. They wrote, "...quality cannot be guaranteed for final tests (in random-samples but only from a combination of in-process tests, end-product tests, and strict controls of the entire manufacturing process." The FDA inspection results from February 1998 already indicate a significant lack of quality controls during manufacturing. It would seem that any damage done could not really be reversed at this point. Can you provide specific details of just how the supplemental testing process is able to overcome problems already present in the final vaccine product without remanufacturing the lots?

Answer #2:

As an additional quality check of the integrity of the anthrax vaccine in the stockpile, Secretary Cohen, before he authorized the Anthrax Vaccine Immunization Program to proceed, approved the DoD plan to establish a process for supplemental testing of the vaccine by the manufacturer to assure its sterility, safety, potency and purity. The supplemental testing program goes beyond FDA requirements to assure service members and the public that the vaccine stockpile is safe and effective. Supplemental testing is based on the tests required by the FDA for lot release and, as a quality check, provides an added level of confidence in the safety of the

anthrax vaccine in the stockpile. While not required by the FDA, the manufacturer has performed, and continues to perform supplemental testing on lots of anthrax vaccine that had been previously approved for release by the FDA and that were in the DoD's stockpile in December 1997 when the Secretary of Defense approved the policy to immunize the Total Force against anthrax. Supplemental testing by the manufacturer is overseen by an independent, third party organization called Mitretek Systems, Inc., which provides external review of supplemental testing under a contract with the Department. Supplemental tests performed by the manufacturer include: general safety (follows 21 CFR 610.11 guidelines); potency (follows 21 CFR 610.10 guidelines); sterility (follows 21 CFR 610.2 guidelines); and purity (no formal 21 CFR requirements for individual testing of preservatives or additives);

All supplemental testing performed by MBPI/BioPort follows the accepted testing protocols and the manufacturer's current Standard Operating Procedures. Mitretek Systems Inc., which observes all aspects of supplemental testing, provides a written report to the DoD prior to any lots being approved for use and shipment.

Question #3:

The second concern relates to the overall safety of the vaccine. As with any drug, there are concerns about harmful side effects. Since 1970, the primary recipients of the vaccine have been several thousand mill workers and mostly DOD researchers. This limited civilian usage of the drug has resulted in limited evidence of adverse reactions. The one exception to this was the inoculation of approximately 150,000 Gulf War troops. However, the Defense Department's poor record keeping after the Gulf War has made gleaning any useful information about the vaccine's effectiveness or harmful side effects impossible.

Once again, it may be premature to conclude that a drug used on several thousand individuals with a small incidence of adverse effects is safe to administer to 2.5 million military personnel. A simple overall 2% rate would yield 50,000 adverse reactions each and every year. This is an unacceptably high rate (more on the DOD reported reaction rate later). It is also completely unknown what will be the effect of cumulative annual boosters, let alone the combined effects from 15 or so other biological warfare vaccines under development. What other force protection program has, as a built-in component, such a high casually rate and unknown level of future risk?

Answer #3:

To date, our Servicemen and Servicewomen have received nearly 1 million anthrax immunizations, and while side effects do occur in some people, they tend to be temporary, confined to the area around the injection, and mild or moderate in most people. Systemic reactions, if they occur, have for the most part been self-limited. Although we have seen the isolated emergence of several patients who have developed significant symptoms or diagnosable

illnesses temporally in relation to the administration of the vaccine, we have not established any pattern of causality.

The rate of adverse reactions related to administration of the anthrax vaccine is comparable to many other commonly given vaccines that have been administered to many millions of adults and children in the US. For purposes of comparison, the studies of the anthrax vaccine that were used at time of licensure showed that in 16,000 doses approximately 3-20% exhibited mild reactions and fewer than 1% severe side effects. In the case of hepatitis A vaccine, soreness at the injection site was reported by 56% of adult vaccine recipients. Headache was reported by 14%. For the typhoid vaccine, local tenderness was reported by 98%, pain by 56%, malaise by 24% and headache by 11%. The pneumonia vaccine, which is a recommended vaccine for all Americans over the age of 50, has a 71% rate for localized soreness. The hepatitis B vaccine reports a local reaction rate of 17% and a systemic reaction rate of 15% in adults. The recently licensed Lyme disease vaccine produced unsolicited reports of injection site pain in 21% and fever in 2.5% of vaccine recipients. When a subset of Lyme disease vaccine recipients were surveyed, 93% reported local soreness, 41% reported local redness, and 3.4% reported fever. The safety and efficacy data for licensure of the Lyme disease vaccine came from clinical trials involving 6,478 individuals who received a total of 18,047 doses of vaccine; most had follow-up for 20 months after receiving the first dose of the vaccine.

With respect to the comment regarding an unacceptably high casualty rate, we respectfully suggest the appropriateness of comparing adverse vaccine effects with the predictable casualties resulting from anthrax exposure among unvaccinated personnel. We believe the balancing of risks overwhelmingly supports vaccination against this highly lethal biological agent.

Question #4:

Another source of safety concerns comes from the vaccine plant. It is well known that the original manufacturer of the vaccine, Michigan Biologics Products Institute (MBPI), "voluntarily" closed down in March 1998 in order to make $ 1.9 million in renovations and a $15 Million expansion which was Funded by the Defense Department. Prior to this, MBPI had been cited repeatedly by the FDA for quality control problems and manufacturing violations dating back to 1990. Will you inform us as to what steps the new owner of the manufacturing site, Bioport Corporation, is taking to improve the production and testing process for the safety of the vaccine?

Answer #4:

The anthrax production facility currently owned and operated by BioPort has been manufacturing vaccines for decades. In recent years, the manufacturer has upgraded and added to its existing facility in a staged fashion in order to comply with current good manufacturing

practices (cGMPs). The anthrax production line was closed by the manufacturer for planned renovation in March 1998. Although the decision to close the facility for planned renovation was part of the manufacturer's facility improvement strategy, it was, in part, also based on a 1996 DoD assessment that concluded that the facility was inadequate to meet future requirements. This renovation project included upgrades of the anthrax vaccine manufacturing space along with the addition of a negative air pressure sink, a reach-in environmental chamber, and a state-of-the-art closed inoculation system. The physical aspects of the renovation were completed in January 1999. Validation and FDA inspection of the facility, which must occur before full production resumes, are scheduled for completion by January 2000. DoD has provided significant administrative, scientific, technical, and consultative assistance to BioPort to facilitate its continuing efforts to comply with regulatory requirements.

DoD was aware that the manufacturer had undergone FDA inspections in November 1996 and February 1998 that had found a number of deficiencies related to compliance with cGMPs. Following the November 1996 FDA inspection, the manufacturer teamed with the DoD to devise a Strategic Plan for Compliance on April 9, 1997 that addresses in detail how it plans to implement quality systems and cGMP improvements to achieve compliance with applicable FDA standards and regulations. Although the facility was not manufacturing anthrax vaccine at the time of the FDA inspection of February 1998 due to its planned renovation, a number of deficiencies with the manufacturing process were cited by the FDA. The FDA also acknowledged that the manufacturer had made progress toward implementing its strategic plan for achieving compliance with FDA standards and regulations. The manufacturer, with support from the DoD, continues to diligently implement these quality and cGMP improvements. It should be pointed out that at no time were deficiencies reported by the FDA considered serious enough to warrant recall of the anthrax vaccine in the stockpile. With continued assistance from the DoD, BioPort continues to make progress toward full implementation of its Strategic Plan for Compliance.

Question #5:

The Subcommittee briefing from the April 29 hearing, stated that the vaccine "is dangerous enough the manufacturer demanded, and received indemnification from the Army against the possibility that persons vaccinated may develop anaphylaxis or some unforseen reaction of serious consequences, including death. Private indemnity insurance was considered too costly." If the manufacturer was highly concerned about potential civil litigation, why was the Defense Department so quick to convey the message that the vaccine was safe for general use?

Answer #5:

Indemnification for the anthrax vaccine was done for reasons of insurance, not vaccine safety. Congress has clearly recognized that reliance on private liability insurance for injuries

potentially arising from vaccine use is ineffective. In the legislative history of the National Childhood Vaccine Injury Act of 1986, the House Committee on Energy and Commerce (H. Rept. No. 99-908, page 6) said:

> Manufacturers have become concerned not only with the problems of time and expense [of litigation], but with the issue of the availability of affordable product liability insurance that can be used to cover losses related to vaccine injury cases. Whether current problems with liability insurance arise from a crisis in the tort system or from a particularly bad downturn in the business cycle of the insurance industry remains a matter of great controversy. Nevertheless, *there is little doubt that vaccine manufacturers face great difficulty in obtaining insurance.* This lack of insurance was the stated reason for one manufacturer to withdraw temporarily from the vaccine market in 1984. Others have suggested that they may follow a similar course of action. This factor, coupled with the possibility that vaccine-injured persons may recover substantial awards in tort claims, has prompted manufacturers to question their continued participation in the vaccine market. [Emphasis added.]

Based on the need for an alternative to reliance on private liability insurance for vaccine manufacturers, Congress created the Vaccine Injury Compensation Program (administered by the Department of Health and Human Services). The goals of this program were to provide no-fault compensation for injuries associated with vaccines routinely administered to children and to reduce the adverse effect of tort claims on the vaccine supply, the cost of vaccines, and the development of improved vaccines. The special program for handling vaccine liability applies to vaccines for diphtheria, tetanus, pertussis, measles, mumps, rubella, polio, hepatitis B, and selected other widely used vaccines. By addressing the unusual liability insurance problem associated with these vaccines, the Vaccine Injury Compensation Program is credited with stabilizing vaccine supplies and costs and promoting further vaccine research and development.

Because anthrax vaccine is not covered by the statutory Vaccine Injury Compensation Program, indemnification provides a similar method for addressing potential liability. As general rules: a) the government assumes responsibility for actions of its agencies and employees; and b) government contractors buy private insurance for liability arising from performance of the contracts and obtain reimbursement for the premium costs from the government. There are many exceptions to the general rules. One exception is that in certain cases, in which private insurance is not reasonably available, the government provides contract indemnification instead of requiring and reimbursing for private insurance. The circumstance in which private insurance is not reasonably available is referred to as "unusually hazardous risk." In the case of anthrax vaccine, the manufacturer demonstrated that, similar to the vaccines covered by the Vaccine Injury Compensation Program, private liability insurance is not reasonably available. Therefore, rather than requiring the manufacturer to obtain extremely expensive insurance and pass the premium cost back to DoD, the Department granted indemnification. The result is, similar to the

handling of vaccines were changed to ensure that upon receipt, the lot number and expiration of all vials of vaccine in the shipment are recorded. Upon issue, the expiration date of the vial of vaccine all vials of vaccine will be checked by the health care provider administering the immunization.

Currently, the Services use different interim automated immunization tracking systems (ITS) to record and track the anthrax immunization status of Service members. A core set of anthrax immunization data in a standard format is transmitted to the DoD's central personnel database, the Defense Enrollment and Eligibility Reporting System (DEERS). While DoD immunization regulations require documentation of the name of the immunization given, dosage number in the multi-dose series, lot number, manufacturer, name of the health provider administering the immunization, and date when the next dose is due, recording the expiration date in the ITS and/or medical records is not required by military or federal regulation. Therefore, the use of the ITS would not prevent administration of expired vaccine since this information is not currently documented in the ITS. As with any immunization or medication, the best way to prevent the use of an expired product is for the health care provider administering it to visually check the expiration date directly before its use.

Question #7:

Moreover, it appears that adverse exclusionary categories, such as respiratory conditions, previous reactions, chills and fever, and pregnancy are not being adequately reviewed by the personnel in charge of administering the shots. Rather, the subcommittee has received reports that many of those administering the vaccine are simply glossing over communicating the exclusionary requirements in an effort to inoculate as many individuals as rapidly as possible. Likewise, we are also concerned that the reporting of adverse reactions among troops who have received the vaccine, is being discouraged, so as not to cause undue alarm in those units which have not received their first round of shots.

In that same regard, the official Defense department's reported reaction rates of between .0002% and .007% this year is not reassuring for several reasons. We have received reports that VAERS forms are not available to service members, not filled out, or not forwarded. FDA and JAMA sources indicate extremely low percentages of reactions are ever reported anyway, and the military's record of reaction reports with the 1970s swine flu vaccine is far below that of civilian rates. Given these qualifiers, why are the DOD reported reaction rates not accompanied by reasonable disclaimers?

Answer #7:

The Department has a robust risk communication and education program that endeavors to inform Service members about the anthrax vaccine and the AVIP. Prior to receiving the first

anthrax immunization, Service members are provided written and oral information on the benefits and risks of the anthrax vaccine and details of the overall program by medical personnel and Commanders, to include reasons for exemptions and deferrals. Service members are also given the opportunity to have follow-up individual discussions with medical personnel and/or Commanders to answer specific questions or concerns that they may have regarding the program and the vaccine. The written trifold that is given to each individual prior to the first immunization contains information about the safety of the anthrax vaccine, some of the expected side effects, general information about the program and vaccine, and the address of the DoD website where more information about the anthrax vaccine can be obtained. Prior to orally briefing individuals on the anthrax vaccine and details of the program, medical personnel and Commanders are provided with anthrax briefing materials that discuss the adverse event reporting, contraindications/precautions, medical deferrals (such as pregnancy), and details about the program. The Department continuously stresses the importance of informing Service members about the benefits and risks of the anthrax vaccine and details about the overall program.

With respect to adverse event reporting for the anthrax vaccine, the DoD uses a passive surveillance developed collaboratively by the FDA and CDC called the Vaccine Adverse Event Reporting System, or VAERS. Passive surveillance is a common surveillance method employed for the collection of adverse events potentially related to vaccines and drugs. We know that a passive surveillance system under-reports the true number of adverse events. In addition, a passive surveillance system for adverse events seeks to identify those serious, rare, and/or unexpected events that potentially may be related to a vaccine. It is not a system for capturing all of the expected side effects after vaccine administration, such as local pain or swelling or expected systemic symptoms.

A passive surveillance system for reporting adverse events does provide us a large pool of vaccine recipients from whom we can collect information regarding rare but serious adverse events (such as anaphylaxis) and unexpected adverse events that may be associated with the vaccine. For the purposes of anthrax adverse events, only those reactions resulting in: (1) hospital admission; (2) quarters greater than 24 hours; or (3) suspected to have resulted from contamination of vaccine lots, are required to be submitted. However, any adverse event can be submitted within the military and directly to the Food and Drug Administration (FDA), at the discretion of the healthcare provider. It is also important to mention that patients themselves can input information into the VAERS system and some have done so. VAERS is an effective surveillance tool for the early identification of an unexpected adverse event or pattern of adverse events that may be related to a vaccine. In-depth evaluation and research is necessary to establish a causal link between the vaccine and any potential adverse event.

Reaction rates that the Department has reported reflect the rate or occurrence of adverse events that meet its VAERS criteria. It does not represent expected reactions to any immunization that are not captured by the VAERS. The Department has set up a process to have

all VAERS reports, those reported by providers as well as patients, reviewed by an independent external-review panel called the Anthrax Vaccine Expert Committee (AVEC). The AVEC consists of a special panel of civilian physicians from a component of the Department of Health & Human Services' Vaccine Injury Compensation Program. The AVEC uses explicit criteria for attributing causality to adverse events coincidentally associated with administration of the anthrax vaccine. To date, the AVEC has found no pattern of causality stemming from use of the anthrax vaccine. Over time, if the AVEC observes patterns of adverse events, it may recommend additional study or changes in practice guidelines.

The Department is and will continue to be vigilant in our surveillance for any unexpected adverse events that may potentially be associated with the anthrax immunization. We are committed to fully investigating all concerns or questions about the safety of anthrax vaccine and will continue full and complete disclosure of all risks, based on objective evidence.

Question #8:

The fourth area of concern deals with the operational plans to administer the vaccine. There appears to be some confusion deadlines as some units begin their shots and frequent deadline adjustments for unit personnel to receive their shots. Some of those deadline adjustments appear due to commander fear of excessive personnel losses because of the vaccine. Additionally, as reserve component personnel express an interest in transferring or terminating their participation because of the vaccine, we are hearing they are met with delays, instructions to not list the vaccine as a reason, and even threats or poor evaluation reports. Last we heard, this is still a voluntary force. If members are convinced after careful research that a policy truly threatens their civilian livelihood, they should be allowed to communicate the truth about their perspective. What assurances can you provide that these repressions will not occur in the future?

Answer #8:

There is no confusion regarding the execution of the AVIP. Due to limitations in the availability of anthrax vaccine, the AVIP is being implemented in several phases. Clearly, our first priority must be to protect our Service members deployed in areas that pose the greatest risk for encountering anthrax as a weaponized agent. Phase I, the current phase of the AVIP, requires all uniformed Service members and Emergency-Essential DoD civilians and contractors who are assigned, deployed, or on temporary duty in the Joint Staff designated high threat areas and contiguous waters of Southwest Asia and the Korean peninsula be immunized against anthrax first. Essentially, the "deadline" for individuals in phase I is prior to movement into the high threat areas to ensure that each member of the Armed Forces operating in these areas is protected. No scheduled deployment of units has been preempted due to concerns about the program, nor have there been any reports of adverse effects on the combat readiness of units involved in these deployments. More than 99 percent of all service members readily accept the anthrax immunizations.

Regarding the allegations of consequences for refusing anthrax vaccination, it should be understood that every Service member has an obligation to comply with lawful orders. The Secretary of Defense's order that all personnel receive the vaccinations (unless covered by a specified exception) is a lawful order. Service members who fail to comply with their obligation to follow lawful orders are subject to administrative or disciplinary action. There is no policy to single out anthrax vaccine compliance for any special actions relating to ongoing personnel matters, such as evaluation reports, unit transfer requests, voluntary separation requests, the recording of separation codes on personnel documents, or other matters, or for any special actions concerning administrative or disciplinary authorities that accompany all military obligations.

Question #9:

Furthermore, the Reserve Officers Association (ROA) has recommended that all National Guard and Reserve units should receive shots from lots of newly made vaccine. The ROA is chartered by Congress to review defense policies to ensure their adequacy. Since they represent 80,000 current, experienced, and retired reservists, their opinion should be considered carefully. Given that Bioport Corporation is not due to begin production of new vaccine until next year, and we know Guard and Reserve units are being vaccinated, why has this recommendation for new lots been ignored?

Answer #9:

The Reserve Officers Association (ROA) of the United States Resolution Number 99-8 specifically appeals for the use of only newly manufactured anthrax vaccine. The existing stockpile of anthrax vaccine is used for the active and reserve component without distinction between old or newly manufactured vaccine. Every dose of vaccine we administer to our Service members must first meet strict inspection requirements by the FDA for potency, purity, sterility and general safety. Each lot is then supplementally tested at the plant for these same specifications with oversight from an independent quality assurance agency before it is released for use. The viability and consistency of any lot released for use is exactly the same, therefore, there is no reason to distinguish between vaccine lots based upon date of manufacture.

The ROA recommendation to inoculate Reserve Component (RC) members only with lots of newly made vaccine also does not address the Total Force concept or recognize the increased emphasis on the Guard and Reserve to support current missions. If Guard and Reserve members are required to wait for the newly made vaccine lots, it would delay immunization and delay when the member would have adequate protection. The Department would be negligent in total force health protection measures if it did not take steps to use this safe and effective vaccine to ensure protection from anthrax.

Question #10:

We would also appreciate data the DOD collected, if any, regarding how many and what percent of service members were inoculated to be protected prior to deploying to the Allied Force operation in Kosovo. Also, what percent of members deployed without the vaccine's protection? Given Russian support for Serbia, we assume DOD took into account the possible anthrax supply provided to the enemy for use against our forces or the Kosovars.

Answer #10:

The high threat areas validated by our intelligence community for the potential use of anthrax as a biological weapon of mass destruction includes Korea, Israel, Jordan, Kuwait, Saudi Arabia, Bahrain, Qatar, Oman, UAE and Yemen. The EUCOM CINC intelligence threat analysis of the risk of biological warfare in the Balkans did not necessitate immunizing the force in that region against anthrax. We continue to immunize and protect our forces in accordance with the AVIP phased concept of execution.

Question #11:

Finally, we have serious concerns about the independent review of the medical aspects of the vaccination program. The reviewer in question, Dr. Gerald N. Burrow, has been cited by the Defense Department as approving of the safety and effectiveness of the vaccine. Yet in a letter to the Subcommittee dated April 26, 1999, Dr. Burrow stated: "The Defense Department was looking for someone to review the program in general and make suggestions, and I accepted out of patriotism. I was very clear that I had no expertise in Anthrax and they were very clear they were looking for a general oversight of the vaccination program. . . I had no access to classified information. The suggestions I made were to utilize focus groups to be sure the message they wanted to send to force personnel was being heard, and to use the vaccination tracking system as a reminder for subsequent vaccinations. I had no further contact after delivering my report and do not know whether my suggestions were implemented."

Given that the independent reviewer was admittedly not an expert in the field of anthrax, how can the Defense Department stand by his earlier claims that the vaccine was safe for distribution and the "best protection against wild-type anthrax?" Given past poor credibility in these issues, the history with Gulf War illnesses, and the enormous potential risk to our entire population of uniformed defenders, why was this individual, and not someone with a background in large programs or biological agents like anthrax, selected for the independent review?

Answer #11:

Before the Secretary made his decision for total force anthrax vaccination, he established four conditions to be met, and, also before he made the decision to proceed, he determined that

they were met. A very important condition was that an independent expert would review the program, including the vaccination's safety and efficacy, and advise the Secretary. In order to assure an independent review, it was important to seek out someone not already deeply involved with the anthrax issue and not already identified with a particular point of view. Dr. Gerard Burrow was and is a well-known health expert who has been involved with and was respected for his work at Yale University and with the Institute of Medicine of the National Academy of Sciences. He was asked to bring a fresh and unbiased perspective in advising the Secretary on this very critical decision. Dr. Burrow provided that independent perspective and advised the Secretary that: "The anthrax vaccine appears to be safe and offers the best available protection against wild-type anthrax as a biological warfare agent. Steps have been taken to ensure the safety and quality of the Department's anthrax vaccine stockpile."

Question #12:

One more specific concern we have relates to the approach of our allies to the biowarfare issue. We know Britain has a voluntary vaccine policy which yields only 30% cooperation. We know the French didn't force their troops to take anthrax or other vaccines in the Gulf War and don't have the illnesses our Service members - complain about. We know the Canadians have faced the same controversies and even more severe logistics problems with the vaccine and are not currently administering it to their troops. We know Israel, which is conceivably at the greatest risk in the Middle East and has received SCUDs attacks, does not rely on vaccines, but antibiotics. And the State Department, which arguably has more personnel risk because embassies are less well protected than military units, has only a voluntary policy. It is almost inescapable that this policy appears as a captive research market. Why in light of everyone else's lack of forced inoculations is it necessary to put US. Service members trust on the line when two surveys have indicated that 80% of the civilian and military respondents oppose the program?

Answer #12:

Many of our allies share our concerns for the global proliferation of biological warfare and have adopted similar policies and strategies in responding to it. Since the start of the AVIP in March of last year alone, the DoD has provided on request anthrax vaccine to Canada, Germany, Israel, Denmark, and Australia. To our knowledge, Canada has not suspended their immunization program against anthrax, and Israel does not rely solely upon the use of antibiotics.

The primary task of our Nation's Armed Forces is to deter aggression, and if that fails, to fight and win on the battlefield. The American people expect us to win and to accomplish this, our Armed Forces must be prepared to conduct successful military operations worldwide at a moments notice. While interaction with our military friends and allies is a critical part of all operations, the policies of DoD must be clearly focused on accomplishing the goals and objectives that support our national interests and national security strategy. DoD does not base its policies on those of our allies or coalition partners. Our mandatory AVIP is clearly in our best interests and strongly supports our national security and military strategies.

Furthermore, a voluntary program that yields only 30 percent compliance, as you assert that the British voluntary anthrax program experiences, would mean that a large number of our Service members would be casualties if exposed to weaponized anthrax and the military mission would be in jeopardy. The threat of anthrax represents a clear and present danger to our forces that has been validated by our intelligence agencies. Neither gas masks nor prophylactic antibiotic therapy provides adequate protection because our detection equipment cannot reliably warn troops prior to lethal exposure. It would be unconscionable to place any service member at risk when we maintain a protective countermeasure that is FDA-licensed, has an excellent safety record, and is effective.

Question #13:

Above and beyond the specific concerns mentioned here, we are concerned about the public perception of the anthrax vaccination program and its impacts on service member morale. We must ensure that this single force protection measure: which addresses only one of a myriad of biological threats is not itself a more real threat to our citizens in uniform.

Answer #13:

We firmly believe that public confidence in the United States military remains high and that the morale of military personnel, affected by many operational, personnel, and quality of life matters, has not been adversely affected by the AVIP. We are also convinced that the overwhelming majority of our Service members understand the threat represented by anthrax and strongly support our program.

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

DEPSEC DEF
SEP 30 1999

MEMORANDUM FOR SECRETARY OF DEFENSE
DEPUTY SECRETARY OF DEFENSE

THROUGH: USD (PERSONNEL AND READINESS)

FROM: ASD (Health Affairs)
(Prepared by: LTC (b)(6) Program Director, Chemical-Biological Warfare and International Affairs, OASD (Health Affairs), (b)(6))

SUBJECT: Congressional Letter on Anthrax Vaccine Immunization Program (AVIP) from Representatives Gilman, Shays, Kelly, Souder, Ose, and Talent

PURPOSE: To secure SECDEF signature on the letter responding to questions from Congressional members on the AVIP.

DISCUSSION: The enclosed letter of July 20, 1999 from Congressional members' (TAB A) requests responses to a number of questions about the anthrax vaccine and the Department's AVIP. The responding letters to Representatives Gilman (TAB B), Shays (TAB C), Kelly (TAB D), Souder (TAB E), Ose (TAB F), and Talent (TAB G) address all of the questions and concerns about the anthrax vaccine and the AVIP that are mentioned in the Congressional letter. The letter and accompanying responses were coordinated with the Office of the General Counsel, Army Office of the Surgeon General/Army AVIP Agency, Joint Program Office for Biological Defense, and Reserve Affairs.

COORDINATION:
GC
LA

RECOMMENDATION: Sign the letters to Representatives Gilman, Shays, Kelly, Souder, Ose, and Talent.

SECRETARY OF DEFENSE DECISION:
APPROVED:
DISAPPROVED:
OTHER:

Authorized SOM Hand delivered today 9/30

U15131 /99

PRS/PRD ITEMS
DATE RECEIVED IN OSD: 7-21-99
SUSPENSE DATE: 8-4-99
RECEIVED IN CLD: 9-28-99
DAYS LATE: 38

9/8/99 Still awaiting Signature
9/23/99 - Going to SecDef w/Undersecretary for signature

CONGRESSIONAL or SPECIAL CORRESPONDENCE

Office of Special Assistant for Gulf War Illnesses
Internal Routing/Tasking Sh

CMAT: 9207-005
Date: 7-26-99

Coord/ Routing	Position/Organization		Action	Info	Comments
	Special Assistant	(SA)			
	Deputy Special Assistant	(DSA)			
	Executive Assistant to SA	(EA)			
	Executive Assistant to DSA	(EADSA)			
	☐ Director, Investigation & Analysis _____	(IAD)			
	☐ DepDir _____ ☐ MED _____ ☐ VDM _____ ☐ C/B _____ ☐ ENV _____ ☐ PAG _____				
	Dir Lessons Learned Implementation	(LLI)			
	Dir Public Affairs & Outreach	(PA)			
	Dir Legislative Outreach	(LA)			
	Dir Medical Outreach & Issues	(MOI)	X		
	Legal Advisor	(LGL)			
	PM, Gulf War Illnesses Support	(PM)			
	Editorial Review ☐ AMB _____ ☐ Editors _____	(ER)			
	CMAT	(CMAT)			
	Action Management Call (b)(6) ☐ COMEBACK COPY TO: _____ ☐ GET CMAT NUMBER WHEN SIGNED & SENT ☐ READING FILE ☐ THANK YOU FILE ☐ CHRON FILE ☐ ADD TO GulfNEWS				

Note: We are not responding to the Congressional - Pete. Capt Willcox just wants a bullet in case issue that shows the POR answer. PM

SUSPENSE: 10 Aug 99

Prepare reply for signature of:
☐ SA/GWI ☐ SD ☐ DSD ☐ DepSA/GWI

695-3333

- get a copy of OSD PR response to Senator's for Dr Roetler's information
- Notify AMB; will close after completed action

☒ Congress ☐ Oversight ☐ FOIA ☐ OSD ☐ WBM ☐ VSO/MSO
☐ Ltr to SA ☐ IR ☐ E-Mail ☐ OGA ☐ Other ☐ Veteran

KEYWORDS:
Anthrax vaccine program

07/23/99 Issuance

Highlights of the Response to MOC Benjamin Gilman Regarding Anthrax

- All four prerequisite conditions, supplemental testing of the vaccine; assured tracking of immunizations; approved operational and communications plans; and review of the health and medical aspects of the program by an independent expert, were met before the Total Anthrax Vaccine Immunization Program (AVIP) was approved and implemented.
- An adverse event reporting and tracking system is in place to assure expert review of any adverse events possibly related to the vaccination. There have been very few instances of serious adverse events.
- The evidence of the efficacy of the FDA-licensed anthrax vaccine is based upon data from both human and animal models. The only clinical human study was completed by Brachman in 1962 and evaluated the efficacy of a precursor to the current licensed vaccine. In the non-human primate model that best approximates inhalation anthrax in humans, the FDA-licensed anthrax vaccine is able to provide close to 100% protection against an aerosol challenge.
- Los Alamos National Laboratory reviewed questions on the effectiveness of the vaccine against altered or multiple strains and concluded "...there is no experimental data or evidence to suggest that such a mixture is resistant to the FDA-licensed anthrax vaccine used by the US military."
- Before Secretary Cohen authorized the AVIP to proceed he approved a DoD plan to establish a process for supplemental testing of the vaccine by the manufacturer to assure its sterility, safety, potency, and purity. This program goes beyond FDA requirements.
- To date almost 1 million vaccinations have been given. There have been a few cases of side effects, but they tend to be mild to moderate, temporary, and confined to the area of injection.
- The rate of adverse reactions for the anthrax vaccine is comparable to many other commonly given vaccines.
- The Bioport anthrax vaccination production facility was closed in March 1998 for renovations as part of the manufacturer's facility improvement strategy, and in part due to a 1996 DoD assessment that the facility was inadequate to meet future requirements. Before full production can resume the facility must be validated and meet FDA inspection. This is expected to occur by January 2000.
- Bioport underwent FDA inspections in 11/96 and 2/98 and the FDA found a number of deficiencies related to compliance with current good manufacturing practices. In 1997, DoD teamed with Bioport and devised a Strategic Plan for Compliance that addressed how to comply with FDA standards. That plan is currently in place. At no time were deficiencies reported by the FDA serious enough to warrant a recall of stockpiled anthrax vaccine.
- The anthrax vaccine is not covered by the statutory Vaccine Injury Compensation Program and private insurance for the manufacturer is extremely expensive. Therefore, so that the high cost of insurance is not passed back to DoD, the manufacturer was granted indemnification.
- Handling procedures are in place to ensure that upon receipt, the lot number and expiration date of all vials of the vaccine are recorded. The expiration date is also checked upon administration of the vaccine.
- The Services are using automated immunization tracking systems to record and track the anthrax immunization status of Service members. This information is also placed in the DEERS system.

- Prior to administration of the vaccine service members are provided written and oral information on the benefits and risk of the anthrax vaccine and details of the overall program by medical personnel and Commanders, to include reasons for exemptions and deferrals.
- DoD uses the Vaccine Adverse Event Reporting System (VAERS) to report adverse events. For the purpose of anthrax adverse events only reactions resulting in either hospitalization, quarters greater then 24 hours, and suspected to have resulted from vaccine contamination are required to be reported. All VAERS reports are reviewed by the Anthrax Vaccine Expert Committee, who to date have found no pattern of causality from the vaccine.
- The AVIP is being executed in stages. It is currently in Phase I, where those who are assigned, deployed, or TDY in the JCS designated high threat areas and contingous waters of Southwest Asia and the Korean peninsula are being vaccinated. No scheduled deployments have been preempted due to concerns about the vaccine.
- The Secretary of Defense's order that all personnel receive the vaccination is a lawful order and any service member who fails to comply is subject to administrative or disciplinary action. More then 99% of all service members accept the anthrax vaccination.
- The Reserve Officers Association recently recommended that National Guard and Reserve units only receive shots from lots of the newly made vaccine. However, DoD concluded that this recommendation does not address the Total Force concept or recognize the need for the Guard and Reserve to support current missions. If they waited for newly made vaccine lots, it would delay when the member would have adequate protection. Additionally, the existing stockpile of vaccine is used for both active duty and reserve components.
- The current AVIP Phase 1 immunization plan does not include Kosovo, because the EUCOM CINC intelligence threat analysis of the risk of BW in the Balkans did not reveal the potential use of anthrax.
- Dr. Gerald Burrow, a well known-health expert, was asked to act as an independent expert and review the AVIP for safety and efficacy before the program was implemented. He concluded that the program appears to be safe and offers the best protection against the use of anthrax.
- Since the start of the AVIP program DoD has provided on request anthrax vaccine to Canada, Germany, Israel, Denmark, and Australia. Unlike the U.S. some countries have a voluntary vaccination program. DoD maintains a mandatory program, because we feel those who were not vaccinated would be casualties if exposed and thus it would be unconscionable to place any service member at risk.
- DoD believes that public confidence in the military remains high and that the morale of personnel has not been affected by the AVIP, because the overwhelming majority of service members understand that anthrax represents a clear and present danger to our forces and vaccination is our best weapon against it.

Congressional

CMAT Control #
1999216-0000025

(10)

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	DEPUTY SECRETARY OF DEFENSE		
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	EXECUTIVE SECRETARY		
	UNDER SEC FOR ACQUISITION & TECHNOLOGY		
	Director, Defense Research & Engineering		
	UNDER SECRETARY FOR POLICY		
	ASD (International Security Affairs)		
	ASD (Special Operations/LIC)		
	ASD (Strategy &Threat Reduction)		
	UNDER SECRETARY (COMPTROLLER)		
	Director, Program Analysis and Evaluation		
1	UNDER SEC FOR PERSONNEL & READINESS	X	
	ASD (Force Management Policy)		
	ASD (Health Affairs)		X
	ASD (Reserve Affairs)		
	ASD (C3I)		
	ASD (LEGISLATIVE AFFAIRS)		X
	ASD (PUBLIC AFFAIRS)		
	GENERAL COUNSEL		
	INSPECTOR GENERAL		
	DIR, OPERATIONAL TEST & EVALUATION		
	DIR, ADMINISTRATION & MANAGEMENT		

		ACT COPY	INFO COPY
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	SECRETARY OF THE NAVY		
	SECRETARY OF THE AIR FORCE		
	CHAIRMAN, JOINT CHIEFS OF STAFF		
	Director, Joint Staff		
	BALLISTIC MISSILE DEFENSE ORGANIZATION		
	DEFENSE ADVANCED RESEARCH PROJECTS AGENCY		
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	DEFENSE FINANCE & ACCOUNTING SERVICE		
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	DEFENSE LEGAL SERVICES AGENCY		
	DEFENSE LOGISTICS AGENCY		
	DEFENSE SECURITY COOPERATION AGENCY		
	DEFENSE SECURITY SERVICE		
	DEFENSE THREAT REDUCTION AGENCY		
	NATIONAL IMAGERY AND MAPPING AGENCY		
	NSA/CENTRAL SECURITY SERVICE		
	GWI		X

TYPE OF ACTION REQUIRED

	PREPARE REPLY FOR SEC OF DEF SIGNATURE		COMMENTS AND/OR RECOMMENDATIONS
	PREPARE REPLY FOR DEP SEC OF DEF SIGNATURE		INFORMATION AND RETENTION
1	REPLY DIRECT *(Forward copy of reply to CCD, Room 3A948)*	X	COORDINATE REPLY WITH LA
	APPROPRIATE ACTION		

Remarks:

ACTION DUE DATE *(YYMMDD)*	ROUTING DATE *(YYMMDD)*	OSD CONTROL NUMBER	
990818	990728	U12053-99	

THOMAS H. ALLEN
1ST DISTRICT OF MAINE
1717 LONGWORTH HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
(202) 225-6116
234 OXFORD STREET
PORTLAND, ME 04101
(207) 774-5019

Congress of the United States
House of Representatives
Washington, DC 20515–1901

COMMITTEE ON ARMED SERVICES
SUBCOMMITTEES:
MILITARY PROCUREMENT
MILITARY RESEARCH AND DEVELOPMENT
MERCHANT MARINE PANEL
COMMITTEE ON
GOVERNMENT REFORM
SUBCOMMITTEES:
NATIONAL SECURITY, VETERANS AFFAIRS, AND INTERNATIONAL RELATIONS
CIVIL SERVICE
DEMOCRATIC AT-LARGE WHIP

July 23, 1999

OSAGWI

AUG 03 1999

Ms. Sandra K. Stuart
Assistant Secretary of Defense
U.S. Department Of Defense
The Pentagon, Room 3E966
Washington, D.C. 20301-1300

Dear Ms. Stuart:

I am enclosing a letter from two constituents, (b)(6). As you will see, the (b)(6) are very concerned about their son, (b)(6), receiving the anthrax vaccination.

On the (b)(6) behalf, I would appreciate your review and comment on their concerns about the safety of this vaccine. If you have any questions, you may contact Mark Ouellette of my Portland, Maine district office. He is familiar with this request and can be reached at (207)774-5019.

Thank you for your cooperation.

Sincerely,

Tom Allen
Member of Congress

THA/mo

U12053 /99

JUL 20 1999

P.O. Box 167
China, ME 04926
July 16, 1999

Congressman Tom Allen
24 Oxford Street
Portland, ME 04103

Dear Congressman Allen,

I am writing to you on behalf of our son, (b)(6), who has served for three years in the U.S. Navy, stationed in Jacksonville, Florida. (b)(6) for refusing to take the anthrax vaccination. We fully support (b)(6 in his refusal to take the vaccine, and ask for your help. Since he is on a training mission aboard the John F. Kennedy, he can not contact you directly. Here are our concerns:

1. While the military contends that "the anthrax vaccine has been approved by the F.D.A. and in use since 1970", it appears that the actual vaccine being given to military personnel today is not at all the same vaccine that was approved by the F.D.A. Therefore, military personnel are being expected to take a vaccine that is not approved for use on the general public.

2. While the military denies this, there appears to be a high correlation between the use of at least certain types of this vaccine and chronic long-term, serious illness. The Government Reform and Oversight Committee's Subcommittee on National Security hearing transcripts address some of this, as do several national press reports, such as "Vanity Fair's" May issue.

3. It appears that this vaccine is a Department of Defense-contracted vaccine. The sole supplier of the vaccine is apparently about to undergo bankruptcy due to safety and product reliability issues.

It is our belief that this great nation's military establishment could and should be using its considerable resources to see that a safe vaccine is developed. While we understand that the military cannot allow each individual to decide what vaccines seem appropriate case by case, and while we understand that the military has a duty to protect its forces from biological weapons such as the anthrax vaccine, we are appalled that our military continues not only to administer an apparently shoddy vaccine without a major effort to perfect a better one, but to punish personnel who refuse it.

Our son enlisted when he was seventeen years old, never thinking that he would be asked to inject such a dangerous substance into his veins. After having served three years in the Navy, (b)(6)

(b)(6)

We are -- and so far all of the people we have talked with about this are – very alarmed that the Department of Defense holds such sway as to be able to get away with this.

We look forward to your response. Thank you.

(b)(6)

CMAT Control #
1999223-0000003

(11)

Congressional

	SECRETARY OF DEFENSE ROUTING SLIP	ACT COPY	INFO COPY			ACT COPY	INFO COPY
	SECRETARY OF DEFENSE				SECRETARY OF THE ARMY		
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	THE SPECIAL ASSISTANT				SECRETARY OF THE AIR FORCE		
	EXECUTIVE SECRETARY						
	UNDER SEC FOR ACQUISITION & TECHNOLOGY				CHAIRMAN, JOINT CHIEFS OF STAFF		
	Director, Defense Research & Engineering				Director, Joint Staff		
	UNDER SECRETARY FOR POLICY						
	ASD (International Security Affairs)				BALLISTIC MISSILE DEFENSE ORGANIZATION		
	ASD (Special Operations/LIC)				DEFENSE ADVANCED RESEARCH PROJECTS AGENCY		
	ASD (Strategy &Threat Reduction)				DEFENSE COMMISSARY AGENCY		
	UNDER SECRETARY (COMPTROLLER)				DEFENSE CONTRACT AUDIT AGENCY		
	Director, Program Analysis and Evaluation				DEFENSE FINANCE & ACCOUNTING SERVICE		
1	UNDER SEC FOR PERSONNEL & READINESS	X			DEFENSE INFORMATION SYSTEMS AGENCY		
	ASD (Force Management Policy)				DEFENSE INTELLIGENCE AGENCY		
	ASD (Health Affairs)		X		DEFENSE LEGAL SERVICES AGENCY		
	ASD (Reserve Affairs)				DEFENSE LOGISTICS AGENCY		
	ASD (C3I)				DEFENSE SECURITY COOPERATION AGENCY		
	ASD (LEGISLATIVE AFFAIRS)		X		DEFENSE SECURITY SERVICE		
	ASD (PUBLIC AFFAIRS)				DEFENSE THREAT REDUCTION AGENCY		
	GENERAL COUNSEL				NATIONAL IMAGERY AND MAPPING AGENCY		
	INSPECTOR GENERAL				NSA/CENTRAL SECURITY SERVICE		
	DIR, OPERATIONAL TEST & EVALUATION						
	DIR, ADMINISTRATION & MANAGEMENT						
					GWI		X

TYPE OF ACTION REQUIRED

	PREPARE REPLY FOR SEC OF DEF SIGNATURE		COMMENTS AND/OR RECOMMENDATIONS
	PREPARE REPLY FOR DEP SEC OF DEF SIGNATURE		INFORMATION AND RETENTION
1	REPLY DIRECT *(Forward copy of reply to CCD, Room 3A948)*	X	COORDINATE REPLY WITH LA
	APPROPRIATE ACTION		

Remarks:

ACTION DUE DATE *(YYMMDD)*	ROUTING DATE *(YYMMDD)*	OSD CONTROL NUMBER
990825	990804	U12469-99

SD FORM 14, OCT 98 PREVIOUS EDITIONS ARE OBSOLETE. Designed using Perform Pro, WHS/DIOR, OCT 98
Overprint approved by OSD/WHS/DIOR, OCT 98

JOHN EDWARDS
NORTH CAROLINA

RALEIGH OFFICE
301 CENTURY POST OFFICE BUILDING
300 FAYETTEVILLE STREET MALL
RALEIGH, NC 27602
(919) 856-4245

United States Senate

WASHINGTON, DC 20510-3201

August 3, 1999

Mr. Derrick Lavalle
Special Assistant to Assistant Secretary for Health Affairs
U.S. Department of Defense
The Pentagon
Washington, DC 20301-1300

Dear Mr. Lavalle:

Enclosed is a copy of correspondence I have recently received from (b)(6) regarding the Anthrax Vaccine Immunization Program.

I appreciate your reviewing this material and providing any assistance or information possible under the governing statutes and regulations. Please forward your response to Marilyn Dixon in my Raleigh office.

Thank you for your attention to this matter. I look forward to hearing from you soon.

Yours sincerely,

John Edwards

JE/md

Enclosure

3 August 1999

Dear Senator Edwards,

I am North Carolina native and civilian employee of the US Navy living in Naples Italy. Recently I have been told I must participate in the Anthrax Vaccine Immunization Program (AVIP), in accordance with a memorandum signed by an Under Secretary of Defense. I have numerous doubts and questions, none of which have been addressed to my satisfaction through normal channels. Please find attached a letter from myself and three co-workers which provides detail about our situation.

Also attached is a copy of the emergency essential personnel agreement which I was required to sign this past May, after I had been in my current overseas position as an (b)(6) for 20 months. Note that it *could not* reasonably be interpreted as consent to participate in AVIP. To be sure, I even asked if it obligated me to take the anthrax vaccine and was told "no."

My involvement in this began 30 June 1999 when I was first given notice that I would be required to take the vaccine. I immediately expressed reservations to my officer in charge. I have been researching the issue since then and requested guidance from my local Human Resources Office (HRO) as well as the Office of Personnel Management (OPM) on 14 July 1999. HRO has twice told me that I can be disciplined for declining AVIP, and also told me that the US Navy is not liable for any adverse health effects caused by AVIP. OPM told me they do not handle these issues and passed my request along to Mr. (b)(6) at Navy headquarters. I have been unable to locate Mr. (b)(6) office.

On 28 July 1999, my officer in charge took written questions from me and two co-workers to forward up the chain of command. We have heard nothing since then, but based on what HRO has told us we are very concerned.

I hope you can sympathize with my position as a private citizen--who provides his own medical insurance--who is being forced to choose between pursuing a civil service career and taking unnecessary health risks.

I request any assistance your office can provide. You have my permission to conduct an inquiry on my behalf. I would ask you to encourage the Under Secretary to at least put a moratorium on this questionable program (as applied to civilians) until an independent agency such as GAO has studied its long term effects.

Respectfully,

(b)(6)

3 August 1999

Dear Senator Edwards,

We are writing you as DoD civilians working for the US Navy in Naples, Italy. Our job is to examine badly damaged Navy and Marine Corps aircraft, and implement repairs to them in a safe, expedient manner. As you can imagine, with today's operational tempo, our jobs require us to be willing to go anywhere at any time and work side-by-side with military folks to help fix their aircraft. We stand ready to fulfill this commitment, even though we receive *no extra pay*.

Our duties as emergency essential civilians

Before coming to our overseas station, we performed this same class of work for state-side Naval Aviation Depots at North Island (San Diego, CA) and Cherry Point (Havelock, NC). We were carefully screened for overseas duty as part of being hired by our current command, Naval Air Pacific Repair Activity.

At the time we agreed to our jobs we understood that, while our primary place of work would be an office, we would sometimes find ourselves working under difficult conditions, traveling to third world countries, or working in close quarters aboard ship. We could even be involved in supporting US air operations such as Operation Desert Storm.

Our positions are considered emergency essential by our command. In approximately May 1999, we were asked to sign a form acknowledging our emergency essential status. We were all experienced in our NAPRA roles: Mr. (b)(6) has been at NAPRA for 33 months, Mr. (b)(6) for 32 months, Mr (b)(6) for 29 months, and Mr. (b)(6) for 6 months. Having this experience, we had no qualms about signing the emergency essential paperwork. Mr. (b)(6) did, however, ask the senior civilian in the office (who typically serves as our interface to the Human Resources Office, HRO) if his signature would obligate him to receive the anthrax vaccine. He was told flatly "no."

On 31 March 1999, an Under Secretary of Defense released a memorandum stating that the Anthrax Vaccine Immunization Program (AVIP) "will be applied to all U.S. military personnel and Department of Defense emergency essential civilian employees and contractor personnel assigned, deployed, or on duty in the high threat areas..."

Through our chain of command, we were told on 27-28 July 1999 that we will comply with the AVIP program because we are emergency essential and sometimes deploy to the affected areas for short duration (less than one week).

Significant safety concerns over AVIP

As you know, this vaccination program is surrounded by a swarm of controversy. In our view the most credible reporting on the vaccine has been undertaken by the Government Accounting Office. In testimony[1] given by Mr. Kwai-Cheung Chan to the House Subcommittee on National Security (29 April 1999), the GAO stated that "the long term safety of the vaccine has not yet been studied." Mr. Chan went on to testify that the efficacy of the vaccine against inhalation anthrax has not been assessed. Finally, the GAO representative testified about the significant quality control lapses committed by

[1] GAO/T-NSIAD-99-148

the sole manufacturer of the vaccine, MDPH (now BioPort). These lapses culminated in the FDA threatening to revoke MDPH's license in March 1997.

BioPort is required to provide a small slip of paper with each vaccine dose, the intent of which is to inform the patient. This slip of paper states our concerns very clearly:

> "Studies have not been performed to ascertain whether Anthrax Vaccine Adsorbed has carcinogenic action, or any effect on fertility."[2]

Additional testimony given by servicemen in the House Subcommittee on National Security related disturbing first hand accounts of short-term adverse reactions. This testimony is part of the public record.

Testimony from Meryl Nass, MD, states that of the 37 lots of vaccine manufactured before 29 April 1999, *all but six* had been quarantined. Seventeen of these were quarantined as a result of quality concerns raised by an FDA inspection in February 1998.

The leading British medical journal *The Lancet* has published a study (of British veterans) regarding Gulf War Illness and the anthrax vaccine:

> "Vaccination against biological warfare and multiple routine vaccinations were associated with this... syndrome in the Gulf War cohort."[3]

A comment relating to this study from a researcher at the National Institutes of Health, also published in *The Lancet*, states:

> "Vaccination against plague and anthrax before deployment to the Gulf correlated highly with illness. The investigators speculate that these vaccines--more so than routine ones given to service personnel--had unanticipated effects."[4]

We feel AVIP, which consists of six shots over 18 months plus a yearly booster, does not yet meet the "reasonable person's" test for what is safe and effective.

<u>We are responsible for our own health care</u>

Civilian employees, as private citizens, have a dubious safety net against harmful effects of this program. We procure our own medical and life insurance, contribute our own savings into our retirement program, and have a limited number of "sick leave" days. A serious adverse reaction could leave us in a "leave without pay" status. At the time we agreed to our jobs, we understood that we would sometimes be working under hazardous conditions. We accepted these risks as controllable, and worked under the assumption that the DoD would stand behind us in the event we were injured while carrying out our duties.

---

[2] F-483 30M 8/90 Rev. 10/87 "Anthrax Vaccine Adsorbed"

[3] Catherine Unwin, et al. "Health of U.K. Servicemen who served in the Persian Gulf War." <u>The Lancet</u> vol. 353, January 16, 1999.

[4] Stephen E. Straus, NIAID, NIH. "Commentary on the Unwin Study." <u>The Lancet</u>, vol 853, January 16, 1999.

Our local HRO, however, has informed us that the DoD has *no responsibility* to us if we suffer adverse effects due to AVIP. Any sick leave, medical expenses, or other consequences will be borne by the employee alone. We submitted a letter to HRO on 3 August 1999 seeking the Director's written confirmation of this policy.

We have been told verbally by our chain of command and our HRO that we can be found in violation of our employment agreements for not complying with this *retroactive* requirement of our emergency essential classification. This could entail being terminated outright, or being forced to leave our overseas assignments *at our own expense*. This could easily cost us $20,000 each.

We submitted letters to our chain of command (28 July 1999) and HRO (3 August 1999) requesting written clarification.

AVIP participation is an unreasonable retroactive requirement

We stand ready to continue our obligation to support our national defense overseas--without participating in the AVIP program. We remain ready to enter high threat areas, but without this vaccine. Until last week, *nobody* in our command had *ever* questioned our shot records before sending us *anywhere*. Each of us is a seasoned global traveler--combined we have 71 years of federal service--and we have always taken responsibility for obtaining our own inoculations.

Our employment with NAPRA was not contingent on participating in AVIP. Indeed, AVIP did not exist when Mr. (b)(6) Mr. (b)(6) and Mr. (b)(6) were transferred to NAPRA. Making a questionable program like AVIP a *retroactive* condition of our employment and then holding over us the possibility of disciplinary action is clearly an unfair practice.

We respectfully request any assistance or guidance which can be provided by your office as soon as possible. You have our permission to initiate an inquiry on our behalf. Due to the operational nature of our work, we could be required to travel to the AVIP-mandatory countries at any time. We have provided faithful service to the US Navy and do not want to be forced to choose between our careers and our health. Undoubtedly there are many other DoD civilians scattered throughout the world who are also facing this difficult issue.

Respectfully,

(b)(6)

(b)(6)

(b)(6)

(b)(6)

3)

(b)(6)

DOD CIVILIAN EMPLOYEE OVERSEAS EMERGENCY - ESSENTIAL POSITION AGREEMENT

PRIVACY ACT STATEMENT

AUTHORITY: Legal authority for the personal information, including Social Security number, required on this form is 5 USC 301.

PRINCIPAL PURPOSE: To establish emergency procedures to ensure that qualified personnel are identified to fill emergency-essential DoD civilian position overseas.

ROUTINE USE: To fill vacant emergency-essential DoD civilian position overseas.

DISCLOSURE: Voluntary. If information is not furnished, the employee will be reassigned as soon as possible without the loss of pay or grade to a non-emergency-essential position.

SECTION A - EMPLOYEE IDENTIFICATION

1. TYPED NAME *(Last, First, Middle Initial)*	2. SOCIAL SECURITY NUMBER

SECTION B - POSITION IDENTIFICATION

1. ORGANIZATION NAME		2. POSITION NUMBER	
3. POSITION TITLE	4. PAY PLAN	5. SERIES	6. GRADE

SECTION C - SUPERVISOR'S STATEMENT

1. The position identified above is emergency-essential. In the event of a crisis or war, performance of the duties of this position is essential to the support of assigned *(Enter DoD Component)* _____ missions.

2. Performance of the duties of this position during a crisis situation or wartime will require that you *(X one)*

☐ a. Relocate *(TDY or PCS)* to a duty station in an overseas area.

☐ b. Continue to work in an overseas area after the evacuation of others who are not in civilian emergency-essential positions.

3. The incumbent of/designated alternate for *(Line through one)* this position may also be required to participate in emergency plans exercises.

4. As the incumbent of/designated alternate for *(Line through one)* this position, request you complete the agreement in SECTION D below.

5. SUPERVISOR

a. TYPED NAME *(Last, First, Middle Initial)*	b. SIGNATURE

c. TITLE	d. DATE SIGNED

SECTION D - EMPLOYEE'S AGREEMENT

1. I agree:
   a. To perform the duties and requirements of the position identified above in the event of crisis situation or wartime.
   b. To participate in emergency plans exercises when required.

2. I understand that:
   a. Failure to perform the duties of this position in an emergency may result in appropriate action - defined as separation for the efficiency of the Federal Service under the procedures contained in Federal Personnel Manual 752.

   b. Provisions have been made to evacuate my dependents from the hostile or potentially hostile zone with the same priority as other DoD sponsored dependents *(DoD Directive 5100.51)*.

   c. Steps will be taken to authorize danger pay allowance for my post if it meets the criteria established by the Department of State *(Title 5, United States Code, Section 5928 (Public Law 96-465, Section 2311) "Foreign Service Act of 1980")*.

   d. I will be given a Geneva Convention Identity Card, DD Form 489 or DD Form 1934, as appropriate, to identify me as a non combatant. *(DoD Instruction 1000.1)*

3. EMPLOYEE

a. SIGNATURE	b. DATE SIGNED

DD FORM 2365, MAR 85 *(EF)*

FAX

TO: Derrick Lavalle

FROM: Honorable John Edwards
U.S. SENATE
300 Fayetteville Street Mall
Raleigh, North Carolina 27601
(919) 856-4245
(919) 856-4408 (Fax)

(b)(6)

Marilyn Dixon
Staff Member

NUMBER OF PAGES (including cover page)

DATE: 8/3/99

COMMENTS: Concern from constituent regarding Anthrax Vaccine Immunization Program

(12)

Congressional

CMAT Control #
1999197-0000010

SECRETARY OF DEFENSE ROUTING SLIP	ACT COPY	INFO COPY
SECRETARY OF DEFENSE		
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Director, Program Analysis and Evaluation		
1 UNDER SEC FOR PERSONNEL & READINESS	X	
ASD (Force Management Policy)		
ASD (Health Affairs)		X
ASD (Reserve Affairs)		
ASD (C3I)		
ASD (LEGISLATIVE AFFAIRS)		
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TYPE OF ACTION REQUIRED

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	APPROPRIATE ACTION		

Remarks:

ACTION DUE DATE *(YYMMDD)*	ROUTING DATE *(YYMMDD)*	OSD CONTROL NUMBER
990803	990713	U11173-99

OSAGWI

JUL 15 1999

il Gramm
Texas

United States Senate

MEMORANDUM

1999 JUL 13 PM 2:39

Date: JUL 07 1999

Office of the Assistant Secretary
for Legislative Affairs
Department of Defense
The Pentagon, Room 3E966
Washington, DC 20301

A constituent has sent the enclosed communication. A response which addresses his/her concerns would be appreciated.

Please send your response to the following address:

Office of Senator Phil Gramm
2323 Bryan Street, #2150
Dallas, Texas 75201

Attention: SHANNON SUMMERS
(214) 767-5217
(214) 767-8754 (fax)

U11173 /99

Author: (b)(6) at Internet
Date: 6/21/99 4:05 AM
Subject: My Son in The Marines

From:
(b)(6)

JUN 25 1999

Senator Gramm:

Mr. Gramm thank you for attending to my letter. We appreciate your many years of service to our Great Country. My son (b)(6) has just started his Marine boot camp training in San Diego. He graduated High School as a member of the National Honor Society. He also is one of the top drummers in the State of Texas. He chose to join the Marines after auditioning and getting accepted into the Marine Band. This is no small feat for any music student especially just out of High School, but I do have an exceptional son. He scored above the perfect score of 99 on the enlistment test. His love for his Country is also great. He has been involved politically in his High School, was president of the Band Council, and is also a staunch Republican. He has probably supported and spoke out for the Republican cause more than any other student in his school. I say this just to give you some background on one of my reasons for writing. I heard in the news the other day that a Marine was dishonorably discharged for refusing to take a anthrax vaccine. This got my attention. If someone would ruin their career for such a cause is there reason to be alarmed? Has there been enough research on this vaccine to prove that there will be no side effects? Or, is the government using our countries finest men and women as guinea pigs? I for one find it hard to trust our Government. With the President talking about "Doing the right thing" all the time but proving by his actions his real intentions are rarely there and more often cloaked in self service. His disdain for our safety and well being I believe could be catastrophic, and when the details of this Chinese espionage unfold, it would not surprise me at all if his name becomes synonymous with Benedict Arnold. These are my own personal feelings, not of anger, but alarm that our great country could be led into diaster. If we allow our military to be used as a testing ground and it is made to be vulnerable, then we as a nation could be a target for attack. I am also concerned as a parent for my sons well being. Please check into this and share your information and insite with us. I would also appreciate if you would put my son on your mailing list. His address is:

(b)(6)

I will also be sending similar letters to Senator Kay Bailey Hutchison and Representative Ralph Hall. Thank you for your time.

Sincerely,

(b)(6)

Sincerely,

(b)(6)

(13)

Congressional

~~OSAGWI~~

CMAT Control #
1999201-0000044

JUL 2 0 1999

	SECRETARY OF DEFENSE ROUTING SLIP	ACT COPY	INFO COPY			ACT COPY	INFO COPY
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1	UNDER SEC FOR PERSONNEL & READINESS	X			DEFENSE INFORMATION SYSTEMS AGENCY		
	ASD (Force Management Policy)				DEFENSE INTELLIGENCE AGENCY		
	ASD (Health Affairs)		X		DEFENSE LEGAL SERVICES AGENCY		
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	ASD (LEGISLATIVE AFFAIRS)		X		DEFENSE SECURITY SERVICE		
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	INSPECTOR GENERAL				NSA/CENTRAL SECURITY SERVICE		
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	DIR, ADMINISTRATION & MANAGEMENT						
					GWI		X

TYPE OF ACTION REQUIRED

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990802	990719	U11504-99	

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ED BRYANT
7TH DISTRICT, TENNESSEE

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COMMITTEE ON THE JUDICIARY

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House of Representatives
Washington, DC 20515–4207

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http://www.house.gov/bryant

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CLARKSVILLE, TN 37040–3210
931–503–0391

5909 SHELBY OAKS DRIVE
SUITE 213
MEMPHIS, TN 38134
901–382–5811

810½ SOUTH GARDEN ST.
COLUMBIA, TN 38401
931–381–8100

July 14,1999

Secretary of Defense
William Cohen
1000 Defense
The Pentagon
Washington, DC 20301-1000

Dear Secretary Cohen,

I recently heard from one of my constituents, (b)(6), who was expressing his concerns over the anthrax vaccine.

I have enclosed a copy of his letter to me and my reply for your information; no reply is necessary.

Thank you for your attention to the concerns of my constituents.

Sincerely,

Ed

Ed Bryant, M.C.

EGB:als

Enclosure

U11504 /99

ED BRYANT
7TH DISTRICT, TENNESSEE

COMMITTEE ON COMMERCE
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SUITE 213
MEMPHIS, TN 38134
901-382-5611

810½ SOUTH GARDEN ST.
COLUMBIA, TN 38401
931-381-8100

June 29, 1999

(b)(6)

Dear (b)(6):

Thank you for contacting me with your concerns over the anthrax vaccine. I appreciate your taking the time to reach me, and I enjoy hearing your views.

I can certainly understand your position on this issue, and I think you make some good points. You are naturally concerned for the health and safety of military personnel, and want to protect our service members from serving as guinea pigs. On your behalf, I have shared your concerns with the Secretary of Defense, so that he can have the benefit of your views on this matter. I will be sure to share his response with you.

Again, thank you for contacting me. Please continue to keep in touch. I look forward to hearing from you again.

Sincerely,

Ed Bryant, M.C.

EB:als

(b)(6)

From: writerep
Sent: Thursday, June 17, 1999 11:04 PM
To: TN07, WYR
Subject: WriteRep Responses

DATE: June 17, 1999 9:58 PM
NAME: (b)(6)
ADDR1:
ADDR2:
ADDR3:
CITY: (b)(6)
STATE: (b)(6)
ZIP: (b)(6)
PHONE:
EMAIL: (b)(6)
Message:
In regards to the service members refusing to take the Anthrax vaccination. If I were still on active duty I would refuse to take it myself. I believe in serving my country and putting my life on the line. However, I dont believe our service members should be guinea pigs. Please do something to intervene on their behalf. Thanks.

(b)(6)

Congressional

CMAT Control #
1999201-0000045

(14)

	SECRETARY OF DEFENSE ROUTING SLIP	ACT COPY	INFO COPY
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	ASD (International Security Affairs)		
	ASD (Special Operations/LIC)		
	ASD (Strategy & Threat Reduction)		
	UNDER SECRETARY (COMPTROLLER)		
	Director, Program Analysis and Evaluation		
1	UNDER SEC FOR PERSONNEL & READINESS	X	
	ASD (Force Management Policy)		
	ASD (Health Affairs)		X
	ASD (Reserve Affairs)		
	ASD (C3I)		
	ASD (LEGISLATIVE AFFAIRS)		X
	ASD (PUBLIC AFFAIRS)		
	GENERAL COUNSEL		
	INSPECTOR GENERAL		
	DIR, OPERATIONAL TEST & EVALUATION		
	DIR, ADMINISTRATION & MANAGEMENT		

		ACT COPY	INFO COPY
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	SECRETARY OF THE NAVY		
	SECRETARY OF THE AIR FORCE		
	CHAIRMAN, JOINT CHIEFS OF STAFF		
	Director, Joint Staff		
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	DEFENSE FINANCE & ACCOUNTING SERVICE		
	DEFENSE INFORMATION SYSTEMS AGENCY		
	DEFENSE INTELLIGENCE AGENCY		
	DEFENSE LEGAL SERVICES AGENCY		
	DEFENSE LOGISTICS AGENCY		
	DEFENSE SECURITY COOPERATION AGENCY		
	DEFENSE SECURITY SERVICE		
	DEFENSE THREAT REDUCTION AGENCY		
	NATIONAL IMAGERY AND MAPPING AGENCY		
	NSA/CENTRAL SECURITY SERVICE		
	GWI		X

TYPE OF ACTION REQUIRED

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	PREPARE REPLY FOR DEP SEC OF DEF SIGNATURE		INFORMATION AND RETENTION
1	REPLY DIRECT *(Forward copy of reply to CCD, Room 3A948)*	X	COORDINATE REPLY WITH LA
	APPROPRIATE ACTION		

Remarks:

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ED BRYANT
7TH DISTRICT, TENNESSEE

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Washington, DC 20515–4207

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SUITE 213
MEMPHIS, TN 38134
901-382-6811

810½ SOUTH GARDEN ST.
COLUMBIA, TN 38401
931-381-8100

July 15, 1999

The Honorable William Cohen
Secretary
United States Department of Defense
The Pentagon
Washington, DC 20301

Dear Secretary Cohen:

I recently heard from one of my constituents, (b)(6), regarding his concerns about an anthrax vaccine.

I have enclosed a copy of his letter to me for your information. I would appreciate it if you could address his concerns in your response to my Washington, D.C. office.

Thank you for your attention to the concerns of my constituent.

Sincerely,

Ed

Ed Bryant, M.C.

EGB:eog
enclosure

ED BRYANT
7TH DISTRICT, TENNESSEE

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931-802-[illegible]

5909 SHELBY OAKS DRIVE
SUITE 213
MEMPHIS, TN 38134
901-382-5811

[illegible] SOUTH GARDEN ST.
COLUMBIA, TN 38401
931-381-[illegible]

FAX TRANSMISSION

CONGRESSMAN ED BRYANT
5909 SHELBY OAKS, #213
MEMPHIS, TN 38134
901-382-5811 FAX 901-373-8215

Date: 5-28-99 Fax #: Phone:

To: Legis/DC

From: Susan

Pages: Lots!, including this cover sheet.

Comments:

(b)(6) wanted this to be faxed up asap.

He is a retired Col for the US Public Health Service

IF THERE IS A PROBLEM WITH THE TRANSMISSION OF THIS FAX,
PLEASE CALL THE MEMPHIS OFFICE AT (901) 382-5811 OR FAX (901) 373-8215

5-26-99

(b)(6)

Dear Congressman Ed Bryant:

Attached is a very important article re: "Gulf War Illnesses" in American Veterans. This is a very very serious problem. Please read the article very carefully. The "government" is definitely covering up the fact that, they put in a substance, "Squalene", in the anthrax vaccine given to servicemen + women. This was not cleared by FDA. It caused the "Gulf War Illness". It was put in the anthrax vaccine to speed up the effectiveness of the vaccine. The "govt" denies using this drug.

This needs to be investigated by the Senate and Congress immediately, as another Anthrax vaccine is scheduled to be given to our troops in July 1999. We must be 100% certain that "squalene" is not put in the vaccine again.

This will be given to all troops, Active duty, and National guardsmen. If this fact re "Squalene" is true + I definitly feel it is true, this fact could cause many armed service personel to leave the service to avoid the shot, or

may develop more Tragic illnesses.

I know you have many other problems to worry about, but what can be more important than the safety of our Troops.

I have a son in Air National Guard in Memphis, who received the anthrax Vaccine & served in Gulf War. Fortunately he has not become ill, yet. He + I are worried about receiving the next vaccine in July or are all the military Troops, that are aware of this problem. I'm sure you also, would be quite concerned if you had a son or daughter in the military + had to take this vaccine shot again, not being able to Trust our goverment.

Thank you sincerly for any help you may give to this matter

Respectfully

(b)(6)

SUPER TROOPER
Colonel Herbert Smith with his pointer, Raisin, at home in Ijamsville, Maryland. A former Green Beret, he can now barely walk.

THE PENTAGON'S TOXIC SECRET

Thousands of American veterans suffer from debilitating Gulf War–related illnesses. But the origins have remained a mystery. A crusading molecular biologist and internal military documents now suggest a shocking scenario: the Pentagon's possible use on its own soldiers of an illicit and secret anthrax vaccine

BY GARY MATSUMOTO

Veterinarian Dr. Herbert Smith negotiates the nine paces across his porch to the driveway of his house as though he were on a high wire, adjusting each deliberate step, shifting his weight from a walking cane in his left hand to another in his right. Smith lives in Ijamsville, Maryland, a subdivision no-man's-land of two-acre lots and empty vistas where the exurbs of Washington, D.C., commingle with those of Baltimore.

He wears black leather wrist pads Velcro'd from palm to forearm and a pair of rugged government-issue elbow pads to protect himself from the falls he frequently experiences. "I'm subject to what's called neurapraxia—damage to the nerves," explains Smith. "Like with diabetics, who then wind up with amputations. I'm trying to avoid that."

On reaching the driveway, he straightens up to shake my hand. You can still see the outlines of the

elite athlete he once was. Dr. Smith, 59 years old, is also Colonel Smith, Green Beret. His subordinates nicknamed him "Super Trooper," in deference to his gung-ho attitude and his once Olympian physique. When he entered airborne school at Fort Benning in April 1966 he set out to be No. 1 in a class of 687 by baiting his drill instructors to drive him harder than the others. "So, they targeted me. I must've done a thousand push-ups a day. But I knew it was all a game. I never got mad, never lost my cool. There were a couple of navy SEALs there. They were pretty tough guys. But they weren't as tough as me." Until 1991, Smith ran P.T. (physical training) programs; the ones back in the 80s were notoriously grueling, earning him a nickname: "Dr. Death." He smiles at this but is unapologetic. "I wore 'em into the ground. In a fun way, not in a brutal way."

Today, a thick purple welt juts from Smith's forehead—an angry bulge from hairline to brow. Even on perfectly flat ground, he falls a lot.

The symptoms first appeared in January 1991, the same month, Smith says, that he got his first shot of something that does not appear on his immunization card or in his records: a mysterious vaccine, described to him only as "Vac A." He was then in Saudi Arabia training Kuwaiti medical personnel in disaster relief. Sometimes the pain was so bad in his right hand he couldn't hold a fork at meals. The next time it would be his left hand, never both hands at the same time. By May his joints ached and his lymph nodes were swollen, and he had a fever and a red rash on his chest and legs. He was constantly fatigued. It hurt to walk. It hurt to brush his teeth. After the invasion he wanted to stay on to help the Kuwaitis rebuild, but the symptoms were getting worse, and he had no idea what was wrong. He knew he needed treatment back in the States.

Just before he got on a transport heading home, one of his medical officers, who had seen similar symptoms in other soldiers, came up to him and said, "When you get home, check out the vaccines. I think you've got a problem with them." Smith had received vaccinations for hepatitis and tetanus, and a second shot of Vac A, which was entered into his records on February 14, 1991.

Back at Fort Meade, Smith was given a desk job while the military doctors investigated his condition—without success. In October 1991 he left active duty, but continued to see physicians at the Walter Reed Army Medical Center in Washington, D.C. He didn't regard the problem as serious until the seizures started. Not grand mal, fall-on-the-floor, foam-at-the-mouth seizures, but complex partial ones, in which he appeared to be functioning normally but was actually on autopilot, without awareness of what he was doing. "I skipped periods of time," he explains. "I was in a car driving towards Baltimore on I-70, and the next thing I know, I'm outside of Washington, D.C., on I-95, and I've got no clue how I got there."

One night, his worst, Smith became completely disoriented. "I had blacked out for an hour, hour and a half. I had to call my wife on the phone to find my way home. I was probably 25 miles away. I was an emotional mess because by then I had to admit to myself that something was wrong with me."

By this time Smith was seeing Dr. Michael Roy, an internist at Walter Reed. Roy diagnosed Smith's condition as "somatization disorder," a psychosomatic illness in which a patient becomes so obsessed with an imaginary disease that he begins to exhibit its symptoms.

Smith was not the only Gulf War veteran experiencing mysterious symptoms. In late 1991 and early 1992, some from a reserve unit at Indiana's Fort Benjamin Harrison reported sick with a constellation of symptoms that have since been associated with Gulf War syndrome: joint pain, headaches, fatigue, memory loss, and rashes. Reservists in Georgia and Alabama made similar complaints. Military doctors mostly dismissed the symptoms as psychosomatic or stress-related. As the number of people affected began to grow, several government studies were commissioned, including those of the Presidential Advisory Committee on Gulf War Veterans' Illnesses, the Institute of Medicine, and the Senate Committee on Veterans' Affairs. By 1996 all of them had concluded that there was no single disease that could account for all the different symptoms associated with Gulf War syndrome. The Department of Defense has examined at least 20 possible health hazards, including pyridostigmine bromide (PB) pills taken by the Gulf War troops to help protect against chemical warfare, the insect repellent DEET and various pesticides used by the soldiers, and Kuwaiti oil-fire smoke. A frequently repeated theory, still unproven, blames the syndrome on low-dose exposures to chemical-weapons fallout.

About 40,000 veterans have registered with the Department of Defense's Comprehensive Clinical Evaluation Program (C.C.E.P.) for Gulf War illnesses; another 70,000 or so are tallied by the V.A. A C.C.E.P. spokesperson says the numbers do not overlap; i.e., the total number of 110,000 to 115,000 is accurate. Of these, 18,000 are undiagnosed, and are merely being treated for their symptoms. To date, the federal government has sponsored 140 or so related research programs, exploring everything from microwaves to biological weapons, which have been funded at a cost to the taxpayer of more than $130 million.

"A doctor there accused me of bleeding myself to fake anemia," says Colonel Smith.

Colonel Smith is one of the highest-ranking officers on full disability for Gulf War syndrome. He believes he might have never known the nature of his illness had it not been for the efforts of Dr. Pamela Asa, a Ph.D. molecular biologist who for the past five years has waged a one-woman battle with the Pentagon over the diagnosis of Gulf War syndrome and its cause. She has conducted her own research without a penny from the government or any other benefactor. Because of Asa's work, Colonel Smith has become more than a poster boy for a public-health disaster. Asa believes that in Smith's blood there is evidence that may hold the answer to why so many veterans of the Gulf War are sick.

Vanity Fair has uncovered military documents that show the Department of Defense made plans to run a clandestine trial of experimental vaccines and medical products during Desert Shield and Desert Storm. Military physicians called this effort "the Manhattan Project." While many of these vaccines were never used, *Vanity Fair* has found evidence suggesting that the Pentagon may have developed a modified version of its F.D.A.-licensed anthrax vaccine during an operation called "Project Badger." If Pam Asa is right, an experimental substance that causes incurable diseases in lab animals was mixed into an unknown number of doses—in essence creating a new, untested anthrax vaccine. The actual administration of such a vaccine would have violated the 10-point Nuremberg Code, which in 1947 established the conditions for experiments on human beings—the cardinal point being informed consent. Speaking for the Pentagon, Dr. Ronald R. Blanck, a three-star general in the army's medical com-

mand, denies that any of this took place. "Absolutely not," he says. "I will tell you flat out it wasn't done."

There are echoes of the antebellum South in Pam Asa's accent, in the way she can stretch three syllables out of a word like "hey." Her speech is a genteel drawl, evoking images of hoopskirts, silk hats, and magnolia blossoms. Asa, 46 years old and the mother of four, lives in Memphis, Tennessee. "American by birth, southern by the grace of God," she likes to say, especially in the presence of Yankees. During the Civil War, Union cavalrymen arrested her great-great-grandfather the Reverend John Murray Robertson for refusing to pray for Abraham Lincoln, and then turned his church, Huntsville, Alabama's Episcopal Church of the Nativity, into a horse stable. But though Asa is fond of making jokes about "the War of Northern Aggression," she is no regional chauvinist. Members of her family have fought in just about every American conflict, from the Revolutionary War up through Vietnam. Francis Scott Key, who wrote the words to the national anthem, is one of her ancestors. Her father retired from the Marine Corps as a captain in the early 1960s, then worked as a quality-control director for NASA's Redstone Arsenal in Huntsville. Asa's reverence for the military borders on idolatry. "My father taught me ever since I can remember to have respect for anyone who serves in the military, because they protect us. They're willing to take bullets for us."

It was patriotism that motivated Asa to approach the Pentagon in 1994 about vaccines administered to the troops for Operation Desert Storm. By then, the symptoms related to Gulf War syndrome had been widely publicized. They were vague enough to point to anything from a stroke to allergies to mere tension. "But when these particular symptoms are taken together," Asa says, "they point to autoimmune disease"—when a person's immune system goes haywire and attacks his or her own body.

Mostly, doctors don't know what causes autoimmune disease. Many victims develop it from unknown causes. Since 1984, Asa had been working with her husband, Kevin—an M.D. certified in both internal medicine and rheumatology—to treat a group of women with such autoimmune diseases as rheumatoid arthritis and lupus. After a series of landmark legal cases in the early 1990s which alleged a relationship between silicone breast implants and autoimmune disease (the lawsuits put the main manufacturer, Dow Corning, into bankruptcy), a large number of the Asas' patients revealed that they had received breast implants. Pam Asa became convinced that silicone had induced diseases such as scleroderma and lupus in her patients—a conclusion that embroiled her in one of the most contentious public-health disputes of the 90s. It is a view that has propelled her into what promises to be an even more bellicose scrap.

Asa suspected that the autoimmune illnesses showing up in Gulf War troops were also induced by a toxic substance. For one thing, the gender breakdown of the victims was suspicious. Women develop autoimmune diseases far more often than men do. With lupus the ratio of female to male sufferers can be as great as 14 to 1. But among Gulf War veterans the victims were overwhelmingly male (an anomaly only partially explained by the fact that women made up a mere 6.8 percent of the U.S. force serving there).

"They're not going to equate my son with a lab rat," says Asa. "It's not right."

BAD MEDICINE
Pamela Asa holds a jar of squalene, which she suspects was added to military vaccines and is causing autoimmune diseases.

Another startling fact pointed to the vaccination program. Many of Asa's Gulf War–syndrome patients had never deployed to the Persian Gulf. They had never been exposed to petroleum fires, chemical-weapons fallout, pesticides, or the other suspected causes of Gulf War syndrome. But, she says, they did have one thing in common with the troops who were in theater: they had rolled up their sleeves and gotten their shots.

For Asa, all of this pointed to an adjuvant. Adjuvants are toxic substances which make vaccines more effective by stimulating an even stronger response from the immune system than a virus or bacterium might on its own. In the course of investigating the possible connection between her earlier patients' breast implants and their illnesses, Asa says she came across a confidential Dow Corning document showing that the company had conducted research with silicone as a vaccine adjuvant in 1974. The term "adjuvant" comes from the Latin word *adjuvare*, "to aid." But the quest for a safe, effective adjuvant has been like the medieval alchemist's

quest to turn lead into gold. Adjuvants work because they are toxic, generally too toxic. Eighty years of research has produced a grand total of one that is considered safe for human use: a salt called aluminum hydroxide, also known as alum. Other adjuvants have been rejected as too dangerous; in tests on animals, adjuvants have been used over and over again to induce autoimmune disease.

At first, Asa suspected sabotage. "If the vaccine manufacturers were overseas, their loyalties could lie elsewhere or be bought for the right price." If an enemy wanted to undermine our fighting forces undetected, she says, this would be one way to do it. "I can't think of a more effective and insidious way to reduce the effectiveness of a military force going into combat. This disease process affects people's minds. Patients suffer mood swings, blackouts, and cognitive disorders where a person loses the ability to read or understand language or remember directions. This is not what you want to see happening to people who handle guns, bullets, and bombs." Asa contends this "process" can develop into full-blown, debilitating, and sometimes fatal autoimmune diseases such as lupus, rheumatoid arthritis, and multiple sclerosis.

In June 1994, Asa phoned Colonel John Dertzbaugh of the Pentagon's Defense Science Board with her theory. Dertzbaugh said it made a lot of sense, and promised to check it out. But the Science Board had just completed a report concluding that there was "no persuasive evidence" of Gulf War syndrome and no single cause of illness related to service in the Persian Gulf. The report had gone to press, and no one wanted to reopen the investigation. Still, Dertzbaugh couldn't shake the feeling that it was important to give Asa's theory a closer look. In December 1994, he asked her to write a report and submit it to the Office of the Army Surgeon General. Dertzbaugh even made a personal pitch; he told the office that Asa's theory appeared to explain the patients' problems, as he understood them. Asa says she asked the office for vaccine samples to test free of charge—to no avail.

Herb Smith didn't call Pam Asa. She called him. In March 1995, *60 Minutes* ran a segment on Gulf War syndrome that made a case for chemical weapons as its cause. Promoting this view was one of the veterans whom newsman Ed Bradley interviewed, Colonel Herbert Smith. "We were getting hammered with a lot of information about us getting affected by chemicals. I was getting sick enough where I couldn't argue with anyone. As you noticed," Smith recalls now, "they were talking about chemicals. [Former] senator Don Riegle [Democrat, Michigan], his team, and Jay Rockefeller [Democrat, West Virginia] and his team—they all said it was chemicals."

Watching the program, Asa noticed that Smith's knuckle joints had a particular swelling that she had seen before. She was convinced he had an autoimmune disease.

Asa decided to track down Colonel Smith. "*60 Minutes* called me and said, 'We got people calling and they wanna talk to you,'" says Smith. "And I said, 'Fine, you know, doesn't bother me, let 'em call.' I was getting people calling me up and saying, 'You've got Lyme disease; you've got chronic fatigue syndrome; you need to take vitamin C.' They were trying to help, but they were nuts. When Pam called, I thought, Well, here's another one gonna tell me, you know, what I've got and how to fix it. And then she starts talking and it just makes sense to me." About one month later, Smith says, he flew to Memphis to be treated by the Asas.

After examining Smith, Dr. Kevin Asa agreed with his wife that the diagnosis was systemic lupus erythematosus (S.L.E.). Physicians back at Walter Reed balked. Smith recalls them protesting, "You can't have lupus! You're a white male in your 50s. People like you don't get autoimmune diseases!" They refused to run their own tests. Smith was not surprised at this response from the people who had been telling him that his problems were all psychological. "I had a doctor there, a guy named Michael Roy [major, U.S. Army]. He accused me of bleeding myself to fake my anemia," says Smith. "I have a degree in chemistry as well as being a doctor of veterinary medicine. Anyway, he says I'm a pretty smart guy, so I must know how to screw up my lab results." [Dr. Roy could not be reached for comment.]

Smith wouldn't let this insult go. "I wrote a letter to the commanding general, and I told him I had an officer, a major, accuse a superior officer, me, of conduct unbecoming an officer, and perjury. They gave me this new doctor, and he comes in saying, 'Well, you know, Dr. Roy says you got all these psychological problems.' And I said, 'What about all the V.A. findings [which supported the conclusion that Smith was physically ill]?' 'The V.A.? They're wrong. They don't know what they're doing.' So I asked, 'If you won't believe the V.A., who will you believe?' And this new doctor says, 'We'll believe either N.I.H. [National Institutes of Health] or Johns Hopkins.'"

Smith sent his lab results to the N.I.H.'s Dr. John Klippel, who had co-edited a standard medical-school text in this field called *Rheumatology*. "He reviewed the case," says Smith, "and he said the Asas' diagnosis was correct, but he couldn't see me, because he wasn't accepting new patients." (Dr. Klippel could not be reached for comment.) Smith then sent his records to another leading rheumatologist, Dr. Michelle Petri of Johns Hopkins University Medical School. "She called me up and said the Asas' diagnosis was correct, but she's going to have to run her own tests to confirm this. I gave more blood. Did a brain scan. And the results were pretty much the same."

When the Asas treated Smith for lupus,

"I would have declined to give the vaccine. You do not obey an unlawful order."

his pain subsided. He could get out of his wheelchair and walk again, provided he used canes.

Word about Asa had spread on the Internet's Gulf War–veteran grapevine, and others started to get in touch with her. One was Dr. Charles Jackson, a general practitioner who used to work at the V.A. hospital in Tuskegee, Alabama. Jackson told her he had hundreds of Gulf War–syndrome patients; he didn't know what it was or how to treat it. Asa asked him to run standard diagnostic tests for autoimmunity. Jackson says the lab values suggested that a full quarter of his Gulf War patients had autoimmune problems.

But if Gulf War syndrome is adjuvant-induced autoimmunity, what is the adjuvant? In 1995, Asa got the clue she sought. An official with the Senate Committee on Veterans' Affairs introduced her to a patient who had volunteered for an N.I.H. experimental-herpes-vaccine trial. The patient complained of chronic fatigue, muscle and joint pain, headaches, and photosensitive rashes—the same baseline symptoms as in Gulf War syndrome. She also had arthritis and other autoimmune disorders, diagnosed through lab tests. But this particular patient had never received the herpes vaccine. She'd been injected with a placebo, a single shot of a compound called MF-59, which contained an adjuvant that is much stronger than alum: squalene. This was in 1991, the same year as Desert Storm. Asa discovered from published scientific papers that squalene was a cutting-edge adjuvant used in at least three experimental vaccines

in the 1990s. These were used in tightly controlled experiments on animals and humans, but vaccines containing squalene have never been approved by the F.D.A. for human use.

Squalene is a lipid, or fat, that can be found in sebum, an oily substance secreted by the human sebaceous glands. Commercial squalene is extracted from shark livers. You can buy it in health-food stores in capsules which are purported to boost the immune system. It is also used in some cosmetics as a moisturizing oil. Squalene manufacturers say it's safe, and it appears to be when swallowed or rubbed on the skin. But injecting it is another matter. The adverse effects of vaccines containing squalene have been documented in papers published in such peer-reviewed scientific journals as *Vaccine* and the *Annals of Internal Medicine*. Since the mid-1970s researchers studying autoimmunity have used squalene to induce rheumatoid arthritis and a multiple-sclerosis-like disease called experimental allergic encephalomyelitis (E.A.E.) in rats. Like every other oil-based adjuvant ever concocted, squalene is apparently unsafe.

SWAN'S WAY
Jeff Swan with his mastiff, Bob, in Gosport, New Hampshire, March 1999. A military doctor told him he "wasn't in the right place" to get Gulf War illness.

"For almost 20 years I held a top-secret clearance. Suddenly I'm psychotic?" says Swan.

A rheumatologist who conducts research into adjuvants at the N.I.H. disputes the idea that adjuvants can induce autoimmune disease in humans. The researcher, who did not wish to be named, calls these allegations "junk science." He admits that squalene can induce rheumatoid arthritis, but alleges that it does so only in one species of rat. Published scientific studies, however, show that squalene has been linked to the development of autoimmune disease in rats, mice, and macaque monkeys. When asked if he thinks the F.D.A. will ever approve squalene as an adjuvant, the N.I.H. researcher says no. "The F.D.A. has not had a track record of approving oil-based adjuvants."

Research with squalene has been done at Stockholm's Karolinska Institute, which names the finalists for the Nobel Prize in Medicine each year. Dr. Lars Klareskog, a rheumatologist at the affiliated hospital, concurs that compounds with squalene could be dangerous for humans. "It's true that adjuvants can, in these experimental models, turn a potential autoimmune reaction that is otherwise not pathogenic into pathogenic immune reactions. That is true in experimental animals. Whether that is true in humans, we do not really know. But we believe that is so. Where the event occurs in reality very much depends on the genetic background."

In early 1995, Asa submitted to the army surgeon general the report Oertzhaugh had asked her to write. In response, the Department of Defense in March 1996 published a report on the Internet, refuting her theory without ever putting it to the test. A letter to the commander of the U.S. Army Medical Research and Materiel Command from Dr. Walter Brandt, who works for the Science Applications International Corporation, a Pentagon contractor, summarized the army's critique of Asa's theory, claiming that the only adjuvant the military used in vaccines was alum. He also criticized Asa's use of the phrase "human adjuvant disease" (H.A.D.), a term used by Japanese doctors in the 1960s to describe autoimmune problems in women who had received silicone injections to enlarge their breasts. Brandt's letter said, "The term was coined 30 years ago and is generally not used by most informed physicians today. . . . There is similarity between H.A.D. and *Gulf War Syndrome* in their symptomatology. However, the development of symptoms in H.A.D. requires years, not months."

After the Internet report came out, Asa's initial frustration with the army's lack of response turned to anger. "Adjuvant disease doesn't take years to create symptoms," Asa says. "And I wrote them about squalene and they hardly mentioned a word about it." Recently, Dr. Brandt explained to *Vanity Fair*, "The presence of squalene or squalene antibodies in blood samples would seem to be a natural occurrence and not an indicator of adjuvant injection." According to Dr. Robert Garry, a professor of microbiology at Tulane University School of Medicine who works with Asa, this contradicts the fundamental definition of autoimmunity. "If that were true, we'd have antibodies to all the proteins, all the tissues in our bodies, and the immune system wouldn't function at all," he says.

In August 1997, Vice Admiral Harold M. Koenig, then the surgeon general of the navy, wrote that the army "has used squalene as an adjuvant in several experimental vaccines . . . over the past ten years. . . . Military members who served in the Persian Gulf received standard vaccines, licensed by the FDA, with one exception [botulinum toxoid, which approximately 8,000 troops received]. . . . Squalene was not a component of any vaccine product given."

In June 1996, after denying for years

that Iraq had ever forward-deployed chemical weapons during Desert Storm, the Defense Department admitted that the U.S. had destroyed a large cache of chemical munitions at the Khamisiyah depot in Iraq in March 1991. Using only limited data on weather and detonation patterns, in 1997 the D.O.D. and C.I.A. released computer models of a toxic plume emanating from Khamisiyah, wafting downwind and possibly contaminating 100,000 troops—by remarkable coincidence the approximate number of veterans who at the time were believed to be sick. (In September 1998, after conducting its own study, the Senate Committee on Veterans' Affairs would censure both the D.O.D. and C.I.A. for faulty analysis and for sending letters to Gulf War vets suggesting, without sufficient evidence —that Gulf War syndrome may have been due to fallout from Khamisiyah.)

The Khamisiyah computer models were suspect, but the spin was effective. The C.I.A.-produced animations were played and replayed on television news shows. Almost overnight, chemical-weapons contamination became the conventional wisdom on the cause of Gulf War syndrome. Saddam did it, sort of. So did the wind. And maybe army engineers should have taken more precautions. As shots in the dark go, this seemed to make sense. The appearance that the Pentagon and C.I.A. had disclosed a possible cover-up lent the idea credibility.

But even if a toxic plume had actually existed and moved in the direction the Pentagon said it did, enveloping 100,000 troops with minute doses of nerve agent, the theory collapses on several points with regard to autoimmune disease. First, the symptoms don't match: the effects of chemical weapons—acute headache, nausea, shrinkage of the pupils to pinpoints, and muscle paralysis—are well documented. In more than 50 years of data on nerve gases, published since the Nazis invented the chemical weapons sarin and soman, there isn't a single recorded instance of a nerve agent causing autoimmune symptoms or diseases.

Second, veterans suffering from the symptoms of Gulf War syndrome who never deployed to the Gulf could not have been exposed to chemical-weapons fallout, or any other toxic agent in the region. Some of the veterans never left the United States; some went to other countries, such as Egypt. These veterans did not take P.B. pills. Moreover, had chemical weapons caused Gulf War syndrome, one would expect to see it among those who are native to the region. Yet according to U.S. defense intelligence documents, there are no reports of Gulf War syndrome among the Kuwaitis or Israelis. The Egyptians, who contributed some 40,000 troops to the coalition force, don't have it; neither do the French or the Belgians. All of them sent troops. Another cohort of people who do not significantly report cases are the journalists who covered the war, myself included. These groups all have at least one thing in common: they did not receive shots for biological-warfare agents.

Retired air force master sergeant Jeffrey Swan, 40, says he got his shots at Fort Belvoir in Virginia sometime around March 1991. Only one of the vaccines he received was identified (smallpox), so he doesn't know which other shots he was actually given. Because Swan speaks Arabic, French, and Greek, the air force sent him to Egypt in April 1991 to serve as a liaison with the Egyptian military. About four months later the tremors started, which made him look as though he were suffering from an alcoholic's D.T.'s. He developed joint and muscle pain and experienced seizures similar to Smith's. In 1996, back home in Tamworth, New Hampshire, he felt his car accelerating out of control and he slammed on the brakes. But it wasn't moving; he was parked at a shopping center.

Swan's symptoms were the same as those of veterans who had Gulf War syndrome, but a V.A. physician refused to put him on the government registry for it. "He told me that I had Gulf War illness, but he couldn't write that in the records, because I hadn't been deployed there, I wasn't in the right place. So he wrote 'undiagnosed illness.'" Air-force physicians have listed Swan's problem as "Major Depression with psychotic features." "For almost 20 years I held a top-secret security clearance," Swan says. "On my medical chart there was a big red-and-white sticker that said, 'SENSITIVE DUTIES.' I never had a doctor or dentist once note anything suspicious about my behavior. Any hint of instability had to be reported immediately. . . . Anything that might affect my performance had to be reported, even a teaspoonful of codeine. Suddenly I'm psychotic?"

Swan thinks he knows why he and other veterans have encountered this penchant to call their problems psychosomatic, if not psychotic. "Anything I said could be dismissed. It got to a point where I didn't even believe I was having these symptoms . . . that I was imagining everything. If we were registered for Gulf War syndrome, then everybody would know that the sickness couldn't be due to chemical weapons. We're the proof." According to Asa's reading of Swan's lab tests, Swan has lupus. He says a V.A. rheumatologist also told him that he may have atypical lupus, but that it would take more time to confirm the diagnosis. Asa has tested Swan +2 positive for squalene on a scale of 4.

In early 1997, Asa bought 200 milliliters of squalene from Acros Organics in Geel, Belgium. She developed a scratch test to measure sensitivity to the substance. All 16 of her Gulf War patients were "reactive." Some suffered symptoms such as rashes or swelling at the injection site. She also tested a control group of healthy patients who had never taken military vaccines; none of them reacted. Still, Asa didn't have her evidence. The scratch test indicated exposure, but didn't prove squalene had been injected.

Around this time, Asa teamed up with Robert Garry at Tulane University. Garry and the university received a U.S. patent in 1997 for an assay that could detect antibodies to polymers, of which squalene is one. Asa sent Garry an initial batch of serum samples, including one from the subject who had volunteered for the N.I.H. herpes-vaccine trial. Asa didn't tell Garry which polymer he would be testing for, or which patients might have been exposed to it. This would be a blind study.

When the samples all came back positive for antibodies to the unknown polymer, Garry repeated the tests and got the same results. He also tested frozen serum samples from Gulf War veterans sent directly to him in 1993 by Department of Defense and V.A. researchers. He had originally been asked to test the blood for evidence that the patients had been exposed to retroviruses including H.I.V., for which they were virtually all negative. Garry got these samples out of cold storage and ran the new assay on them. He had been told that some of the samples were from healthy control subjects; now 69 percent of the samples tested positive for antibodies to the unknown polymer.

It was at about this time, Asa says, that the phone calls started. She would answer the phone, and no one answered back. Her phone would occasionally dial 911 by itself in the middle of the night. A year and a half earlier, just after she had submitted her report to the D.O.D., there had been two attempted break-ins at her house. Her husband opposed any further involve-

"All I know is, my son and other people are getting sick after getting the anthrax shots."

BURDEN OF PROOF Professor Robert Garry at Tulane University School of Medicine, New Orleans, His tests revealed Asa's patients were positive for antibodies to squalene.

convened the first meeting of the task force, which began to draft plans to "surge" the production of vaccines for anthrax and botulinum toxin. At the next meeting, on October 12, the acting chairperson, Colonel Garland McCarty, and a team of 13 other officers decided to give the task force and its mission the code name Project Badger.

Of more than 160 companies that were asked to make anthrax vaccine, all but one said no. Only Lederle-Praxis Biologicals of Pearl River, New York, signed on. Under the supervision of General Ronald R. Blanck and Colonel Harry Dangerfield, Project Badger organized the production of additional anthrax vaccine at the National Cancer Institute's Frederick Cancer Research and Development Center, located at Fort Detrick. Both Lederle and N.C.I. were unlicensed and unregulated by the F.D.A. The plan called for subcontractors to ship vaccine to the only F.D.A.-licensed manufacturer of anthrax vaccine, Michigan Biologic Products Institute (now BioPort), in Lansing, Michigan, for bottling, labeling, potency testing, and storage. This would have been another breach of federal safety regulations. As an earlier task force memo from October 10 stated,

"Our commander told us to destroy everything connected with the vaccine," says Dr. Dubay.

ment with the Gulf War–syndrome patients after the harassment began. If it was tied to this work, their children could be in danger, he believed. But Asa persisted, partly, she says, *for* the safety of her children. Her eldest, Chris, was in high school and would soon register for the draft. "They're not going to equate my son with a lab rat. I don't care what the vaccine is, I don't care what they claim it's supposed to do for mankind. It's not right to experiment on people, ever."

Asa sent Garry more samples, and by the fall of 1997, Garry had the results. Ninety-five percent of Asa's Gulf War syndrome patients had tested positive for antibodies to the unknown polymer. Colonel Smith was positive. The subject from the N.I.H. vaccine trial was positive. Of those sick veterans who had never deployed to the Gulf, but who said they had received shots, 100 percent were positive.

In all, Asa and Garry tested some 350 subjects, half of them controls. "So what was that stuff?" he asked Asa.

"Squalene," she said.

This left one major question unanswered. If the military used a squalene adjuvant, in which vaccine did they use it?

In August 1990, the month Iraqi troops invaded Kuwait, there was palpable anxiety at the Pentagon over the prospect that Saddam Hussein might use biological weapons to defend his newly annexed territory. On August 8, intelligence intercepts of Iraqi military communications indicated that Baghdad had produced and probably weaponized (i.e., made suitable for warfare) many deadly biological agents, including botulinum toxin and anthrax. The U.S. Army had been purchasing small amounts of vaccine for both, but its stocks were woefully short of what would actually be needed. A high-ranking army source confirms that by August 1990 the United States had stockpiled between 11,000 and 12,000 doses of anthrax vaccine. We eventually deployed 697,000 troops in the Persian Gulf.

According to declassified military documents, in August 1990 the army surgeon general at the time, General Frank E. Ledford Jr., ordered a team of doctors and researchers from the army, the navy, and the air force to form a secret Tri-Service Task Force on vaccinations for troops in the Gulf. On October 9, 1990, in a conference room at the army's Fort Detrick in Frederick, Maryland, the Defense Department

"It must be noted that any firm other than Michigan will produce a vaccine under an I.N.D. and not a licensed product." I.N.D. stands for "investigational new drug," which requires special approval from the F.D.A. for use. The army—as the executive agent for the Defense Department's biological-warfare vaccine program—should have sought that approval. It did not, and N.C.I. confirms that it never applied for an I.N.D. to produce anthrax vaccine. (Wyeth-Ayerst International, which now owns Lederle-Praxis, could not be reached for comment.) The F.D.A. must approve all vaccines used in the United States and also license the production sites, military vaccines not excepted. General Blanck disputes this scenario unequivocally. "I have no knowledge of anybody producing any anthrax vaccine other than Michigan," he says. "Nobody provided us or produced any vaccine, because the war ended, basically, is what happened."

By the first week of December 1990, Project Badger had begun plans to test other experimental vaccines on U.S. troops in the Gulf. Project scientists referred to this endeavor, rather portentously, as a "Manhattan-like project," or simply

a "Manhattan Project." They organized a crash program to manufacture, or purchase, at least four experimental vaccines: Enterotoxigenic E. Coli, Hepatitis A, Centoxin, and Shigella. At least two other experimental products were ultimately used: PB pills and botulinum toxoid vaccine, for both of which the army received from the F.D.A. a waiver of informed consent.

As for the mysterious "Vaccine A," variously cited as Vac A, Vac A-1, or Vac A-2 in the shot records of sick veterans such as Colonel Smith, declassified Defense Department documents identify it as anthrax vaccine. Dr. Gregory Dubay, who commanded the 129th Medical Company, a former Alabama National Guard unit out of Mobile, gave thousands of anthrax vaccinations to troops. He says, "Each soldier had to read a classified sheet of instructions, stating that he, or she, was receiving a secret shot, and that this was so for reasons of operational security. You don't want to tell the enemy that you're getting protection against one of his weapons." Dubay—who both administered and took the vaccinations—says that he was under orders not to record the inoculations in the soldiers' medical records, and that the troops were not given a chance to decline the shots. "You were just marched through, and that was it. . . . Then our commander told us to destroy everything connected with it—the empty vials, the boxes, and the package inserts. We burned them all in 55-gallon steel drums back behind the tents."

The Pentagon says that 150,000 Gulf War troops received anthrax inoculations. There are no documents available proving that the army used a squalene adjuvant in the unapproved vaccines, and the army has specifically denied it. But that still leaves Asa and Garry with more than 100 sick veterans who had their shots and now test positive for antibodies to squalene.

Why might the army have used squalene instead of alum, the only adjuvant approved for human use? Probably because squalene was stronger. The licensed anthrax vaccine was relatively weak. Immunity wasn't achieved with one shot. It took six shots, administered over a period of 18 months, then an annual booster. In 1991, tens of thousands of U.S. troops arrived in Saudi Arabia only a month before the coalition forces began the ground war. Most could get only two shots out of the six-shot regime; some just got one. And there was, perhaps, an even more compelling reason to enhance the vaccine. Two former members of Project Badger say the coalition suspected that Iraq had engineered a more powerful anthrax bio-weapon. "We were concerned that Saddam may have made anthrax resistant to penicillin," says one, who does not wish to be identified. "We knew he had the skills to do that—people who had trained in the United States, who had the skills to turn the bug into a resistant bug. . . . The Brits were the ones who gave us the information, actually. We actually knew who those people were." The anthrax vaccine licensed by the F.D.A. back in 1970 was designed to protect against anthrax germs that occasionally infect woolsorters and veterinarians. It was not known to be effective against a biowarfare agent that Iraq had possibly made more lethal. It is plausible that the army thought an experimental anthrax vaccine was worth the risk, especially since squalene was considered to be a superior adjuvant. However, this was a hypothesis. Administering such a vaccine to the troops would have been tantamount to a human experiment. In order to conduct a legal trial with squalene, one would have to file an "investigational new drug" application with the F.D.A. and have that application approved. This did not happen. In October 1997, the British revealed their attempts to boost the efficacy of their anthrax vaccine during the Gulf War by using a pertussis vaccine as an adjuvant. This controversial combination had caused serious side effects in animals. But Asa believes she has evidence that the British also boosted at least one of their vaccines with squalene. In 1998, she tested five British veterans suffering from symptoms similar to those of Gulf War syndrome. Four were positive for antibodies to squalene. (The British Ministry of Defence denies using squalene in vaccines given to Gulf War troops.)

Among the 1991 coalition allies, the United States, Britain, Canada, and the Czech Republic have reported possible Gulf War–related illnesses. Of these, the first three admit to immunizing troops against biological-warfare agents.

Production of anthrax vaccine in unlicensed facilities did not end with the war. On August 29, 1991, six months after Iraq's surrender, the army surgeon general approved a $154 million contract for a company called Program Resources, Inc. (P.R.I., a National Cancer Institute subcontractor that managed some of N.C.I.'s labs at Fort Detrick. Contracts were drawn up for fiscal years 1992 and 1993. In a secret Pentagon log kept continuously between August 8, 1990, and February 7, 1992, there are numerous references to the army's expanded vaccine-production program, but no record of any decision to halt it or to cancel the contract with P.R.I. Chuck Dasey, a spokesman at Fort Detrick, says that no anthrax vaccine was ever produced through the contract.

Presumably, the vaccines made during the Gulf War are part of the stockpile now being administered in the wake of the D.O.D.'s December 1997 decision to immunize all 2.4 million people in the armed services against anthrax. When Pentagon officials held a press conference about the mandatory immunizations last summer, they insisted that there had been only seven reported adverse reactions to the nearly 140,000 anthrax vaccinations that the military had given in the preceding six months. But according to the F.D.A.'s Vaccine Adverse Event Reporting System, there were at least 64 reports of reactions to the vaccine between September 2, 1998, and March 9, 1999. Activist Lori Greenleaf, a day-care provider in Morrison, Colorado, says that, based on her E-mail, there are a lot more military personnel reporting problems. Greenleaf began a grassroots campaign against mandatory antithrax immunizations because of her 23-year-old son, Erik Julius, who she says fell ill after taking the second of three anthrax shots in March 1998. She is swamped with messages from fearful enlisted men and women. Some of them have already received their anthrax shots. "They've got rashes, chronic fatigue, hair loss, memory loss, muscle and joint pain, numbness in their extremities." Greenleaf says she does not know what an adjuvant is, and she has no idea what is ailing her son. "All I know is, my son and many other people are getting sick after getting the anthrax shots, and it sounds an awful lot like Gulf War syndrome."

Two servicemen who received their anthrax shots last year have tested positive for antibodies to squalene. One received vaccine from Lot No. FAV020, the same lot sold to Canada and Australia. The other serviceman received vaccine from Lot No. FAV030. Doses from this lot were also sold to Canada, according to that country's Department of National Defence. There is no evidence that every dose in FAV020 and FAV030 is contami-

"No one in their right mind would volunteer for something like that," says Jeff Rawls.

nated with squalene, but the antibodies in these two veterans suggest that anyone immunized from these lots may be playing "vaccine roulette." The U.S. has shipped anthrax vaccine from other lots to Germany, Israel, and Taiwan.

If the first casualty of war is truth, then the rule of law is a close second. As Cicero wrote, "Laws are silent in time of war." In the fall of 1990, the Pentagon began petitioning the F.D.A. to waive informed-consent requirements on so-called investigational new drugs for the Persian Gulf. This was an ethical powder keg. In 1947, under the authority of the U.S. military in Nuremberg, Nazi scientists and physicians stood accused of war crimes and crimes against humanity for performing experiments on prisoners. Seven were hanged. Following the trials, U.S. judges drafted the 10-point Nuremberg Code, which was intended to govern all future experiments involving human subjects. The code's first and best-known principle was voluntary, informed consent. Until the Gulf War, the U.S. military had never argued that there should be any exceptions. In the end, the F.D.A. decided to grant waivers for P.B. pills and for the rarely used and as yet unlicensed vaccine botulinum toxoid.

In 1994, the Senate Veterans' Affairs Committee called this a violation of Nuremberg, the moral equivalent of the army's World War II–era mustard-gas tests on troops and its LSD experiments in the 50s and 60s. "We'd like to think these kinds of abuses are a thing of the past, but the legacy continues," said the committee chairman at the time, Senator Rockefeller. "During the Persian Gulf War, hundreds of thousands of soldiers were given experimental vaccines and drugs . . . these medical products could be causing many of the mysterious illnesses those veterans are now experiencing." Rockefeller could barely contain himself: "The D.O.D.'s failure to provide medical treatment or information to soldiers was unjustifiable, unethical, sometimes illegal, and caused unnecessary suffering."

He was referring to the experimental P.B. pills and botulinum-toxoid vaccine. Rockefeller and his staff made no mention of unapproved anthrax vaccine, Project Badger, or the Persian Gulf "Manhattan Project."

Declassified documents show that Dr. Walter Brandt, who helped organize the Internet report attacking Asa's theories, was one of the original members of Project Badger. Dr. Michael Roy, the physician who diagnosed Colonel Smith's illness as psychosomatic, also worked with members of the team in early 1991: the same doctors who planned the "Manhattan Project." The Pentagon says that most of the unit logs in which biological-warfare vaccinations were recorded are missing. *Vanity Fair* has found an army document showing that at least some of these records were ordered sent to the Office of the Surgeon General. General Ronald Blanck, who led the Project Badger Working Group on expanded vaccine production, is the current army surgeon general.

Some might understand the decision to accelerate vaccine production by any means possible when faced with the prospect of biological warfare. But Dr. Greg Dubay believes he should have been told if he was administering an altered version of an existing vaccine. "If I'd known it was a vaccine that had been tampered with: if it was tampered with—I would

Production of anthrax vaccine in unlicensed facilities did not end with the Gulf War.

PARADE'S END
Sergeant Jeff Rawls with his father, Don, at home in Utica, New York, March 1999. Rawls's illness caused part of his brain to shrink.

have declined the order to give it," he says. "You do not obey an unlawful order. If I knew it was done clandestinely, and had solid evidence, I would have disobeyed the order. The first oath of every physician is to do no harm. I don't know any physician who would purposely do something that is truly harmful, unless you're a Mengele or something."

A spokesman for BioPort says parts of Project Badger remain classified. Pentagon officials deny using a squalene adjuvant in any Gulf War vaccines and balk at Asa's allegation that some undiagnosed Gulf War illnesses are autoimmune diseases. Can a substance that induces autoimmune disease in a rat or a mouse be dangerous to a human being? Former Marine Corps tank commander Jeff Rawls has a solution for the naysayers. Rawls is a 31-year-old Gulf War veteran who now lives with his parents in upstate New York. He has experienced severe shrinkage of part of his brain and can barely walk. At +3, he is almost off the scale for antibodies to squalene. "Inject them with the same thing and see what happens," Rawls says in a slurred and halting voice. "No one in their right mind would volunteer for something like that." ▮

ED BRYANT
7TH DISTRICT, TENNESSEE

COMMITTEE ON COMMERCE
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HEALTH AND ENVIRONMENT
OVERSIGHT AND INVESTIGATIONS

COMMITTEE ON THE JUDICIARY

Congress of the United States
House of Representatives
Washington, DC 20515–4207

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MEMPHIS, TN 38134
901–382–5911

810½ SOUTH GARDEN ST.
COLUMBIA, TN 38401
931–381–8100

July 7, 1999

(b)(6)

Dear (b)(6)

Thank you for contacting me with your concerns over the anthrax vaccine. I appreciate your taking the time to reach me, and I enjoy hearing your views.

I can certainly understand your position on this issue, and I think you make some good points. You are naturally concerned for the health and safety of military personnel, and want to protect our service members from serving as guinea pigs. On your behalf, I have shared your concerns with the Secretary of Defense, so that he can have the benefit of your views on this matter. I will be sure to share his response with you.

I have also sent the information you mailed me on this issue to Representative Christopher Shays, the chairman of the House Committee on Government Reform's National Security, Veterans Affairs, and International Relations Subcommittee, so that he will have the benefit of your input. Representative Shays has held a number of oversight hearings on both Persian Gulf War illness and the Department of Defense's Anthrax Vaccine Program; your information could be of great benefit to him as he further investigates this matter.

Again, thank you for contacting me. Please continue to keep in touch. I look forward to hearing from you again.

Sincerely,

Ed

Ed Bryant, M.C.

EB:als

Congressional

CMAT Control #
1999201-0000046

(15)

	SECRETARY OF DEFENSE ROUTING SLIP	ACT COPY	INFO COPY			ACT COPY	INFO COPY
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					C&D		X

TYPE OF ACTION REQUIRED

	PREPARE REPLY FOR SEC OF DEF SIGNATURE		COMMENTS AND/OR RECOMMENDATIONS
	PREPARE REPLY FOR DEP SEC OF DEF SIGNATURE		INFORMATION AND RETENTION
1	REPLY DIRECT *(Forward copy of reply to CCD, Room 3A948)*	X	COORDINATE REPLY WITH LA
	APPROPRIATE ACTION		

Remarks:

REPLY DIRECT - MUST BE SIGNED BY COMPONENT HEAD

ACTION DUE DATE *(YYMMDD)*	ROUTING DATE *(YYMMDD)*	OSD CONTROL NUMBER	
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JOHN ELIAS BALDACCI
SECOND DISTRICT, MAINE

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OSAGWI

JUL 20 1999

July 16, 1999

OFFICE OF THE SECRETARY OF DEFENSE
1999 JUL 19 PM 4:43

The Honorable William Cohen
Secretary
U.S. Department of Defense
The Pentagon, Room 3E880
Washington, DC 20301-1000

Dear Mr. Secretary:

I am writing on behalf of Mr. and Mrs. Robert Johnson, (b)(6) (b)(6), regarding their son Zachary Johnson who is currently pending court martial for refusing to submit to the anthrax vaccine. Zachary is currently on board the USS JOHN F. KENNEDY.

Enclosed is a copy of an e-mail I have received from Mr. and Mrs. Johnson, along with newspaper articles, expressing specific concerns after having completed research on the subject. It is my understanding that a pre-trial hearing is scheduled for August 9. Mr. and Mrs. Johnson are especially concerned that their son's attorney be allowed to present a defense on his behalf. I would appreciate your reviewing this matter and providing me with information in order that I might respond directly to the their concerns in a timely manner.

Thank you for your attention to this matter.

Sincerely,

John E. Baldacci
Member of Congress

Enclosure
Please Reply to:
Congressman John E. Baldacci
P. O. Box 858
Bangor, Maine 04402-0858

U11544 /99

Zachary Johnson-Anthrax vaccine

Janet -
Call
A.

Subject: Zachary Johnson-Anthrax vaccine
Date: Wed, 14 Jul 1999 14:50:33 -0400
From: (b)(6)
To: <baldacci@me02.house.gov>, <senator@collins.senate.gov>, <olympia@snowe.senate.gov>
CC: "Johnson, ATAN (HS-11)" (b)(6)

Dear people,

Last week, we contacted your office to ask for some help with regard to our son Zachary's pending court marshal for refusal to submit to the anthrax vaccine while serving in the U.S. Navy. We were told that Zachary himself would have to contact your office. Since he is currently on board the U.S. John F. Kennedy, his only means of communication is through e-mail, and we understand that he e-mailed you last week to ask for your help.

We have read the military's "position papers" regarding this issue, and ask that you help us in any way that you can, with the following in mind:

1. It appears that the vaccine that is currently being given to military personnel is NOT the same vaccine that was approved by the FDA in 1970. We are concerned that Zachary is being asked to submit to a vaccine that is not approved for use by the general public.

2. While the military denies it, there is evidence -- that we happen to find convincing or at least alarming -- that there is a correlation between the use of certain types of the vaccine and auto-immune illnesses.

3. The sole manufacturer of the vaccine is about to go bankrupt and has been cited for numerous safety and product quality violations.

Zachary has served three years in the Navy. If he is found guilty of "failure to obey a lawful order", he faces up to six months imprisonment and a bad conduct discharge from the Navy.

We would appreciate, as he would, hearing from you about this issue. A pre-trial hearing has been scheduled for August 9. His Attorney is LTCOMMANDER Todd Wyncoop, telephone # (b)(6)

We can be reached by e-mail or by telephone: (b)(6)

Thank you.

Sharon and Bob Johnson
(b)(6)

Mainer refuses Navy's vaccine

BDN 7/12 P<BC

Anthrax issue goes to military court

The Associated Press

CHINA — A Navy airman from China has refused to take the anthrax vaccine and will be tried in military court in April.

Zachary A. Johnson, 22, is expected to be the first person in the Navy to be tried for refusing to take the vaccine, according to his military lawyer, Lt. Cmdr. Todd A. Wynkoop. His court-martial is scheduled for Aug. 16.

"He is not the first man in the Navy to refuse to take it," Wynkoop said. "He is the first one I'm aware of to be tried for it."

Johnson is charged with disobeying a direct order to take the vaccine, on June 6, Wynkoop said.

"His personal position is that he should not have to take the vaccine because he is not clear that it is not lawful, and that it serves a purpose," Wynkoop said.

Defense Secretary William Cohen last year ordered all 2.4 million active duty and reserve troops to get the anthrax vaccine as protection against biological warfare. Nearly 300,000 service members have been immunized so far, though there have been scattered cases of some troops refusing the inoculations out of safety concerns.

The Pentagon says more than 40 have reported adverse affects, but all have recovered.

In an e-mail to the Morning Sentinel, Johnson said there have been no long-term studies on the vaccine, and that studies that have been done reveal little about its effectiveness against airborne anthrax.

"One of the main reasons I am doing this is because I believe that my body is the only thing on this Earth that I truly own," he wrote. "I, alone, should decide what goes into my body, not some bureaucrat with lobbying interests."

Wynkoop said the Navy offered to allow Johnson to face a nonjudicial punishment in the case, but he refused.

"This was a matter of principle," Wynkoop said.

A handful of U.S. Marines who refused to take part in the six-shot immunization procedure have been convicted of disobeying orders and received sentences that included confinement in military prisons and bad-conduct discharges.

Johnson, a member of a helicopter anti-submarine squadron, is stationed at the U.S. Naval Air Station in Jacksonville, Fla. The aviation electronics technician is doing training exercises on the USS John F. Kennedy in the Caribbean and is scheduled to return to port in July.

Johnson has received a mixed reaction from others stationed with him on the USS John F. Kennedy.

"The majority of the junior personnel are excited that I am doing this," he said. "Most of the older people here don't really agree with me."

Morning Sentinel
Sunday, July 11, 1999

China man nixes shot, faces trial

By MARY CALDER
Staff Writer

CHINA — Zachary Johnson of China may become a guinea pig for the anthrax vaccine.

A guinea pig that will see what happens to a member of the U.S. Navy who refuses an order to take the vaccine.

Johnson has scheduled to appear April 16 at a military court in Florida where he will be the first person in the Navy to be tried for refusing to take the vaccine.

JOHNSON ... on training exercises aboard the aircraft carrier U.S.S. John F. Kennedy in the Caribbean

An aviation electronics technician, Johnson has been in the Navy for three years. He currently is on training exercises aboard the aircraft carrier U.S.S. John F. Kennedy in the Caribbean.

On June 6, Johnson refused to take the vaccine, which is designed to protect against an anthrax attack. Anthrax is a highly lethal biological agent used as a weapon.

A member of Helicopter Antisubmarine Squadron Eleven, stationed at the U.S. Naval Air Station in Jacksonville, Fla., Johnson disobeyed a direct order to take the vaccine, according to Lt. Commander Todd A. Wynkoop, his military defense lawyer.

ANTHRAX

Anthrax [illegible]
deadly, silent and invisible
according to information
released by the U.S.
Department of Defense. The
cost to produce a [illegible]
information about making it easily
widely available and it is easy
to produce in large quantities.

Johnson should not have to take the vaccine because he is not classified as a lawful [illegible] that [illegible] pose, Wynkoop said. Wynkoop has his office at the naval air station in Jacksonville, Florida.

Johnson, a graduate of China Senior High School, [illegible] personnel [illegible] take the vaccine, which [illegible] highly [illegible] recipients [illegible] made them sick.

[illegible] Navy [illegible] said. He [illegible] of to be [illegible]

•Anthrax

Continued from A1

In an e-mail letter sent Thursday from his ship to the Morning Sentinel newsroom, Johnson wrote that while he was told the anthrax vaccine was completely safe, he researched the issue and found there have been no long-term studies on the vaccine. Studies that have been done reveal little about its effectiveness against airborne anthrax.

"One of the main reasons I am doing this is because I believe that my body is the only thing on this Earth that I truly own. I alone should decide what goes into my body, not some bureaucrat with lobbying interests."

A growing number of military personnel are refusing to take the vaccine, according to reports. Some have been demoted and fined, others have been discharged other than honorably.

According to Pentagon records, about 300,000 members of the armed services have started the anthrax vaccine's six-shot series, with more than 900,000 shots given so far. During the Persian Gulf War, 150,000 service personnel were vaccinated against anthrax, according to reports in The New York Times.

The U.S. Marine Corps has court-martialed and punished eight men since last year for refusing to take the vaccine, according to the San Diego Union-Tribune. The Navy and Army have not court-martialed anyone yet for refusing.

Johnson's stepmother, Sharon Marden Johnson, and father, Robert, of China, back their son in his decision.

"We can do nothing but support him because we think he's smart and we just really wish that the case could be heard fairly," Mrs. Johnson said. "If it is found that the vaccine is unsafe, let him finish his tour of duty."

Wynkoop, the defense attorney, said the Navy offered to let Johnson face a nonjudicial punishment in the case, but he refused.

"This was a matter of principle," Wynkoop said.

Wynkoop would not say whether he thinks Johnson can win the case, but indicated his client is brave to try in the wake of others who have lost.

"I think it's a very difficult and courageous stance that he's taken on this," Wynkoop said.

IS VACCINE SAFE?

Anthrax is preserved as a biological warfare agent because it is highly deadly, silent and invisible, according to information issued by the U.S. Department of Defense.

When inhaled, it is always fatal.

The cost to produce anthrax is low, information how to make it is widely available and it is easy to produce in large quantities. A naturally occurring disease in plant-eating animals, such as goats, sheep and cattle, anthrax is caused by a bacteria.

A medical countermeasure to anthrax is an anthrax vaccine approved by the U.S. Food and Drug Administration and taken prior to exposure. The vaccine contains anthrax.

In December 1997, Secretary of Defense William S. Cohen announced that all 2.4 million American service members would be immunized with the anthrax vaccine.

That vaccine was licensed by the FDA in 1970 and has been safely administered for nearly 30 years to veterinarians, laboratory workers and people at risk of coming into contact with potentially infected livestock, according to literature issued by the U.S. Navy.

An anthrax vaccine was administered to members of the military who served in Desert Shield and Desert Storm, and there have been any reported cases of adverse reproductive outcomes, such as infertility, miscarriages or birth defects, or cancer, according to Navy literature.

The majority of side effects are limited to local redness, tenderness and an occasional subcutaneous nodule. It may cause

But thousands who received the vaccine and served in the Persian Gulf have become ill. Their illnesses, which are unknown, vary and range from aching joints, fatigue and sudden weight loss to blackouts and seizures.

While the military's anthrax vaccine program is growing, numbers of service personnel and reservists refusing the vaccine are growing. The military asserts that the vaccine is safe, whether the [illegible] the same vaccine that received FDA approval [illegible]

VACCINE RESEARCH

The Johnson family has questioned the anthrax vaccine's safety, saying they're sure the vaccine is not always FDA-approved.

Dr. Pamela Asa, a molecular biologist who has argued with the Pentagon over the diagnosis of Gulf War-related illnesses and their causes, also questions the safety of the vaccines.

The May issue of Vanity Fair magazine features a story about Asa's research, which suggests an experimental substance that causes incurable diseases in laboratory animals was mixed into an unknown number of doses of the anthrax vaccine, creating a new, untested vaccine.

The actual [illegible] such a vaccine would have [illegible] the 10-point [illegible]

which in 1947 established the conditions for experiments on human beings — the cardinal point being informed consent," according to the Vanity Fair article, written by Gary Matsumoto.

But Gen. Dr. Ronald Blank of the U.S. Army denies that the untested vaccine was ever created and used, according to the article.

Asa suspects that autoimmune illnesses (those in which a person's immune system attacks one's own body) suffered by Gulf War veterans were induced by a toxic substance.

Since some service personnel who were not deployed to the Gulf War still became ill, Asa suspected an adjuvant, or toxic substance mixed into vaccines to make them more effective, might be the cause.

Asa and Robert Garry of Tulane University ultimately determined that most of Asa's patients who suffered Gulf War illnesses tested positive for antibodies to the adjuvant squalene, a fat extracted from shark livers, according to the article. Of sick veterans who never went to the Gulf but said they received shots, 100 percent tested positive, according to the Vanity Fair article.

The Pentagon denied using a squalene adjuvant in vaccines used during the Gulf War, or that undiagnosed illnesses from that war are autoimmune diseases.

Miriam A. Lareau, deputy public affairs officer for the U.S. Navy Region Southeast in Jacksonville, said Thursday she is not aware of the squalene issue.

"I can't even comment on that," she said. "I don't have that background."

FACES COURT-MARTIAL

Johnson has been arraigned on charges that he violated an order to take the vaccine, according to Lareau.

On Aug. 9, Wynkoop and military prosecutor Lt. Chris Ludmer will present motions in the case.

Ludmer's superior officer, Capt. Daniel McCarthy, deferred comment on the case, referring questions to the Navy's public relations department.

Wynkoop says he will probably submit motions Aug. 9 to dismiss the charges that his client disobeyed a lawful order. It is up to Johnson, who is being defended free of charge, to decide if there will be jury at his trial on Aug. 16, Wynkoop said.

"We haven't gotten that far yet," Wynkoop said.

According to Lareau, if Johnson loses, the maximum punishment is six months confinement, a two-thirds cut in pay for six months, class reduction to E-1 and a bad conduct discharge.

Johnson's ship is scheduled to return to Jacksonville at the end of July.

In his e-mail, Johnson wrote that before his refusal to take the vaccine, his commanding officer told him and another sailor that should they decide to take the shot any time after their refusal, there would be no retribution. The other sailor took the vaccine and was taken to Captain's Mast and fined $200, according to Johnson.

Johnson said that after he refused the vaccine, he was told he would be sent to Captain's Mast, found guilty, receive a reduction in rank, 45 days restriction, and a half-month's pay taken away for two months, each time he refused the shot.

"There are six shots in the series," he wrote. "That would mean going on our upcoming six-month deployment as an E-1 and being restricted to the boat for the whole time, not being allowed off the boat. So I requested to go to court-martial."

Johnson was selected to advance to the next pay grade, but because of the anthrax case that has not occurred, pending conclusion of the court martial, he said.

The attitude of others on the ship to Johnson's situation differs with rank, he wrote.

"The majority of the junior personnel are excited that I am doing this. Most of the older people here don't really agree with me."

Asked if he was being treated well, he replied: "I am being treated well, I guess. Everyone I work with has been instructed not to talk to me about the proceedings. Many of the officers here are extremely wary of me, especially the commanding officer. I believe they are worried that I am trying to bring everyone down with me."

Johnson asked that people contact congressional representatives to help him in the case.

"An independent thinker who was an avid reader and played varsity soccer and ran track in high school, Johnson is well-liked, according to his stepmother. While his grades were not great in high school, his Scholastic Aptitude Test scores were strong, according to Mrs. Johnson.

"Zachary's a real charmer," she said. "There's not a teacher that I run into who doesn't say, 'How is Zachary?' He's a real personable guy."

She said when she and her husband first learned of Johnson's anthrax vaccine stand, she suspected he may have wanted an early release from the Navy. But she quickly was convinced her stepson was sincere and his refusal to take the vaccine was based on principle, she said.

"He thinks for himself," Mrs. Johnson said. "He travels to the beat of his own drummer."

The trial is the only fair way to go, she contended.

"Zach is just hoping that a judge and jury — a panel of fair-minded people — have a question of whether this is a lawful order," she said.

CONGRESSMAN JOHN BALDACCI

Bangor District Office: P.O. Box 858 Bangor, Maine 04402-0858

FROM:
- [X] Janet Dennis
- [ ] Lennie Mullen
- [ ] Doug Dunbar
- [ ] John Ripley
- [ ] Sally Polyot
- [ ] Other

DATE: 7-16-98

TO: Alice Stewart

COPY: Hassan

NOTES: Any help you can give on this would be appreciated. Hope all is well!

Number of pages (including this cover page): 7

Please respond to this office via:

FAX: 207-942-5907 or VOICE: 207-942-6935

Thank you!

(16)

SUSAN M. COLLINS
MAINE

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(202) 224-2693 (FAX)

CMAT Control #
1999201-0000048

COMMITTEES:
GOVERNMENTAL AFFAIRS
HEALTH, EDUCATION, LABOR, AND PENSIONS
SPECIAL COMMITTEE ON AGING

United States Senate

WASHINGTON, DC 20510-1904

OSAGWI

JUL 20 1999

11 Lisbon Street
Lewiston, Maine 04240
(207) 784-6969
July 13, 1999

Mr. Bernard Rostker
Special Assistant for Gulf War Illnesses
1000 Defense Pentagon
Washington, DC 20301-1000

Dear Mr. Rostker:

I am writing to you on behalf of one of Senator Susan Collins' constituents, (b)(6) (b)(6)

(b)(6) received a letter from your office approximately two years ago, indicating that there is a possibility that he may have been exposed to the nerve agents sarin and cyclosarin. To date, he has not experienced any symptoms which he believes are a result of such an exposure. However, (b)(6) has had difficulty obtaining information relevant to his situation and would like to know how to receive updated information on this subject. Specifically, he would like to know what symptoms, if any, are being experienced by his fellow Gulf War veterans as a result of exposure to these nerve agents. Also, is there any evidence indicating the possibility of long-term effects from this exposure?

Enclosed please find copies of the letter (b)(6) sent to Senator Collins requesting her assistance and his privacy form. Thank you for your consideration and the Senator's office looks forward to your reply.

With best wishes, I am

Sincerely,

Kara Marcoux

Kara Marcoux
Staff Assistant to
Susan M. Collins
United States Senator

02 June 1999

Senator Susan Collins
1 City Center
Portland, Maine, 04101

Dear Senator,

I am writing this letter as a concerned Gulf War veteran. I am a recipient of a letter dated 27 July 1997 and signed by a Bernard Rostker at the Office of the Secretary of Defense. The letter indicates that my unit may have been exposed to low levels of sarin and cyclosarin nerve agents. This is disturbing but not as disturbing as the reception I get when trying to obtain more information. When calling the numbers listed on the letter, to the DoD Comprehensive Clinical Evaluation Program and the Department of Veterans Affairs Persian Gulf Registry, I am routinely asked about my symptoms. When I explain that I cannot accurately answer that question due to lack of information I am put into hold/transfer limbo.

I am simply seeking information. The internet is so rife with "conspiracy theory" websites on this issue that I cannot determine if any of the information is accurate or not! My concern is simply what are other Gulf War vets experiencing? What ARE the symptoms so far exhibited by vets? And what about the Pyridostigmine Bromide (PB) tablets and the anthrax vaccine I was compelled to take? How do I ensure that I will receive information as it becomes available?

Let me make clear that I do not believe that I am suffering from any illness I have contracted during the Gulf War. However I am concerned about what sort of long term effects I may experience. And what about children? I do not have any yet, but I need to know what may occur because of the possible exposure to agents and the drugs and vaccines I took. I realize there may be no conclusive answers yet. How do I get in the loop so that information gets to me? I have already noted my experience with the Registry.

I know you are a busy person. You are probably not reading this yourself and that is fine. Any information, or sources where I can obtain information, that your office can provide would be greatly appreciated.

My thanks to you.

(b)(6)

02 JUL 1999

SUSAN M. COLLINS
MAINE

172 RUSSELL SENATE OFFICE BUILDING
WASHINGTON, DC 20510
(202) 224-2523
(202) 224-2693 (FAX)

United States Senate

WASHINGTON, DC 20510-1904

COMMITTEES:
GOVERNMENTAL AFFAIRS
LABOR AND HUMAN RESOURCES
SPECIAL COMMITTEE
ON AGING

To Whom It May Concern:

In accordance with the requirements of the Privacy Act of 1974, which protects my records from unauthorized release, I am taking this opportunity to give U.S. Senator Susan M. Collins and her staff permission to receive information in my confidential records relative to her inquiry on my behalf.

(b)(6)

Checklist and Guidance on Sending "Plume" and "Non-Plume" Letters

1. ☒ Veteran's unit was on the original plume list. Veteran was previously sent a "plume letter."
   Action: Provide another copy of the "plume letter" if requested.

2. ☐ Veteran's unit was on the original plume list. Veteran wasn't sent a "plume letter" for some reason.
   Action: Provide a copy of the "plume letter" if requested.

3. ☐ Veteran documents his/her status as assigned/attached to a unit on the original plume list.
   Action: Provide a copy of the "plume letter" if requested.

---

4. ☐ Veteran's unit was on the original plume list, but his unit has been identified by the S3/G3 Conferences as being outside of the plume.
   Action: This situation may arise if someone writes in requesting a copy of their plume letter – coordinate carefully with CMAT and the PM on the course of action. A possible response may be to send a copy of original plume letter, but explain that attendees at the S3/G3 Conferences are analyzing unit locations and his/her status is subject to change -- findings will be released when the analysis is complete.

5. ☐ Veteran's unit wasn't on the original plume list, but his unit has been identified by the S3/G3 Conferences as being under the plume.
   Action: Explain only that attendees at the S3/G3 Conferences are analyzing unit locations Findings will be released when the analysis is complete.

---

6. ☐ Veteran's unit wasn't on the original plume list. Veteran was previously sent the "non-plume" letter because his unit was inside the 50-kilometer radius.
   Action: Provide another copy of the "non-plume" letter if requested

7. ☐ Veteran's unit wasn't on the original plume list, the veteran wasn't ever sent a letter about the plume, the veteran was outside the 50-kilometer radius, but the veteran asks for information about the plume.
   Action: Explain that if he/she was with the unit at the time, the plume didn't affect him/her. Don't send a "non-plume" letter.

8. ☐ Veteran's unit wasn't on the original plume list, the veteran wasn't ever sent a letter about the plume, the veteran was outside the 50-kilometer radius, and the veteran hasn't asked for information about the plume.
   Action: Address the veteran's issues and concerns. Don't send a "non plume" letter.

---

9. ☐ Special circumstances explained in memorandum.

Comments:

1. Fill out this sheet and attach it to all correspondence pertaining to Gulf War veterans.
2. Unit location data (e.g., map plots) may be released upon request.

(b)(6)

CONGRESSIONAL or SPECIAL CORRESPONDENCE

CMAT: 9201-048

Date: 03-Aug-99

Office of Special Assistant for Gulf War Illnesses
Internal Routing/Tasking Sheet

Coord/ Routing	Position/Organization		Action	Info	Comments
8	Special Assistant	(SA)			
(W) 6	Deputy Special Assistant	(DSA)			
7	Executive Assistant to SA	(EA)			
	Executive Assistant to DSA	(EADSA)			
3	☐ Director, Investigation & Analysis _____ (IAD) ☐ DepDir _____ ☐ MED _____ ☐ VDM _____ ☐ C/B _____ ☐ ENV _____ ☐ PAG _____		M/A 10 AUG		see edits dave 8/3/99
	Dir Lessons Learned Implementation	(LLI)			
V	Dir Public Affairs & Outreach	(PA)			
	Dir Legislative Outreach	(LA)			
	Dir Quick Reaction Team	(QR)			
4	Dir Medical Outreach & Issues	(MOI)		10 Aug	See edit + suggested chart/format.
	Legal Advisor	(LGL)			
5	PM, Gulf War Illnesses Support	(PM)	M/A	10 Aug	
1	Editorial Review ☒ AMB ✓ ☒ Editors w/edits	(ER)			
	CMAT	(CMAT)			
9	Action Management Call 845-8369 ☒ COMEBACK COPY TO: MOI ☐ GET CMAT NUMBER WHEN SIGNED & SENT ☐ READING FILE ☐ THANK YOU FILE ☒ CHRON FILE ☐ ADD TO GulfNEWS				

SUSPENSE:

Prepare reply for signature of:

☐ SA/GWI ☐ SD ☐ DSD ☐ DepSA/GWI

☐ Congress ☐ Oversight ☐ FOIA ☐ OSD ☐ WBM ☐ VSO/MSO

☐ Ltr to SA ☐ IR ☐ E-Mail ☐ OGA ☐ Other ☐ Veteran

KEYWORDS:

02/05/99 Issuance

OFFICE OF THE SECRETARY OF DEFENSE
1000 DEFENSE PENTAGON
WASHINGTON, DC 20301-1000

SPECIAL ASSISTANT
FOR
GULF WAR ILLNESSES

Honorable Susan M. Collins
United States Senate
Washington, D.C. 20510-1904

AUG 13 1999

Dear Senator Collins:

This is in reply to your recent inquiry on behalf of your constituent, (b)(6). As the Special Assistant to the Deputy Secretary of Defense appointed to oversee the Department of Defense (DoD) investigation of Gulf War illnesses, I assure you that we are fully committed to investigating the events of the Gulf War to understand why many of our Gulf veterans are ill.

(b)(6) primary stated concern is a need for information. We have two excellent sources: the GulfLINK web site (*http://www.gulflink.osd.mil*) and *GulfNEWS*, our free, bi-monthly newsletter. To ensure our findings are readily available to the public, we publish all of our reports and other documents on GulfLINK. The site contains all of the public information we have collected related to Gulf War illnesses. We also offer e-mail communications on the site (*brostker@gwillness.osd.mil*). Through this service we are able to quickly respond to inquiries from veterans and the public. I hope (b)(6) will be able to use these resources to monitor our progress and resolve his questions.

(b)(6) asked for a list of symptoms related to nerve agent exposure. There is no set of symptoms identified for potential low-level exposures to chemical warfare agents. Current medical evidence indicates that long-term health problems are unlikely. There are several studies studying the issue funded by the Departments of Defense and Veterans Affairs. The most common symptoms reported by Gulf War veterans are fatigue, skin rashes, headaches, muscle aches, joint pains, abdominal pain, diarrhea, hair loss, memory loss, insomnia, depression, and mental concentration problems. These are symptoms not specifically associated with any single, possible cause. I have enclosed some background information about his potential exposure for (b)(6) reference.

If (b)(6) is healthy, there is no need to for him to seek medical attention. However, he is entitled to an examination if he would like one for peace of mind. If he is still on active duty, active in a Reserve Component, or has retired from the military, he can contact the Comprehensive Clinical Evaluation Program at (800) 796-9699. If he has separated from the military, the VA Persian Gulf Registry offers a similar examination; he may schedule by calling the VA at (800) 749-8387. (b)(6) has spoken with both of these agencies previously, but only with respect to getting information about chemical exposures which they are not set up to provide. Both programs offer a physical examination and laboratory studies, but he should know that there are no medical tests to detect if a person was exposed to low-levels of nerve agents some years ago. There is no charge to the veteran for these programs.

In his letter (b)(6) expressed concern about health problems related to reproduction. On June 6, 1997, the *New England Journal of Medicine* provided the results of an epidemiological study

of more than 75,000 children of Gulf War veterans and other service members on active duty during the Gulf War. Evaluating data on all live births at 135 military hospitals in 1991, 1992, and 1993, this study found no overall increase in birth defects among children of Gulf War veterans. The study provides strong scientific evidence that the children of Gulf War veterans are not more likely to suffer birth defects. We believe the work suggests that service in the Gulf War should not affect family planning or a veteran's decision on having children. I have enclosed a copy of the study for your information.

(b)(6) also expressed concern about the anthrax vaccination he received and the pyridostigmine bromide tablets he took. Anthrax vaccine was given to a limited number of service members for protection against biological warfare agent attack. The anthrax vaccine was then and is still a licensed, commercially-available product with an excellent health record in more than 30 years of use. Approximately 150,000 Gulf War veterans received at least one dose of the vaccine.

During Operation Desert Storm, the threat of nerve agent use by Iraq was very high. After careful deliberation by a specially constituted human-use review committee of the Food and Drug Administration, it was determined that pyridostigmine bromide could be instrumental in saving the lives of many service members. Their approval was based on extensive scientific information that supported the safety and effectiveness of pyridostigmine bromide as a preventive treatment.

Pyridostigmine bromide is not an exotic or experimental drug. The FDA approved it in 1955 for use in treating myasthenia gravis, a neuromuscular disease that causes muscle weakness and fatigue. However, when approved for use in the Gulf, the approval was as an investigational new drug – this classification signifies that it had not been formally approved for general commercial marketing as a nerve agent antidote. Part of our investigation of Gulf War illnesses aims to better understand how individuals during the war used the pretreatment drug. We are also seeking information on how it acted in the presence of other factors to determine if it played a role in the illnesses experienced by our Gulf War veterans. The Department of Defense is also supporting research to further evaluate the health effects of pyridostigmine bromide. A number of research projects are underway and a scientific review of the literature that we commissioned will be released soon.

I hope this information is useful to (b)(6) If he has additional questions he can contact our office via e-mail at the address above, or call (800) 497-6261 and speak with a member of my staff. You have my assurance we are doing everything possible to investigate and explain Gulf War illnesses – we owe it to the brave men and women who served our country. Unless we understand what went on in the Gulf and what may be making our veterans sick, we will never be able to make the changes necessary to ensure our forces are protected in the future. People are our first concern.

Sincerely,

Bernard Rostker

Enclosures

Congressional

CMAT Control #
1999145-0000014

(17)

	SECRETARY OF DEFENSE ROUTING SLIP	ACT COPY	INFO COPY			ACT COPY	INFO COPY
	SECRETARY OF DEFENSE		X		SECRETARY OF THE ARMY		
	DEPUTY SECRETARY OF DEFENSE		X		SECRETARY OF THE NAVY		
	THE SPECIAL ASSISTANT				SECRETARY OF THE AIR FORCE		
	EXECUTIVE SECRETARY		X				
	UNDER SEC FOR ACQUISITION & TECHNOLOGY				CHAIRMAN, JOINT CHIEFS OF STAFF		
	Director, Defense Research & Engineering				Director, Joint Staff		
	UNDER SECRETARY FOR POLICY						
	ASD (International Security Affairs)				BALLISTIC MISSILE DEFENSE ORGANIZATION		
	ASD (Special Operations/LIC)				DEFENSE ADVANCED RESEARCH PROJECTS AGENCY		
	ASD (Strategy &Threat Reduction)				DEFENSE COMMISSARY AGENCY		
	UNDER SECRETARY (COMPTROLLER)				DEFENSE CONTRACT AUDIT AGENCY		
	Director, Program Analysis and Evaluation				DEFENSE FINANCE & ACCOUNTING SERVICE		
1	UNDER SEC FOR PERSONNEL & READINESS	X			DEFENSE INFORMATION SYSTEMS AGENCY		
	ASD (Force Management Policy)				DEFENSE INTELLIGENCE AGENCY		
	ASD (Health Affairs)		X		DEFENSE LEGAL SERVICES AGENCY		
	ASD (Reserve Affairs)				DEFENSE LOGISTICS AGENCY		
	ASD (C3I)				DEFENSE SECURITY COOPERATION AGENCY		
	ASD (LEGISLATIVE AFFAIRS)		X		DEFENSE SECURITY SERVICE		
	ASD (PUBLIC AFFAIRS)				DEFENSE THREAT REDUCTION AGENCY		
	GENERAL COUNSEL				NATIONAL IMAGERY AND MAPPING AGENCY		
	INSPECTOR GENERAL				NSA/CENTRAL SECURITY SERVICE		
	DIR, OPERATIONAL TEST & EVALUATION						
	DIR, ADMINISTRATION & MANAGEMENT						
					C&D		X
					GWI		X

TYPE OF ACTION REQUIRED

	PREPARE REPLY FOR SEC OF DEF SIGNATURE		COMMENTS AND/OR RECOMMENDATIONS
	PREPARE REPLY FOR DEP SEC OF DEF SIGNATURE		INFORMATION AND RETENTION
1	REPLY DIRECT *(Forward copy of reply to CCD, Room 3A948)*	X	COORDINATE REPLY WITH LA
	APPROPRIATE ACTION		

Remarks:

102-18-1

REPLY DIRECT - MUST BE SIGNED BY COMPONENT HEAD

ACTION DUE DATE *(YYMMDD)*	ROUTING DATE *(YYMMDD)*	OSD CONTROL NUMBER
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JOHN E. PETERSON
5TH DISTRICT, PENNSYLVANIA
(202) 225-5121
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COMMITTEES:
APPROPRIATIONS
RESOURCES

Congress of the United States
House of Representatives
Washington, DC 20515-3805

May 14, 1999

The Honorable William S. Cohen
Secretary
Department of Defense
The Pentagon
Washington, D.C. 20301

Dear Mr. ~~Secretary~~ Bill:

As I am certain you are aware, there exists a growing concern among our armed services personnel as to the appropriateness of the Department of Defense's Anthrax Vaccine Immunization Program (AVIP). These concerns are mirrored by many Members of Congress, of which I am one.

Specifically, anxieties arise over the anthrax vaccine's long term safety as it relates to possible use of yet-to-be approved adjuvant formulations, and the soundness of its manufacturing process as it relates to numerous unflattering Food and Drug Administration inspections of the Michigan-based manufacturer of the vaccine. Giving further credence to service personnel's skepticism with AVIP is DoD's and the FDA's reluctance to clearly answer these concerns as posed by Government Reform Subcommittee on National Security, Veteran's Affairs, and International Relations Chairman Christopher Shays, and other subcommittee members, at several hearings on the vaccine's safety.

(b)(6) a constituent, was among those testifying at an April 29 hearing before the subcommittee. My rural congressional district is home to many armed service personnel who rely on G.I. Bills and other financial aid generated by their service, and lack the economic resources required to endure a dishonorable discharge or loss of benefits resulting from their noncompliance with AVIP. Many feel they must choose between their immediate economic livelihood and their future quality of life, which -- as subcommittee witnesses have testified -- could be negatively impacted by AVIP compliance.

In light of the questions raised by these young service men and women, by congressional hearings, and by the recent General Accounting Office report which found possible linkage of veterans' illnesses to vaccine administration, I respectfully request your consideration of administering AVIP on a voluntary basis -- or perhaps halting AVIP altogether until congressional have ultimately been addressed.

U08077 /99

STATE COLLEGE
1524 WEST COLLEGE AVENUE
STATE COLLEGE, PA 16801
(814) 238-1776
(814) 238-1918 (FAX)

TITUSVILLE
116 WEST SPRING STREET
TITUSVILLE, PA 16354
(814) 827-3985
(814) 827-7307 (FAX)

WARREN
224 LIBERTY STREET #3
WARREN, PA 16365
(814) 726-3910
(814) 726-0269 (FAX)

We owe, at least, this modest assurance to the brave men and women who serve our nation everyday. Not doing so may wrongfully obligate them to accept into their bodies a health-deteriorating agent with inadequately proven safety and effectiveness.

Thank you for your time and consideration over this matter. I eagerly await your reply.

Sincerely,

John E Peterson

JOHN PETERSON
Member of Congress

JEP/jlv

(18)

ONE HUNDRED SIXTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON GOVERNMENT REFORM
2157 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6143

MAJORITY (202) 225-5074
MINORITY (202) 225-5051
TTY (202) 225-6852

CMAT Control #
1999085-0000007

SUBCOMMITTEE ON HUMAN RESOURCES
Christopher Shays, Connecticut
Chairman
Room B-372 Rayburn Building
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Statement of Rep. Christopher Shays
March 24, 1999

This morning we begin the Subcommittee's oversight of the Department of Defense (DoD) force-wide Anthrax Vaccine Immunization Program (AVIP).

We begin with questions: Why now? Why this vaccine? Why a mandatory program? And why would active duty, Reserve and National Guard personnel jeopardize their military careers, and even their liberty, rather than take the vaccine?

After what has been described as a multi-year and deliberative, but for the most part closed process, DoD launched the AVIP in 1997. But anthrax was a known threat in the 1991 Gulf War. Vaccine development and acquisition against biological threats have been an explicit element of U.S. force protection policy since 1993.

Yet only now has anthrax been deemed the preeminent threat requiring this additional medical force protection measure unique to that single organism. If, as has been argued, it would be irresponsible, even immoral, not to use the available vaccine, what took so long?

To meet tomorrow's very real threat of biological weapons cocktails and genetically altered anthrax strains, DoD selected the vaccine approved by the Food and Drug Administration (FDA) almost 30 years ago. It has been described as crude and dated medical technology. The sole production plant is under renovation to address serious failures to follow good manufacturing practices which in turn can effect vaccine purity, potency and safety. Is that the best we can do?

The missing element of the mandatory anthrax vaccine program is trust. Radiation testing, Agent Orange, the reckless use of experimental drugs and mysterious Gulf War illnesses have made military men and women understandably distrustful of the Pentagon on medical matters. Although DoD appears to acknowledge the problem, AVIP brochures and web sites still seem heavy-handed and one-sided, glossing over legitimate concerns about the safety and efficacy of the vaccine, minimizing adverse reaction reports and blaming the Internet for fanning dissent.

But it's what they don't find on the Internet that gives many pause. There are no long term studies of the anthrax vaccine. Limited use by veterinarians and researchers since 1970 does not provide the statistical weight to project the vaccine's effects in 2.4 million young men and women. After vaccinating 150,000 Gulf War troops, DoD had a unique pool of subjects to study, but due to poor record keeping no large scale research has been conducted.

So those being ordered to take the vaccine face a profoundly personal choice, whether or not to put something in their bodies they fear may do more harm than good. After military service, the uniform comes off, but the anthrax vaccine stays with you for life. It's just not the commitment many dedicated men and women made to their country when they volunteered for military service.

We arrive at this inquiry after traveling a road that began for many veterans in the toxic battlefields of the Gulf War, where they were exposed to multiple vaccines, experimental anti-nerve agent pills and botulism toxoid vaccine, depleted uranium, low levels of chemical warfare agents, pesticides, oil fire smoke and more. We will follow it until we are sure medical force protection means assuring the long term health of U.S. forces not just short-term mission capability.

Thanks to all our witnesses for being here today. We look forward to your testimony.

(19)

WALTER B. JONES
3D DISTRICT, NORTH CAROLINA

ROOM 422
CANNON HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
TELEPHONE: (202) 225-3415

COMMITTEES:
COMMITTEE ON BANKING AND FINANCIAL SERVICES
COMMITTEE ON NATIONAL SECURITY
COMMITTEE ON RESOURCES

DISTRICT OFFICE
102-C EASTERNOOK DRIVE
GREENVILLE, NC 27858
(252) 931-1003
(800) 351-1697

Congress of the United States

House of Representatives

Washington, DC 20515–3303

April 22, 1999

OSAGWI

MAY 04 1999

The Honorable William S. Cohen
Secretary of Defense
3E880 The Pentagon
Washington, D.C. 20301

Dear Secretary Cohen:

I am writing with regard to the health and safety of our men and women in the military. Specifically, I am concerned about the impact of the required inoculation of the anthrax vaccine upon military personnel in light of disturbing reports that the Department, in some cases, may be administering non-FDA approved vaccines to military members.

After hearing from a number of my constituents, I now feel that I would be failing in my responsibility if I did not call attention to the legitimate questions of safety that surround the Department's policy of administering the anthrax vaccination. I have heard from too many military officers from the state of North Carolina alone, whose fierce loyalty and dedication to this country has forced them to offer their resignation from the service rather than disobey a direct order to receive a potentially unsafe immunization.

I fully recognize the imperative to provide our men and women in uniform protection against unconventional threats such as biological weapons. However, I am concerned that the Department may be moving ahead with implementation of an anthrax vaccine program prior to conducting the full range of scientific and medical tests necessary to appropriately reduce the risks of unintended health consequences for those required to receive the inoculation.

In this regard, I believe the Department must proceed with maximum caution in light of its inadequate response to veterans who have contracted serious and debilitating illnesses as a result of their service to the nation during the Gulf War. In particular, I find it troubling that the Department of Defense continues to deny a correlation between military personnel receiving inoculations administered by the Department during the 1990-1991 period and such illnesses irrespective of a recently released General Accounting Office (GAO) report that has confirmed the presence of the squalene antibodies in sick veterans. These antibodies have been found in the blood of uniformed personnel who served overseas as well as of those who remained within the continental United States throughout the conflict.

Mr. Secretary, I am certain you share my conviction that we, in both the Congress and Executive Branch, cannot falter in our responsibilities to ensure the health, safety, and welfare of those who serve their country in uniform. The GAO report recommended to Congress that the Department of Defense immediately begin studying the discovery of antibodies in the blood of military personnel exhibiting characteristics of so-called Gulf War Illness for the presence of squalene anitbodies. I believe the recommendation of the GAO is sound and I request the Department expeditiously move forward on such analysis. Additionally, I urge you to impose a moratorium on involuntary anthrax vaccinations until a more thorough examination of the connection between previous vaccinations and adverse health affects has been completed.

I appreciate your attention to this critical issue. I look forward to your action and reply.

Sincerely,

Walter B. Jones

Walter B. Jones
Member of Congress

(20)

STENOGRAPHIC MINUTES
Unrevised and Unedited
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PROTECTING THE HEALTH OF DEPLOYED FORCES:

LESSONS LEARNED FROM THE PERSIAN GULF WAR

Tuesday, March 25, 2003

House of Representatives,

Subcommittee on National Security,

Emerging Threats, and

International Relations,

Committee on Government Reform,

Washington, D.C.

Committee Hearings

of the

U.S. HOUSE OF REPRESENTATIVES

OFFICE OF THE CLERK
Office of Official Reporters

I'm a tennis fan. I think we'll start with you, Dr. Winkenwerder.

STATEMENTS OF WILLIAM WINKENWERDER, JR., M.D., M.B.A., ASSISTANT SECRETARY OF DEFENSE FOR HEALTH AFFAIRS, DEPARTMENT OF DEFENSE, ACCOMPANIED BY MICHAEL E. KILPATRICK, DEPUTY DIRECTOR FOR THE DEPLOYMENT HEALTH SUPPORT DIRECTORATE, DEPARTMENT OF DEFENSE; ROBERT H. ROSWELL, M.D., UNDER SECRETARY FOR HEALTH, DEPARTMENT OF VETERANS AFFAIRS, ACCOMPANIED BY K. CRAIG HYAMS, CHIEF CONSULTANT, OCCUPATIONAL AND ENVIRONMENTAL HEALTH, DEPARTMENT OF VETERANS AFFAIRS

STATEMENT OF WILLIAM WINKENWERDER, JR.

Dr. WINKENWERDER. Thank you, Mr. Chairman. Mr. Chairman, members of the subcommittee, thank you for the opportunity to appear here today. With your permission, I will summarize my written statement. And also with me today to answer questions, if that is acceptable to you--.

Mr. SHAYS. That is fine.

Dr. WINKENWERDER. --is Dr. Michael Kilpatrick, whom you've already introduced.

I want to begin--.

Mr. SHAYS. Let me just ask, can you all hear in the back of the room? No. I need you to speak up a little louder. Thank you very much. It is the silver mike that projects your voice.

Dr. WINKENWERDER. All right. Thank you.

I want to begin by adding my condolences to those of President Bush and the Secretary of Defense for the families' of the United States casualties since operations began last week. Each of you is in our prayers. Our country's ultimate weapon against any enemy is the valor of the men and women in our armed services who serve the cause of freedom. They comprise the most powerful force on Earth, and, in this particular case today, a force for peace and liberation of the Iraqi people.

On behalf of all the men and women in medical service to our Armed Forces, I want to recognize the cause for which many have now given their lives and the efforts to ensure the safety of everyone engaged in this conflict. The courage, skill and discipline of our military medical personnel is matched only by the high-quality, swift and effective medical care that they provide.

You have already seen reports by embedded media of heroic acts by U.S. Armed Forces medics to save lives; for example, the MediVac crews and surgical teams that have gone into very dangerous situations. We can be assured that today such acts

will continue, and they will continue until our final mission is accomplished. In Operation Iraqi Freedom we have more than sufficient capability to move casualties from their point of wound to any level of care their injuries might require. We have more than sufficient medical supplies, including blood supplies, for all of our troops operating in the field, and all of this is regulated by an integrated logistics system in the theatre.

Our medical and soldiers--our medical medics and soldiers are trained, equipped and prepared to operate in the contaminated environment, if necessary, with equipment decontamination and antidotes. We are prepared for what Saddam Hussein might attempt to deliver to United States forces.

As the Assistant Secretary of Defense for Health Affairs, safeguarding the health and safety of our military members is my highest priority. Our force health protection program has made great strides based on the lessons learned from the Gulf War and subsequent deployments. I believe our efforts are in line with your own objectives, as these have been expressed in public law.

The Department is committed to providing an ongoing continuum of medical service to service members from entrance into the military through their separation and as many transition to the Department of Veterans Affairs after their

service.

The vigorous requirements of entrants' physical exams, periodic physical examinations, periodic HIV screening, annual dental examinations, routine physical training and periodic testing and then regular medical record reviews are all part of this continuum.

We've established a comprehensive program to sustain and document our service members' health and fitness for duty. All deploying personnel are required to complete individual predeployment health assessments. These health assessments are coupled with a review of medical and immunization records. We look at whether there is a DNA sample on record, and if a blood serum sample has been drawn within the prior 12 months. This information is considered, along with the availability of personal protective and medical equipment. Predeployment briefings on deployment-specific health threats and countermeasures are also provided. All personnel complete postdeployment health assessments when they return.

Any indication of health concerns results in an individual health review and, if appropriate, referral for further medical evaluation or testing. These health assessments are to be maintained in the individual's medical records and centrally in electronic format in the defense medical surveillance system.

Additionally, all immunizations are tracked by

service-specific systems, and the data are fed into a central database. We're currently transitioning from paper-based medical records to automated medical records for patient encounters and reporting of nonbattle and disease events.

Health care focused on postdeployment health concerns is available through both military and VA providers who are using jointly the postdeployment health clinical practice guidelines. These guidelines were designed to ensure that the medical providers render effective and appropriate responses to the medical concerns of our deployed service members and their families upon return.

We've established three deployment health centers. One focuses on deployment-related health care, one on related health surveillance, and the third on health research. All are working towards prevention, treatment and understanding of deployment-related health issues.

Desert Shield, Desert Storm taught us knowledge of the environment is vital if we're to protect the health of our service members. Today the Army's Center for Health Promotion and Preventive Medicine conducts environmental health assessments that enable intelligence preparation of the battlefield before and during deployments. This unit employs equipment to monitor the combat environment, and it samples soil, air and water. They also perform extensive environmental assessments of staging areas and base sites.

This information is used to make determinations of where we can safely put our military people. We also archive that information so that we can go back amend, look at it later to evaluate for correlation between an area of known or suspected exposure and illness that may appear in the future.

In the past few months, we've been working to develop and have implemented a joint medical workstation. This is an important development. We're using a Web-based force health protection portal to our classified system, and DOD now has the electronic capability to capture and disseminate real-time and near real-time information to commanders about in-theatre medical data, patient status, environmental hazards, detected exposures and critical logistics information like blood, beds and equipment availability.

The transition from paper-based processes to automated systems offers us a much greater opportunity for collecting and analyzing medical information that is useful in real time. We proceed with that work with an awareness of operational security and personal security for our service members who expect their medical records to remain confidential.

When we deploy, we bring a formidable medical capability. This includes far-forward surgical care, and we've seen this on the battlefield just in the past few days; medical evacuation assets, with the ability to provide intensive

care, ICU care, inside an airplane; and ship-based medical capabilities.

In the event of a biological or chemical attack, we also maintain significant decontamination equipment and the ability to treat both chemical and biological casualties. All services have made training improvements, and they've been significant to do that, to assure that their medical personnel can work successfully in a contaminated environment and decontaminate and rapidly evacuate their patients to safer environments.

Much has been accomplished in the past decade. Our level of effort and our capability to protect our forces is unprecedented in military history. However, today we face new and deadly threats and the possibility that a brutal regime would use chemical or biological weapons.

As military professionals and as health professionals, we're well aware that war, and particularly this war, involves real risks, but our message to you, to our service members, to their families, to the American people is that we're prepared, and we have extraordinary capability to protect and care for our people.

Mr. Chairman, I thank you again for inviting me here today. I'm pleased to answer your questions, and I know there will be many. Thank you.

Mr. SHAYS. I thank you.

I'm pretty clear, when we voted on this law, what that meant to me. I'm just curious to know why we're not seeing it implemented. And, Dr. Winkenwerder, would you kind of tell me why not?

Dr. WINKENWERDER. We believe that we are following the law, and that we're doing it in a way that makes sense. As you read--and I think it is very helpful to read the actual language of the law here--you note the fact that we're required to develop a system to assess the medical condition. I think that's the operative point. It is to understand what is the baseline health, and when one is looking at a young generally healthy population, the most useful information to ask--or to determine the health of the--the health status of that individual is a set of questions. I think, from my experience as a physician, that history-taking is really the most useful information to get a picture of the health status of the individual, not so much a hands-on physical examination. Usually those types of examinations are of very limited value.

We do perform periodic full physical examinations, along with the drawing of blood, but it is our view that we are meeting the letter and the spirit of the law--.

Mr. SHAYS. Let me just tell you, from my standpoint, you're not meeting the letter of the law clearly, and I don't even think you're meeting the spirit of the law.

So I'd like to know where it says that this examination should be a self-assessment. Where in the law do you read self-assessment?

Dr. WINKENWERDER. Well, it is not only a self-assessment. There is a review by a medical provider with questioning by the medical provider that gets at the history of the individual, the medical history of that individual.

Mr. SHAYS. The challenge that I have is that we've had countless numbers of hearings since Gulf War, because our folks came home sick; 125,000 thousand are registered with the VA out of 700,000. And it started out when we had our hearings that the government officials would respond and say, no one came home sick, and our second panel were people who were sick, and you knew they were sick just looking at them. And then when you heard their history--so we then reversed it. So we had them go first and then had the VA and DOD come second and be the second panel.

What I'm struggling with right now is we didn't accept self-assessment when our VA folks--when our military folks came back. We gave them a physical. And we didn't ask them to fill out a questionnaire. With we gave them a physical. I can understand you'd have them fill out a questionnaire, but doesn't the law say that there's supposed to be a medical examination?

Dr. WINKENWERDER. Well, again, medical examination and physical examination are not synonymous. Some may have read that to be the same, but as a physician, I would say that they're not the same.

Mr. SHAYS. You know--.

Dr. WINKENWERDER. What we're attempting to do ~~to~~ really--to answer your question, which I think is a very fair question, is to ensure that we have a good baseline of information for every individual that gives us what we need to know about the health status of that individual.

Now, I will--I'll stop at that. I was going to go into the issue of the postdeployment.

Mr. SHAYS. Well, I'm sure you'll have an opportunity.

Let me just say before I recognize Mr. Kucinich that one of the challenges with the concept of medical examination versus physical examination is that it reminds me of what was alluded to by Mr. Kucinich when we went to DOD and questioned whether our troops had been exposed to chemical weapons, and we found them using the word, they weren't exposed to offensive use of chemicals.

And then we had a hearing in which we had a video of the blowing up of Khamisiyah, and DOD has a press conference on Friday at 4 o'clock before our Tuesday hearing to disclose that our troops were exposed to defensive chemical exposure. And I just hope we're not getting a play on words here.

So at any rate, Mr. Kucinich, you have the floor.

Mr. KUCINICH. Thank you very much, Mr. Chairman. Again, I want to thank you for demonstrating your concern for the men and women who serve by calling this hearing.

Dr. Winkenwerder, I would like to ask you about the press release that you issued in January. In it you made a broad statement. You said the U.S. military is prepared to protect its personnel against the use of biological weapons. That's a direct quote. You stated that, quote, America's troops are well trained and protected with a robust multilayered set of defenses against bioweapons, unquote.

Now, you say the troops are prepared. Does your definition of prepared include training in a realistic environment?

Dr. WINKENWERDER. Yes.

Mr. KUCINICH. But, Dr. Winkenwerder, the GAO testified before this subcommittee last fall, quote, no realistic field exercises for medical personnel of chemical and biological defense have been conducted. None. How can you say that you're prepared with no chem-bio field exercises for your medical personnel?

Dr. WINKENWERDER. That study, if it is the same one that I believe you're referring to, was in 2001. That is the time when that information was collected was approximately 2 years ago. And I can just tell you that since that time there has

been an intensive effort to train a large number of people, both nonmedical and medical.

When I took my position about 18 months ago and then was before this committee about 14 months ago or 13 months ago, I think, now, I committed to you that this matter of training people would be one of my highest priorities.

Mr. KUCINICH. Thank you.

Dr. WINKENWERDER. And let me just say, we issued--.

Mr. KUCINICH. Doctor, I've got a question here that is a follow-up, and I appreciate you taking this time to answer the question, but I have another question.

Dr. WINKENWERDER. Okay.

Mr. KUCINICH. And that is that are you familiar with the war game called Millennium Challenge 2002?

Dr. WINKENWERDER. Generally. So yes, I--.

Mr. KUCINICH. You say we're talking about 2001. Now let's go to 2002. That was the largest war game in American history, and it was also the most expensive at $250 million. It involved over 13,000 soldiers, sailors, airmen. But when the commander claimed the enemy wanted to simulate the use of chemical weapons, he was told to disclose his troop locations and be destroyed. He told the Army Times that instead of testing against the most urgent threats, the game was rigged. Now, how can you say, 2002, that you're prepared, when from this report realistic field testing had not been done?

Dr. WINKENWERDER. I'm not going to try to speak for our commanders in the field, Army officers that planned and conducted those exercises.

Mr. KUCINICH. But how do you answer the question, though? Do you have an answer to that question?

Dr. WINKENWERDER. Well, I can't answer your question, because I'm not in a position--.

Mr. KUCINICH. Let me move on to the next question if you can't give me an answer.

Mr. WINKENWERDER. Well, let me just stay this. I stand by what I've said in terms of the preparation of our medical personnel to operate in those environments, the preparation and training to care for people, whether there's been exercises--.

Mr. KUCINICH. Doctor, Doctor, with all due respect, you said you stand by what you said, but I gave you an example that contradicted what you said, but you still stood by what you said. Now, I just want that on the record.

Does your definition of "prepared" include providing troops with the minimum level of necessary chem-bio equipment as said by you and the Defense Department?

Dr. WINKENWERDER. The minimum level of equipment to protect people would be part of being prepared, absolutely.

Mr. KUCINICH. And in light of all the equipment shortages identified by the GAO, the critical deficiencies

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identified by the Army audit agency and the false inventories identified by the inspect general, tell me, Doctor, how can you assert that you're prepared?

Dr. WINKENWERDER. The first thing I would say to you is you're bringing up issues that are not directly within my area of responsibility, but I will tell you, based on my conversations with other people in the Department of Defense who do have some responsibility in that area, that the concerns about suits and equipment have been addressed, and that there is confidence, a high level of confidence, that the issues that you refer to have been addressed and that people believe that we are prepared.

Mr. KUCINICH. Mr. Chairman, thank you. I just want to conclude with this. Now, the doctor has said that the problem has been fixed, and we were told this as well, and that's why Congresswoman Schakowsky, who was part of our last committee, wrote to Secretary Rumsfeld and asked him to certify to Congress that these minimum required levels of chem-bio equipment have been met. She got her answer 3 weeks before the war, and her answer was no.

Dr. WINKENWERDER. I'm not sure--I might respond, because I think this is an important issue.

Mr. SHAYS. Sure. I do want you to respond. And I would like the gentleman to put on the record the letter. I think the letter didn't say no. I think it said they had two

JSLIST suits, which then you could interpret as not meeting the minimum requirement. The JSLIST suits have 30 days each to them.

Dr. WINKENWERDER. Right.

Mr. KUCINICH. Mr. Chairman, here is the letter.

Mr. SHAYS. We'll put that in the record.

[The information follows:]

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Mr. KUCINICH. Here's the letter, here's the response, and it's very clear the answer was no.

Mr. SHAYS. For the record, since this is so technical, find the--where the no is on that letter.

Mr. KUCINICH. The text of this does not answer the question as far as certification.

Mr. SHAYS. Okay.

Mr. KUCINICH. She asked for certification. If the Secretary of Defense will not certify that these suits are okay, the American people have a right to know that. The answer was no.

Mr. SHAYS. I got the same letter, and my interpretation of it was that he was certifying that they would have--well, I first have to make sure I have the same letter. I'll look at it and then--.

Dr. WINKENWERDER. I want to attempt to answer your question, even though I want to be clear that the issues you're talking about are not within my area of responsibility, but I don't want to avoid trying to answer the issue that is in front of us.

Mr. SHAYS. I realize we have a 5-minute rule, but I will extend a little more time if a Member, you know, is nervous that the answer is a little long. But I don't want to have the answer not be thorough enough to respond.

Dr. WINKENWERDER. The issue with respect to chemical

protective suits, I believe you're referring to, is the number of them, and each service member has been issued at least two, and I'm told--the information I have is that each will have three within a matter of less than a week.

Now, obviously that's to reach 100 percent. So they've been moving towards that target obviously for the last several weeks. So the--and then I think there was another issue with some defective suits, and, again, I'm going to relate to you my best understanding of that, but my understanding is that those have been removed from the inventory, and there was a very deliberate, scrupulous effort to remove all of those suits, and they are not being used in this situation today.

Mr. SHAYS. Well, we'll be here for a bit, so we can nail this one down.

Mr. Turner.

Mr. TURNER. Dr. Winkenwerder, I just recently met with representatives from the Ohio National Guard, and they were talking to me about the issue of National Guard reservists that do not have a continuous health care coverage. They have indicated numbers between 20 and 40 percent of the reservists do not have continuous health care coverage for insurance.

To what extent do you have a concern that that might have an impact on the medical condition of those deployed?

Dr. WINKENWERDER. If I might just ask you, the 20 to 40 percent, is this without health insurance coverage, and they're sort of private--.

Mr. TURNER. Correct. Correct.

Dr. WINKENWERDER. My hope is that it would not impact upon their health status. We do have a check on that, however, and that is that we require a certain level of medical readiness before people come on to Active Duty, and so we would hope to screen for and identify individuals who are not medically ready to serve.

Obviously the issue of health insurance or the lack thereof among certain members of the population is an ongoing problem.

I will say that with respect to caring for National Guard and reservists and their families, when they come on Active Duty, they are eligible for the military health system benefit program, TRICARE. We've made--in a change that we had just 2 weeks ago, made it easier for them to gain coverage for their families. There had been a glitch in the system where if a person was living, for example, in one part of the country and got deployed from another, that because they weren't residing with their family--or their family wasn't residing with them, they would not be eligible. We changed that. They're now eligible right then and there. There was also a hurdle that one had to be activated for 180

days. We changed that and said they only need to be active for 30 days. So all those benefits are commensurate between reservists and Guard and our ongoing Active Duty.

And we gladly did that. Our reservists and Guard are playing a very important role in this conflict, and particularly so in the medical area. So it's important that we take care of them.

Mr. TURNER. Thank you.

Mr. SHAYS. Thank you. I think we will go to Mrs. Maloney.

Mrs. MALONEY. A few, Mr. Chairman, and I want to be associated with your comments and those of the panel in appreciation of our men and women who are serving in the armed services.

I would like to ask some questions that were raised in this book, Saddam's Bomb Maker. It was written by Khidir Hamza, who says that he was in charge of Saddam's efforts to secure materials from foreign governments to build nuclear bombs, and he also talks about their chemical and biological weapon program. And I would like permission to place in the record page 244 and page 263.

[The information follows:]

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Mrs. MALONEY. And he raises really an alarming statement, and I would like to just quote from his statement here. He says, the Gulf War syndrome was well known to everyone in Iraq, but Saddam remained silent. In this he had a secret ally, the U.S. Pentagon, which continued to deny that there was proof of a war-based disaster--war-based disease despite growing evidence to the contrary. But evidence soon leaked of allied forces blowing up chemical dumps during the war and of the U.S. Government efforts to suppress repeated efforts of reports of the contamination of our troops.

He also on page 244 talks about Saddam's effort to put biological--or that he did put, according to him, biological and chemical weapons into missiles that he was going to fire on the U.S. military if they went into Baghdad, but that he had a more sinister plan in that he buried chemical and biological weapons in southern Iraq, knowing that the tactics of the U.S. military would be to blow up the bunkers; therefore, they would release the contaminated material, they would not even know that they were affected, and that they would then be laden with chemical and biological disease from these terrible weapons.

I'd like to ask you if you, number one, have read the book; number two, your comments on what Saddam's bomb maker, Mr. Hamza, who is now a--has defected to the West and I

understand is working with our military and has been very outspoken against Saddam in hearings and publicly and so forth.

Dr. WINKENWERDER. I have not read the book, Congressman. I have heard of the book. And by all accounts, it is a--from what I understand, is a reliable piece of information.

Mrs. MALONEY. Are you aware that our troops were exposed to these biological weapons? The allegation that he makes that out Pentagon knows, that Saddam knows, that people in Iraq know that our troops were exposed to these terrible chemicals in the Gulf War?

Mr. WINKENWERDER. Well, from all the information that I've been presented during my tenure, no one has ever indicated to me that there is any knowledge of an acute exposure or the exhibiting of symptoms that would suggest an acute exposure to chemical or nerve agents during that conflict.

Mr. SHAYS. Would the gentlelady yield? I'll make sure she gets additional time.

Mrs. MALONEY. Sure.

Dr. WINKENWERDER. That is a separate question, an acute exposure, someone who is acutely ill, than the issue of whether there were low levels of exposure--.

Mrs. MALONEY. Were there low levels of exposure?

Mr. WINKENWERDER. Well, that is what the whole Khamisiyah incident is about.

Mr. SHAYS. This is very important, and I don't want--since this is testimony under oath, I do want to make sure. There are really two issues, but one issue is sites. The only one that the Department of Defense has acknowledged is Khamisiyah. So I would love it if you would ask the question of whether there were other sites, and then get into this other shoe. But I want to make--.

Mrs. MALONEY. Were there other sites besides Khamisiyah where they were exposed to chemical weapons?

Dr. WINKENWERDER. Not to my knowledge.

Dr. Kilpatrick.

Dr. KILPATRICK. I can answer that. In looking at--.

Mr. SHAYS. A little closer to the mike, Doctor.

Dr. KILPATRICK. In looking at the air war campaign, it's very clear that his storage sites at Al Muthanna and Mahamadia, that there were releases of chemical agents. In one location we have no indication there were American troops in the area where that plume would have gone, and the other area there were possibly up to 70 Special Forces people in that area, but there were no coalition forces or American forces in that area.

Then Khamisiyah is the third area, and that's been widely publicized and put out, and certainly we've identified the

101,000 American forces who were in that hazard area that was determined.

Mrs. MALONEY. Well, Mr. Hamza alleges that Iraqis were likewise exposed, and women gave birth to deformed children. People died of cancer early. People had Parkinson's-like neurological problems. And he blamed it all on malnutrition, according to this professor, and he likewise said that the same symptoms--or he alleges are now in the troops who regrettably were exposed to these terrible chemicals in the war.

If you have any other information, if you could get back to the chairman on it, on how many troops we think were exposed, where they were exposed and what chemicals--what chemicals do we think they were exposed to? Do you have an idea of what the chemicals were or biological weapon they were exposed to? Do you have an idea what it was?

Dr. WINKENWERDER. Yes.

And Dr. Kilpatrick.

Dr. KILPATRICK. In all three areas, it was sarin--cyclosarin were the agents that we were concerned about. As far as biological agents, we don't have any indication that American troops were exposed to biological agents. We do know that bombs and rockets filled with biological agents were found by the United Nations Special Commission, but we have no indication that they were ever

launched against Americans.

Mrs. MALONEY. Excuse me. Go ahead, Mr. Chairman. My time is up. I'd like to continue with this questioning.

Mr. SHAYS. Why don't you ask the next question, and then we'll--.

Mrs. MALONEY. If you have another question.

Mr. SHAYS. I just want to say to you that it's a little unsettling to me, because we've had so many instances--DOD has insisted that the only place that our troops were exposed was at Khamisiyah, and now we're hearing that we had other troops that were nearby. So I'm not sure whether I should consider this new information or old information, but it is a little unsettling to me, because either way it's new to me. And so I want to be clear that you have said that--there were two other sites. I want you to say what those sites were, and I want you to be very clear as to what level of the amount of chemicals we think were on site and compare them to Khamisiyah.

Dr. KILPATRICK. Those reports we released in the last 2 years, and I can get you specific details. Al Muthanna is one site, and Mahamadia is the other site. These were large production storage sites in Iraq near Baghdad, and they were damaged during the air war. We don't know exactly which day, because the bombing ones in each of those sites were somewhat over 17 days. We don't know whether the release was at one

time or over multiple periods of time. The determination of the hazard area assumed a release of all agent at one time, and the amount of agent is information that we receive from CIA, and they have recently released a report to give that amount. We can provide that to you.

Mr. SHAYS. Well, I understand we have the GAO looking at this, but--the plume modeling--but one thing I want to ask you would be then how many American troops do you think--first off, it's unsettling no matter what humanity was there, but how many Americans do you think were at--.

Dr. KILPATRICK. At Al Muthanna, we don't believe there were any Americans in the area. At Mahamadia, we believe that there were up to 70 Special Forces, and we have identified them and notified them.

Mr. SHAYS. And have you notified the VA?

Dr. KILPATRICK. And that's been done also, yes.

Mr. SHAYS. Okay. I thank the gentlelady for asking those questions.

Mrs. MALONEY. Mr. Chairman, could I follow up with other sites that--.

Mr. SHAYS. Yeah. Why don't we do that real quick.

Mrs. MALONEY. They mentioned that they had it really as a war strategy, burying these chemicals knowing we might bomb them. The symptoms would not arise until weeks, months later. They would not know where it came from.

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[1:59 p.m.]

Mrs. MALONEY. But they mention that--he mentions that they were buried, thousands of chemical weapons in southern Iraq at Basra, Nasiriyah, Simawa, Diwaniyah, and Hilla, the likely routes of the allied invasion. And he says that that's what they did, and that we walked into that trap.

Dr. WINKENWERDER. I think you can conclude that this provides a good window into the twisted mind of Saddam Hussein.

Mr. SHAYS. But is that an answer that is a yes?

Dr. WINKENWERDER. We will take that information for the record, and certainly--.

Dr. KILPATRICK. And I have no information at this time to be able to comment positively or negatively. I have no knowledge that that in fact is true.

Mrs. MALONEY. Just very briefly, for years, literally, the Pentagon denied that they were exposed to chemical weapons, and he says that in the book. Why did we do that when we knew that they were exposed? And when did we acknowledge in the time frame that they were exposed to chemical weapons?

Dr. WINKENWERDER. Let me just say this. I cannot speak for those who had my responsibility or were associated with

those responsibilities 5, 6, 7 years ago, at the time the information began to come to light.

Mrs. MALONEY. But can you get us that information?

Dr. WINKENWERDER. Well, what I can tell you is that I am committed to getting that kind of information out and making it available, and that we know what happened. I think it is in everyone's interest, our service members, their families.

Mrs. MALONEY. And you will get that information to the chairman, so we can--.

Dr. WINKENWERDER. We will take your request. But I just want you to know that I am committed to making that kind of information--and we have sought to establish a track record with this for the release of the information regarding the SHAD.

Mr. SHAYS. Let me just say. You are not just taking the request. You are going to get us the information, correct?

Dr. WINKENWERDER. We will.

Mr. SHAYS. Thank you.

[The information follows:]

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Mr. SHAYS. Mr. Murphy, thank you for being so patient.

Mr. MURPHY. Thank you, Mr. Chairman. Are there differences between British troops and American troops in the Gulf War syndrome incidents?

Dr. WINKENWERDER. I am going to turn to Dr. Kilpatrick for that.

Dr. KILPATRICK. I think the research that has been done to date shows that there is tremendous similarity, not really difference. As far as numbers of British troops, the numbers of course are smaller. They had deployed some 50,000 and they've had some 3,000 people go through their health assessment program, which is very similar to our clinical--comprehensive clinical evaluation program, the VA's Persian Gulf registry program.

Mr. MURPHY. Is anybody still pursuing the line--I found the article from Pain and Central Nervous System Week from a year ago, a year ago last week, saying that research teams identified clusters of postcombat syndrome, some debilitating syndrome from the Boer War and the First World War, somatic disorder focused on the heart from the First and Second World Wars, and neuropsychiatric syndromes, in essence saying that every war seems to have those.

Are people still following that or has that been seen as not scientifically valid to say that perhaps Gulf War syndrome is similar to what is seen after every war?

Dr. WINKENWERDER. My answer to that is that even though different kinds of issues and maybe even some similar kinds of issues do occur in all wars, we saw something and later better understood something coming out of the Gulf War that was a constellation of symptoms and complaints that were quite real, that were occurring in higher proportion among those people who were deployed than among those who didn't deploy.

So I would distinguish what we saw there from what maybe had occurred in other, prior wars.

Mr. MURPHY. I have also read some studies that have looked at animal studies of some chemicals used for example for insect control and other things, particularly DEET, permethrin, and an antinerve gas agent, pyridostigmine bromide--I hope I am pronouncing that right--PB, which was administered to both U.S. and British troops; and have found a number of problems--cell degeneration, cell death, animal behavior differences--and have found that those things were exacerbated more when the animals were under stress, et cetera.

Given that these were--there also seems to be an additive effect, a multiplier effect, that any individual chemical, when used alone, doesn't have that, even when the dosage of those chemicals is low. But when you add them together, you end up with some pretty severe outcomes.

With those, that kind of data, have there been changes in how the military is using such things as immunizations, insect control agents, and other things in dealing with the Gulf War now?

Dr. WINKENWERDER. First of all, let me just say that the area that you are talking about is an area of research that we continue to support and believe is very important to better understand whether a variety of simultaneous or near-simultaneous insults from low-level agents produces these effects. And that is very important work. It is ongoing. We are supporting that.

I would distinguish that from immunizations. From my perspective, particularly with respect to the use of the anthrax vaccine, we have had millions of doses given. We have followed all of that very closely for the last several years, and from my perspective, don't believe that there is any--and I think others would corroborate this, experts, outside experts, Institute of Medicine--that there is any association between the use of that vaccine and any of the symptoms that we saw.

Mr. MURPHY. Not even an interactive effect with these agents?

Dr. WINKENWERDER. Not with respect to the vaccine.

But I think your other point is very well taken in terms of low-level chemical exposure, nerve agents and pesticides.

The way they work in the body is similar, and so you could hypothesize or theorize that there might be this additive effect. And I think that is important work that is ongoing, and we are supporting that.

Mr. MURPHY. Is that changing, though, how--a lot of what is being done that we are talking about here is the epidemiology of exploring pre- and post-data. But I am just wondering if there has been a difference in handling things like insecticides and knowing that there may be nerve agent exposure.

Dr. WINKENWERDER. There have been some changes in the use of pesticides and pesticide management policy, and I think the long and short of that is that they are used more sparingly and more carefully, and with a lot better documentation and control. So that is something that we had already begun to respond to and change practice.

Mr. MURPHY. One other factor I want to ask, perhaps because of my background as a psychologist. But what I see frequently in these studies is the impact or the interactive effect of stress upon any of these.

Can you comment on how that works?

And it also relates to some of the comments--you talked about soldiers who are in the actual theater of war and those who remain home.

Dr. WINKENWERDER. I think it is certainly plausible that

stress could add to any sort of physiologic--yeah, and as Dr. Roswell was saying. But I would distinguish that from saying that stress alone is responsible for the symptoms; I don't happen to believe that.

Mr. MURPHY. I understand. I just think as we discuss these things, as one is looking at pre- and post-histories, that getting some understandings of the mental health, which is oftentimes extremely difficult to get from just a self-disclosing questionnaire, is very important.

That is not to say that these folks have mental illness, that is not--although some may have post-traumatic stress syndrome. It is important to understand that stress has an impact on many diseases, cancer being one on which there has been extensive amounts of research. And one that you can't build a cure to protect you from that, but it is one that we need to be aware of, how we help soldiers with that.

Dr. WINKENWERDER. We agree with you.

Mr. MURPHY. Thank you, Mr. Chairman.

Mr. SHAYS. Thank you, Mr. Bell, your patience. And you have the floor.

Mr. BELL. Thank you very much, Mr. Chairman.

I want to follow up on some lines of questioning that were begun by my colleagues, Congresswoman Maloney and Congressman Kucinich. I want to begin with this letter that Congressman Kucinich referred to, since we didn't really--I

know it's been offered for the record, Mr. Chairman, but we didn't really get to delve into the text.

And I would disagree with my colleague that it was a no; actually, it was a little more disturbing than that in that it was a non-answer completely. And Representative Shakowsky had asked a very direct question in her letter to the Department, requesting information on the suits and would they provide protection for our troops. And I am not going to read the entire letter since it has been entered in the record, but where you come to the paragraph where he could easily answered the question yes or no, he says, instead:

"since Operation Desert Storm, the Department of Defense has fielded a new and improved CD, defense detection equipment and individual protective equipment. Every service member, to support near-term operations in Southwest Asia, will carry at least two of the newer, joint service lightweight integrated suit technology JS list suits and will have an additional two suits in contingency stocks. The contingency suits will be the battle dress overgarments, BDOs, until replaced by JS list suits." .

So we know what they will have in terms of supplies, but we have no idea whatsoever whether they are safe because nowhere in the letter of response does it say that they are safe. And I think the frustration felt by me and some of my colleagues in recent weeks is that it is hard to get a direct

answer.

And the purpose of this hearing is to focus on lessons learned from the Persian Gulf. Persian Gulf War syndrome was not something that was immediately announced after the Persian Gulf War, if I recall correctly. I was not--obviously not serving as a Member of Congress at the time, but if memory serves, it took months, perhaps years in some cases, for all the information regarding that syndrome to filter out regarding what people had been exposed to.

And we are highly critical of our enemies in this conflict as to their propaganda machine. And I am not saying that our information system compares to that in any way, shape, or form, but it does seem that we do engage in misinformation sometimes. And I would like for your comments on that and whether you think that we could learn a lesson from the Persian Gulf War and perhaps do a better job of educating both Members of Congress and the American people as to the risk we face. Because I don't think any right-thinking individual in this country believes that we don't face very serious risk by going forward with this conflict.

Dr. WINKENWERDER. Congressman, I can just assure you there is no thought of misinformation or trying to misinform either our service members or the public. That does not serve any of us in the short run or the long run.

I think that, from my review of what transpired in the past, it did take months and years to find out more about what happened. I do believe that that has informed a lot of action and activity on the part of the Congress, as well as DOD and VA, to put into place better recordkeeping, better tracking, better equipment, better monitoring detection across the whole board.

And my conclusion is that we are prepared. However, we face an enemy that is prepared to use some of the most lethal and awful weapons we have ever known, and that is a daunting situation. So I don't think there is any effort to tread lightly over this issue or to not acknowledge the seriousness of the risks that are out there. These are very serious risks that we face.

Mr. BELL. And I think that is a very important statement, because by putting a statement on the record that we are prepared, basically you put yourself in a position that, if we come up against something that we really didn't know we were going to come up against during the course of this conflict, then you are in a box if we come back and face something and you have to say, well, we weren't prepared completely for that.

But aren't we in a situation, Doctor, where it is almost impossible--based on your statement about what he is prepared to do, almost impossible to completely prepare for what we

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might face?

Dr. WINKENWERDER. That's a judgment. I think we have very good information about what the threats are. We have good information about the detection capabilities. We have good information about the protective capabilities of the equipment and suits. We have good information about the protective capability of medical countermeasures. So I think that we are prepared.

There are certain situations, there are circumstances that one can envision where an enemy can create harm and damage, and we have already seen that in the war thus far. So being prepared does not mean being able to completely prevent any adverse outcome in every single service member serving.

Mr. BELL. Can I ask one more question?

Mr. SHAYS. Sure.

Mr. BELL. As far as the lessons-learned category, are we prepared, after we face whatever we are going to face in this conflict, to come back and say, this is what we are looking at, this is what we are testing our troops for?

Dr. WINKENWERDER. Yes.

Mr. BELL. And to treat that instead of trying to pretend that we didn't face any of those things?

Dr. WINKENWERDER. Absolutely. We will be looking at people very carefully after deployment. And we have a

process in place. We are looking at and currently evaluating that system to ensure that it will collect all the information in a timely way that we want and think that we might need.

Mr. BELL. Thank you very much, Doctor.

Thank you, Mr. Chairman.

Mr. SHAYS. Thank you.

Just for the record, my counsel, our counsel, the committee's counsel reminds me that all three sites had been discussed. The only thing that we think is a bit new is that maybe we had Special Forces near one of those sites, but that the committee is trying to determine where those plumes went. So I just want the record to state that.

Also say--Dr. Winkenwerder, you are getting all the questions right now.

Dr. Roswell, you are going to get some.

But you have--you have, for the record, turned over some stones and have been very cooperative and very helpful with this committee. So these are big issues. But I do want the record to note that you are been pushing DOD to be more candid, to be more open, and to treat these very serious questions that you are being asked with a lot more attention than has been done in the past. I do want the record to note that at well.

Dr. WINKENWERDER. Thank you.

Mr. SHAYS. Mr. Janklow.

Mr. JANKLOW. Thank you very much, Mr. Chairman.

You know, let me, if I can, ask questions kind of like we used to take our English lessons--what, where, when, how, why, and to what extent--if I can.

Let's talk about the current war that we are in. In order to try and make sure that we don't have some of the problems that--and nobody wants to repeat the problems of Desert Storm. One, is it--will it be difficult at all--and you used the phrase before, production areas, storage areas. Would it be difficult now, if we come across any production areas in the country, to document, using GPS, GIS, whatever, exactly where these locations are;

Two, exactly what storage facilities we come across within the country;

Three, exactly where utilization of chemical, biological types of weapons are used--three; and

Four, to the best extent possible, identifying, if not the individuals, at least the units that are in the area so that all of these kinds of problems that we have wrestled with from Desert Storm don't have to be revisited?

Is there a plan in place to deal with it that way?

Dr. WINKENWERDER. I will try to give you the best answer I can. But I will note that, again, you are asking very good

questions. They are out of my--.

Mr. JANKLOW. Are they out of your bailiwick?

Dr. WINKENWERDER. They are really, truly are out of my area of responsibility.

Mr. JANKLOW. Okay. If they are, then could you find somebody that could--could you at least take the message back?

And I've got to believe they're doing this. It isn't that they operate in a vacuum over there. They are the best there are.

Dr. WINKENWERDER. Absolutely.

Mr. JANKLOW. This is a way to try and obviate some of these kinds of problems.

Dr. WINKENWERDER. I can just tell you from my exposure to those types of discussions, there is an exquisite level of sensitivity to the issue of how to deal with the issues that you brought up and to avoid any inadvertent or any kind of contamination.

Mr. JANKLOW. Doctor, based on your position, your experience, your background, are you satisfied that we have a good baseline on the troops that are currently in the field or will be going to the field over in Iraq?

Dr. WINKENWERDER. I am.

Mr. JANKLOW. In terms of a medical baseline for them?

Dr. WINKENWERDER. Yes, sir, I am.

Mr. JANKLOW. And Mr. Roswell, are you satisfied that within the President's budget, the existing budget or the supplemental request, there are sufficient funds to take care of the medical liens, medical needs that are reasonably foreseen--and I realize we could argue about terms--but the medical needs that are reasonably foreseen, that may be necessary for these soldiers, sailors, airmen, Marines when they come home? Or, obviously, in the field, but when they come home?

Dr. ROSWELL. Certainly, based on the current availability of resources we have concerns. But given their high priority, I have no reservation about our ability to--.

Mr. JANKLOW. When you say that, is there any anticipation at all that you will be bumping other people that are currently eligible out of the system or aside to take care of these folks when they come home?

Dr. ROSWELL. That is a contingency that the Secretary of Veterans Affairs, in exercising his statutory authority as mandated by this Congress, would have to consider. So it is possible that if there was an unpredicted demand for care from the Department of Veterans Affairs, by law, Secretary Principi would have to consider other lower priorities of veterans and their ability to continue to enroll in and receive a full health care benefit.

Mr. JANKLOW. Mr. Chairman, can I see that letter for a

second? I guess I have it here, the one that was mailed to you. I am unfamiliar with these letters, until today, that have been talked about. But one of the letters I saw is a letter from Mr. Eldridge--or an E.C. Eldridge, Jr., I am sorry, I assume that is a Mr. Eldridge--to Representative Shays; and in it--I am sorry, one signed by Mr. Eldridge on February 27th of 2003.

And in that one, Mr. Eldridge says to--excuse me--Ms. Schakowsky that every member of Desert Storm will carry at least two--excuse me--every member support near-term operations in Southwest Asia will carry at least two of the new joint service lightweight integrated, the J list suits, and will have an additional two suits in contingency stocks.

Is that the case for the people currently operating in Iraq?

Dr. WINKENWERDER. That is my understanding. Yes.

Mr. JANKLOW. Okay.

Thank you, Mr. Chairman. I have no more questions right now.

Mr. SHAYS. Thank you very much. We are going to put both letters in the record. But the bottom line is, that was the response to my request and also Ms. Schakowsky's.

[The information follows:]

******** COMMITTEE INSERT ********

Mr. SHAYS. Mr. Tierney, you have the floor for a generous 5 minutes.

Mr. TIERNEY. Thank you, Mr. Chairman.

Mr. Chairman, thank you for the long series of these hearings that you've had over the years. I think they have served to benefit the men and women that are there now. I don't think that without having had the hearing on the condition of our suits and things of those materials, that they would have the two new suits; and so I appreciate that, and I am sure their families do.

Mr. SHAYS. It has been a team effort on both sides of the aisle.

Mr. TIERNEY. Doctor, let me--Dr. Winkenwerder, let me ask you for a second:

One of the concerns that we had in doing the homeland security measures and overseeing those was that if there was a contamination, the people responding to that, from medical personnel who oftentimes found themselves unprepared, sometimes exacerbated the situation and completely knocked out an entire medical unit because they hadn't prepared to separate out the contaminated folks, out from the others.

My understanding is that, in the Gulf, most of the medical people, the doctors and nurses sent over there, are Reservists, which would raise the specter that their training is 1 weekend a month or 2 weekends a month and 2 weeks in the

summer; and I would guess that that would probably be barely enough to keep up on their training for medical treatment in the field.

Can you give us some assurance that those Reservists have, in fact, been properly trained to meet what might happen in terms of a chemical or biological attack?

Dr. WINKENWERDER. We expect every service to be trained equally to the Active Duty to take care of those situations.

Mr. TIERNEY. How is that happening if they are getting 1 weekend a month and 2 weeks in the summer, and in that period of time have to keep up with their own medical treatment? How are they getting this additional training? Where are they getting that in a fashion that would give us the comfort that they are really prepared and ready?

Dr. WINKENWERDER. Well, there are a variety of training courses that we offer. And it is part of this overall requirement that I set into place last year that for every medical person in the military health system, professional, that depending upon his or her level, there should be training to deal with chemical and biological events.

And so we expect that. That is a responsibility of each of the services, to provide that training and to ensure that we meet the standards.

Mr. TIERNEY. Have you be monitoring that?

Dr. WINKENWERDER. Yes, we have been.

Mr. TIERNEY. And how much additional training other than that 1 weekend a month and 2 weeks of summer are these personnel getting?

Dr. WINKENWERDER. Well, I had some figures that we recently generated from the three services, and I want to be careful with this, to describe it as accurately as my recollection will allow. But the percentages are in the high double digits now as opposed to the low single digits, what they were a couple of years ago.

So there has been--.

Mr. TIERNEY. Double digits? Single digits? What?

Dr. WINKENWERDER. That means like somewhere between 60 and 80-something percent. And again, there has been an effort to make sure that those that are deploying are the ones that get the training. So when I describe those statistics, that is across the whole system.

Obviously, not everybody is going, so the training has been targeted more towards people that are serving. But I will--I understand the gist of your question and we will try to get back with that information.

Mr. TIERNEY. Would you get that information?

Dr. WINKENWERDER. Yes, sir. We would be glad to.

[The information follows:]

******** COMMITTEE INSERT ********

Mr. TIERNEY. Thank you.

And just, again, because I continue to have concerns about those suits, and even though you've now told me how many suits they have, in my reading anyway, it indicates that that may well not be enough depending on how long this conflict goes.

But you put out the impression at least, that Mr. Kucinich mentioned earlier, about the people being ready; and I am wondering, can you give us the assurance that Secretary Rumsfeld, through Under Secretary Aldridge, was not able to give us? Can you give us the assurance here today that the troops have sufficient equipment to protect them against chemical and biological attacks in quantities sufficient to meet the minimum required levels previously established by the Department of Defense?

Dr. WINKENWERDER. Certainly, from a medical standpoint; and by that I mean the medical countermeasures, the antibiotics, the vaccinations and all of that; those are the issues that come directly under my area of responsibility. The others, my understanding from recent conversations with--Dr. Anna Johnson Winegar, who is the chief responsible person within the Office of the Secretary of Defense for those matters and has testified before this committee and others, has indicated that she believes that we are well prepared on the issues that you have just raised.

Mr. TIERNEY. Well, your impression at least was not contained just to the medical end; it also involved the suits or whatever. Or did it not?

Dr. WINKENWERDER. That is not--and I know from your perspective, as well it should be, you should be concerned about everything, and so I don't want to be bureaucratic here. But--.

Mr. TIERNEY. I appreciate that.

Dr. WINKENWERDER. It is not directly within my area of responsibility. It is another area that does work under Mr. Aldridge. We work ~~real~~ closely, very closely with those people. The responsibility for executing those policies resides within each of those services.

Mr. TIERNEY. Thank you.

And just to finish up my generous 5 minutes, the reason I raised the initial question was that we had an exchange here in committee with Dr. Kingsbury, Nancy Kingsbury, at some point in time; and her answer indicated, to me at least, that in instances of mass casualties she did not believe that the exercises that have been done so far indicated that we could deal with those appropriately.

So whatever assurances you could give the committee in --returning to that in terms of medical personnel being ready would be greatly appreciated.

Dr. WINKENWERDER. We will do that.

[The information follows:]

******** COMMITTEE INSERT ********

Mr. TIERNEY. Thank you.

Mr. SHAYS. Thank the gentleman.

We are going to do a second round here, and I just want to ask--so we can close up the issue of the questionnaire, I want to know why our men and women aren't given physicals when they go into battle, so that we know. What is the logic of that?

Mr. JANKLOW. Aren't given what, sir?

Mr. SHAYS. Aren't given physicals. They are given questionnaires, but they aren't given physical examinations.

Dr. WINKENWERDER. I think, Mr. Chairman, that the logic is that a hands-on physical examination yields not a great deal of information in terms of the baseline health status of young, healthy individuals. And far more important and relevant is a series of questions that are asked that can go into greater detail if a flag goes up that indicates that there is some problem with that person's health.

Mr. SHAYS. I could hear the--first off, I am not going to concede that we didn't intend that they weren't going to have physicals. So I understand your doing the questionnaires, and I understand when we talk about a medical examination versus a physical examination, you have decided that you have some flexibility there.

But what about the Reservists and the National Guard folks who simply, you know, might be eating a little

differently, might--you get my gist. Why wouldn't they have physicals? They might be older. They might not have been active for a while. Why treat them all the same?

Dr. WINKENWERDER. Why treat them all the same?

Mr. SHAYS. Why treat them all the same? Why not have a little bit more of an interest in giving a physical to someone who may not have been in the Active Service?

Dr. WINKENWERDER. You raise a good point. I think it is something we could certainly take a look at.

Dr. Kilpatrick.

Dr. KILPATRICK. If I could, for the Reservists that are called to Active Duty, there is a more stringent process put in place to look at them, having physical examinations, their periodic physical examinations.

For Reservists under 40, they need to have one every 5 years; over 40, every 2 years. I think there is a recent GAO report that showed that people were not meeting the mark--I mean, the numbers were terrible--on doing that. So when people are called to Active Duty at that mobilization center, if they have not had a physical within the last 5 years for under 40 or the last two years over 40, they have to have a physical before they go, so they are caught up.

Mr. SHAYS. Why not at least draw blood and why not do that?

Dr. KILPATRICK. And I think the drawing of blood is--we

do make sure that everyone has an HIV screening sample done within the previous 12 months prior to deployment. That serum sample is banked in a serum bank. It is kept permanently. There is no sort of portfolio of tests to do on a serum sample, but that is kept in the eventuality there is an exposure, either recognized or unrecognized, and then a determination of a set of tests that could be done. So the serum sample is saved, but there is no testing done, prior to leaving, for levels of any agents.

Mr. SHAYS. Dr. Roswell, how much involved were you on--how are you involved in the predeployment questionnaire? How much involvement did you have in this questionnaire?

Dr. ROSWELL. Relatively little, Mr. Chairman.

Mr. SHAYS. Does relatively little mean, really, I didn't have much involvement at all?

Dr. ROSWELL. The survey was shared with us. We have effective communication through the Health Executive Council that Dr. Winkenwerder and I cochair. So there is an active sharing of information.

Mr. SHAYS. But this was basically designed by DOD, Dr. Winkenwerder?

Dr. KILPATRICK. Yes.

Dr. WINKENWERDER. Designed in 1997.

Mr. SHAYS. 1997. Okay. We have a letter that Principi--Principi; I'm sorry, I went to a college called

Principia, so I have a bit of a problem with that name--where the Secretary had written. And he said--and this is a letter he drafted to Mr. Rumsfeld on--Secretary Rumsfeld on February 14th of this year; and the second page says, "In the event of hostilities, VA further requests more extensive postconflict health data. Within the first month after hostilities cease, VA recommends administration of a detailed postwar health questionnaire to accurately document the health status and health risk factors and health in Gulf War troops immediately after the conflict." .

Can you explain that a little to me?

And, Dr. Winkenwerder, can you respond?

Dr. ROSWELL. I think what Secretary Principi was asking for was to get--to get risk assessment and self-reporting--.

Mr. SHAYS. Excuse me. Let me just say for the record, with just three members, I am going to roll to a 10-minute question. So you'll have 10, and we'll go from there.

Thank you. Go ahead.

Dr. ROSWELL. Our concern is that particularly with Reservists and National Guard, when they are demobilized, the immediate concern--and it's true of Active Duty as well--is to get home to family and loved ones. But unlike the Active component, when the Reservists are demobilized, they may be lost to follow-up, and it may be difficult to get information.

We learned, painfully so, in the Gulf War that when we surveyed service members who had separated from military service months or years after their service in the Gulf War, that there was a high level of what we would call "recall bias." they don't really remember the specifics, it is hard to recall a specific date. A service member might not remember an actual grid coordinate or an actual physical location.

So I think what Secretary Principi was asking Secretary Rumsfeld was that, in the event of possible exposures, we get as much information as possible at the time military members are demobilized and separated from service. That would help us evaluate possible symptomatic exposures and health consequences that might have--.

Mr. SHAYS. So there's logic to doing this.

Let me just ask, Dr. Winkenwerder, do you--we had in 1997, you have this--developed this questionnaire we are using today.

Do you have a postsurvey questionnaire that was done in 1997, or is that still a work in progress?

Dr. WINKENWERDER. That was developed in the same time frame.

Mr. SHAYS. We are asking that that questionnaire be updated and improved.

Dr. Roswell?

Dr. ROSWELL. The postdeployment survey that Dr. Winkenwerder speaks of would certainly be helpful. Obviously, we'd seek more complete information if there was a documented or suspected exposure.

Mr. SHAYS. It's just a two-page document?

Dr. ROSWELL. Correct.

Mr. SHAYS. It doesn't even look as extensive. I guess it's the same as--both are two page.

I would hope, Dr. Winkenwerder, that you will give tremendous consideration to Principi's letter and request, and absolutely determine that our troops, shortly after--not after they are sent back home, but you know, a month or two after the conflict ends, that they are going to have this kind of questionnaire.

And I am going to--I am seeing the nodding of heads. I would love to know if you could put something in that we could transcribe here.

Dr. WINKENWERDER. Yes. Well, I share the objective of getting accurate information in a timely way.

Mr. SHAYS. And do you believe that maybe a more than just two-page questionnaire would be helpful?

Dr. WINKENWERDER. I have already initiated an effort to reassess this survey tool to see if it collects all the information that we think it ought to collect.

Mr. SHAYS. Do you give some weight to the Secretary of

Veterans Affairs, who ultimately has to deal with this, that--.

Dr. WINKENWERDER. Oh, absolutely.

Mr. SHAYS. Okay.

Dr. WINKENWERDER. Yeah, absolutely. So I've, number one, done that.

And secondly, ideally, if we could collect that information even before people come back to the United States, it would be great. Logistically, we are still looking at that. Obviously, we have to have a lot of cooperation and assistance from many, many people to--.

Mr. SHAYS. And you may have to do some physicals. You may have to add more than physicals to the questionnaire, and you may have to have more of these folks actually take a physical when they leave.

Dr. WINKENWERDER. Well, I would expect, with a good detailed questionnaire that whenever people gave any reason for concern, they would then be very carefully evaluated.

Mr. SHAYS. Okay.

Mrs. Maloney.

Mrs. MALONEY. Thank you, Mr. Chairman. I would like permission to place in the record an article written by Judith Coburn entitled Suited for War, and it is very thought provoking. In it, she alleges--.

Mr. SHAYS. Without objection, that will be put in.

Mrs. MALONEY. Thank you. In it, she alleges that it took a four-year struggle of Gulf War veterans from Georgia before they got the Pentagon to declassify documents which revealed that Iraq's stocks of sarin gas stored in Khamisiyah had been blown up, and that roughly 140,000 American troops were exposed.

I realize, Dr. Winkenwerder, this did not happen on your watch, but I fail to understand the mentality or the mind frame of a department that would withhold valuable information on the exposure to chemicals that could hurt people.

And I understand this was not on your watch, but if you can find any documentation on what they were thinking about or what, in their minds, they thought they couldn't reveal to our men and women, that they may have been exposed, I would love to get that back in writing.

But my question--and Ms. Coburn further goes on.

Mr. SHAYS. Let me be clear. What do you want back in writing?

Mrs. MALONEY. Why the Pentagon fought the release of information on men and women being exposed to sarin gas when they knew they were exposed in that particular area.

Mr. SHAYS. The record will note that they acknowledged that our troops were exposed, before our hearing, at a press conference. Then there was a question as to how many troops

were ultimately exposed, and the numbers kept going up.

And so what would be helpful is if, in fact, additional information was held and for how long and why. And that will be--it is just not a wish, it is a request that--Dr. Kilpatrick, you are nodding your head--you will get back to us on.

Dr. KILPATRICK. Yes. There is a great deal of information. We will pull out all together and provide it.

[The information follows:]

******** COMMITTEE INSERT ********

Mrs. MALONEY. She further states that 148 Americans died in the war, but that roughly 160,000 have fallen ill; and that 11,000 have died since the Gulf War--much higher than other men and women in the military--and that they have collected a series of 57 symptoms for which there is no known cause, which is the Gulf War Syndrome.

I would want to ask what we are doing to protect the health of the men and women that were exposed and the possibility, God forbid, that they may be exposed yet again. And I am the cochair of the Parkinson's Disease Task Force, along with Fred Upton; it is a bipartisan effort. And my father suffered from Parkinson's.

But it has been reported that some of the Gulf War veterans have suffered symptoms similar to Parkinson's. And each year we have been working with the Defense Department, and we have received funding for Parkinson's research on neurotoxin exposure, seeing if that is a reason for the brain damage that causes Parkinson's. But I would argue that, likewise, it may be a study for what we can do to help the men and women that may have been exposed to chemicals.

So my question right now is more of a proactive one of, what are we doing in research?

As I understand it, we have no cure for Gulf War Syndrome. And what are we doing to find--are we spending some of our research dollars in trying to find a cure for

neurotoxin disease that may be caused by the sarin gas or other things? What are we doing? I am very thankful to the Department of Defense for funding the Parkinson's research.

My question is, is this likewise connected to the Gulf War Syndrome?

Dr. WINKENWERDER. To your general question of what are we doing? We are continuing to fund with millions of dollars ongoing research into many of these questions that you have raised. As I alluded to earlier, it's difficult to determine with the levels of certainty that one would like in this case, if one is talking about evaluating these individuals that served, when the baseline of information and what was collected and what people may or may not have been exposed to is not good.

The information is not good, so--by definition, to do good research, you need good information. That shouldn't prevent us from funding additional research, as we have done, to look at some of these questions of what would low levels of exposures do to laboratory animals. Certainly we would never do this to any individual on an experimental basis. But studying what happens with animals and looking at some of these things is very important.

Mrs. MALONEY. Specifically, is the Parkinson's research that you are funding--and I thank you for that research. Is that connected to the Gulf War Syndrome?

Dr. WINKENWERDER. I am going to turn to Dr. Kilpatrick.

Dr. KILPATRICK. Let me just address it. It is being pursued in two directions.

One is a clinical basis, looking at people; and then that is very tightly tied to a program looking at chemical nerve agents in particular and the effects that they have on brain function. And there are projects funded at $5 million a year over the next 3 years; 1.5 million is looking at repeated low-level exposures of animals to sarin nerve agent, to look at long-term health consequences. That is very applicable to what Gulf War veterans' concerns are.

The other part of the money each year is spent toward what we call the high end of low-level exposure, below symptomatic response to nerve agents, one exposure, and then seeing what are the physiological responses.

And those data from those research sets are really very closely shared with people looking at Parkinson's disease, because they are really looking at the same pathway potentially as far as disease cause.

Dr. ROSWELL. If I may respond to that from a combined perspective.

Since the Gulf War, over $200 million in federally funded research has been focused on possible causes for Gulf War Syndrome. I would like to set the record straight.

One of those studies has looked at death rates in

veterans in the Gulf War, and in fact, the overall death rate for veterans who served in the Gulf War is not increased compared to their military counterparts who were deployed outside the theater of operations. If you look at specific-cause mortality in veterans who served in the Gulf War, there is a very slight increase in death due to trauma, such as automobile accidents. But other than that, the mortality rate is not increased in any subcategory, and the overall mortality is not increased.

And I certainly wouldn't want to create a fear for the men and women currently serving in Iraq.

Let me point out that Parkinson's disease is one of several neurodegenerative diseases that DOD and VA are currently studying. VA recently funded the creation of a neuroimaging Center of Excellence for neurodegenerative diseases to look not only at Parkinson's but also other diseases, even when unpublished data suggested that there might be an increase in a degenerative disease known as amyotrophic lateral sclerosis, or Lou Gehrig's disease.

Secretary Principi moved quickly to presumptively service-connect veterans who suffered from that illness and served in the Gulf War, so that they received disability compensation.

I would also point out that 160,000 veterans of the Gulf War have received approved disability claims. But most of

those claims are for diseases that we would expect to see in a military age population, and it is a relatively small number for undiagnosed illnesses or the Gulf War Syndrome you spoke of.

Mrs. MALONEY. When you mentioned the clinical trials, are you doing them on our veterans? Are we tracking our veterans and seeing if--particularly those that we know were exposed to sarin gas? That would be helpful to see, because some of them apparently--I am talking to doctors that treat Parkinson's. They have told me that they are developing Parkinson's-like symptoms.

Dr. ROSWELL. We have extensively reviewed literature for symptomatic exposures to the organophosphate, which is the class of compounds that sarin nerve gas falls into. The study suggests that there is cognitive impairment in people who suffer symptomatic exposures, but I am not aware of evidence that conclusively links any kind of organophosphate or nerve agent exposure to Parkinson's disease specifically.

Some investigators have reported a possible neurodegenerative disorder that involves part of the vasoganglia, which are structures that are affected in Parkinson's, but in a way different than in Parkinson's disease, which is why we've funded the neuroimaging center.

Mrs. MALONEY. Where is the neuroimaging center?

Dr. ROSWELL. Actually, there are several within the VA.

MEL

There is one in San Francisco; there is--a final selection for the designated center has not yet been made, however.

Mrs. MALONEY. Well, thank you for investing in research for coming up with some cures. And thank you for your testimony. My time is up.

Mr. SHAYS. We have just two more members who will ask some questions, and then we are going to get to the next panel.

Mr. Janklow.

Mr. JANKLOW. Thank you very much, Mr. Chairman.

Help me, if you could. With the testimony--the hearing is about lessons learned from the Gulf. My question is, both of you in your capacities, you, Dr. Roswell, and you, Dr. Winkenwerder, have you looked into the history of why was this so secret so long? With everybody clamoring for information, why did it take so long to get the information out? Why did it have to be dragged out of people? What was the reason for the mystery?

I guess--have you ever been able to find out, or have you ever looked as to the reason for the mystery? It couldn't have been national defense secrets.

Dr. WINKENWERDER. I can't give you a good answer. I will give you the best answer I know, and that is that in many cases it took months and even years for symptoms to develop with people. And that, combined with the poor record

base, made it very difficult to do research or to even develop good, plausible mechanisms, causal-related mechanisms.

Mr. JANKLOW. Have those problems been solved?

Dr. WINKENWERDER. In my judgment, we have a far superior baseline of information. We have a far improved recordkeeping system. We have a far improved ability to surveil and actually keep records in the theater. We have these pre- and postdeployment assessments. So our information base, by all accounts, should be far, far better in our current situation.

Mr. JANKLOW. Doctor, I believe you said you have been in your position about 18 months.

Dr. WINKENWERDER. Yes, sir.

Mr. JANKLOW. And for you, is there anything, at least at this point in time in your tenure in this position, where we have got a lesson we haven't learned?

Dr. WINKENWERDER. Well, I hope we don't have one that I am not attending to.

Mr. JANKLOW. Are there any--do you know of any that concern you or that we ought to be concerned about?

Or you Dr. Roswell?

Either one of you, are there any lessons we haven't learned?

Dr. ROSWELL. If I could, I think the Gulf War was an

unprecedented conflict. The breadth and nature of military occupational exposures had never been experienced by our men and women in any prior conflict. So part of the delay, if you will, the confusion--I think, in retrospect, it is fair to say there was some confusion about exposures and possible health consequences--was because we didn't recognize that a vast number of unprecedented exposures could be factors: the anthrax vaccine, the pyridostigmine bromide that was used, the dense oil fire smoke, the fine particulate sand in the desert, the use of petroleum products to cut down on the blowing sand, the use of permethrin and DEET to protect people from insects--there were so many exposures--the use of depleted uranium as both an armour-piercing munition and a firearm plate, even chemical agent-resistant coating paint, which was applied to vehicles to make them resistant to chemical agents--were just some of the possible exposures that were investigated methodically, consistently over time to try to ferret out possible causes for the illnesses we saw in Gulf War veterans.

And I think that, to me, if there is a lesson learned, it is that we have learned that all of these exposures, singly or in combination, as has been pointed out in this hearing, could be factors in the development of illness. Certainly, every major conflict that U.S. Men and women have served in has yielded unexplained illnesses.

But that doesn't obviate our need to methodically and thoroughly investigate each and every exposure. And that is why we are committed to do that, and I think that is the partnership that VA and DOD, through the Deployment Health Working Group, are vested in right now.

Mr. JANKLOW. Dr. Kilpatrick, are there any unlearned lessons that you know of lingering from the Gulf War?

Dr. KILPATRICK. I think one of the hardest ones is communication. It doesn't matter how good a job you do, you can always do it better.

And I think one of the issues that we are working at very hard now is to make sure that leaders in the field are communicating to their troops that they are concerned about these various exposures, their health. They are concerned about documenting where they are. They are concerned about making sure they have that access to health care when they come home--I think DOD and VA share the same concern for those who are getting off Active Duty; they will be looking perhaps to the VA for health care--that they understand that, in fact, there is the ability for them to have 2 years of health care coming out of a combat zone now. That was not present after the Gulf War in 1991. And I think that that is--getting that communicated to people, so they know they have that access to health care, is so important.

So I think that that is one of the areas where, as good a

job as I think we are doing, we always need to look to say, how can we do it better. And I think doing that, through even this hearing, is very helpful to those men and women who are serving today.

Dr. WINKENWERDER. And if I might add to that to say, you know, you never know when you haven't learned a lesson until--there are many times you don't until you've learned it, which to me speaks to the need culturally to have an open mind, be open to learning things that you didn't know before.

And so if there is one thing that I would continue to hope to convey to our people it is a continued vigilance about different sources and causes of illness and ways to improve. It is sort of a culture of learning and getting better.

Mr. JANKLOW. Assuming we have the baseline data that we need for the current war that we are in, recognizing that our troops could be exposed to biological or chemical warfare, do we have the systems in place?

I mean, that is the key thing. Do we have the systems in place to be able to get the information about the individuals and about the chemical or the agents or the toxins that are being--that they have been exposed to, so that we will have the database of information to address it without all the types of--new types of frustration that we will have to go through in order to find out whether or not there are or

aren't legitimate reasons for illnesses or problems that people have after the war?

Am I making sense to you?

Dr. WINKENWERDER. Yes.

Mr. JANKLOW. Do we have a system in place, is what it comes down to. I realize we had no history before the Gulf War. We now have a history.

Dr. WINKENWERDER. I believe we do have the system in place.

Mr. JANKLOW. Is there anything we can do to make it better?

Dr. WINKENWERDER. Yes.

Mr. JANKLOW. What?

Dr. WINKENWERDER. One of the things that we can do to make it better is to ensure that there is 100 percent compliance with all the policies and all the procedures, the training we have talked about.

Mr. JANKLOW. Have those orders gone out to the military?

Dr. WINKENWERDER. Absolutely.

Mr. JANKLOW. Is there any reason that the military would have for not following orders from above that are lawful?

Dr. WINKENWERDER. No. I have no reason to believe that people have not taken this issue extremely seriously.

Mr. JANKLOW. Do they understand that if they violate direct, lawful orders from a superior, that it sometimes is

far more serious in the military than it is in civilian life?

Dr. WINKENWERDER. Yes. I think there is a good understanding of that.

Mr. JANKLOW. Those are all the questions I have, sir.

Mr. SHAYS. Thank you.

Mr. Tierney.

Mr. TIERNEY. Thank you. I have only a follow-up question.

We know that this 2004 VA budget, Dr. Roswell, has several provisions that are going to restrict the ability of certain classifications of veterans, Priority 7 and Priority 8, to get treated and to get the cost of care covered--I can't get this thing to stop moving up and down.

Isn't that one of the lessons we've learned, though? If we have incidents that are not really showing signs of symptoms or illnesses for several years after people get out of the service, being covered for the first 2 years may not be sufficient. And haven't we learned through some of the Gulf War Syndrome incidents that it can be any number of years before people start coming down with these symptoms?

So having learned that lesson, we put out a budget that still doesn't seem to address these people's concerns.

What are your concerns about that, and what can we do about the fact that some of these people may not exhibit symptoms in the first couple of years? And how is the VA

going to deal with those people without excluding them from coverage?

Dr. ROSWELL. Well, certainly one way to do that is to authorize special access for care for people who have illnesses that occur following a conflict.

We actually had that authority that just expired in 2002 for veterans of the Gulf War. It would be obviously, depending upon the outcome of the current conflict, appropriate for this Congress to consider special authorization for priority care for veterans who have served in this conflict.

The 2 years is a minimum. It would certainly continue beyond that if an identified need were discovered during that period or if an illness, injury, or disability associated with military service were identified that led to a service connection.

Mr. TIERNEY. I think your first recommendation is probably one that we ought to look into, and that is making sure that we provide some sort of flexibility or ability to cover those for people that may be coming out of this conflict, and I appreciate that.

Mr. Chairman, I have no other questions at this time. I want to thank our witnesses for their thoughtful answers and for their assistance here today. Thank you.

Mr. SHAYS. Thank the gentleman. Let me just do a few

little minor points for the record.

Dr. Roswell, we are looking at VA data and reports on mortality in the Gulf War. And its recent reports, based on VA data, have been late. There was one report that showed kind of a real spike in deaths, and it was called back and we are curious about that.

So we are going to invite the VA back to have a dialogue about this, but I just kind of feel your comment about not showing much difference is something that this committee has a big question with.

And I would also just say, Dr. Winkenwerder, that I have some specific questions about the status of the Armed Forces Radiobiology Research Institute and their work on a drug to counteract the effects of radiation exposure.

RPTS BULKLEY

DCMN BURRELL

Mr. SHAYS. And we're going to second these questions in writing to your office and ask that you respond. I don't think we need to take time to do that now, we think.

Dr. WINKENWERDER. We'd be glad to do that.

[The information follows:]

******** COMMITTEE INSERT ********

Mr. SHAYS. And also say, Dr. Hyams, you have the biggest challenge here, and I have a theory and it never fails me that the person who says the least has the greatest contribution at the end to make. So I'm going to just ask--no, I'm not going to do it quite that way. But I'm going to say to you that I would like you to put on the record anything that you think needs to be put on the record or any observation that you would like to put on the record, and then we'll get to the last panel.

And Dr. Hyams, I would also invite you as well. I'm not being facetious. I know all four of you have expertise here, and we didn't ask Dr. Roswell as many questions so you didn't need to jump in, but I'm happy to have all four of you make any final comment. I'll start with you, Dr. Kilpatrick.

Dr. KILPATRICK. Well, I think that the Department of Defense is very focused from the lessons learned in the Gulf on how do we better take care of our men and women in harm's way today. I think the Force Health Protection Program is that cascade effect of programs that will protect health. It does depend on good leadership and cohesive units. We believe we have that that we see that in action today, and it is our duty to make sure from a medical standpoint that those men and women have their health concerns addressed, and our medical department stands by waiting to make sure that their health concerns, whether they are related to the deployment

or any other concern, get addressed with facts about exposures we know occurred.

Mr. SHAYS. Thank you.

Dr. WINKENWERDER. Mr. Chairman, I'd just say we appreciate the opportunity to be here today. I think this has been a productive exchange of information. I hope you've found it that way and useful.

My first comment is just to say that I deeply appreciate the sacrifice that our men and women in uniform are making, and I also deeply appreciate the outstanding job that our medical people are doing. I think we've seen from the TV reports and all just the incredible job they're doing. They've made us all very proud.

We are absolutely committed to trying to protect our people who are taking on a very challenging situation, a brutal regime that has terrible weapons. We've done everything that we know we can do to protect them. We will continue throughout this conflict and after the conflict is over to ensure that we look after people's health care needs and that we do right by them for the good service that they've done. So I'm committed to that.

Mr. SHAYS. Thank you.

Dr. ROSWELL. Mr. Chairman, let me begin by thanking you for your leadership over the last decade in moving our government closer to a more full and complete understanding

of the day. You have the floor and you're asking great questions. I'm done.

Dr. MOXLEY. In our written statement, we--.

Mr. SHAYS. Could I just thank--before--I'm interrupting. I'm sorry. I just wanted to thank Dr. Winkenwerder for staying here and having the courtesy of listening to their points. I'd like to do a little connection between you and them and also to point out Dr. Kilpatrick is here and also Dr. Hyams as well, and thank all three of them for showing you the courtesy and also learning from what you might say. That's very helpful of you.

Thank you.

Dr. WINKENWERDER. Thank you. We're glad to have more interaction here.

Mr. SHAYS. We'll make sure that happens. Thank you.

I'm sorry to interrupt.

Dr. MOXLEY. Well, I was trying to come back to some sort of answer to your question. I was going to say in our written statement we recapitulate our recommendations. I mean, it would be a fairly long list of inquiries, but one could ask whoever is responsible has this been implemented. I don't know that going over it I could improve upon it, and they are in the written record.

Mr. JANKLOW. Sir, after this report was submitted to the Defense Department, did you ever hear back anything?

2002365-0000008

(21)

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Congressional Name: Shelby, Richard USS

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December 11, 2002

Hon. Powell A. Moore
Assistant Secretary of Defense
Legislative Affairs Office
U.S. Department of Defense
Room 3E966, The Pentagon
Washington, D.C. 20301

Dear Hon. Moore:

Enclosed please find a copy of correspondence I received from (b)(6).

Please reply, **in duplicate**, to my aide, RYAN WELCH.

Sincerely,

Richard Shelby

Richard Shelby

RCS/wrw
Enclosure

U20105 /02

CASE DOD

410786

502524

Date: 11/5/2002 8 28 AM
Sender: (b)(6)
To: senator
Priority: Normal
Subject: Please read regarding Anthrax vaccine

(b)(6)

November 5, 2002

The Honorable Richard C Shelby
United States Senate
110 Hart Senate Office Building
Washington, D.C 20510-0103

Dear Sen. Shelby:

I strongly and sincerely recommend that you read and act upon this. I sincerely request that you will look into each military member's records and redress the wrong if they were harassed, courtmartialed, or forced out of their respective branch of service for "noncompliance" for refusing this vaccine. I was in the Air Force and Reserve for 26 years over a 31 year period and took countless doses of vaccine, some of which were only slightly tested and the military used as guinea pigs Heaven knows what caused the bouts of sudden depression I now suffer from but I'm willing to bet that it is a side effect from something I was supposed to over the years, whether military connected or not

During the '80's I refused an AIDS test at Eglin AFB, Florida, along with an AF Officer, until the medical technician washed the blood of a previous patient from his rubber glove that he had not changed His excuse was that they didn't have adequate supplies of gloves to change after each patient I was ostracized by my superiors and co-horts for my adamant stand, but I would have gone home with a court-martial before I would have let him handle me with a bloody glove Of course, I could not have taken this stand during a combat condition, but this was during a training mission or weekend drill

Thank you for your cooperation and consideration in this matter.

(b)(6)

(In case the article does not copy, it is Phyllis Schlafly's syndicated article dated November 5, 2002).

Phyllis Schlafly (archive)
(printer-friendly version)

November 5, 2002

Clinton scandals continue to surface

The General Accounting Office reported last week that 16 percent of our National Guard and reserve pilots and aircrew have transferred out of their combat positions An additional 18 percent of those surveyed have stated their intent to transfer or leave Did they suddenly lose their zeal for flying? Are they fatigued after years of service? Are they avoiding possible deployment for an invasion of Iraq? None of the above; the pilots' departure has nothing to do with flying or with war The GAO

discovered that those pilots departed because the Clinton administration ordered them to receive the anthrax vaccine, and 66 percent of those who did take the shots reported adverse side effects.

Now, after scores of resignations and hundreds of careers destroyed by court-martial, we discover that our brave servicemen and women were right to resist the anthrax orders, and the government was fatally and corruptly wrong. A lawsuit filed by two Connecticut Air Force Reserve pilots asserted that the vaccine used on the military was never properly tested, and the Food and Drug Administration's recent response was to halt use of existing stocks of the vaccine

Several months earlier, the FDA had ordered that a warning be included on the vaccine's package insert stating that the vaccine can harm people with immunity disorders, can cause a host of serious long-term adverse reactions, and could already be responsible for six deaths and a number of birth defects These warnings were based on complaints by military vaccine users since 1998 and show an injury rate that far exceeds casualty rates in combat.

The FDA warning also states that adverse reactions are expected in 5 percent to 35 percent of people who get the injection That is an absolutely shocking danger difference from the advertised 0 2 percent rate when Clinton ordered everyone in the military to be given the vaccine

Clinton saw in the anthrax vaccine a way to stick it to the military he "loathed," literally, while handing a pot of gold to an important political ally It was win-win for the Clintonistas, but lose-lose for our finest servicemen and women.

The biggest beneficiary of the order to force the anthrax vaccine on the military was Adm William Crowe, the former chairman of the Joint Chiefs of Staff, who had provided political "cover" for Clinton at a key moment during his bid for the presidency in 1992 Crowe personally vouched for Clinton against charges that he was a draft dodger.

A grateful President Clinton rewarded Crowe with the plum appointment as Ambassador to England But even that was not enough, Clinton handed BioPort, a corporation where Crowe was a director and a stockholder, an exclusive multimillion-dollar contract to supply 2.4 million servicemen with the anthrax vaccine. Crowe reportedly received substantial stock in BioPort's parent company without paying for it A Pentagon audit in April 2000 revealed that BioPort wasted funds on "excessive travel costs, excessive severance pay and unsubstantiated consulting costs," including $1 28 million in "unreasonable" bonuses for senior management.

About a year after BioPort contractually obligated itself to supply the anthrax for $25 7 million, the Clinton administration nearly doubled its promised payments to $49 8 million, even though the FDA repeatedly cited BioPort for quality deficiencies and BioPort failed federal inspections again and again BioPort was even indemnified against all liability from adverse reactions to the vaccine, which Army Secretary Louis Caldera admitted was "unusually hazardous" for certain recipients

An emergency medicine physician at Keesler Air Force base in Mississippi, Capt John Buck, chose to face a court-martial rather than be injected with the vaccine

"A red lump on the arm is not something that scares me," Buck said, "but an autoimmune disorder for the rest of my life is "

The Clinton administration cruelly court-martialed hundreds of servicemen for declining the unsafe, untested vaccine.

The anthrax vaccine, which was imposed on servicemen and women alike, was never tested for harm to unborn children. Clinton's feminist advisors would never permit treating women differently from men, even for the sake of avoiding birth defects

The number of deaths that the FDA now concedes could have been caused by the anthrax vaccine exceeds the casualties from the anthrax itself when the mails and office buildings were contaminated last year The postal workers showed good common sense when 98 percent of them rejected the government's hard sell to be voluntarily injected with the vaccine

We are waiting for the Department of Defense to do the right thing· restore the careers, with rank and pay, of the hundreds of servicemen and women who were punished for refusing a corrupt order to be injected with the unsafe, untested and unnecessary vaccine. ~~One reason we elected George~~ W. Bush was to remedy Bill Clinton's mistakes, and this is a good place to start

Contact Phyllis Schlafly | Read her biography

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WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

27 APR 1998

Honorable Arlen Specter
Chairman
Committee on Veterans' Affairs
United States Senate
Washington, DC 20510-6375

Dear Mr. Chairman,

Thank you for giving me the opportunity to respond to your letter of March 30, 1998 requesting information to complete the hearing record of March 17, 1998.

I believe that the attached answers to your post-hearing questions underscores our determination to ensure that the health of our men and women in uniform are fully protected against health hazards they may encounter as they deploy around the world in support of our national interests.

Should your office have any further questions, please contact my Chief of Staff, COL Terry Rauch at (703) 697-2113.

Sincerely,

Mary A. Christopherson

Gary A. Christopherson
Acting Assistant Secretary of Defense

HOPPALE
HA-24954

Department of Defense (DoD) Responses
to Post-Hearing Questions from U.S. Senate Committee on
Veterans' Affairs Hearing - March 17, 1998

Question 1: DoD coordination with the Department of Veterans' Affairs

1) What has DoD learned over the last seven years from its experience with Desert Storm/Desert Shield and Bosnia veterans that will change the way veterans will receive post-deployment health care and services?

2) How has DoD coordinated with the Department of Veterans Affairs any strategies to address health problems associated with exposure to BW/CW?

3) What has DoD done to coordinate with the Department of Veterans Affairs the development of individual medical baselines on military personnel who are being sent to the Gulf and who may be sent to future military engagements?

Answer: DoD and the Department of Veterans Affairs (VA) have worked together successfully on several levels to ensure that we have learned lessons from the Gulf War and subsequent deployment experiences and that we apply those lessons to current and future agency and interagency activities. The two Departments and the Department of Health and Human Services (DHHS) have worked together since January 1994 through the Persian Gulf Veterans Coordinating Board. The success of that effort has led to plans to establish a Military and Veterans Health Coordinating Board to continue interagency coordination. Once established, the new Coordinating Board should ensure coordination between VA, DoD, and DHHS on a broad range of health care and research issues relating to past, present, and future military service in the U.S. Armed Forces. The Coordinating Board provides the forum to ensure the agencies develop and provide, as necessary, coordinated and timely registry and evaluation programs, clinical care programs, comprehensive health risk communication, and benefit and compensation determinations.

Under the National Science and Technology Council (NSTC), DoD, VA, and DHHS were the primary participants in development of an interagency plan to address health preparedness for and readjustment of veterans and families after future conflicts and peacekeeping missions. This effort was in response to Presidential Review Directive (PRD)/NSTC-5, which required the participants to review policies and programs and develop a plan that can be implemented by the Federal government to better safeguard those individuals who risk their lives to defend our Nation's interests. The plan focuses on existing policies and lessons learned from the Gulf War and other recent deployments such as those in Bosnia, Haiti, and Somalia. In addition, health preparedness for defense against and the health consequences of deployment-related exposures to biological and chemical warfare agents is an essential part of the plan. The President's Committee of Advisors on Science and Technology is currently reviewing the plan.

Under the leadership of the VA/DoD Executive Council, the Department's are advancing other cooperative efforts. VA and DoD have a commitment to create a computer-based patient record (CPR). The CPR will capture health-related data from the service member's accession into the military, through training and deployments, and to separation or retirement from military service. The CPR and supporting systems will capture (and improve tracking and analysis) of (1) health events (outpatient visits and inpatient hospitalization), (2) periodic, pre-deployment, and post-deployment health assessments, (3) immunizations and other preventive countermeasures, and (4) potential health risk factors (including deployment-related, occupational, environmental, and personal). Upon separation or retirement from active service, the CPR will be transferred to the VA for their use in providing long-term health services and benefits, and in improving our understanding of the health of veterans.

Question 2: Improved medical tracking

In your prepared statement, you mentioned the computer-based patient record (CPR), the Theater Medical Information Program and the Personal Information Carrier (PIC) as systems designed to improve medical tracking. What are the development and fielding schedules for these items?

Answer: The Composite Health Care System II (CHCS II) developmental and fielding schedules are attached. CHCS II is an evolutionary development program which will ultimately provide the CPR. CHCS II consists of incremental deliveries of increased functionality supporting the President's 8 November 97 memorandum and the Department's Force Health Protection (FHP) Program. The Preventive Health Care System (PHCS) and the Personal Information Carrier (PIC), both integral to improved medical tracking capability, are functional components of CHCS II. PHCS and PIC in the near term, will be deployed as a stand-alone system in FY99, pending identification of funding. The long-term plan, however, is to fully integrate PHCS and PIC functionality into CHCS II Increment 3. The CHCS II Program development schedule and deployment plan are attached as Enclosure 1.

Question 3: Pyridostigmine bromide.

1) The records for the documenting use of pyridostigmine bromide (PB) during the Persian Gulf War are incomplete. For example, in June 1994, the Defense Science Board Task Force stated, "Although all units were given PB, the Department of Defense does not have records of which military people actually ingested PB, nor of how many tablets may have been ingested." a) What is DoD's current policy on the use of this drug and how its use will be monitored?

Answer: The Department is committed to working with the Food and Drug Administration (FDA) in the development of a policy that will allow for the use of Investigational New Drugs in combat missions. The Department currently has established working groups to resolve issues relating to the use of INDs in military combat or civilian terrorism emergencies. In the military combat context, the DoD is working to establish a protocol for use of PB which is acceptable to the FDA and which is executable by line commanders. DoD is pursuing the application of the Army's

MEDPROS system to track IND products in operational settings. Additionally, future immunization tracking systems will include capability to record IND usage.

Question:

3. 2) Given DoD's new guidelines that PB will be used only if there is intelligence information indicating threat of the use of soman or tabun, is DoD acknowledging that there may be health risks when PB is used in association to an exposure to other chemical warfare agents, such as sarin? Does DoD now have reason to believe that PB may otherwise be harmful when used by a healthy population?

Answer: The guidelines being developed for use of PB are based on well designed and executed research protocols and on information available from Operations Desert Shield and Storm. The Department believes that the pharmacological action of PB is effective as a pretreatment against the use of soman and possibly tabun. PB is not effective as a pretreatment against sarin. Based on available data, the Department does not believe it is harmful. The FDA has noted that until there have been clinical trials using PB as a nerve agent pretreatment at the proposed dose and schedule, effectiveness in humans cannot be fully evaluated. However, it is unethical to do clinical trials in humans to prove effectiveness for this proposed use. Therefore the FDA is considering the use of surrogate animal data to further evaluate the drug for approval. It should be noted that PB has been licensed for use as a treatment for myasthenia gravis for 5 decades at much higher doses for long periods of treatment. The FDA has not questioned the use of PB at these higher doses for these patients.

Question:

3. 3) Given the disputes between DoD and FDA on DoD's ability to comply with Investigational New Drug (IND) agreements and requirements, what is DoD's policy for current or future application for the use of Investigational New Drugs in peacetime or combat missions?

Answer: The Department is committed to working with the FDA in the development of policies and practical protocols that will allow for the use of Investigational New Drugs (IND) in combat missions and civilian terrorist emergencies. The Department complies with the FDA requirements for use of INDs in medical treatment facilities and in research facilities. However, the doctor/patient or principal investigator/patient relationship required for the use of INDs in a medical treatment facility or research facility is very different from what is required to use an IND in a disaster emergency or combat exigency situation.

Question 4: Anthrax Vaccine Program

1) When Secretary Cohen initially announced that DoD would proceed with inoculation of all U.S. service members against anthrax, he outlined four conditions that needed to be met: (1) safety testing; (2) a plan for tracking of vaccines; (3) approval of operational plans to administer the vaccines and inform troops; and (4) review of the program by an independent expert. The plan to vaccinate troops has been understandably moved up because of the presence of our troops in the Gulf. But, we still need to learn from the lessons of the Gulf in making plans for future

deployments. Please describe DoD's current progress on each of the four conditions that Secretary Cohen initially outlined.

Answer:

(1) The Department requested that the vaccine manufacturer, Michigan Biological Products Institute (MBPI), conduct supplemental or additional testing on all lots of anthrax vaccine in the stockpile that had been previously approved by the FDA for release. The supplemental testing was requested by the Department because the FDA, during one of its routine inspections of MBPI, had raised questions about vaccine production and quality control procedures. Although none of the concerns dealt specifically with anthrax vaccine production, the Department felt it would be prudent to have the manufacturer conduct supplemental testing to assure the general safety, potency, sterility, and purity of the anthrax vaccine in the Department's stockpile. Supplemental testing began in January 1998 and is scheduled to be completed by November 1998. Thus far, the results of all supplemental testing have been satisfactory. Even though supplemental testing will not be completed until November 1998, only those lots of anthrax vaccine in the Department's stockpile that have successfully completed supplemental testing will be distributed to the field for use.

(2) The Services have implemented short-term, interim tracking systems that are currently documenting anthrax vaccinations in Southwest Asia (SWA). The Services interim systems will transmit data to the Department's central data base, the Defense Enrollment Eligibility Reporting System (DEERS). A long-term, immunization tracking system, Preventive Health Care System (PHCS), will begin initial deployment in the fall of this year. When the total force anthrax vaccination program is implemented, the interim tracking systems will be used to document and manage the program until the long-term immunization tracking system is fully operational.

(3) The Air Force operational and communication plan has been approved by the Chief of Staff of the Air Force. The Army and Navy plans are in the final stages of coordination and are expected to be signed by the senior leadership of both Services by the end of April 1998.

(4) Dr. Gerard N. Burrow, Special Advisor for Health Affairs for the President of Yale University, agreed to conduct an independent review of the Department's anthrax vaccination program. Dr. Burrow, who previously chaired the Institute of Medicine Committee on Health Consequences of Persian Gulf War Service, completed his evaluation around 19 February 1998 with the following findings:

- "Anthrax vaccine appears to be safe and offers the best available protection against wild-type anthrax as a BW agent"
- " Steps have been taken to ensure the safety and quality of the Department's vaccine stockpile"
- "The Services are developing a comprehensive plan to design and track the immunization program"
- The communication program will be coordinated by individual Services"

- Other than delaying vaccination during pregnancy and in immunodeficient personnel, there would not seem to be the need for special considerations
- Nor would there seem to be the need for special follow-up"

Question:

4. 2) The current anthrax vaccine program requires military service personnel to receive six shots over a period of eighteen months, followed by a booster shot every year. It is the Committee's understanding that the Department of Defense is exploring the efficacy of a different shot regimen.

(a) If there is indeed a new program being considered, what is DoD's plan for implementation?

Answer: Studies evaluating reduced vaccination schedules for administering the anthrax vaccine are ongoing, to include clinical studies in humans. The initial goal is to reduce the initial part of the primary 6-shot series from three shots given at 0,2, and 4 weeks to two shots given at 0 and 4 weeks (the current 6-shot primary series is administered at O, 2, and 4 weeks and 6, 12, and 18 months). Although some preliminary data has been collected, these studies are scheduled for completion in Fiscal Year 1999. A precise implementation plan has not been established because the clinical data and surrogate animal studies, when completed, will have to be reviewed and approved by the Food and Drug Administration (FDA). The FDA must approve any change in the licensed vaccine regimen. Therefore, as studies are completed, the data will be presented to the FDA. This is necessary because a change in the vaccination schedule represents a change in the labeled use of the anthrax vaccine which must be approved by the FDA. This abbreviated vaccination schedule will not be implemented as part of the current plan to vaccinate the total force.

Question:

4. 3) On March 6, 1998, CNN reported that 200,000 doses of anthrax vaccine had to be recalled because they had been frozen, and thus ruined, during shipment to the Middle East. This illustrates some of the significant logistical hurdles of vaccinating our troops.

(a) Please describe other logistical hurdles needed to be overcome for this plan to work.

Answer: Other logistical concerns that must be adequately addressed to successfully implement the program are:

- Monitoring/rotating vaccine stocks intra- and inter-Service to best ensure use of all vaccine prior to the expiration of vials of vaccine.

- Ordering and distribution of correct size syringes for administering the vaccination to minimize waste in administering the .5 ml shot from a 10 ml vial.

- Ordering and pre-vaccination distribution of anthrax risk communication information and educational materials to service members and other personnel designated to receive the vaccination.

Question:

4. 3) (b) What is the shelf life of this vaccine?

Answer: The shelf life of the FDA-licensed anthrax vaccine is one year from the date the product is bottled and labeled by the manufacturer.

Question:

4. 4) Given DoD's poor performance in maintaining medical records during the Gulf War, what assurances can you provide that this program will be properly administered and documented in the future?

Answer: For both the accelerated program in Southwest Asia and the total force program, the anthrax vaccination program has high-level attention and oversight within the Office of the Secretary of Defense, the Joint Staff, the Services, and the warfighting Commanders in Chief (CINC). The Army Vice Chief of Staff is the Executive Agent for implementation of the anthrax vaccination program in Southwest Asia.

The CINC has placed a high priority on successfully implementing the vaccine program. On February 20, 1998, CENTCOM updated their deployment policy on implementing comprehensive joint medical surveillance measures, as outlined in the August 1997 Department of Defense Instruction 6490.3, Implementation and Application of Joint Medical Surveillance for Deployments. In addition to requirements for pre- and post-deployment health assessment questionnaires and daily and weekly disease and non-battle injury reporting, the CENTCOM policy stresses immunization tracking with special focus on the anthrax vaccine. CINC CENTCOM has directed that deploying personnel hand-carry their immunization record. Guidance on vaccination programs and other force medical protection measures for the theater are explicit regarding the requirement to document, retain, and, if appropriate, archive individual medical information. At the CINC's request, joint medical surveillance teams (JMST) have recently arrived in the CENTCOM area of responsibility to closely monitor and report on compliance with force medical protection/surveillance initiatives, including the anthrax vaccinations administered in theater.

An interim immunization tracking system (ITS) is in place to meet the immunization tracking requirements for the anthrax vaccination program. Currently, the Services use use different systems to capture and retain data locally, but they also transmit a core set of information in a standard format to DEERS. As individuals redeploy or move from one geographic location to another, the interim ITS will allow query of the DEERS database to confirm the vaccination status of an individual or update the individual service member's immunization record.

DoD is proceeding with a single, long-term solution to immunization tracking. In 1995, the Military Health System (MHS) began development of the Preventive Health Care System (PHCS)—a component of the Composite Health Care System (CHCS) II.

Immunization recording and tracking for military members, and all MHS beneficiaries, are essential components of PHCS. Requirements were approved in May 1996. Funding for PHCS was approved in August 1996. Prototype testing is occurring at MacDill Air Force Base, FL, Brooke Army Medical Center, TX, and Naval Hospital, Beaufort, SC. Operational testing is planned for FY 1998 with worldwide deployment anticipated in FY 1999. PHCS is programmed in the FY 99-2003 POM as a part of the Defense Health Program: CHCS II Deployment Surveillance Program. For active, Reserve, and National Guard activities that may lack a ready electronic link to CHCS II, a stand-alone PHCS product is being developed.

Question:

4. 5) Reuters News Service reported on March 7, 1998 that several research articles published within the last three months demonstrate that anthrax can be genetically altered and there is some evidence that forms of resistant vaccines already exist. A March 26, 1998 New York Times article also reported that Russian researchers may have produced strains of anthrax that may defeat the American vaccine. Does DoD have any evidence that anthrax can or has been genetically engineered to defeat the current American vaccine?

Answer: Russian scientists have reported the creation of an antibiotic resistant strain of anthrax--a relatively simple technical manipulation. They also described, in a 1997 publication, a study to improve their own anthrax vaccine. As part of that study, they genetically engineered a strain of anthrax to contain two foreign genes. That strain was resistant to the Russian anthrax vaccine unless the vaccine was modified to contain the same genes. This genetically engineered strain likely causes disease by a different mechanism than that used by naturally occurring anthrax strains. Such an organism would essentially be a new organism and not anthrax, as we know it.

Scientists from Los Alamos National Laboratory have described identification, using gene probes, of multiple strains of anthrax in tissue specimens obtained from victims of the 1979 Sverdlovsk anthrax incident. The laboratory press release implied that mixtures of anthrax strains might overcome the protection afforded by anthrax vaccine. However, this assertion was purely speculative and is not supported by any data.

The current U.S.-licensed anthrax vaccine is considered to be highly effective against naturally occurring strains of anthrax, including antibiotic resistant strains. The development of genetically engineered new organisms using anthrax or any other biological warfare agent is a potential threat that must be evaluated carefully. We are not aware, however, of any information to suggest that these modified strains have been used in any context other than the research laboratory. Creation of a new vaccine would require initiating a substantial research effort. Even a "new" strain hopefully would be susceptible to an antibiotic, and thus treatable. While vaccines offer the best means of protection and are an important component of our overall passive defense posture, physical protection in the form of the mask remains a critical element in our defense against biological weapons.

Question:

4. 6) DoD has decided to invest $130 million, over a six year period, in vaccinating the entire force of about 2.4 million personnel. Were other alternatives considered, for example, vaccinating only those personnel in relative high-risk areas and investing the remaining funds in developing a better biological agent detector?

Answer: The decision to vaccinate all service members against anthrax was made after a thorough two-year review effort and based on the recommendations of the Chairman and Joint Chiefs of Staff. During this review, all available alternatives were considered. Development of vaccines and other medical countermeasures against known biological warfare threats are vitally important because they increase our ability to provide full spectrum protection against these threats. Protective clothing and gas masks provide excellent front-line defense against biological warfare agent threats, but require detection of the agent to be effective. While research is ongoing to improve the threshold of point and stand-off biological warfare agent detectors, variables like weather, wind, and other external factors affect their ability to detect BW agents, particularly at low levels. Vaccines against biological warfare agents are given prophylactically, or before exposure, and provide individual protection when detection is absent or delayed and forces are exposed.

Question:

4. 7) In its May 1997 report, the General Accounting Office (GAO) recognized some progress since the Gulf War in DoD's medical surveillance procedures. However, it also identified some weaknesses during the Bosnia deployment in maintaining accurate deployment information, the timeliness of post-deployment medical assessments, and medical record-keeping. Given the relative small number of personnel involved in Bosnia compared to the pool of 2.4 million personnel DoD now plans to vaccinate, how can DoD ensure that the anthrax vaccination program will not be subject to these same, serious shortfalls?

Answer: The response to Question 4, sub-question 1, documents the requirements in place and the future plans to minimize problems with the anthrax vaccination program. It is important to note that the GAO report focused on the administration of tickborne encephalitis (TBE) vaccine to some service members in Bosnia. TBE vaccine was used as an investigational new drug (IND); anthrax vaccine is a licensed vaccine. While it is important to accurately document all vaccines, IND vaccines have more extensive documentation requirements imposed by the Food and Drug Administration in their regulatory oversight of IND products.

Question:

4. 8) Currently, DoD only requires medical exams every five years for most active and reserve personnel. How will DoD ensure that personnel are notified that they are to receive their annual booster shot and receive that inoculation?

Answer: The immunization tracking systems that will document the anthrax vaccinations will also be used as a management tool to inform commanders about the

status of individual and unit immunizations and to provide reminders when shots are required.

Question:

4. 9) In November 1993, DoD established the policy, responsibility, and procedures for stockpiling biological agent vaccines and determined which personnel should be immunized and when the vaccines should be administered.

(a) Why did it take until now to approve this policy for anthrax?

Answer: The department took a very methodical approach in developing this policy which translated into a slower than usual process. It was the first policy involving total force immunization against a biological agent so an extraordinary amount of analysis and coordination were deemed prudent. Additionally, tracking systems were not fully operational which was a requirement prior to implementation.

Question:

4. 9) (b) What were DoD's concerns about this policy and how were they resolved?

Answer: DoD had no major concerns relative to the efficacy or requirement for this policy.

Question:

4. 9) (c) Are there any other vaccine programs in DoD that have a similar dosage requirement (six shots followed by annual boosters)? Please describe how those vaccines are administered and documented.

Answer: No, there are no other vaccines in current use that have similar dosage requirements (six shots over 18 month time interval with annual boosters).

Question:

4. 10) A number of issues regarding potential problems with implementation of the new anthrax vaccination program with active military personnel have already been raised. Please describe DoD's plan to implement and monitor this program for Reserve and National Guard personnel who are supposed to be prepared for activation and possible deployment to problem areas such as the Persian Gulf and Korea where these threats exist.

Answer: The Service total force anthrax vaccination program implementation plans, which have either been signed or are in the process of being signed by their respectively Service Secretaries, address how each Service will implement and monitor the program with respect to Reserve Component (RC) personnel (i.e., Reserve and National Guard). In general, anthrax vaccinations for the total force will be administered to RC personnel by health care providers at the following locations: Department of Defense medical facilities; Coast Guard medical facilities; Veterans Affairs (VA) or Public Health Service medical facilities; Federal Occupational Health (FOH) Service medical facilities; Indian Health Service medical facilities; and where necessary, by civilian contract teams or facilities.

Phase I of implementation for total force anthrax vaccinations will vaccinate all forces, Active Component (AC) and RC, forward-deployed or assigned to high threat areas of South West Asia (SWA) and Korea. Those RC rotating back to CONUS after deployment will continue the vaccination schedule to complete the six shot series.

Phase II will vaccinate AC and RC early deploying forces (C to C+35) supporting SWA and Korea. The remainder of the total force, accessions, and sustainment (including the remainder of Reserve Component).

Question 5: Why only Anthrax?

Anthrax is not the only biological weapon that U.S. military personnel may be exposed to in future conflicts. During the Gulf War 8,000 doses of botulinum toxoid vaccine were administered to U.S. troops to protect against a weaponized version of that agent. Why only protect our troops against anthrax when exposure to botulinum toxoid is also a possibility?

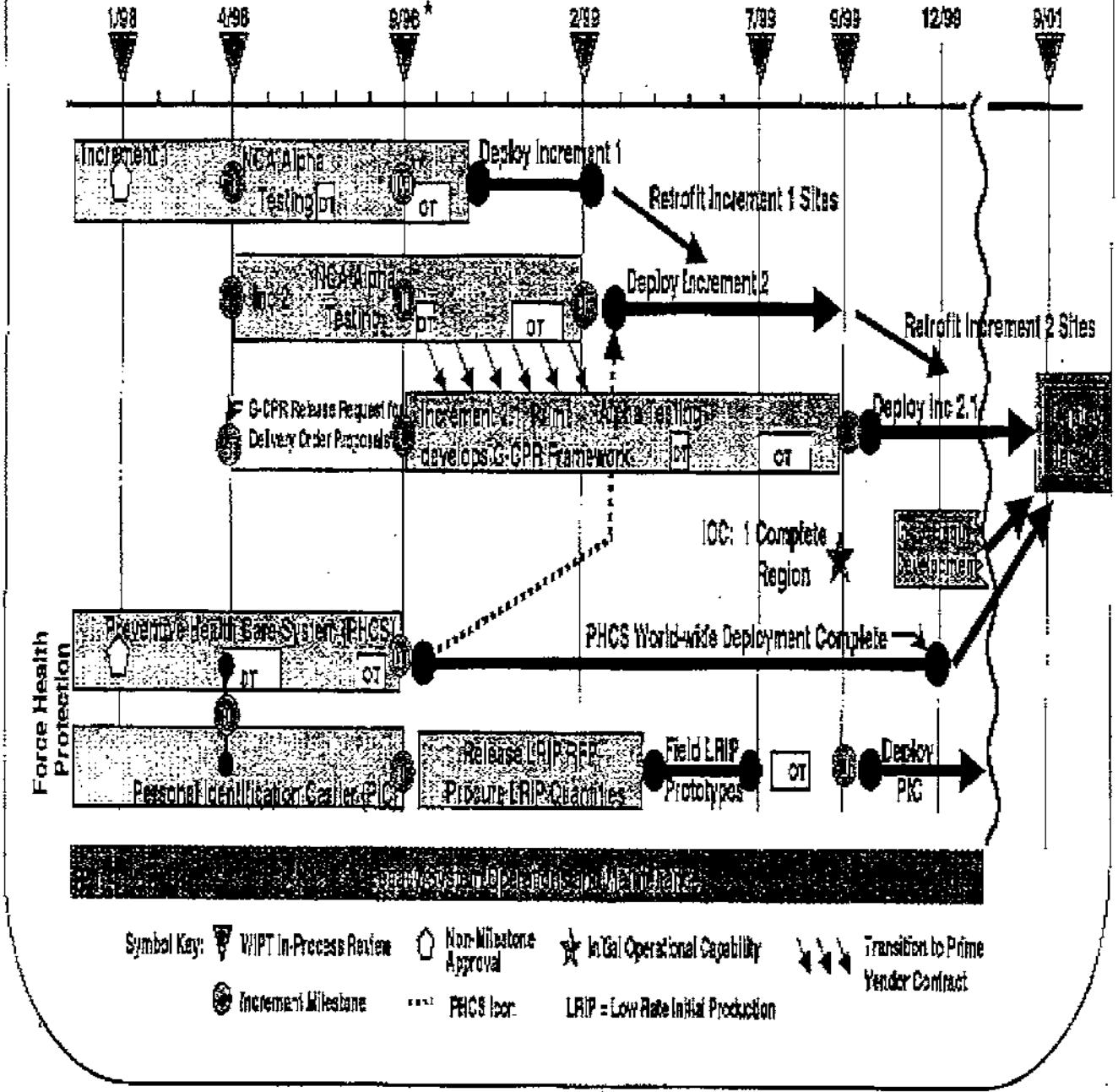
Answer: Although botulinum toxin is a biological weapon threat, we do not have a licensed (FDA-approved) vaccine to use as a countermeasure. Given the technical and logistical considerations associated with a vaccination policy that provides total force protection, the Department currently plans to use only licensed vaccines with the total force. In a military combat emergency, when the best medical defense against chemical and biological warfare agents requires the emergency use of drugs and vaccines not approved by the FDA for general commercial use as a chemical or biological warfare agent treatment/antidote, the Department may require the use of products classified by the FDA as INDs. The use of botulinum toxoid vaccine is in this category.

Question 6: Health Preparedness.

Health preparedness includes ensuring that troops are sufficiently healthy to deploy to a conflict. Reservists who lack health insurance through their regular, non-military employment may lack access to medical care. Since Reservists are only required to have a DoD physical every five years, health problems may go undetected. How can you ensure the health preparedness of Reservists and National Guard personnel?

Answer: In accordance with Section 10206 (a)(2), Title 10, USC, each Reserve Component (Reserve and Guard) member is required to execute and submit annually to the respective Service Secretary a certificate of physical condition. This certificate is completed by the member, and subsequently reviewed by a military medical authority. If a medical condition is identified, the member is informed of the condition, and they are advised to seek medical follow-up (treatment) for corrective action, and continuation in an active Reserve status. Failure to comply may mean separation from Reserve status.

CHCS II Program Schedule with Incremental Milestones/IPRs

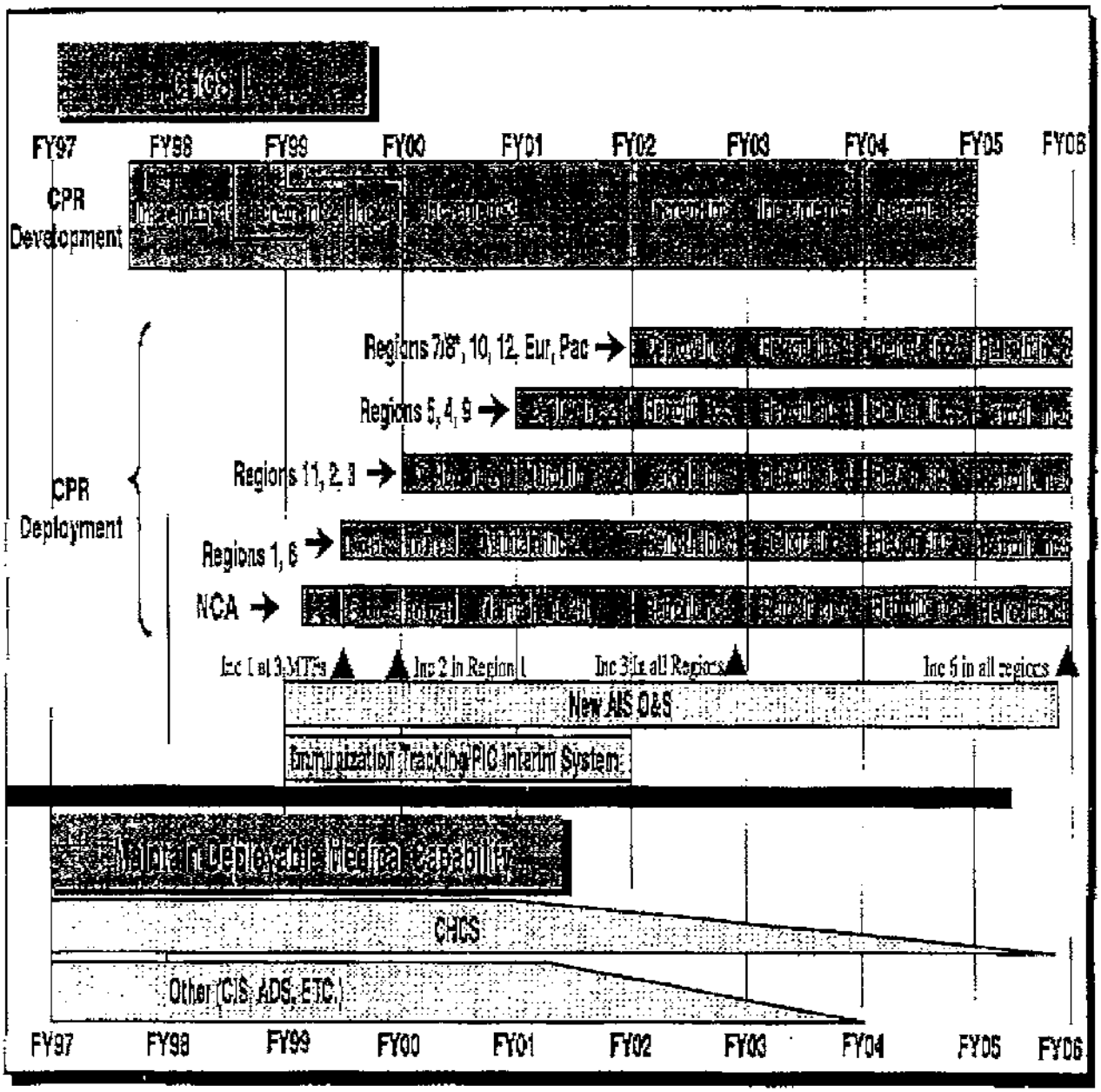


Enclosure 1

* EA and CCA must be reconciled prior to MS II; and the Concept Baseline will be established at MS II.

** Milestone III contingent upon DOT&E Report on successful CT&E results.

CHCS II Deployment Plan



* Regions seven and eight have been combined and are now called the TRICARE Central Region, but for the CHCS II Program, the designation "seven" and "eight," and the number fourteen versus thirteen TRICARE regions, will be retained to match deployment schedules of other MHS programs already underway.

Enclosure 1

United States Senate

COMMITTEE ON VETERANS' AFFAIRS
WASHINGTON, DC 20510-6375

March 30, 1998

Mr. Gary Christopherson
Acting Assistant Secretary
of Defense, Health Affairs
Department of Defense
The Pentagon
Washington, D.C. 20301

Dear Mr. Christopherson:

Thank you for testifying before the Committee on March 17, 1998 about the shortcomings that the Department of Defense has identified in chemical and biological preparedness and medical readiness during the Gulf War, lessons learned from the experience and strategies for future deployments. Unfortunately, time constraints hindered Committee members from asking a number of questions that would have completed the hearing record. We would appreciate your response for the record to the enclosed set of questions by April 6, 1998.

Please forward your responses to:

Senate Committee on Veterans' Affairs
412 Russell Senate Office Building
Washington D.C. 20510-6375
Attention: Mr. Dat Tran

Should you have any questions, please contact Terence Lynch (202-224-4305) of the Committee staff. Thank you for your prompt attention to this matter.

Sincerely,

Arlen Specter

Arlen Specter

2495A

Secretary Christopherson:

DoD coordination with the Department of Veterans' Affairs

1) What has DOD learned over the last seven years from its experience with Desert Storm/Desert Shield and Bosnia veterans that will change the way veterans will receive post-deployment health care and services?

2) How has DOD coordinated with the Department of Veterans Affairs any strategies to address health problems associated with exposure to BW/CW?

3) What has DOD done to coordinate with the Department of Veterans Affairs the development of individual medical baselines on military personnel who are being sent to the Gulf and who may be sent to future military engagements?

Improved medical tracking

4) In your prepared statement, you mentioned the computer-based patient record (CPR), the Theater Medical Information Program and the Personal Information Carrier (PIC) as systems designed to improve medical tracking. What are the development and fielding schedules for these items?

Pyridostigmine bromide

5) The records for the documenting use of pyridostigmine bromide (PB) during the Persian Gulf War are incomplete. For example, in June 1994, the Defense Science Board Task Force stated, "Although all units were given PB, the Department of Defense does not have records of which military personnel actually ingested PB, nor of how many tablets may have been ingested."

a) What is DOD's current policy on the use of this drug and how its use will be monitored?

Anthrax Vaccine Program

6) When Secretary Cohen initially announced that DoD would proceed with inoculation of all U.S. service members against anthrax, he outlined four conditions that needed to be met: (1) safety testing; (2) a plan for tracking of vaccines; (3) approval of operational plans to administer the vaccines and inform troops; and (4) review of the program by an independent expert. The plan to vaccinate troops has been understandably moved up because of the presence of our troops in the Gulf. But, we still need to learn from the lessons of the Gulf in making plans for future deployments. Please describe DoD's current progress on <u>each</u> of the four conditions that Secretary Cohen initially outlined.

7) The current anthrax vaccine program requires military service personnel to receive six shots over a period of eighteen months, followed by a booster shot every year. It is the Committee's understanding that the Department of Defense is exploring the efficacy of a different shot regimen.

a) If there is indeed a new program being considered, what is DoD's plan for implementation? 8)

On March 6, 1998, CNN reported that 200,000 doses of anthrax vaccine had to be recalled because they had been frozen, and thus ruined, during shipment to the Middle East. This illustrates some of the significant logistical hurdles of vaccinating our troops.

a) Please describe other logistical hurdles needed to be overcome for this plan to work.

b) What is the shelf life of this vaccine?

9) Given DOD's poor performance in maintaining medical records during the Gulf War, what assurances can you provide that this program will be properly administered and documented in the future?

10) Reuters News Service reported on March 7, 1998 that several research articles published within the last three months demonstrate that anthrax can be genetically altered, and there is some evidence that forms of resistant vaccines already exist. A March 26, 1998 New York Times article also reported that Russian researchers may have produced strains of anthrax that may defeat the American vaccine. Does DoD have any evidence that anthrax can or has been genetically engineered to defeat the current American vaccine?

11) DOD has decided to invest $130 million, over a six year period, in vaccinating the entire force of about 2.4 million personnel. Were other alternatives considered, for example, vaccinating only those personnel in relative high-risk areas and investing the remaining funds in developing a better biological agent detector?

12) In its May 1997 report, the General Accounting Office (GAO) recognized some progress since the Gulf War in DOD's medical surveillance procedures. However, it also identified some weaknesses during the Bosnia deployment in maintaining accurate deployment information, the timeliness of post- deployment medical assessments, and medical record-keeping. Given the relative small number of personnel involved in Bosnia compared to the pool of 2.4 million personnel DOD now plans to vaccinate, how can DOD ensure that the anthrax vaccination program will not be subject to these same, serious shortfalls?

13) Currently, DoD only requires medical exams every five years for most active and reserve personnel. How will DOD ensure that personnel are notified that they are to receive their annual booster shot and receive that innoculation?

14) In November 1993, DOD established the policy, responsibilities, and procedures for stockpiling biological agent vaccines and determined which personnel should be immunized and when the vaccines should be administered.

a) Why did it take until now to approve this policy for anthrax?

b) What were DOD's concerns about this policy and how were they resolved?

15) Are there any other vaccine programs in DOD that have a similar dosage requirement (six

shots followed by annual boosters)? Please describe how those vaccines are administered and documented.

Why only Anthrax?

16) Anthrax is not the only biological weapon that U.S. military personnel may be exposed to in future conflicts. During the Gulf War 8,000 doses of botulinum toxoid vaccine were administered to U.S. troops to protect against a weaponized version of that agent. Why only protect our troops against Anthrax when exposure to botulinum toxoid is also a possibility?

Posthearing Questions
Concerning March 17, 1998 Hearing

For The Honorable Gary Christopherson
Acting Assistant Secretary of Defense, Health Affairs
Department of Defense

From Senator John D. Rockefeller IV
Ranking Minority Member
Senate Committee on Veterans' Affairs

Pyridostigmine Bromide

1) Given DoD's new guidelines that PB will be used only if there is intelligence information indicating threat of the use of soman or tabun, is DoD acknowledging that there may be health risks when PB is used in association to an exposure to other chemical warfare agents, such as sarin? Does DoD now have reason to believe that PB may otherwise harmful when used by a healthy population?

2) Given the disputes between DoD and FDA on DoD's ability to comply with Investigational New Drug (IND) agreements and requirements, what is DoD's policy for current or future applications for the use of Investigational New Drugs in peacetime or combat missions?

Anthrax Vaccine Program

3) A number of the issues regarding potential problems with implementation of the new anthrax vaccination program with active military personnel have already been raised. Please describe DoD's plan to implement and monitor this program for Reserve and National Guard personnel who are supposed to be prepared for activation and possible deployment to problem areas such as the Persian Gulf and Korea where these threats exist.

Health Preparedness

4) Health preparedness includes ensuring that troops are sufficiently healthy to deploy to a conflict. Reservists who lack health insurance through their regular, non-military employment may lack access to medical care. Since Reservists are only required to have a DoD physical every five years, health problems may go undetected. How can you ensure the health preparedness of Reservists and National Guard personnel?

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Subject: SENATOR HAS CONCERNS REGARDING CHEMICAL AND BIOLOGICAL PREPAREDNESS AND MEDICAL READINESS DURING THE GULF WAR

Date Written: 03/30/98 **Date Received:** 04/06/98 **Signature:** AASD

From: SPECTER, ARLEN SENATOR

Action Office(s): HOP

Coord Office(s):

– Cirone Norris
– Trump
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Ent Ofc Note: THE LEAD ACTION OFFICE IS HOP.

Ack 28 Apr 98 - BB

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(23)

CMAT Control #
2002198-0000037

HA/TMA Document Profile

2002198-0000037

38321

Subject:	Anthrax Vaccine Policy		
Author:	MOC Richard G. Lugar	Congressional Name:	Richard G. Lugar
Date of Document:	6/24/2002	Input By:	ASARDO
OSD #:	U10648-02	Profiler's Directorate:	HA
PR #:	0101237	Response Signed By:	
Organization:		Dt Response Signed:	
Department:		Doc Type:	102-18
Assigned To:	FHP&R	Application:	DOCSIMAGE
Prepared For:	USD(P&R)	Previous Documents:	
Suspense Date:	7/8/2002	Related Documents:	
Coord Office(s):	LA		

Notes:
On 7/16/02 A&CD fwd signed actio memo/pkg to USD(P&R).(gjs)
On 7/16/02 rec'd LA chop and inserted in orig pkg. (aas)
On 7/16/02 packaged hard copy in A&CD and fwd to HA FO for review.. Copies to LA and OGC for coordination. (aas)
Fwd to HA Admin for packaging 7/16/02–jlw-r. On 7/2/02 submitted 391 to request extension until 7/15/02. (aas)
On 7/2/02 rec'd tasker in A&CD, scanned and routed to FHP&R.

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INDIANA
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WASHINGTON, DC 20510
202-224-4814

AGRICULTURE, NUTRITION, AND FORESTRY
FOREIGN RELATIONS
SELECT COMMITTEE ON INTELLIGENCE

United States Senate

WASHINGTON, DC 20510-1401

June 24, 2002

The Honorable Donald H. Rumsfeld
Secretary of Defense
1000 Defense Pentagon
Washington, DC 20301-1000

Dear Secretary Rumsfeld:

I have noted recent developments in the Department of Defense's anthrax vaccine policy. Reports suggest that you have signed off on a plan to set aside your predecessor's policy to vaccinate the entire force in favor of a plan that will only vaccinate those who are at risk for exposure. As you finalize details of the new plan, I ask you to review carefully the effects that the old program had on the uniformed military who refused to submit to the shot series and left the military.

In October 2001. my staff and I were inconvenienced for over three months by contamination resulting from the famed "Daschle letter," which contained a highly virile strain of anthrax. We all gained new understanding about the effectiveness of anthrax vaccines as well as the great degree of variance in susceptibility of individuals to anthrax spores. We also came to the realization that what we knew previously about anthrax was limited and that supposed protections against exposure may not have had any effect in this instance.

More recently, I read a book by Lieutenant Colonel Thomas S. Heemstra, entitled *Anthrax, a Deadly Shot in the Dark,* which was given to me by (b)(6) a constituent who refused to take the shots and was subsequently discharged from the (b)(6) (b)(6). LCOL Heemstra writes eloquently of the plight of those who believed that the anthrax vaccine was not effective and was not safe, and perhaps more so, felt that the government they served was not dealing honestly with them. I recommend it to you.

The old policy was promoted as a lawful order and used the Uniform Code of Military Justice to bring members into compliance, but neither the policy or the UCMJ were implemented uniformly across or within the services. For example, in the Indiana Air National Guard, 16 pilots (nearly half the squadron) were dismissed or resigned from a single squadron and no longer serve. LCOL Heemstra notes the glaring disparity between those actions and the lengthy informed consent procedures used when postal workers and Senate staff were offered the same vaccine last year.

As you review the actions of the past Administration and the institutional military that carried out the orders involving the anthrax vaccine, and as you lay out the road ahead seeking best protections of our troops against this deadly substance, I urge you to carefully consider the individuals who were victims of a policy that at can easily be called flawed, particularly (b)(6)

(b)(6) and the other pilots of the (b)(6) And, I hope you will find it appropriate to extend to them invitations to return to military service.

Thank you for your attention to these issues.

Sincerely,

Richard G. Lugar
united States Senator

RGL/pem
Cc: (b)(6)

U.S. SENATOR
RICHARD G. LUGAR
Indiana

FAX TRANSMISSION

To: Secretary Rumsfeld

Office: OSD

Fax #: (b)(6)

Page: 1/ 3 Date: 6/28/02

From: Patrick Garvey

Please Note:

Hard copy in mail.

Patrick

Senator Richard G. Lugar
306 Hart Senate Office Building
Washington, DC 20510-1401
Phone: 202224.4814
Fax: 202228.0360

Congressional

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Action Agency: UPR

Suspense Date: 7/8/02

1. ACTION TAKEN (Check one)

- [ ] a. ACTION HAS BEEN COMPLETED (Copy attached)
- [x] b. REQUEST EXTENSION OF SUSPENSE DATE TO 07/15/2002 *(Justify below)*
- [ ] c. *INTERIM* REPLY HAS BEEN SENT (Copy attached) EXTEND SUSPENSE TO (J u s t i f y below)
- [ ] d. REQUEST CANCELLATION *(Justify below)*
- [ ] e. **REQUEST** TRANSFER TO _____ *(Justify below* /include POC Name & Phone Number)
- [ ] f. REQUEST DOWNGRADE TO _____ *(Justify below)*

2. JUSTIFICATION

Respectfully request extension due to the holiday and the coordinations necessary to prepare a complete and accurate response on this issue.

3. REPORTING AGENCY

a. ACTION AGENCY: HA

b. NAME OF ACTION OFFICER: Anita Sardo

c. TELEPHONE NO.: (b)(6)

d. DATE: 07/02/2002

e. APPROVING AUTHORITY (Service Secretary/Under Secretary/ASD/Military/Executive Assistant Level)

Signature: Anita Sardo

Date signed: 7/2/02

4. CCD CONTROL #: U10648-02

5. ACTION TAKEN (For EXSEC/ Correspondence Control Division Use Only)

a. EXT	[ ] Approved	[ ] Disapproved
b. CANX	[ ] Approved	[ ] Disapproved
c. DWNGRD	[ ] Approved	[ ] Disapproved
d. TRANSFER	[ ] Approved	[ ] Disapproved
e. OTHER (Specify)		

Signature: _____ Date Signed: _____

SD FORM 391, JAN 2000

ACTION MEMO

July 9, 2002, 4:30PM

FOR ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ellen P. Embrey, DASD, Force Health Protection and Readiness

SUBJECT: Response to Anthrax Vaccine Policy letter from Senator Lugar

- Tab A is proposed response to a letter from Senator Richard Lugar requesting Secretary Rumsfeld review the judicial punishments associated with the Anthrax Vaccine Immunization Program. He also suggests that Secretary Rumsfeld consider issuing invitations to return to the military service to any service member discharged for refusal to comply with the AVIP.

RECOMMENDATION: USD (P&R) sign proposed response at Tab A.

COORDINATION: Tab B.

Prepared By: COL Denise Baken, OASD (HA)/FHP&R (b)(6)
PCDOC: 38321 R/ 38543

ACTION MEMO

FOR: UNDER SECRETARY OF DEFENSE (PERSONNEL AND READINESS)

FROM: Assistant Secretary of Defense (Health Affairs)

SUBJECT: Response to Anthrax Vaccine Policy Letter from Senator Lugar

- Tab A is the proposed response to a letter from Senator Richard Lugar requesting Secretary Rumsfeld review the judicial punishments associated with the Anthrax Vaccine Immunization Program. He also suggests that Secretary Rumsfeld consider issuing invitations to any service members who were discharged for refusal to comply with the AVIP to return to military service.

- Tab B is the incoming letter from Senator Lugar to Secretary Rumsfeld.

RECOMMENDATION: USD (P&R) sign proposed response at Tab A.

COORDINATION: Tab C.

Attachments:
As stated

Prepared By: COL Denise Baken, OASD (HA)/FHP&R ((b)(6)
PCDOCS # 38543,38321

The Honorable Richard G. Lugar
United States Senate
Washington, DC 205 10

Dear Senator Lugar:

Thank you for your letter to Secretary Rumsfeld on behalf of your constituent (b)(6) (b)(6) I appreciate your concern for our military members.

In your letter, you cite Lieutenant Colonel Thomas Heemstra's book, and his reference to the recent use of the anthrax vaccine for postal workers and Congressional staff personnel as a reason for military members to view the Anthrax Vaccine Immunization Program as unfair. I would like to clarify the difference between the Centers for Disease Control (CDC) use of the anthrax vaccine and that of the Department of Defense. The CDC offered anthrax vaccine to U.S. Postal Service workers and Congressional staff as a post-exposure treatment, a use for which the anthrax vaccine is not Food and Drug Administration (FDA) licensed. The CDC had to, therefore, adhere to FDA accepted procedures of administering the vaccine under an "investigational new drug" protocol with informed consent. The Department of Defense, on the other hand, uses the anthrax vaccine as a pre-exposure prevention, the use that is consistent with its FDA license.

You also raise the issue of members discharged after refusing a lawful order. A member is discharged for refusing to obey a direct order only after a commander's assessment has determined the unique factors of the case warrant it. While there are standards to guide the commander in the range of disciplinary actions that can be taken for a refusal, each is unique.. The options available to a commander to resolve disciplinary problems range from taking no action, imposing administrative action, imposing or nonjudicial punishment, with Article 15, Uniform Code of Military Justice or referring the charges to a court-martial_

It is the policy of the military justice system to use the lowest level of disposition that will further the interests of justice and discipline. The disposition should be warranted, appropriate and fair. No superior officer may attempt to improperly influence the commander in the exercise of his or her independent discretion when disposing of an offense. More importantly, the Manual for Courts-Martial, the Uniform Code of Military Justice, and Service regulations provide a host of due process rights that are guaranteed to every solider, sailor, airman or marine who refuses an order to receive the anthrax vaccination. Among those rights are the right to consult with a military attorney at no cost, legal representation by an attorney in any special or general courts-martial, the right to notification of adverse administrative proceedings and an opportunity to present matters at those same proceedings, the right to appeal adverse decisions to superior commanders, and the right to request discharge upgrades from service review boards. We believe, therefore, that disciplinary issues associated with the Anthrax Vaccine Immunization Program have been concluded in the most appropriate manner available.

In view of the recent bioterrorism events, the validated threat associated with anthrax, and the defined parameters of our present policy, we do not anticipate that service members will refuse immunization. Further, any concerns that are raised by service members during this process will be directly addressed by medical personnel who are knowledgeable on the safety and efficacy of the vaccine. Again, thank you for your letter and the opportunity to discuss the program.

Sincerely,

David S. C. Chu

The Honorable Richard G. Lugar
United States Senate
Washington, DC 205 10

Dear Senator Lugar:

Thank you for your letter to Secretary Rumsfeld on behalf of (b)(6) I share your concern for the health and well-being of all of our dedicated men and women serving or who have served in our Armed Forces.

I want to emphasize that the anthrax vaccine has continually proven to be safe and effective. Numerous human studies, some dating back almost 50 years, support this fact. There are no known long-term side effects to anthrax vaccine. At Fort Detrick, more than 1,500 laboratory workers have been followed for 20 or more years after receiving anthrax vaccine. Most of these workers received 150 to 200 vaccinations and skin tests; some received more than 300 injections during their tenure at Fort Detrick.

More recently, the National Academies of Sciences, Institute of Medicine, was asked by the Department of Defense to review data on the safety and efficacy of the anthrax vaccine based on concerns expressed by some military members and members of Congress. This report, released in early 2002 after a comprehensive 15-month review, found that the anthrax vaccine is safe and effective in protecting against anthrax infection, including inhalation anthrax. The study concluded that anthrax vaccine side effects are common but tend to be local reactions commonly seen in all vaccines. There is no evidence to suggest that long-term health effects were associated with receipt of anthrax vaccine.

Thank you for highlighting Lieutenant Colonel Heemstra's book, "Anthrax; a Deadly Shot in the Night." I appreciate that it provides a perspective that is not unlike the various theories promulgated as causes of unexplained illnesses associated with the Gulf War. We continue to allocate significant resources towards this issue in a deliberate effort to prevent or mitigate similar events in future contingencies.

While Lieutenant Colonel Heemstra exercises his first amendment rights in writing his book, his views are not consistent with those of the expert panels advising the Department of Defense on this vaccine. Views expressing concerns about short- and long-term vaccine consequences in the United Kingdom where childhood vaccination is voluntary have led to lowered uptake of vaccine and increased morbidity and mortality in children from common childhood illnesses like measles, mumps, rubella, etc.

The Department of Defense has consistently used the anthrax vaccine as a pre-exposure protection against anthrax, a purpose for which the vaccine is fully licensed by the Food and

Drug Administration. The information provided to servicemembers prior to the vaccination focuses on the threat, safety and efficacy of the vaccine. After U.S. Postal Service workers and Congressional staff were exposed to anthrax spores in letters, the anthrax vaccine was offered under an investigational new drug protocol because it is not FDA licensed for use after exposure. The use of an investigational new drug requires extensive information to the individual, is voluntary, and requires a written informed consent. These two situations are extremely different.

The DoD's anthrax vaccination program remains mandatory for those determined to be at risk. If individuals refuse after being counseled and ordered to take the vaccination, they are subject to the Uniform Code of Military Justice (UCMJ) for disobeying a direct order. Under the UCMJ, individuals are fully informed of their rights and options. While there are standard policies to guide the commander in the range of disciplinary actions, it is the policy of the military justice system to use the lowest level of disposition that will further the interests of justice, discipline, and good order. The National Guard Bureau's records show a total of 13 rated officers (pilots) voluntarily separated as a result of the anthrax vaccine. Additionally, six enlisted guard members voluntarily separated for this same issue.

Under separations that are voluntary in nature, a former Guard member can apply for re-instatement. Hypothetically, if separations were involuntary with adverse information in his or her record, the servicemember could appeal to the board of military records and, if favorably adjudicated, apply for reinstatement to the Air National Guard.

I thank you for your letter and the opportunity to discuss our anthrax vaccination program.

Sincerely,

David S. C. Chu

SUBJECT: Response to Anthrax Vaccine Policy letter from Senator Lugar

COORDINATION PAGE

DASD (FHP&R)	7/i 6/02
cos (HA)	_____
PDASD (HA)	_____

SUBJECT: Response to Anthrax Vaccine Policy letter from Senator Lugar

COORDINATION PAGE

OLA _____

OGC _____

ACTION **MEMO**

July 9, 2002, 4:30PM

FOR ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ellen P. Embrey, DASD, Force Health Protection and Readiness JUL 16 2002

SUBJECT: Response to Anthrax Vaccine Policy letter from Senator Lugar

- Tab A is proposed response to a letter from Senator Richard Lugar requesting Secretary Rumsfeld review the judicial punishments associated with the Anthrax Vaccine Immunization Program. She also suggests that Secretary Rumsfeld consider issuing invitations to return to the military service to any service member discharged for refusal to comply with the AVIP.

RECOMMENDATION: USD (P&R) sign proposed response at Tab A.

COORDINATION: Tab B.

Prepared By: COL Denise Baken, OASD (HA)/FHP&R (b)(6)
PCDOC: 38321 R/ 38543

[redacted]

Personnel and Readiness Internal Tracking Sheet

JUL 17 2002

_____
_____
_____ CAPT (b)(6)
_____ LTC (b)(6)

POC: COL Baken HA 681-1711
Originator: Dr. Winkenwerder
Tracking # 0101237
ECD # U10648-02
Subject: Response to Anthrax Vaccine Policy Letter from USS Lugar – ACTION MEMORANDUM

Action Taken

Date: _____
Signed: _____
Sent to: _____
Returned for Edits: _____
Return to: _____

NOTES

Please ASAP

1) Date – DoD report on Anthrax safety
2) Comment on Lot Release Book
3) Comment on Indiana National Guard dismissal and court martial numbers

Can Paul Clarke

38543, 38321

U.S. House of Representatives

COMMITTEE ON VETERANS' AFFAIRS
ONE HUNDRED SEVENTH CONGRESS
335 CANNON HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
http://veterans.house.gov

February 7, 2002

Ms. Ellen Embry
Secretary of Defense
Deputy Assistant Secretary of Defense for
Force Health Protection and Readiness
Department of Defense
The Pentagon, Washington, DC 20301

Dear Ms. Embry:

In reference to our Subcommittee oversight hearing of January 24, 2002, please answer the enclosed questions by the close of business February 22, 2002

Please provide your answers consecutively on legal size paper, single-spaced and restate the question in its entirety before the answer.

Sincerely,

Jerry Moran

JERRY MORAN
Chairman
Subcommittee on Health

Enclosure

JM:khc

Questions for Department of Defense

1) I appreciate both views of DoD and VA in respect to actions now being taken to protect troop health, and to ensure transitions of records and information from DoD to VA. Can you help us by forecasting how your improved systems will deal with veterans coming home from this new war?

2) Ms. Embrey, Senator Riegle asserted char thousands of chemical alarms were sounded during Desert Storm, but the Defense Department maintained that every one was a false alarm-that our troops in fact were not exposed to dangerous chemical substances in Kuwait or Iraq. Many efforts to review the Gulf War referred back to those alarms and the Department's posture that chemicals were not involved, Is that the Department's current position in light of the health status of Gulf War veterans?

3) Whst actions have you taken to upgrade chemical alarms and develop biological alarms? Do the troops in Afghanistan now have access to better chemical alarms?

4) General Blanck's written statement reviews the issue of missing or non-existent records having hindered the Army's work in crying to discover the underlying causes for problems Gulf War troops were experiencing. Give me a bit of insight into what kinds of records DoD and VA would have needed to be able to capture information sufficient to address a cause and effect. In other words, what kinds of records were missing or non-existent?

5) Ms. Embrey, your statement placed a separation between what DoD is attempting to do for the active duty members and your references to veterans, whom you say would be, and I quote, "best served" by scientific research to address their health concerns. All of your active duty members eventually become veterans, because veterans are "made" by military service, not "born" as veterans. Does the Department intend to continue to make such a distinction with respect to the current deployment in Central Asia, or do you acknowledge some responsibility within DoD for the health status of all veterans?

6) Ms. Embrey, you indicate the Department of Defense is, and I quote, "assessing and monitoring current deployments" for health care needs. What kinds of mechanisms is the Department using to carry out such assessment and monitoring?

7) Ms. Embrey, you testified about the Institute of Medicine's three-year study that made a series of recommendations to the Department on protecting the health of deployed U.S. forces. Can you tell us among the recommendations made, how many have been implemented and explain those that haven't been accepted and why?

8) I am especially concerned about reserves and their status. As I said in my opening statement, I recently witnessed the deployment of a reserve unit in Kansas. These are civilians who are called up, coming from all walks of life. In terms of preparation, da members of activated reserves get the full platter of preventive training, health baseline examination, equipment and other facets of DoD's policies? In other words, is there one standard applied to borh the "'professional" soldier and the activated reserve? How do you monitor the reserves co ensure this is so?

9) Law-level environmental hazards are generally difficult to detect. Is the Department developing technologies with chemical and biological sensors capable of detecting sub-lethal doses of chemical or biological agents? What is the state of development of such devices?

10) Can you confirm for the Committee that DoD has developed better operational tracking systems for personnel and units so that the costly effort of trying to learn where people were located after we discover a problem -- such as an exposure to chemical weapons -- can be reduced and we can bener identify who may be at risk? Would you call this a lesson learned from the Gulf War?

11) What other lessons did we learn from the Gulf War that we are now putting to use in Operation Enduring Freedom? Can you give me specific examples of something identified then as an error or commission that is now implemented and is specifically addressed in the current deployment?

12) Will we be able to know where every uniformed DOD member has served on the ground during Enduring Freedom? In other words, should

we identify a disease or illness after the fact associated with particular areas, in Kandahar or Tora Bora for example, will we be able to overlay troop movements to determine the individuals who may have been exposed? What is the mechanism DoD is using to do such tracking, and will you be able to transfer this data to VA for VA's use in providing health care, conducting biomedical research and for benefits purposes?

13) The Committee understands that the Office of the Special. Assistant far Gulf Wax Illnesses has spent in excess of $130 million over rhe past five years on publishing "case narratives" and "literature reviews?" Are these activities subjected to scientific peer review?

14) How much funding has DoD expended for Gulf-related medical research over the past five years? Can you point to anything you learned from either rhe case narratives, reviews or research char has been put to use for the troops in the field today, particularly for those in Afghanistan?

15) The Senate Committee on Veterans' Affairs made a significant investigation in researching rhe possible causes of Gulf War veterans' health problems. That effort was thoroughly documented in a 199 8 report. Among its findings were failures on the part of the Department of Defense to protect troops we sent to thc Gulf. Specifically cited were failures in issuing proper equipment, training, vaccinations, documentation and record keeping. The report included 29 important recommendations in all, most directed at DoD and VA. How many of these recommendations hsvc bccn implemented, and do you believe these recommendations helped Dob and VA learn some of the lessons of the Gulf War'? How so?

16) As you are probably aware, patient advocates are often included as voting members on peer-review panels within NIH-funded programs. Given that fact, why are veteran advocates excluded from representation on the Research Working Group, thc body responsible for deciding which Gulf War illness studies will or will not be funded? What is your justification for excluding advocates from this body?

17) Recent media reports indicate that a new, as-yet unpublished study concerning the anthrax vaccine shows, for women, an association between anthrax inoculation and an increase in risk for birth defects. Are you aware of thie study and what is the Department planning to do with

respect to women active duty members and the anthrax vaccine? Are you coordinating your work with VA, and how so?

18) Section 765 of the 1998 National Defense Authorization Act (PL 105-85) requires the Defense Department to conduct pre-and post-deployment health examinations including mental health screenings and blood sample to record the baseline health of each active duty member before deployment and any changes in health during the course of deployment. Are they being done and can you provide the Subcommittee evidence to confirm this is rhe policy?

19) What role has VA played in helping DoD develop appropriate pre- and post-deployment health survey instruments and testing procedures to be used by DoD?

20) Ms. Embrey, despite the difficulties with the vaccination program in the Persian Gulf War, the Department's vaccination protocol is of interest to the Committee. Please provide a copy of this proroco1; the current official protocol for vaccinations applicable to the forces being deployed in Central Asia; and, the vaccinations protocol for troops now deployed in the Philippines operation.

21) Ms. Embry, you stated DoD has implemented 12 policy changes. based on lessons learned following the Gulf War, to improve the delivery of health care to our active duty Personnel. What are those policies and how has their implementation changed the pre and post-deployment health assessment protocol? Is DoD better informed to quickly identify health hazards and to forward that information to the Department of Veterans Affairs? Please provide the Committee each of the 12 directives or other documentation establishing these new post-Persian Gulf War force protection policies.

Question 1:
I appreciate both views of DoD and VA in respect to actions now being taken to protect troop health, and to ensure transitions of records and information from DoD and VA. Can you help us by forecasting how your improved systems will deal with veterans coming home from this new war?
Answer:
Both the DoD and VA healthcare systems will respond to veterans of the new war by addressing their health concerns as individuals. The key to recognizing there may be a problem is the use of the Post Deployment Clinical Practice Guideline by all DoD and VA healthcare providers when evaluating health concerns of these veterans and their families. The DoD and VA systems will be actively monitoring both our active duty members and our veterans for health issues. We are training our health care providers to specifically ask returning troops if they believe or are concerned that a medical problem may be related to a deployment. If there appears to be an increase in various symptoms or recognized illnesses researchers will have access to baseline medical information on individuals before and after their deployments and to environmental surveillance data from the theaters.

Question 2:
Ms. Embrey, Senator Reigle asserted that thousands of chemical alarms were sounded during Desert Storm, but the Defense Department maintained that every one was a false alarm-that our troops in fact were not exposed to dangerous chemical substances in Kuwait or Iraq. Many efforts to review the Gulf War referred back to those alarms and the Department's posture that chemicals were not involved. Is that the Department's current position in light of the health status of Gulf War veterans?
Answer:
After reviewing the relevant evidence, the Department of Defense has concluded that chemical alarms that alerted during Desert Shield/Desert Storm were likely to have been false alarms. The evidence can be summarized as follows. The M8A1 chemical alarms are capable of detecting only nerve agents and not blister agents. The M8A1 alarms begin to signal a warning at a concentration of nerve agent which can cause noticeable physical effects in people exposed to that concentration. That is why such alarms are positioned upwind of troops so that troops can don protective equipment before the nerve agent vapors reach them. There were no confirmed instances of nerve agent poisoning in any troops who were in the vicinity of chemical alarms that alerted. There were no definitive reports of confirmation of chemical nerve agent presence with more sensitive equipment. M8A1 alarms will sound in the presence of other, common, non-toxic substances and when their batteries need replacement. The Central Intelligence Agency assessed that Iraq did not use its chemical warfare agents against Coalition forces. The United Nations Special Commission on Iraq testified to the Presidential Advisory Committee that they found no evidence that Iraq moved chemical warfare agent munitions or bulk agents any farther south than Khamisiyah, Iraq, and our investigations support this conclusion. The Department of Defense does recognize that small numbers of special forces operating in Iraq may have possibly been exposed to chemical nerve agents during the allied bombings of a chemical warfare storage facility at Muhammadiyat during the Air Campaign. Over 100,000 US forces were possibly exposed to low levels of chemical nerve agent when US troops unknowingly destroyed rockets filled with sarin and cyclosarin at Khamisiyah, Iraq, in March 1991. There were no confirmed instances of nerve agent poisoning in any troops who were in the vicinity of Khamisiyah. In summary, there is no evidence that M8A1 chemical alarms were exposed to chemical agents in concentrations capable of setting them off. Given that premise, the explanation for the alarms sounding is that they were false alarms.

Question 3:
What actions have you taken to upgrade chemical alarms and develop biological alarms?
Do the troops in Afghanistan now have access to better chemical alarms?
Answer:
Since the Gulf War, we have developed and fielded more sensitive chemical agent detectors which detect blister agent in addition to nerve agents. The policy remains to evaluate any chemical alarm with a more sensitive chemical detector to confirm if a chemical agent caused the initial alarm. These detectors are also less prone to the false alert problems that we experienced in the Gulf. We have also developed and fielded a biological detection and identification capability. In addition, doctrine and training has addressed and is still addressing the technological advances being made in detection to ensure commanders have the tools to accurately assess their current situation. Our forces in Afghanistan have access to the best equipment we have fielded consistent with the expected threat.

Question 4:
General Blanck's written statement reviews the issue of missing or non-existent records having hindered the Army's work in trying to discover the underlying causes for problems Gulf War troops were experiencing. Give me a bit of insight into what kinds of records DoD and VA would have needed to be able to capture information sufficient to address a cause and effect. In other words, what kinds of records were missing or non-existent?
Answer:
The Institute of Medicine, in its literature review of various substances to which Gulf War veterans were exposed, has stated that to determine cause and effect or even association, it is necessary to know the concentrations of airborne substances, duration of exposure and the amount inhaled. For things like drugs taken or vaccines received, it is necessary to know who, how often, how much and for how long. Examples of Gulf War records that do not exist include those described below. There were no centralized records kept of troops vaccinated with the anthrax vaccine or the botulinum toxoid vaccine. From the amount of vaccine taken to the theater, it is estimated about 150,000 US personnel received at least one anthrax vaccination and 8,000 US troops received the botulinum toxoid vaccine. In some instances, these vaccines were recorded on the yellow World Health Organization (WHO) immunization record carried by the individual. In some cases, recipients' names were recorded in log books indicating the vaccines they received. There was no plan in place to consolidate the contents of these log books after the war. There are no records of troops who took pyridostigmine bromide tablets as a pre-treatment for exposure to the nerve agent soman, nor are there records of the duration the drug was taken. From the amount of drug taken to the theater, it is estimated about 250,000 US forces took pyridostigmine bromide. Paper health care records for individuals were kept by the medical units responsible for their care However, if treatment was received at another unit, the individual health record was not available. Standard Forms 600 (Chronological Record of Care) documenting health care were often kept in a box at treatment facilities, but there was no plan for uniting them with the individual health record. Even if paper records of medications, vaccines, and health care were complete and were all placed in individual health records, such paper records are kept in hundreds (if not thousands) of clinics, units, and archives. This distributed storage of paper health records is an insurmountable obstacle to developing a consolidated record of persons with common characteristics, such as receipt of a particular vaccine, in order to study potential health effects. Overcoming this obstacle is one of the principal benefits anticipated from the fielding of automated medical records keeping systems with a central data repository.

Question 5:
Ms. Embrey, your statement placed a separation between what DoD is attempting to do for the active duty members and your references to veterans, whom you say would be, and I quote "best served" by scientific research to address their health concerns. All of your active duty members eventually become veterans, because veterans are "made" by military service, not "born" as veterans. Does the Department intend to continue to make such a distinction with respect to the current deployment in Central Asia, or do you acknowledge some responsibility within DoD for the health status of all veterans?
Answer:
In addition to providing active duty servicemembers care for illness and injury, DoD has direct responsibility for protecting their health. That responsibility for protection underlies the Department's long-standing commitment to safety, occupational health, health promotion, preventive medicine, and what is called force health protection. Each of these is aimed at minimizing the occurrence of preventable illness and injury. Such preventive efforts are crucial for the Department's goal of fielding a fit and healthy force in support of its mission to defend the country. One result is a veteran population whose health status has been affected as little as possible by their military service. This outcome is crucial, for the extent to which DoD protects the health of the men and women who volunteer for military service can affect the confidence of the American people in its military. DoD efforts must be guided by knowledge about the impact of military service on both active duty personnel and veterans. The latter group is best assessed through coordination with the VA on questions or concerns about service-connected health problems that occur in veterans after they leave active military service. There are many examples of DoD and VA cooperating on issues that are health related for those who are currently serving and for those who have previously served. The DoD - VA Millennium Cohort study will follow 140,000 servicemembers and chronicle their health status for 21 years to determine possible effects from military service in general and from deployments in particular. The VA centers to study war related illnesses and DoD's Deployment Health Centers share a common goal of better understanding health effects from military service. The DoD -VA Post Deployment Clinical Practice Guideline, which has DoD and VA healthcare providers asking patients if health concerns are believed to be related to a deployment, is an example of a unique concern about veterans' health that DoD and VA share.

Question 6:
Ms Embrey, you indicate the Department of Defense is, and I quote, "assessing and monitoring current deployments" for health care needs. What kinds of mechanisms is the Department using to carry out such assessment and monitoring?
Answer:
The implementation of Force Health Protection policies is done at the individual Service level. In the pre-deployment process, baselines for each individual's health are established by their periodic medical examination and validated prior to deployment with the pre-deployment medical assessment. Data are also generated on reasons personnel are found not to be qualified for deployment. During deployments, data from outpatient healthcare visits and inpatient hospitalizations are monitored for the possible need for preventive measures. Post deployment medical assessments document individual's health status when they return home. After that, the Post Deployment Clinical Practice Guideline being implemented by DoD and VA healthcare providers will monitor for trends of health issues for which veterans are seeking care.

Question 7:

Ms. Embrey, you testified about the Institute of Medicine's three-year study that made a series of recommendations to the Department on protecting the health of deployed U.S. forces. Can you tell us among the recommendations made, how many have been implemented and explain those that haven't been accepted and why?

Answer:

The IOM study contained six major strategies with 32 recommendations to protect the health of deployed forces. The Department of Defense concurs with these strategies and has created the position of Deputy Assistant Secretary of Defense for Force Health Protections and Readiness in the Office of the Assistant Secretary of Defense for Health Affairs. The Department has made significant progress with 20 recommendations to date and we continue to work to implement the remaining 12 where possible. Some recommendations, such as using Global Positioning System for unit and individual locations, will require considerable deliberation and analysis before a workable solution can be achieved. Several recommendations for a closer working relationship between the military intelligence communities and the declassified medical community will also require some effort for a solution. Recommendations to integrate risk communication into the medical and operational communities will first require a recognition of risk communication in all phases of training, probably to include training prior to entry into the military. An admirable recommendation of obtaining medical information from civilian healthcare providers caring for Reserve Component personnel will require major changes in the medical ethics and privacy regulations.

Question 8:
I am especially concerned about reserves and their status. As I said in my opening statement, I recently witnessed the deployment of a reserve unit in Kansas. These are civilians who are called up, coming from all walks of life. In terms of preparation, do members of activated reserves get the full platter of preventive training, health baseline examination, equipment and other facets of DoD policies? In other words, is there one standard applied to both the "professional" soldier and the activated reserve? How do you monitor the reserves to ensure this is so?
Answer:
Across the Department of Defense, there is a single standard of medical readiness that applies to the reserve component and active component alike. Preparation for mobilization is a constant in all unit and individual training. DoD recognizes that for some units, especially in the reserves, there may not be adequate personnel or training for medical and dental assessments, or preventive medicine and environmental surveillance. The FedsHeal program was instituted by DoD to utilize VA capacities to provide the medical and dental evaluations for reserve component personnel being activated. Active component activities such as the Army's Center for Health Promotion and Preventive Medicine work to provide support and training in preventive medicine and environmental surveillance whenever necessary. For deployments, reserve units are expected to receive the same pre-deployment disease threat and prevention training as active units. Topics would include individual hygiene and sanitation, vector control, unit sanitation, and food and water sanitation. Additional material would cover unique environmental threats and hazards associated with the area of operations. Monitoring of the reserve component medical readiness is done by unit commanders, by Reserve Affairs, and by Force Health Protection and Readiness in Health Affairs.

Question 9:
Low-level environmental hazards are generally difficult to detect. Is the Department developing technologies with chemical and biological sensors capable of detecting sub-lethal doses of chemical or biological agents? What is the state of development of such devices?
Answer:
The Department has had detectors capable of detecting sub-lethal doses of chemical warfare agents for over thirty years. We are currently developing detectors with greater sensitivities in the event on-going research reveals that even lower doses have a negative long term health effect.
Unlike detecting sub-lethal levels of chemical poisons, detection of biological agents means that an exposure to a disease-causing organism has occurred. Whether that exposure actually results in disease depends on a number of factors: virulence, availability of vaccines, etc. Some are more virulent than others. We can detect and identify most of the biological agents we feel constitute the threat. We do not have preventive measures, such as vaccines, for all biological agents that could potentially be used as weapons or an unintended exposure

Question 10:
Can you confirm for the Committee that DoD has developed better operational tracking systems for personnel and units so that the costly effort of trying to learn where people were located after we discover a problem — such as an exposure to chemical weapons — can be reduced and we can better identify who may be at risk? Would you call this a lesson learned from the Gulf War?
Answer:
The need to improve tracking and archiving of individual assignment and unit location data was a key lesson of the Gulf War. To track individuals and units on the fluid battlefield remains a challengefor the Department. Generally, one must associate individuals with units (a personnel function) and units with locations (an operations function). Since the Gulf War, the Department has enhanced the ease and accuracy of both types of tracking. The Services and joint commands regularly forward individual assignment and unit location data to the Defense Manpower Data Center (DMDC) in Monterey, CA, where it is archived indefinitely. We continue to take action to insure programs like Personnel Tempo (Pers-Tempo), Joint Personnel Asset Visibility (JPAV), and Defense Integrated Military Human Resources System (DIMHRS) will further refine the space and time resolution, accuracy, and accessibility of personnel and unit tracking information. Tracking systems for personnel and units is a lesson from the Gulf War which DoD is working hard to make a "lesson learned." Unit locations are an operational database and data are maintained at the company level, a significant improvement since the Gulf War. DoD is working to integrate the operational database for unit locations with the personnel database for individual assignments and the healthcare database to create a system that can be shared with the VA for care of veterans years after their deployments.

Question 11:
What other lessons did we learn from the Gulf War that we are now putting to use in Operation Enduring Freedom? Can you give me specific examples of something identified then as an error or commission that is now implemented and is specifically addressed in the current deployment?
Answer:
A very important lesson was that we need to listen to the veterans. This has led to the cooperative DoD -VA development of the Post Deployment Clinical Practice Guideline. DoD and VA healthcare providers will be asking veterans and their families seeking care if they believe their health concerns may be related to a deployment. We also have information for veterans and their families on DoD Websites such as GulfLINK, DeploymentLINK, and the Anthrax Vaccine Immunization Program, as well as an 800 hot-line for people to call with concerns or problems. The creation of the U.S. Army Center for Health Promotion and Preventive Medicine provides environmental surveillance data to identify hazardous sites in the theater. All personnel receive awareness training on depleted uranium and training on chemical warfare agent detectors, which includes their limitations and the importance of informing troops about alarms that are not confirmed with more sensitive testing. Healthcare systems in the theater are reporting weekly on rates of diseases and injuries and the Defense Medical Surveillance System serves as the repository and does analysis for trends.

Question 12:
Will we able to know where every uniformed DOD member has served on the ground during Enduring Freedom? In other words, should we identify a disease or illness after the fact associated with particular areas, in Kandahar or Tora Bora for example, will we be able to overlay troop movements to determine the individuals who may have been exposed? What is the mechanism DoD is using to do such tracking, and will you be able to transfer this data to VA for VA's use in providing health care, conducting biomedical research and for benefits purposes?
Answer:
It is impossible to track every servicemember's exact location during a deployment due to the nature of the operation. For example, Special Forces Units work in small, highly mobile units with classified locations. Using technologies such as Global Positioning Systems (GPS) is not an option because of the risk of mission compromise. Unit locations are an operational database and data are maintainedat the company level, a significant improvement since the Gulf War. DoD is working to integrate the operational database for unit locations with the personnel database for individual assignments and the healthcare database to create a system that can be shared with the VA for care of veterans years after their deployments.

Question 13:
The Committee understands that the Office of the Special Assistant for Gulf War Illnesses has spent in excess of $130 million over the past five years on publishing "case narratives" and "literature reviews?" Are these activities subjected to scientific peer review?
Answer:
Much of the information for The Office of the Special Assistant for Gulf War Illnesses case narratives, environmental reports and information papers came from interviews with Gulf War veterans who provided their first-hand accounts of what they encountered during the war. Through the use of an 800 hot-line call center, over 21,500 veterans have contributed their first-hand accounts of service in the Gulf. Using public forums – "town hall meetings" – outreaches were conducted in 13 major metropolitan areas so that we could obtain veteran feedback. In order to ensure that the active duty, National Guard, Reserves, military health care providers and family members received information on Gulf War issues and provided their experiences, total force outreach programs were conducted at 96 military installations and their surrounding communities, worldwide. Additionally, briefing teams provided exhibits at 81 conferences hosted by veterans, service organizations, military support offices, and health organization associations. Since outreach began in 1997, these programs provided the Office of Special Assistant for Gulf War Illnesses the opportunity to reach out to more than 70 thousand active duty military personnel, reserve component members, veterans, family members, military health care providers, and the general public. The 800 hot-line number remains available for servicemembers and their families to call and get instant feedback to their first-hand reports, questions and concerns.
From November 1996 to October 2001, DoD has obligated $148 million through the Office of the Special Assistant for Gulf War Illnesses. The purpose of that office was to listen to the concerns of Gulf War veterans about why some believed they were ill, toensure those with health problems had the access to healthcare they deserved, and to investigate what Gulf War veterans were reporting as suspected chemical or biological events during the Gulf War.
Some $35 million was spent going across the country and listening to Gulf War veterans, interviewing Gulf War veterans and telling Gulf War veterans what was being done to find answers as to why some were ill.
Some $500K was spent coordinating with coalition countries' military and civilian medical personnel to evaluate if their Gulf War veterans were experiencing health problems similar to those of our veterans.
Some $15 million was spent identifying and declassifying medically relevant documents from the Gulf War to fully explain incidents that veterans believed may have been biological or chemical exposures.
Some $64 million was spent on the investigation of these incidents and on the analysis of the data to produce the interim case narratives, environmental exposure reports and information papers. The peer review of these products was done by the Gulf War veterans, both those involved with the incidents and others who were in the theater. Their comments, questions, concerns and additional information were used to create the final reports. These interim and final reports are present on our Website GulfLINK, which continues to get over 200,000 hits per week.
Some $4 million was spent on the medical literature reviews done by the RAND Corporation. The 11 subjects that were addressed reflected the concerns of Gulf War veterans about various exposures they believed could possibly be related to subsequent symptoms. These literature

reviews are a RAND product and were peer reviewed through the usual RAND process. The Office of the Special Assistant did review these RAND products for factual accuracy of events that occurred in the Gulf War.

Some $3.5 million was spent in response to questions and concerns raised by organizations responsible for oversight of the work of the Office of the Special Assistant. These included the Presidential Advisory Committee, the Presidential Special Oversight Board, the GAO, the Senate Investigative Unit, the House Veterans Affairs Committee, and the SenateVeterans Affairs Committee.

Finally, some $26 million was spent on office space and administrative support.

Question 14:
How much funding has DoD expended for Gulf-related medical research over the past five years? Can you point to anything you learned from either the case narratives, reviews or research that has been put to use for the troops in the field today, particularly for those in Afghanistan?
Answer:
DoD has been a partner with VA and MS on Gulf War-related medical research since The DoD commitment of over $120 million has resulted in evaluations of two major treatment programs, which have documented the increased rate of medically undiagnosed symptoms in Gulf War veterans, determined that birth defect rates are not higher in Gulf War veterans' children, and led to better health monitoring for current deployments and a Post Deployment Clinical Practice Guideline for DoD and VA healthcare providers. The DoD-VA Millennium Cohort study is evaluating 140,000 active duty personnel, some deployed today, for the next 21 years to monitor their health. The DoD Birth Defects Registry is actively monitoring all births to military personnel. Appropriate training on the health risks of depleted uranium is being given to all servicemembers, and technicians for chemical warfare agent detectors are better trained in the limitations of their equipment and the importance of notifying troops of the results of test confirmation with more sensitive equipment whenever there is an alarm.

Question 15:
The Senate Committee on Veterans' Affairs made a significant investigation in researching the possible causes of Gulf War veterans' health problems. That effort was thoroughly documented in a 1998 report. Among its finding were failures on the part of the Department of Defense to protect troops we sent to the Gulf. Specifically cited were failures in issuing proper equipment, training, vaccinations, documentation and record keeping. The report included 29 important recommendations in all, most directed at DoD and VA. How many of these recommendations have been implemented, and do you believe these recommendations helped DoD and VA learn some of the lessons of the Gulf War? How so? (Is this part of the answer?)Answer:
The Senate Committee on Veterans' Affairs report was a comprehensive review and affirmation of issues which surfaced from many sources. This helpful compendium had 29 recommendations, with 11 applying to DoD, 6 applying to DoD and VA, 11 applying to VA and 1 applying to Congress. Six of the recommendations to DoD have been implemented, two deal with the military intelligence community and there is some progress(can this be said better?), two deal with HHS developing technology or information that is not yet ready for military mission use, and one deals with a tracking system that has not been approved. All six of the DoD/VA recommendations have been implemented. The VA-managed depleted uranium medical follow-up program at the Baltimore VA has been expanded to over 60 individuals involved with friendly fire. Urine testing is available to any veteran with a concern about possible depleted uranium exposure. No adverse depleted uranium health effects have been identified in any veteran to date. In general, the recommendations helped to focus DoD efforts on what were agreed to be the more significant issues from the Gulf War.
How have these recommendation helped?

Question 16:
As you are probably aware, patient advocates are often included as voting members on peer-review panels within NIH-funded programs. Given that fact, why are veteran advocates excluded from representation on the Research Working Group, the body responsible for deciding which Gulf War illnesses studies will or will not be funded? What is your justification for excluding advocates from this body?
Answer:
The Federal Advisory Committee Act allows government departments to create civilian advisory panels to provide input from advocates on specific issues or broad topics. The secretary of Veterans Affairs has created such an advisory panel to provide input on research on medical research on the symptoms and illnesses seen in Gulf War veterans. This advisory panel under the sponsorship of the VA is charged to review and comment on the recommendations of the Research Working Group, which is staffed by members of three governmental departments; Defense, Veterans Affairs, and Health and Human Services. This oversight is similar to the review process in place at the National Institute of Health in regard to medical research. However, current Federal law reserves the authority of the Research Working Group to obligate funds for research to be solely by government representatives.

Question 17:
Recent media reports indicate that a new, as-yet unpublished study concerning the anthrax vaccine shows, for women, an association between anthrax inoculation and an increase in risk for birth defects. Are you aware of this study and what is the Department planning to do with respect to women active duty members and the anthrax vaccines? Are you coordinating your work with VA, and how so?

Answer: DoD is aware of this work, done by researchers from the Naval Health Research Center. The work is preliminary. Review of these preliminary data indicated important limitations in computerized medical records that underlay the data analyzed in this study. Investigators are conducting a systematic evaluation of original medical records, including vaccination and infant health records. This evaluation will require several months. In the interim, the DoD has reinforced its existing policy to avoid immunization of pregnant women. The VA is already aware of this information and action.

The outcome of the above review is not relevant to the process of seeking waivers from the FDA for investigational new drugs (IND). The anthrax vaccine is not an investigational product. The process by which DoD might seek waivers from the FDA for military use of IND is well spelled out in law (Section 1107 of title 10, United States Code), presidential executive order 13139, and Department of Defense Directive 6200.2. Both DoD and the FDA would consider the available evidence about safety and efficacy of any IND product for which it would consider requesting a waiver.

Question 18:
Section 765 of the 1998 National Defense Authorization Act (PL 105-85) requires the Defense Department to conduct pre-and post-deployment health examinations including mental health screenings and blood sample to record the baseline health of each active duty member before deployment and any changes in health during the course of deployment. Are they being done and can you provide the Subcommittee evidence to confirm this is the policy?

Answer: The Assistant Secretary of Defense for Health Affairs Policy of October 6, 1998, established the requirement for pre- and post-deployment health assessments and blood samples. The value of these assessments is not to record the medical condition of members but, rather, to ensure that their medical condition is checked before they deploy and as they return. If there is an indication of a medical problem, then the full and accurate documentation of that medical problem and its management employs the usual systems of inpatient and outpatient treatment records. The forms which document the performance of the pre- and post-deployment assessments are sent to the Defense Medical Surveillance System at the U.S. Army Center for Health Promotion and Preventive Medicine. These assessments complement the rigorous physical examination required for entry into the military, the periodic physical examinations, the annual dental screenings, and the annual medical record check for updating routine vaccinations for all military personnel. Coupled with the immediate access to military healthcare providers for all military personnel, these routine evaluations assure that those serving in today's military are fit and healthy. While this office believes that the percentage of servicemembers completing pre-deployment health assessments is significantly higher than for the early days of the Bosnia deployment, actual figures are not yet available for a more precise answer. The paper forms have not yet been incorporated into a computer database.

Question 19:
What role has VA played in helping DoD develop appropriate pm-and post-deployment health survey instruments and testing procedures to be used by DoD?
Answer:
The VA partnered with DoD in the development of the Post Deployment Clinical Practice Guideline for use by DoD and VA healthcare providers when evaluating health concerns of service members, veterans, and their families.
DoD formulatedthe pre- and post-deployment health assessments through several versions. These questionnaires are designed to identify outstanding health problems just before and after deployment. This type of screening is essential to ensure that troops are healthy before being sent on deployment and to identify troops who should receive health care immediately on their return.
The Clinical Practice Guidelines establish standard criteria to be used by both departments when conducting physical evaluations of veterans for illnesses and injuries attributed to active service.

Question 20:
Ms. Embrey, despite the difficulties with the vaccination program in the Persian Gulf War, the Department's vaccination protocol is of interest to the Committee. Please provide a copy of this protocol; the current official protocol for vaccinations applicable to the forces being deployed in Central Asia; and, the vaccinations protocol for troops now deployed in the Philippines operation.
Answer:
DoD's basic policy for vaccinations is in the DoDI 6205.2 - Immunizations Requirements, which was signed in 1986. Updates to this instruction have been for specific vaccines like hepatitis A and B, anthrax and influenza. A recent Chairman of the Joint Chiefs of Staff Memorandum MCM-0006-02, effective March 1, 2002, provides standardized procedures for assessing health readiness and conducting health surveillance in support of all military deployments. This instruction requires the combatant command to determine the need for deployment-specific medical countermeasures, including immunizations, chemoprophylactic medications and other individual personal protective measures. Attached are the CENTCOM and PACOM instructions for immunizations for travel to its area of operations.

Question 21:
Ms. Embrey, you stated DoD has implemented 12 policy changes, based on lessons learned following the Gulf War, to improve the delivery of health care to our active duty personnel. What are those policies and how has their implementation changed the pre and post-deployment health assessment protocol? Is DoD better informed to quickly identified health hazards and to forward that information to the Department of Veterans Affairs? Please provide the Committee each of the 12 directives or other documentation establishing these new post-Persian Gulf War force protection polices.
Answer:
A list of the twelve policies and directives is attached. Copies of the documents are also enclosed. A thirteenth, a recent update of the Joint Staff Memorandum on Deployment Health Surveillance and Readiness, is also enclosed.
DoDD 6490.2, DoDI 6490.3, the Joint Staff Memoranda on Deployment Health Surveillance and Readiness, and the ASD Health Affairs Policy for Pre- and Post-Deployment Health Assessment and Blood Samples all describe the pre- and post-deployment procedure and forms to be used. The implementation of these assessments gives all deploying servicemembers an opportunity to declare their health concerns or problems that require attention. The objectives are to verify deployability of individuals, provide prompt health interventions they may require, and track changes in their health status possibly due to exposures and experiences during deployment. DoDD 6490.2, DoDI 6490.3, and the Joint Staff Memoranda on Deployment Health Surveillance and Readiness spell out the steps (called environmental surveillance) in identifying and documenting the occurrence of possible health hazards in the environment where troops' are deployed. When significant exposures are identified and documented in troops health records, that information will be provided to the VA in the servicemembers' health records when they leave military service.

Major DoD FHP Policies

Policy Name/Number	Title	Date
DoD Directive 6490.2	Joint Medical Surveillance	30-Aug-97
DoD Instruction 6490.3	Implementation and Application of Joint Medical Surveillance for Deployments	7 Aug-97
Joint Staff Memorandum MCM-251-98	Deployment Health Surveillance and Readiness	4-Dec-98
Joint Staff Memorandum MCM-0006-02	Updated Procedures for Deployment Health Surveillance and Readiness	1 -Feb-02
ASD Health Affairs Policy	Policy for Pre- and Post-Deployment Health Assessment and Blood Samples	6-Oct-98
DoD Directive 4715.1	Environmental Security	24-Feb-96
DoD Directive 6490.5	Combat Stress Control Programs	23-Feb-99
DoD Directive 6205.3	DoD Immunization Program for Biological Warfare Defense	26-Nov-93
DoD Instruction 6055.1	DoD Safety and Occupational Health Program	19-Aug-98
ASD Health Affairs Policy	Policy for National Surveillance for Birth Defects Among Department of Defense Health Care Beneficiaries	17-Nov-98
ASD Health Affairs Policy	Establishment of DoD Centers for Deployment Health	30-Sep-99
DoD Directive 6200.2	Use of Investigational New Drugs for Force Health Protection	1-Aug-00
ASD Health Affairs Policy	Implementation of Post-Deployment Health Clinical Practice Guideline [URL unavailable]	7-Dec-00

House Committee on Veterans Affairs
Health Subcommittee
Questions to the VA
(POA: Craig Hyams)

Question 1:
The Senate Committee on Veterans' Affairs made a significant investigation in researching the possible causes of Gulf War veterans' health problems. That effort was thoroughly documented in a 1998 report. Among its findings were failures on the part of the Department of Defense to protect troops we sent to the Gulf. Specifically cited were failures in issuing proper equipment, training, vaccinations, documentation and records keeping. The report included 29 important recommendations in all, most directed at DoD and Va. How many of these recommendations have been implemented, and do you believe these recommendations helped VA learn some of the lessons of the Gulf War? Please enumerate the lessons.
Answer:
The Senate Committee on Veterans' Affairs report had 29 recommendations, with 11 applying to DoD, 6 applying to DoD and VA, 11 applying to VA and 1 applying to Congress. Six of the recommendations to DoD have been implemented, two deal with the military intelligence community and there is some progress along those recommended lines, two deal with HHS developing technology or information that is not yet ready for military mission use, and one deals with a tracking system that has not been approved. All six of the DoD/VA recommendations have been implemented. The VA-managed depleted uranium medical follow-up program at the Baltimore VA has been expanded to over 60 individuals involved with friendly fire. Urine testing is available to any veteran with a concern about possible depleted uranium exposure. No adverse depleted uranium health effects have been identified in any veteran to date.

Question 2:
At this point, do you expect DoD to provide VA any health-related data concerning troops now serving in Afghanistan? What kind of data are expected, if any? Is VA aware of the mechanism(s) DoD may be using to track troop health, and will you be able to employ any such data for VA use in providing health care, conducting research or in making benefits decisions? Please expand on your answers.

Answer:
The Department routinely cooperates with the VA to provide data on servicemembers necessary to meet the VA's needs.
DoD will provide to the VA any and all relevant information from its records to aid in the VA's delivery of health care and in making benefits decisions for troops exiting the military after service in Afghanistan. Expected data include service health records. Possible data include the findings from environmental surveillance, document exposure to substances with possible health effects. Although some data might prove useful in generating research hypotheses, the purposes of collecting health data during a deployment do not include research.

Question 3:
What role has VA played in helping DoD developed appropriate pre- and post-deployment health survey instruments and testing procedures to be used by DoD? Will the results obtained through these instruments be made available to VA?

Answer:
VA has been involved in the formulation of the pre- and post-deployment health survey instruments. These questionnaires are designed to identify outstanding health problems just before and after a hazardous deployment. This type of screening is essential to ensure that troops are healthy before being sent on a dangerous deployment and to identify troops who should receive health care immediately on their return. These screening questionnaires are not designed to collect comprehensive health data. VA assumes it will have access to this data when needed for patient care and disability determination.

C*O*N*G*R*E*S*S*I*O*N*A*

CMAT Control #
2001277-0000086

(25)

CHIEF OF LEGISLATIVE LIAISON
CONGRESSIONAL INQUIRY DIVISION
ROOM 2C600
1600 ARMY PENTAGON
WASHINGTON, D.C. 20310-1600

October 1, 2001

OFC OF THE SPEC ASS'T FOR GULF WAR ILLNESSES
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH VA 22041

Control ID: 11000072 Task Officer: (b)(6)

Tasked Agency: GULF Action: **Direct Reply**

Suspense Date: OS-OCT-2001

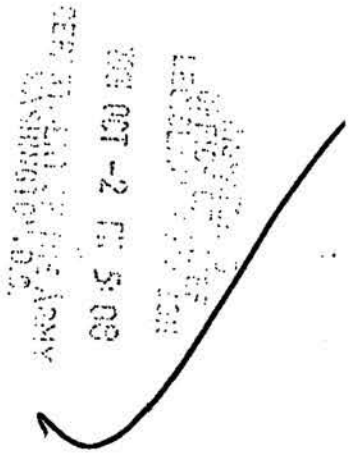
Constituent: (b)(6)

Subject: Anthrax Vaccine

Member of Congress: Senator Rick Santorum

Remarks:

Keyword: ANTHRAX VACCINATION PROGRAM



24-hour FAX Service:
(b)(6)

If there is a'problem with this FAX, please call (b)(6)

(3)

*DSN: (b)(6)
E-Mail Address: (b)(6)@hqda.army.mil
REMINDER: Direct replies require a courtesy copy be provided to OCLL

RICK SANTORUM
PENNSYLVANIA

COMMITTEES:
REPUBLICAN CONFERENCE CHAIRMAN
ARMED SERVICES
CHAIRMAN, SUBCOMMITTEE ON AIRLAND FORCES
RULES
AGING
BANKING

Pre

PHILADELPHIA OFFICE:
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PHILADELPHIA, PA 19107
(215) 864-6900

United States Senate

WASHINGTON, DC 20510-3804
202-224-6324

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DATE 9 26 01 NUMBER OF PAGES, INCLUDING THIS _____

PHILADELPHIA OFFICE
Fax 215-864-6910 PHONE 215-864-6900

TO: Michelle Cromwell FAX# 703-697-6988

FROM:

___Sean Reilly, State Director Randy Urquhart, Community Affairs
___Michelle Turner, Director of Constituent Services
___Jaime Howard, Director of Economic Development
_Michele Rajsic, Special Assistant, Scheduler
Mary A. Fanstino, Special Assistant
X Janet Perez, Special Assistant
Carolyn Strickland, Special Assistant
Intern _____

MESSAGE:

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LEGISLATIVE LIAISON
2001 SEP 27 PM 12:59
DEPARTMENT OF THE ARMY
WASHINGTON, D.C.

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SCRANTON OFFICE:
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SCRANTON, PA 18503
(570) 344-8729

View e:\emailobj\200109\924125643.txt

From: (b)(6)
Date: 9/24/01 12:37:11 PM
To: webmail@santorum-iq.senate.gov
Subject: www_email

Senator Santorum:
I am writing to you for information on how I may be able to receive an Anthrax vaccination. I am aware that the vaccine is available to military personnel, and am hoping to receive a vaccination at a nearby military facility. In light of recent national events, it is apparent that the military is not the only group that could benefit from the vaccine, and I hope that you will give some consideration to the welfare of Pennsylvania's civilan population. The first step in this process is allowing civilians to obtain vaccinations on an "As Requested" basis. I live in the bourough of Lansdowne, and work for the federal government in Philadelphia. Please provide me with information on how J can begin the process of vaccination at a nearby military base. J am hoping that J will receive a response from your office as soon as possible since this is an issue affecting tbc health and well-being of your Pennsylvania constituents. Thank you for your help.

Sincerely,
(b)(6)

Original Formatted Message Starts Here

<APP>SCCMAIL
<PREFIX>(b)(6)</PREFIX>
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<LAST>(b)(6)</LAST>
<ADDR1>(b)(6)</ADDR1>
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<HPHONE>(b)(6)</HPHONE>
<WPHONE>(b)(6)</WPHONE>
<EMAIL>(b)(6)</EMAIL>
<ISSUE>IMADE</ISSUE>
<MSG>Senator Santorum:
I am writing to you for information on how I may be able to receive an Anthrax vaccination. I am aware that tbe vaccine is available to military personnel, and am hoping to receive a vaccination at a nearby military facility. In light of recent national events, it is apparent that the military is not the only group that could benefit from the vaccine, and I hope that you will give some consideration to the welfare of Pennsylvania's civilan population. The first step in this process is allowing civilians to obtain vaccinations on an "As Requested" basis. I live in the bourough of Lansdowne, and work for the federal government in Philadelphia. Please provide me with information on how I can begin the process of vaccination. at a nearby military base. I am hoping that I will receive a response from your office as soon as possible since this is an issue affecting the health and well-being of your Pennsylvania constituents. Thank you for your help.

Sincerely,
(b)(6)

</MSG>
</APP>

CMAT Control #
2001100-0000021

(26)

Congress of the United States

Washington, DC 20515

November 3, 1999

The Honorable Jane E. Henney, M.D.
Commissioner
Food and Drug Administration
14-7 I Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Henney:

We are writing to express our serious concerns regarding the pending license supplement application of BioPort to produce the anthrax vaccine. We strongly urge that each of the items contained in the letter be fully addressed and a response provided to us prior to the approval of BioPort's license supplement application.

As you are aware, in 1997 the Department of Defense mandated the implementation of a force-wide Anthrax Vaccine Immunization Program (AVIP). Since the announcement of this plan to inoculate all 2.4 million members of our Armed Services, FDA documented deficiencies in the manufacturing process have caused widespread and persistent concerns regarding the safety of the vaccine.

Of particular concern is that despite the licensure of the anthrax vaccine in 1970, 23 years passed before your agency physically inspected the anthrax-specific portion of the manufacturing facility. In testimony before the House Government Reform Committee, Dr. Zoon, the Director of FDA's Center for Biologics Evaluation and Research, indicated that two inspections of the production facilities in 1997 and 1998 revealed significant deviations from the Federal Food, Drug, and Cosmetic Act, FDA's regulations, and the standards in the Michigan Biological Product Institute (MBPI) license. Inspection reports of the production facilities following its purchase by BioPort revealed some progress but many remaining deviations. In large part, the significant ongoing deviations prompted the company to close the facility for remodeling rather than face the likelihood of FDA revoking their license.

Given the documented deviations from approved practices in the manufacturing process, it is imperative that the FDA follow it's own prescribed regimen of thorough testing for purity, potency, identity, and sterility. As a prerequisite for approval of the license supplement, the testing must reveal lot-to-lot consistency for the vaccine. Included within the testing requirements, the FDA must ensure lot-to-lot consistency for the antigen level. FDA mandated lot-to-lot consistency will ensure we can accurately measure the efficacy of the vaccine. The lack of clinical data detailing the relationship between antigen levels and the amount of protection provided argues strongly for greater vaccine consistency data so correlates of

No. 99-7003

immunity can be studied. In that regard, please provide information on the status of FDA's request of BioPort to characterize the vaccine. Any failure to characterize the vaccine must preclude the approval of the license supplement application.

We also urge that the FDA place the anthrax vaccine back under Investigational New Drug (IND) status. As Dr. Zoon testified before the Government Reform Committee, the MBPI vaccine was licensed for use by a limited population of individuals at risk for coetaneous exposure to anthrax through infected animals or animal products. The December 13, 1985 Federal Register and the FDA approved package inserts indicate: "Since the risk of exposure to anthrax infection in the general population is slight, routine immunization is not recommended." However, the Department of Defense, in its implementation of the AVIP, is performing a large-scale inoculation for protection against inhalation anthrax. The scope of the vaccination program and the form of exposure anticipated by DoD were not addressed in the initial license. A March 13, 1997, letter from Dr. Michael Friedman, FDA Lead Deputy Commissioner, to Stephen Joseph, then Assistant Secretary of Defense for Health Affairs, acknowledged the "paucity of data regarding the effectiveness of the anthrax vaccine for prevention of inhalation anthrax." This lack of significant data strongly suggests the need for further study under IND status.

Additionally, the data submitted for licensure of initial vaccine did not include scientifically valid support for the current dosing structure. GAO stated that no studies have been conducted to determine the optimum number of doses of the anthrax vaccine. Although annual boosters are recommended, the need for a six-shot regimen and annual booster shots has not been evaluated. There is also no clinical data to accurately conclude that the prescribed regimen provides a consistent level of protective antigen to be efficacious against inhalation anthrax. A September 29, 1999 letter from Dr. Zoon to Dr. Sue Bailey, the Assistant Secretary of Defense for Health Affairs indicated that there is lack of data on the impact of deviations from the approved vaccine regimen. Prior to the approval of the license supplement application, the FDA must scientifically verify the clinical data supporting the six-dose regimen. We would like to be apprised of FDA's plans to accomplish this goal and be provided the clinical data supporting the correlation between the dosage and anti-body levels.

We are also requesting the status of FDA's proposed rule regarding the use of animal data to support claims of human efficacy. Human efficacy information for the current license and the license supplement application is based overwhelmingly upon the application of data from animal anthrax vaccinations and exposure. However, there have been great discrepancies between various animal models regarding the efficacy of the anthrax vaccine. We acknowledge and support the moral argument against human testing to determine the efficacy of the vaccine. At the same time, we must ensure there is a scientifically verifiable extrapolation from animal data that can be applied to humans. It is our understanding the proposed rule would attempt to establish protocols to provide that information. If that rule has not been approved, we would like

Should you have any questions regarding this letter, please do not hesitate to contact us or any member of our staffs. Please provide this information by November 18. Thank you for your consideration of these serious matters. We look forward to your prompt reply.

Sincerely,

Walter B. Jones
Member of Congress

Dan Burton
Member of Congress

Benjamin A. Gilman
Member of Congress

Christopher Shays
Member of Congress

(27)

United States Senate

COMMITTEE ON VETERANS' AFFAIRS
WASHINGTON, DC 20510-6375

SUMMARY OF

PRELIMINARY STAFF FINDINGS

"Is Military Research Hazardous to Veterans' Health?: Lessons from the Persian Gulf"

When the Department of Defense (DoD) began preparations for Desert Shield and Desert Storm in 1990, officials were extremely concerned about the need to protect U.S. troops against chemical and biological weapons that were believed to have been developed by Iraq. Under current law, all vaccines and medical products must be proven safe and effective by FDA in order to be sold and distributed in the United States. However, DoD officials wanted to use a botulinum toxoid -- a vaccine to prevent botulism -- that was not approved by FDA. They also wanted to use pyridostigmine bromide, a medication, to protect U.S. troops against certain chemical weapons, such as soman. Although approved by the FDA for treating patients with a neurological disorder, pyridostigmine is not proven safe or effective for repeated use by healthy persons under any circumstances.

DoD told FDA that these investigational products had well-established uses and were safe. However, these claims are not supported by the research that DoD has provided to FDA.

Pyridostigmine Bromide

Pyridostigmine bromide is a chemical which is believed to enhance the effectiveness of established drugs for the treatment of nerve agent poisoning. Pyridostigmine is also a nerve agent itself.

The Pentagon believes that all 695,000 U.S. troops in the Persian Gulf War were issued pyridostigmine bromide, and officials estimate that approximately two-thirds took the drug for varying periods of time, sometimes exceeding several weeks.

Efficacy. In research studies, animals given pyridostigmine, followed by two antidotes (atropine and 2-PAM), were more likely to survive exposure to a nerve agent called soman. However, pyridostigmine pretreatment may make individuals more vulnerable to other nerve agents, such as sarin. The DoD scientists concluded that **pyridostigmine should only be used when the chemical warfare threat is soman.** Iraq was believed to have both soman and sarin, and the only verified report of chemical weapons in the Gulf War concluded that sarin was present.

In addition, DoD documents indicate that the **treatment regimen for U.S. troops during the Persian Gulf War may have included an inadequate dose of atropine. Therefore, even if Persian Gulf soldiers had been exposed to soman, it is questionable if the pyridostigmine pretreatment would have provided any protection, since the dose of atropine was apparently inadequate.**

Safety. Committee staff reviewed the studies that DoD officials claim prove that the drug is safe for healthy individuals. Most of the studies included less than 35 people; several studies included as few as two or four individuals. All the studies apparently excluded women.

Because of the DoD researchers' concerns about serious adverse reactions, virtually all of the studies screened the male subjects to determine whether they were hypersensitive to pyridostigmine before allowing them to participate in the experiment. In addition, individuals with many medical conditions, those on medications, and those who smoked, were excluded from the studies. Study participants were told not to drink any alcoholic beverages.

Despite these precautions, serious adverse reactions were reported for several of the studies, including **respiratory arrest**, abnormal liver tests, unusual electrocardiograms, gastrointestinal disturbances, memory loss, and anemia.

In a study DoD conducted just before Desert Storm, they excluded men with bronchial asthma, peptic ulcer, liver, kidney, heart disease, or hypersensitivity to pyridostigmine or related drugs. They warned the men that possible adverse side effects included nausea, vomiting, slow heart rate, sweating, diarrhea, abdominal cramps, increased salivation, increased bronchial secretions, pupil constriction, weakness, muscle cramps, and muscle twitches. All subjects were admitted to a hospital so that they could be observed at night.

Lack of Safeguards Regarding Pyridostigmine in the Persian Gulf. **In contrast to these extensive precautions taken before giving pyridostigmine every 8 hours for 3 days to four volunteers, a few months later the same dosage of the drug was given for longer periods of time to approximately 400,000 U.S. soldiers, none of whom had been screened for any of the diseases mentioned in the informed consent form given to the four men.** None of the Persian Gulf War troops were adequately warned about the risks associated with the drug, and few if any were given a choice of whether or not to take it.

Recent Research on Pyridostigmine. Last year, Dr. James Moss, a scientist at the U.S. Department of Agriculture, conducted research on cockroaches that could have important implications for Persian Gulf War veterans. He found that when used in combination with pyridostigmine, a common pesticide called DEET became 10 times as toxic as when used alone. DEET and many other pesticides were widely used in the Gulf War. If individuals who took pyridostigmine pills became more vulnerable to pesticides (or vice versa), this could explain the serious neurological symptoms experienced by so many Gulf War veterans.

Botulinum Toxoid

Botulinum toxoid is an unapproved vaccine that is used to protect laboratory workers and others who are likely to be exposed to botulism. The recommended schedule for immunization with the vaccine includes three injections at 0, 2, and 12 weeks, followed by a booster shot 12 months after the first injection.

Efficacy. **According to DoD, the botulism vaccine was given too late to be of any use had the Iraqis actually used biological warfare during Desert Storm.** DoD officials informed SVAC staff that botulism vaccine was not administered to most military personnel in the Persian Gulf until January 23, 1991, which was 7 days after the onset of the air war. Approximately 8,000 individuals received the vaccine, but most received only one or two inoculations. Furthermore, there is research evidence that the vaccine would not be effective against all botulism toxins.

In summary, 99% of the U.S. troops received no protection from botulism due to the shortage of toxoid, and the remaining 1% were probably not protected because the vaccine distribution started too late.

Safety. In 1974, the Centers for Disease Control considered terminating the distribution of the vaccine because of hypersensitivity and adverse reactions.

Anthrax Vaccine

Anthrax vaccine is an FDA-approved vaccine that is recommended for individuals who may come in contact with products such as hides, hair, or bones of animals likely to have been exposed to anthrax.

The anthrax vaccine was given to approximately 150,000 individuals in the Persian Gulf. Anthrax vaccine is believed to be effective in preventing anthrax contracted through skin exposure to the bacteria. However, when used as biological warfare, anthrax is aerosolized. At the time of the Gulf War, it was unknown whether the vaccine would protect against aerosolized anthrax, which would be inhaled.

DoD/FDA Agreements to Waive Informed Consent for Investigational Drugs During the Persian Gulf War

In August 1990, DoD contacted FDA to review FDA's plans to use pyridostigmine and botulism vaccine for U.S. troops in the Persian Gulf. DoD did not want to abide by informed consent regulations, while FDA officials pointed out that pyridostigmine and botulism vaccine were investigational and that there are laws regulating how they can be used.

After several months of debate, an agreement was reached on December 31, 1990. DoD officials agreed that information about the investigational products would be provided orally to all soldiers, and when possible, in writing. DoD's Central Command subsequently decided that the vaccine would be administered on a **voluntary** basis.

DoD described several other safeguards that would be in place regarding the distribution of the vaccine. DoD officials promised that the soldiers would be observed for 30 minutes after receiving the vaccine, and if possible, they would also be checked again 48 hours later. In addition, DoD claimed that they would provide all three vaccine injections, since all three were necessary to provide protection.

Despite these agreements between FDA and DoD, and DoD's subsequent decision to administer the vaccine voluntarily, many PGW veterans claim that they were not told what vaccine they were being given, or what the risks were, either orally or in writing. Many report that they were told not to tell medical personnel that they had received a vaccination, even if the vaccination caused pain or swelling. No record of the vaccine was available in medical records; as a result, physicians who were concerned about any local or systemic reactions often had no information about the possible causes of those symptoms. Veterans who claim they were harmed by the vaccines or pyridostigmine frequently have no proof that they were vaccinated or took the pills, or that they had an adverse reaction. Moreover, virtually none of the soldiers received more than two of the botulism vaccinations, even though DoD had informed FDA that three shots were necessary for protection against botulism.

CMAT Control #
2001159-0000017

(28)

United States Senate

COMMITTEE ON VETERANS' AFFAIRS
WASHINGTON, DC 20510-6375

October 2, 1996

The Honorable David A. Kessler, M.D.
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Kessler:

I am deeply concerned by today's announcement that anthrax vaccine will be given to our military personnel for potential exposure to inhaled anthrax. Given the multitude of questions surrounding the after-effects of dispensing pyridostigmine bromide to 697,000 troops in the Persian Gulf, detailed information about testing, side effects, and recordkeeping should be provided to the troops, the Congress, and the public before soldiers are ordered to take another vaccine.

As Ranking Member of the Committee on Veterans' Affairs, I request that you provide, immediately, the following:

- Any and all information which in any way relates to the testing, safety, efficacy, and review of anthrax vaccine for protection against inhaled anthrax, including all scientific studies and reviews, and including all NDA, IND, and waiver requests relating to the use of anthrax by the military;

- All memoranda, letters, and other communications, including those maintained in electronic form, which in any way relate to the decision to inoculate military personnel with anthrax vaccine at this time. This should include any information in your possession regarding the assessment that anthrax vaccine administration is necessary at this time, and all memoranda supporting that decision.

This information request includes all written and electronic information in your possession or control, whether in draft or final form, and regardless of whether it was created by, and/or for, the United States Government.

Due to the time-sensitive nature of this information, please provide all of the requested documents no later than the close of business on Wednesday, October, 9, 1996.

Thank you for your attention to this request.

Sincerely,

John D. Rockefeller IV
Ranking Minority Member

SECRETARY OF DEFENSE CORRESPONDENCE ROUTING SLIP

Action Agency: **Senior Advisor to DSD for Chemical & Biological Protection**
Action Required: **PREPARE REPLY FOR SECRETARY OF DEFENSE SIGNATURE**
Coordinate With: **LA UPR**

Remarks:

Special Instructions:

Suspense Date: **June/28/2001**	Routing Date: **June/22/2001**	OSD CONTROL #: **U11302-01**

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Congress of the United States
Washington, DC 20510

June 21, 2001

The Honorable Donald Rumsfeld
Secretary of Defense
The Pentagon
Washington, DC 20301-1000

Dear Secretary Rumsfeld:

As you continue your strategic review of the Defense Department's strategy and policies, we write to express our interest in and concern about reports regarding the Pentagon's continued use of an anthrax vaccine on our military personnel. We recognize that your review is addressing a myriad of issues with large implications for our national security. However, we think you will agree with us that no issue you are currently considering is more important than how to best ensure the health and well being of our military personnel while they serve their country.

As a result, we are troubled by several reports and actions that raise questions about whether continuing to administer the current anthrax vaccine is in the best interests of our personnel. First, we have been made aware of the fact that a number of military and civilian personnel have come to believe that the vaccination given to our military personnel is neither safe nor effective for its intended use. As you know, the Food and Drug Administration's underlying prerequisite for the approval of any vaccine or drug is that it be proved safe and effective for its intended use. A growing number of people believe that the use of the anthrax vaccine as currently formulated to protect humans against inhalation of anthrax spores fails to meet this test.

Second, earlier this month, the Defense Department announced that it will further slow the administration of the anthrax vaccine. The current slowdown, the third in less than one year, was brought about by the continuing inability of the vaccine manufacturer to obtain FDA approval of its production facility. Under the revised policy, the scope of the vaccination program will be limited to special mission units, manufacturing and research personnel, and congressionally mandated research. In light of the questions surrounding the safety and effectiveness of the vaccine and the inability of the vaccine manufacturer to obtain FDA approval, many have asked why the Pentagon has not halted the vaccination program for all military personnel until these outstanding questions are satisfactorily addressed.

Third, the Defense Department has already taken disciplinary action against a number of people who have refused to take or administer the anthrax vaccination and has stated its intention to pursue legal action against others who act similarly in the future. Although a number of questions about the safety and effectiveness of the anthrax vaccination would appear to remain unanswered, the Pentagon has made it clear that it does not intend to revisit either the punishments already meted out or its decision to discipline those who act similarly in the future.

We all acknowledge that the threat posed by biological weapons, including anthrax, is a real one that the Administration and the Congress have a responsibility to address. Ignoring such threats is not an option. However, we also have an obligation to our military personnel to ensure that we do nothing to increase the risks they already face for their decision to serve their country. We would welcome your response to the issues raised here. In addition to your written response, our staff is prepared to discuss this matter with appropriate Defense Department officials.

Sincerely,

Tom Daschle

Dick Gephardt

(30)

CMAT Control #
1999085-0000011

THE HOUSE OF REPRESENTATIVES

STATEMENT OF

Private First Class Stephen M. Lundbom

Before the Subcommittee on National Security,

Veterans Affairs, and International Relations

of the Committee on Government Reform

of the House of Representatives

March 24, 1999

Good afternoon, my name is Stephen Michael Lundbom and I am from Livermore, California. I am currently serving as a Private First Class in the United States Marine Corps, at 29 Palms, California.

I am here to tell you of my own personal experiences after I decided that I would not accept the mandatory anthrax vaccine. I believe that other Marine refusers have also shared some or all of my experiences. The views that I express here are my own and are not meant to reflect those of the U.S. Marine Corps.

Since this is the first time I've visited Washington, my dad and I spent Sunday afternoon touring some of the historic sites, such as the Lincoln Memorial, the Washington monument, and the Vietnam Veterans War Memorial. At each, I saw the words "justice", "democracy," "liberty" and

"independence." These are concepts that this great capitol represents to me. They are the things America is based on and they are the things our military is sworn to protect and uphold.

I enlisted in the Marine Corps in June 1997 because I believed in its stated values of pride, honor, and dedication. However, when I and other Marines began to ask our commanders questions about the safety and effectiveness of the anthrax vaccine, they responded in ways that, in my opinion, lacked respect for our fundamental legal and democratic rights as citizen-soldiers.

Like many Americans of my generation, when I felt I needed to learn more about the vaccine, I went first to the internet. Here, I quickly learned that there were a number of unanswered questions about this vaccine, particularly as it was being used to protect us from inhaled anthrax spores. I was especially concerned that there was much debate about whether the vaccine would keep us safe if bio-weapons were to be used on the battlefield. The fact that there had been no research into whether the vaccine could cause sterility, birth defects, or cancer also worried me.

He said that they didn't use the "usual procedure" of giving shots to anyone at once - they used the mail.

When we were called to take the shot for the first time on Okinawa, twenty-seven of us announced that we would refuse the shot. After much pressure and many threats, all but five of the initial resisters gave in and

accepted vaccination. Like the other four, I was given Non Judicial Punishment (Article 15). My sentence was: 30 days restriction, 30 days extra duty, and the forfeiture of $539.00 pay (one-half months pay for one month). Some of the other refusers were forced to walk approximately sixteen miles each day during the weekend and holidays, and many miles other days, since the battalion office was a half-mile from the barracks and the we had to sign the duty book at that location almost every hour from 7 am to 9:45 pm.

When two weeks of the punishment period had passed, another anthrax vaccination was scheduled and, once again, I was called in and ordered to take the shot. I was again charged and put up for another Non Judicial Punishment. During this Article 15 proceeding Lt. Colonel Stuart Navarre, my battalion commander, ordered me to provide him with the phone number of my mother's employer, a doctor in general practice back in California. This frightened me because I didn't want my refusal to affect my mother's job as a nurse. Despite my fear, I told Colonel Navarre that I didn't believe I had to answer questions like that. He then punished me a second time. This time I received 45 more days restriction, 45 more days of extra duty (including signing the log book every hour) another half months pay

loss for each of two months and a reduction in rank from Lance Corporal to Private First Class.

To be honest, this constant harassment and punishment wore heavy on my spirit and morale. Yet, I was able to stick to my resolve not be vaccinated because of the strong support I received from my wife (who is also a Marine) and my family. My four fellow refusers were a source of support also.

Finished with our six month deployment to Okinawa, my unit returned to Twenty Nine Palms, California where I naively perhaps hoped that my situation might change for the better.

Once I had completed all the punishment from both Non Judicial Punishments I submitted a request for leave. I was not even allowed to fill out a leave request. My command made it clear that any leave requests would be denied. I was told that I could not leave the base because I had refused the anthrax shot and therefore did not deserve to go on leave.

At this point, my family and I agreed that I needed outside legal help to help me cope with the unending harassment. My brother had attended an anthrax town meeting which had been sponsored by the GI rights group Citizen Soldier of New York. The event was held in San Diego. My father

contacted the director, Tod Ensign, and he put me in touch with Louis Font, a Boston lawyer who specializes in military defense work.

I learned that on April 10, 1998 the deputy Assistant Judge Advocate General had sent an internal memorandum to all Navy and Marine Corps Judge Advocates. This memo concludes that after punishment for a first refusal:

> Refusal to obey additional orders to be vaccinated for anthrax cannot form the basis for additional convictions at NJP [Non Judicial Punishment] or courts-martial.

The Marines had violated this attorney's memorandum in my case. I had been doubly punished, and faced a special court.

I believe it is immoral, unethical, illegal and wrong that I have been punished twice at NJP and now face a court-martial, when Marine Corps lawyers have before them the internal memo that states this is unlawful.

My father called my battalion commander, Lt. Col. Navarre, and he said that his hands were tied and that he was only following the Marine Commandant's policy. He said the policy is an NJP for the first refusal, another NJP for the second refusal, and a special court-martial for the third.

After my attorney explained to me the legal issues, I gladly signed a Petition for Extraordinary Writ which we filed on Monday, March 22, 1999, before the Navy/Marine Corps Court of Criminal Appeals at the Washington

Navy Yard. It asks that the second NJP be set aside and that no court-martial be allowed for this refusal.

I ask that Congress investigate whether the Commandant of the Marine Corps has an illegal policy and whether subordinate commanders, such as my battalion commander, are subjecting enlisted men, such as myself, to multiple punishment as a result of this policy. It seems to me that the reason for the policy and the reason the Marine are disregarding their own legal memorandum is to keep the number of refusers so low that Congress will be misled into thinking that compliance is virtually total.

I had never before disobeyed an order and my unblemished record reflects my desire to be a dedicated Marine. I love the Marine Corps and everything it stands for. But when it came time for me to accept this vaccine I felt in my heart, mind, body and soul that I was doing the right thing by refusing it.

I appreciated hearing the testimony of the highest-ranking military health authorities who have testified today and it made me respect even more this Committee's willingness and desire to hear the point of view of an enlisted person at the lowest echelons.

Thank you very much for having me testify today. I welcome any questions you may have.

(31)

CMAT Control #
1999085-0000012

PREPARED STATEMENT OF MARK S. ZAID, ESQ.*
EXECUTIVE DIRECTOR, THE JAMES MADISON PROJECT

BEFORE THE SUBCOMMITTEE ON NATIONAL SECURITY,
VETERANS AFFAIRS AND INTERNATIONAL RELATIONS
COMMITTEE ON GOVERNMENT REFORM
U.S. HOUSE OF REPRESENTATIVES

WEDNESDAY, MARCH 24, 1999

"THE PERFORMANCE OF THE ANTHRAX INOCULATION PROGRAM"

Mr. Chairman, distinguished members of the Subcommittee, thank you for the opportunity to appear before you and offer my comments on the growing concern over the military's forced inoculations of our servicemen with the anthrax vaccine. I have been involved with this issue since April 1998, when the first shots were administered to Naval personnel serving in the Gulf region, and I was requested to provide legal counsel to those who were refusing the inoculations aboard the *U.S.S. Independence*.

Then, in my position as General Counsel for the non-profit organization Veterans for Integrity in Government (VIG), I litigated a Freedom of Information Act case against the government which resulted in the release of thousands of pages of previously unseen documents pertaining to the anthrax vaccine and the Pentagon's vaccination program. Most recently, through The James Madison Project, I served as the lead civilian defense

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*The James Madison Project (JMP), 1501 M Street, N.W., Suite 1175, Washington, D.C. 20005. Tel. No. (202) 785-3801; Fax No. (202) 223-4826; E-Mail: JaMadPro@aol.com. JMP is a Washington, D.C.-based non-profit organization with the primary purpose of educating the public on issues relating to intelligence gathering and operations, secrecy policies, national security and government wrongdoing. JMP also handles litigation under the Freedom of Information and Privacy Acts, including representation of news organizations, journalists, authors, intelligence officers, whistleblowers or others who allege harm at the hand of a government, foreign or domestic, in matters involving intelligence, national security and government accountability issues. The views expressed by Mr. Zaid are his own and do not necessarily reflect the views of any organization or entity with which he is or has been affiliated. A biographical sketch is attached at Exhibit "1".

counsel for Airman Jeffrey Bettendorf, who was the first serviceman to face court-martial for refusing to take the vaccine under orders of a superior commissioned officer.

The Pentagon has embarked upon a massive unprecedented public relations' campaign to minimize any potential objections to the vaccination program. Despite these efforts, a tide of dissention is rising among many servicemen and their families. Indeed, it has been far more widespread than the Defense Department has publicly acknowledged. Senior Pentagon officials have publicly alleged that those refusing the vaccine have been misinformed, the victims of a paranoid Internet community, or the prey of small groups with agendas. These allegation are false. The individuals with whom I have been in contact with have thoroughly researched the issue and have based their decision on a personal, well reasoned and deep-seated desire for preservation of themselves and their loved ones. It is almost certain that in all of the cases a sense of fear contributes to the decision to refuse the vaccine. Regardless of whether the fear is justified, the Pentagon's actions and lack of credibility have led its personnel to make such that choice.

Those refusing have primarily been enlisted personnel under the age of 25. The paucity of protest from more senior rank simply reflects the greater risks and consequences faced by career personnel who oppose official policy. Based on my communications with military personnel, it appears that fear and dissention has spread throughout the services. While it might not always lead to a refusal, it has negatively impacted moral and possibly recruitment as well.

My remarks today will primarily focus on two specific areas: (1) the legal issues that surround this controversy and the options and repercussions involved when a member of the military refuses the vaccine; and (2) the fundamental problems with the Anthrax Vaccination Immunization Program (AVIP) as evidenced by documentation obtained from the government through litigation.

IMPLEMENTATION OF THE AVIP

On December 15, 1997, Secretary of Defense William S. Cohen announced the implementation of a military-wide anthrax immunization plan that had been under review for two years.[2] However, prior to the actual implementation of the program, four conditions were to have been met:

(1) Supplemental testing, consistent with Food and Drug Administration (FDA) standards, to assure sterility, potency and purity of the vaccine;
(2) Implementation of a system to fully track personnel who receive the anthrax vaccine;
(3) Approval of appropriate operational plans to administer the immunizations and communications plans to inform military personnel of the overall program; and
(4) Review of health and medical issues of the program by an independent expert.[3]

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[2]News Release, Office of Assistant Secretary of Defense (Public Affairs), December 15, 1997, "Defense Department to Start Immunizing Troops Against Anthrax, available at http://www.defenselink.mil.

[3]The Joint Program Office for Biological Defense contracted with Mitretek Systems, Inc. to fulfill the first condition and perform independent evaluation of supplemental testing. The process began in January 1998, and was scheduled to have been completed in November 1998. See Memorandum for Secretary of Defense from Assistant Secretary of Defense (Health Affairs), May 1, 1998 (copy on file with the Subcommittee and the author). Although the memorandum indicates that the initial lots passed supplemental testing, none of the test results have been publicly released. Conditions two and three were sufficiently completed by mid-Spring 1998. The independent review referenced in condition four was conducted by Dr. Gerard N. Burrow, Special Advisor for Health Affairs for the President of Yale University, and completed on February 19, 1998. His findings appear to merely reflect a review and regurgitation of the literature provided by the Pentagon and telephone inquiries and consultations, no details of which are provided. See Exhibit "1A". No evidence suggests Dr. Burrow was aware of the multitude of problems associated with the manufacturing process, the unusually high rate of systemic reactions or the possibility that the Department of Defense may have modified the existing vaccine. This Subcommittee may wish to consider contacting Dr. Burrows to further explore the extent of his actual knowledge of the AVIP and how that might have effected his decision.

These conditions were deemed to have all been met by May 1998. As a result those troops in high-threat areas were ordered to take the vaccine. On May 18, 1998, Secretary of Defense William Cohen approved implementation of the program for the total force.[4]

When the Pentagon first began to administer the vaccine in the Gulf region and reports of the refusals reached the media, I undertook sincere efforts to quietly quash the "mutiny" by requesting a meeting with the appropriate officials of the Department of Defense. I also posed a series of questions regarding the anthrax vaccine.[5] No response was received. Nine days later, as the tension continued to mount on the *U.S.S. Independence*, I reiterated my request for a meeting and submitted additional questions.[6] I noted that "the decision to inoculate U.S. military personnel with the anthrax vaccine remains an issue that will only continue to escalate into public controversy unless full disclosure is forthcoming from the Department of Defense. Fear, whether founded or not, is running rampant throughout the military system and future refusals of the vaccine are to be expected."[7] Nearly one year later it appears my predictions were unfortunately true. Finally, nearly one month after I submitted my first letter, on May 8, 1998, I received a written response to my questions from Gary A. Christopherson, Acting Assistant

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[4]Memorandum from The Secretary of Defense, "Implementation of the Anthrax Vaccination Program for the Total Force," May 18, 1998 (copy on file with the Subcommittee and the author); see also News Release, Office of Assistant Secretary of Defense (Public Affairs), "Total Force Anthrax Vaccination Decision Announced," May 22, 1998, available at http://www.defenselink.mil.

[5]Letter dated April 13, 1998, from Mark S. Zaid, Esq. to Honorable William S. Cohen, attached at Exhibit "2".

[6]Letter dated April 22, 1998, from Mark S. Zaid, Esq. to Honorable William S. Cohen, attached at Exhibit "3".

[7]Id. at 2.

Secretary of Defense.[8] The meeting that I requested never occurred. As a result, some colleagues and I explored the option of a class action lawsuit in order to halt the entire vaccination program. The strategy was to challenge the safety, effectiveness and necessity of the vaccine. Legal research, however, soon revealed that the likelihood of success in federal court was virtually non-existent at best.

A. The Nuremberg Principles On Informed Consent Collapse

Following the end of World War Two, the United States took the lead in ensuring that accountability was attained for the unconscionable and inhuman acts committed by the Nazis. Not only did the United States actively participate in the International Military Tribunal at Nuremberg, but it continued the work on its own for three years through prosecutions of both German and Japanese officials for various war crimes. From the ashes of Nuremberg and the dramatic revelations of the horrific experiments conducted by the Nazis arose a code concerning voluntary consent that has been recognized throughout the world.

> The voluntary consent of the human subject is absolutely essential. This means that the person involved should have the legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the

[8]Letter dated May 8, 1998, from Gary A. Christopherson to Mark S. Zaid, Esq., attached at Exhibit "4".

effects upon his health or person which may possible come from his participation in the experiment.[9]

As a result of Nuremberg, varies laws were enacted to ensure that the notion of informed consent was upheld. Federal funding cannot be used by the Department of Defense for research involving a human being unless "the informed consent of the subject is obtained in advance."[10] Safeguards were established to ensure that both Congress and local civilian officials are made aware of any testing of a chemical or biological agent.[11]

The Nuremberg code, in fact, was meant to be absolute.[12] In fact, "[t]here is no exception for soldiers or for wartime, and until Desert Shield, the U.S. military had never argued that there should be such an exception."[13] Following the August 1990, invasion of Kuwait by Iraq, the Department of Defense "argued that informed consent under combat conditions was 'not feasible' because some troops might refuse to consent, and the military could not tolerate such refusals because of 'military combat exigencies.'"[14] As a result the FDA issued a new general regulation, rule 23 (d), that waived the need for the

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[9]THE NAZI DOCTORS AND THE NUREMBERG CODE, HUMAN RIGHTS IN HUMAN EXPERIMENTATION 2 (George J. Annas & Michael A. Grodin, eds., 1992).

[10]10 U.S.C. § 980 (1998); see also 32 C.F.R. Part 219 (1991)(Defense Department policies governing research involving human subjects).

[11]50 U.S.C. § 1520 (1998).

[12]See Washington v. Harper, 494 U.S. 210 (1990)(holding that forcible injection of medication into a nonconsenting person's body represents a substantial interference with that person's liberty).

[13]Annas, George J., *Changing the Consent Rules for Desert Storm*, 326 The New England Journal of Medicine 770, 770 (1992).

[14]Id. (citation omitted).

Defense Department to obtain informed consent.[15] Some believe the FDA was strong harmed into providing such an extreme waiver.[16] Not surprisingly, litigation soon ensued.

B. Prior Legal Challenge To The Military's Vaccination Program

Many members of the American public seem to be genuinely surprised to learn that service in the U.S. military comes with a harsh price. Not only is your life placed in jeopardy, but many of the normal constitutional protections afforded to American citizens, and even aliens, disappear.[17]

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[15]21 C.F.R. § 50.23 (d)(1997). The waiver terminated on March 15, 1991. For additional background see Robyn Pforr Ryan, *Should Combat Troops Be Given The Option Of Refusing Investigation Drug Treatment?* 52 Food & Drug L.J. 377 (1997); Claire Alida Milner, *Gulf War Guinea Pigs: Is Informed Consent Optional During War?* 13 J. Contemp. Health L. & Pol'y 199 (1996); Elliott Schuchardt, *Distinguishing Between Research And Medical Practice During Operation Desert Storm* 49 Food & Drug L.J. 271 (1994).

[16]In fact, at least circumstantial evidence of this premise exists. Internal Defense Department documentation that discussed the military's efforts to use certain vaccinations during Operations Desert Shield and Storm noted that "[t]he FDA's position on licensing products produced elsewhere is that they will not commit themselves without seeing the data. *Leverage may be needed* in the future if this becomes a problem. "Memorandum for Record, "Third Tri-Service Task Force (Project Badger) Meeting, October 18, 1990, at 2-3 (copy on file with the Subcommittee and the author)(emphasis added). "Project Badger" was apparently a Desert Shield endeavor to ensure that certain experimental vaccines, including those that became the subject of Doe v. Sullivan, were accelerated through production and implementation in time for Desert Storm. The various minutes of the Task Force meetings were obtained through VIG's FOIA litigation.

[17]Interestingly, in planning a change to the current anthrax vaccination program, BG Walter L. Busbee, Joint Program Manager for Biological Defense, informed those in attendance at a meeting that "the DoD position is 'soldiers are citizens first;' and whatever studies are formulated, the have to be done with this concept in mind. *Soldiers have the same Constitutional rights as other citizens.*" Memorandum for See Distribution, "Minutes of the Meeting on Changing the Food and Drug Administration License for the Michigan Department of Public Health (MDPH) Anthrax Vaccine to Meet Military Requirements," November 13, 1995, at 3 (emphasis added) ("November 13, 1995 Meeting")(copy on file with the Subcommittee and the author).

During the Gulf War a serviceman and his wife sought an injunction to prevent the Department of Defense "from using unapproved drugs on troops taking part in Operation Desert Storm without first obtaining informed consent from the individual military personnel."[18] The court refused to intervene particularly because the "DoD's decision to use unapproved drugs is precisely the type of military decision that court's have repeatedly refused to second-guess."[19] Even though the Defense Department was also collecting efficacy information while utilizing the experimental drugs under a FDA-waiver of informed consent, the plaintiffs' arguments that unlawful experimentation was being conducted was rejected. "The primary purpose of *administering the drugs is military, not scientific. The fact that the DoD will collect* information on the efficacy does not transform the strategic decision to use the unapproved drugs in combat into research."[20]

Upon appeal, although the court acknowledged that "deference is owed to the political branches in military matters", it did not agree that "judicial review of the matter here at issue is out of order."[21] Nevertheless, after further review the Court of Appeals deferred to the judgment of the FDA and still dismissed the case.[22]

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[18]John Doe et al. v. Louis Sullivan et al., 756 F.Supp. 12, 13 (D.D.C. 1991).

[19]Id. at 15. The court also noted a long line of cases dissuading intervention into military matters. Chappell v. Wallace, 462 U.S. 296 (1983); Gilligan v. Morgan, 413 U.S. 1 (1973); Feres v. United States, 340 U.S. 135 (1950). These and other cases concluded that courts are "ill-equipped to determine the impact upon military discipline that any particular intrusion on military authority might have." Chappell, 462 U.S. at 305.

[20]Doe et al., 756 F.Supp. at 15-16.

[21]John Doe et al. v. Louis Sullivan et al., 938 F.2d 1370, 1380 (D.C.Cir. 1991).

[22]Id. at 1383.

C. VIG's Freedom of Information Act Lawsuit

Given the disappointing results of our legal research, the focus turned to obtaining information concerning the anthrax vaccine and the inoculation program. It was now our hope that a concerted effort could be made to convince both the Congress and the American public, through use of the media, of the problems with the Pentagon's vaccination program. In June 1998, I filed a Freedom of Information Act (FOIA) lawsuit against the Departments of Army, Navy and Air Force and the Food & Drug Administration based on requests filed by Patrick G. Eddington, VIG's Executive Director and a former CIA Whistleblower on Gulf War Syndrome.[23]

This comprehensive lawsuit sought the disclosure of all records pertaining to:

(1) the anthrax vaccine;
(2) any studies regarding the anthrax vaccine;
(3) the composition of the anthrax vaccine as administered to U.S. military personnel;
(4) policies governing the discipline of U.S. military personnel who refuse to take the anthrax vaccine;
(5) the Michigan Biologic Products Institute.[24]

The lawsuit, which has essentially concluded, brought about the release of thousands of pages of documents relating to the anthrax vaccine, the majority of which had never been reviewed outside of government channels. Most revealing, however, was what was not disclosed: no evidence that the government has ever attempted to study whether the vaccine is safe over the long-term.

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[23] Veterans for Integrity in Government v. Department of the Army et al., Civil Action No. 98-1649 (D.D.C. June 29, 1998)(RWR).

[24] The FDA was specifically tasked for more detailed information concerning, but not limited to, anthrax licensing data, lot production, labeling, any memoranda's of understanding between the FDA and Defense Department, proposed rules governing informed consent and biological warfare vaccine production.

The documentation we obtained reveals some very troubling aspects of the Pentagon's AVIP policy and refutes many of the broad conclusory statements that it offers to justify its actions. I will address specific aspects of concern in more detail later in my testimony.

D. Legal Ramifications Of Refusing The Anthrax Vaccine

No apparent military policy exists governing how anthrax refusers will be dealt with, except to the extent that they should be handled through the appropriate and available administrative and judicial framework governing military discipline in general. In the wake of the initial refusals aboard the *U.S.S. Independence*, the need to emphasize counseling and education before punishment was highlighted.

> Whenever military members are directed to take the initial shot and voice any misgivings, they should be referred to our medical personnel to answer their concerns. If there is still some uncertainty, commanders and first sergeants should get involved in attempting to allay the individual's mistrust. Finally, we should make sure a defense counsel is readily available to answer any additional concerns the individual may have. Only after all available education and counseling type efforts have been exhausted should UCMJ [Uniform Code of Military Justice] action be initiated.[25]

Alarmingly, many servicemen have been and continue to be threatened with forcible inoculation, i.e., they would be tied down, if they did not submit voluntarily, despite Departmental policy that "force should never be used to administer the vaccinations."[26]

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[25]Memorandum for all ACC Staff Judge Advocates, BG William A. Moorman, USAF, Staff Judge Advocate, dated May 6, 1998 (copy on file with the Subcommittee and the author). The document also notes that the military "must be highly sensitive to the concerns of the military member, particularly after the DESERT SHIELD/STORM controversy over immunization." Id.

[26]Memorandum from Deputy Assistant Judge Advocate General (Criminal Law) to All Navy and Marine Corps Judge Advocates, April 10, 1998, at 3 ("JAG Memo")(Copy on file with the Subcommittee and the author). There seems to be a great deal of confusion

Indeed, the threat of force convinced many would-be refusers to accept the vaccination.[27]

Ultimately "[a] member refusing vaccination should be issued an order to submit to the vaccination by a superior commissioned officer."[28] If a servicemember refuses the vaccine, the commander has a "full range of options, from taking no action at all to taking administrative action (letters of counseling, letters of reprimand, referral OPR/EPR, etc.) to taking punitive action under the Uniform Code of Military Justice (UCMJ)."[29] Prosecution under the UCMJ will probably take one of two forms. If the order was given by the member's commanding officer, than a charge under UCMJ

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throughout the branches over whether force should be threatened or utilized, at least at the Command level on the ground. While it is the military's position that "Commander's have authority to order involuntary medical treatment of soldiers in cases where such treatment is deemed militarily necessary," see Unclassified Memorandum, "Refusal of Soldiers to be Vaccinated Against Anthrax," July 17, 1998, attached at Exhibit "6', various branches, such as the Navy, have explicitly declared that, as a matter of policy, force will not be used. Id. Indeed, the decision to avoid the use of force appears to be departmental policy. See AVIP, Program Review for the Deputy Secretary of Defense, August 1998 ("Force Should Never Be Used To Administer The Vaccinations"), attached at Exhibit "7". Nevertheless, reports of threats - most likely for intimidation purposes - still continue to be received. See Sean D. Naylor, *Fighting the anthrax vaccine: AWOL soldier faces discharge over the shots*, Army Times, Aug. 17, 1998.

[27]Over the last year I have been contacted by many servicemembers throughout the different branches of service who informed me of initial wide-spread refusals. Follow-up communications revealed, however, that many servicemen reluctantly consented to the vaccine following threats of severe punishment or even forcible inoculations. The Pentagon has significantly downplayed the actual number of initial refusals by only reporting those who were actually disciplined.

[28]JAG Memo, *supra* note 26, at 3; See Order to Take Anthrax Vaccination, September 30, 1998, attached at Exhibit "8".

[29]"Air Force Approach to Anthrax Immunizations," undated, at 3 ("Air Force Approach")(copy on file with the Subcommittee and the author).

Article 90(2) will likely be preferred.[30] If someone other than a superior commissioned officer gives the order (i.e., the member's first sergeant or a NCO medical practitioner), action under UCMJ Article 92(2) is more appropriate.[31]

Following refusal the commander can either impose UCMJ Article 15 nonjudicial punishment (NJP) or prefer charges to a general or special court-martial.[32] Article 15 proceedings are meant to address "minor offenses", and punishments include admonition and reprimand, restriction, arrest in quarters, correctional custody, confinement on bread and water or diminished rations, extra duties, reduction in grade and forfeiture of pay.[33]

During the last year the different branches of the military have been fairly consistent in the penalties they have imposed upon those who refuse the vaccination. The typical course of events following a refusal has been a NJP with the imposed sentence including reduction in grade, a forfeiture of pay, restriction to ship or base and assignment of extra duty.[34] Ultimately the service member would be administratively discharged from the

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[30]Article 90(2) states in relevant part that "[a]ny person subject to this chapter who ... willfully disobeys a lawful command of his superior commissioned officer ... shall be punished...."

[31]Article 92(2) states in relevant part that "[a]ny person subject to this chapter who ... having knowledge of any other lawful order issued by a member of the armed forces, which it is his duty to obey, fails to obey the order ... shall be punished...."

[32]It is important to note that this applies only to active-duty personnel and not reservists of national guardsmen. Members of these organizations can simply quit prior to punishment being imposed. The true test of the military's ability to withstand the growing dissent against the anthrax vaccine will depend on the actions taken by the reserve and guard units. Already several units have almost become non-deployable, particularly because of pilots refusing the vaccine. See Eddington, Patrick G., *Contamination fears drive reservists who refuse vaccine*, Army Times, Jan. 18, 1999, at 10, attached at Exhibit "9" ("Eddington").

[33]Manual for Courts-Martial, Part V, paragraph 5(c)(1)-(8)(1998 ed.).

[34]As the AVIP calls for a series of six shots, three of which are to be administered within a one month period, servicemen have faced the prospect of disobeying repeated orders to

military.[35] If the individual had a clean disciplinary history the likelihood was that he would receive, as the vast majority did, a General Discharge under Honorable Conditions. Some who refused that had only a few months left in their tour of duty were permitted to quietly leave without suffering significant administrative punishment. Indeed, even individuals who went AWOL based solely on their concerns about the vaccine received such a discharge.[36]

As the vaccination program spread throughout the world and more individuals in each branch of the service began to refuse, it was only a matter of time before someone would proceed to a court-martial. Airman Jeffrey Bettendorf, who was stationed at Travis Air Force Base in California, became that unfortunate first person.

On December 1, 1998, Airman Bettendorf refused the vaccine. He was offered an Article 15 for his failure to submit to the anthrax vaccine on December 11, 1998. As the many others who preceded him, he was found guilty and received similar non-judicial punishments; a grade reduction and 45 extra days of duty. Prior to this time A1C Bettendorf had a completely clean disciplinary record. Furthermore, A1C Bettendorf was

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take the vaccine. Many servicemen have been punished more than once for refusing essentially the same order, apparently in contradiction to established policy. "Refusal to obey additional orders to be vaccinated for anthrax cannot form the basis for additional convictions at NJP or courts-martial." JAG Memo, *supra* note 26, at 3, citing U.S. v. Greene, 8 M.J. 796 (NCMR 1980). See also Manual for Courts-Martial, Part V, paragraph 1(f)(1)-(3)(1998 ed.)(prohibiting double, increased and multiple punishments). Documentation obtained by VIG through its FOIA lawsuit reveal that a disparity of policy among the branches. See USCENTCOM Anthrax Update, July 31,1998 (commenting on differences between Air Force and Navy)(copy on file with the Subcommittee and the Author).

[35]"The discharge can be characterized as honorable, general or under other than honorable conditions, depending upon the circumstances surrounding the member's service." Air Force Approach, *supra* note 29, at 4.

[36]This is based on information received from individual servicemembers whom I have represented or maintained communications.

> religion, or personal philosophy cannot justify or excuse the disobedience of an otherwise lawful order.[38]

The test for determining the lawfulness of an order was set forth in U.S. v. Flynn[39], where the court held that "[t]he order must be: (1) reasonably in furtherance of or connected to military needs; (2) specific as to time and place and definite and certain in describing the thing or act to be done or omitted; and (3) not otherwise contrary to established law or regulation."[40]

The biggest hurdle facing anthrax refusers is that the vaccine allegedly being administered is FDA-approved. Under those circumstances the likelihood, absent extraordinary circumstances and the flexibility to conduct discovery, in securing an acquittal of a serviceman facing an Article 90(2) charge is slim. Orders are presumed to be lawful on their face.[41]

However, at the beginning of the AVIP information had begun to circulate that the anthrax vaccine as administered by the Pentagon was, in fact, not the same FDA-approved vaccine. It had allegedly been modified in some manner in order to strengthen its effect.[42] Therefore, our primary defense in A1C Bettendorf's case, and one that should be utilized alongside any other available defenses in every anthrax refusal court-martial case is that the order is not lawful because it is "contrary to established law or regulation," i.e., the vaccine may not be the same one approved by the FDA.

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[38]Part IV, paragraph 14(c)(2)(a)(iii)(1998 ed.).

[39]34 M.J. 1183 (AFCMR 1992).

[40]Id. at 1188.

[41]Unger v. Ziemniak, 27 M.J. 349 (C.M.A. 1989).

[42]One theory that emerged was that the vaccine had been spiked with squalene as an adjuvant to enhance the immune response. Report of the Special Investigation Unit on Gulf War Illnesses, Senate Committee on Veterans' Affairs 123 (1998).

Therefore, the vaccine converts to experimental and as a matter of law and requires the consent of the individual. It was also our defense position that we had every right to present evidence addressing whether the vaccine was safe, effect or even necessary to accomplish a military mission.[43] Ample precedent exists to permit such a defense.

In U.S. v. Chadwell et al.[44], two Marines were tried and convicted by a special court-martial under Articles 90 and 92 for having "willfully disobeyed a lawful order of their superior officer to submit to certain medical treatment, to wit: immunization against smallpox, typhoid, paratyphoid and influenza ..."[45] The Court recognized that "[t]here is no doubt that the legality of an order may be questioned and the courts are required to determine such issue when raised. Individual rights that are protected by the Constitution and statute are not subject to military orders which are arbitrary and unreasonable."[46] Chadwell reiterated a conclusion now more than forty years old held by a prior military court that:

> Persons in the military service are neither puppets nor robots. They are not subject to the willynilly push or pull of a capricious superior, at least as far as trial and punishment by court-martial is concerned. In that area they are human beings endowed with legal and personal rights which are not subject to military order.

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[43]We also argued that A1C Bettendorf had the right to present evidence concerning his views of the vaccine's safety, effectiveness and necessity in any sentencing phrase in order to mitigate any punishment. The Government conceded that A1C Bettendorf had the right to make a sworn or unsworn statement regarding how his state of mind had been effected by information he had compiled about the vaccine, but opposed the introduction of any evidence subsequently obtained.

[44]36 C.M.R. 741 (1965).

[45]Id. at 742.

[46]Id. at 749.

> Congress left no room for doubt about that. It did not say that the violation of any order was punishable by court-martial, but only that the violation of a lawful order was.[47]

Although the Chadwell court did hold that the vaccination order in that case was legal, particularly because the accused did not contest the fact on appeal[48], most importantly it was noted that the trial court "permitted medical testimony offered by the defense that the shots were unnecessary...."[49] Thus clear precedent exists granting anthrax refusers the ability to challenge the underlying policy of the Pentagon to implement the AVIP.

Therefore, in furtherance of A1C Bettendorf's defense we requested as part of the discovery process samples of the vaccine so that independent testing could be undertaken in order to determine whether or not the Defense Department had modified or altered the vaccine in any way.[50] This request was, of course, refused but before the issue was litigated the Air Force agreed to accept Airman Bettendorf's Chapter 4 request for a discharge and he was processed out of the Air Force under Other Than Honorable conditions.[51]

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[47]U.S. v. Milldebrandt, 8 USCMA 635 (1958)(citation omitted).

[48]Id. at 748.

[49]Id. at 750.

[50]According to the manufacturer, the final product should contain no more than 2.4 mg aluminum hydroxide (equivalent to 0.83 mg aluminum), 0.02% of formaldehyde and 0.0025% of benzethonium chloride, per 0.5 ml dose. IND at 002.

[51]See Steven Lee Myers, *Airman Discharged for Refusal to Take Anthrax Vaccine as Rebellion Grows*, New York Times, Mar. 11, 1999. A1C Bettendorf's final discharge disposition was, therefore, more harsh than many of the refusers who preceded him. However, facing a possible penalty of six months in jail, he had earlier filed for such a discharge in order to avoid the court-martial. Nevertheless, A1C Bettendorf's cases raises valid concerns for the consistency in the treatment of refusers. In 1995, when the Defense Department implemented its DNA-identification program, several UCMJ cases arose after servicemembers refused to submit to blood and tissue sampling. An Air Force

THE PROBLEMS WITH THE PENTAGONS' AVIP

Much of the blame for the growing hysteria arising from the AVIP must fall on the Pentagon itself. The Defense Department has continually relied on conclusory statements of fact that have little or no basis, set forth misleading information concerning the vaccine, unfairly ridiculed those who have sought to bring to light inconsistencies and problems with the AVIP program and, whether fair or not in these particular circumstances, suffers from a significant lack of credibility.

A. Brief History Of The AVIP

The AVIP is being implemented under the authority of the Secretary of Defense in accordance with DoD Directive, 6205.3, "DoD Immunization Program for Biological Warfare Defense" (November 26, 1993), which established the policy, responsibilities and procedures for stockpiling biological agent vaccines. It also determined which personnel should be immunized and when the vaccines should be administered. The Army serves as the Executive Agency of the AVIP.

The present AVIP calls for a series of six shots over an 18 month period administered in intervals of 0, 2 and 4 weeks for the first three shots, and then boosters at 6, 12 and 18 months. The original immunization schedule for humans was three doses at 0, 2 and 4 weeks "based on a regimen developed for animals."[52] The genesis for the six shot series arose from three immunized workers falling sick in the 1950s which led "an investigator to recommend arbitrarily three more immunizations (6, 12, and 18 months) as boosters."[53]

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technical sergeant who refused was found guilty at a special court-martial of an Article 92 violation and sentenced to grade reduction and 14 days hard labor. However, he submitted a request for voluntary discharge, which was accepted, and he received an honorable discharge. See Air Force Approach, *supra* note 29, at 3.

[52]November 13, 1995 Meeting, *supra* note 17, at 2.

[53]Id.

Criticism of the program was inevitable given the Pentagon's history. Questions regarding informed consent, particularly after the horrendous lack of appropriate medical record-keeping experienced during Desert Shield/Desert Storm, and cries of "guinea pigs" were expected from the outset.[54] All the more reason why it is shameful that the anthrax vaccine controversy was not resolved much earlier by the Pentagon.

B. History Of Medical Mistreatment And Experimentation Has Fueled Fear

This topic requires very little in the way of introduction. The historical record is not only quite clear, it is despicable. "Examples of use of physicians for governmental purposes include the U.S. military and cold war radiation experiments and the use of investigational drugs on U.S. soldiers in the Gulf War without consent, both done in direct violation of the Nuremberg Code."[55] Another military low point includes the use of Agent Orange.[56]

Both the FDA and the Presidential Advisory Committee on Gulf War Illnesses criticized the Pentagon for its past history of using experimental drugs and vaccines during the Gulf War and exercises in Bosnia. The FDA criticized the Pentagon for "failing to document immunizations in soldiers' permanent medical records and for touting the vaccine in handouts given to troops as 'very safe and extremely effective'

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[54]Anthrax Vaccine License Amendment Project Plan, "Information Briefing for Joint Program Manager, DoD Biological Defense, SAIC, October 20, 1995, at 18 (copy on file with the Subcommittee and the author).

[55]Editorial, *Legacies of Nuremberg: Medical Ethics and Human Rights*, 276 JAMA 1682, 1683 (Nov. 27, 1996)(citations omitted). See also Final Report, Advisory Committee on Human Radiation Experiments (1995)(conducted extensive inquiry into the history of government-sponsored human radiation experiments that occurred between 1944 and 1974); Thomas, Gordon, JOURNEY INTO MADNESS (Bantam Books: 1989)(CIA mind control and medical abuse).

[56]See *Fatal Flaws: How the military misled Vietnam veterans and their families about the health risks of Agent Orange*, San Diego Union Tribune, Nov. 1, 1998.

when the FDA never authorized such glowing language."[57] The President's Committee went even further and declared that the Pentagon "currently is incapable" of handling unapproved drugs.[58] Nor have the concerns regarding the government's predilection to utilize experimental drugs on both military and civilian populations abated.[59]

Of course, vaccines, including anthrax, have been raised as potential contributing causes to the mysterious illness known as Gulf War Syndrome.[60] Again, the issue is not as much whether any specific historical incident is factually accurate or not, but the credibility, or more precisely lack thereof, of the Pentagon to implement new medical programs. Concern is heightened when the program itself is fraught with controversy, as is the anthrax vaccine.

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[57]Patrick Pexton, *Pentagon Can't Be Trusted With Experimental Drugs*, Navy Times, Feb. 16, 1998 ("Pexton").

[58]Id. With respect to the AVIP, because of past deficiencies, Senator John D. Rockefeller IV stated that "[w]hile this may be the only reasonable choice at this point, I am doubtful about DoD's ability to do it properly." Deborah Funk, *Vaccinations: Senate Warns DoD To Get It Right*, Navy Times, Mar. 30, 1998.

[59]Deborah Funk, *Military Proposes Use Of Experimental Drugs At Home*, Navy Times, Oct. 27, 1997. Included within the Defense Department's proposal was an anthrax vaccine post-exposure treatment. Id. See also Pexton, *supra* note 57 (FDA "pointed out an underlying inability for the Defense Department to carry out its obligations" for handling experimental substances).

[60]See Declan Barber, *Admission on Gulf War vaccines spurs debate on medical records*, 390 Nature 3 (Nov. 6, 1997)(British confirmed that pertussis vaccine combined with anthrax vaccine). The Presidential Advisory Committee on Gulf War Veterans' Illnesses concluded, however, that "it is unlikely that health effects reported by Gulf War veterans today are the result of exposures to the BT or anthrax vaccines, used alone or in combination." Final Report, The Presidential Advisory Committee on Gulf War Veterans' Illnesses 114 (1996). Despite this finding, even the Pentagon would likely admit doubts and suspicions remain prevalent.

C. No Long Term Studies On The Effect Of The Vaccine Have Ever Been Conducted And Most Available Studies Are Limited In Scope

It has widely been reported that the anthrax vaccine is safe primarily because of the length of time in which it has been available for use. Repeatedly the Defense Department has emphasized that the vaccine has been FDA-approved since 1970, and in use since the 1950s. Moreover, it has been asserted that the vaccine has received wide-spread use throughout the veterinary and livestock communities. This is, however, not entirely accurate. In fact, the vaccine has apparently only been used by approximately 20,000-30,000 people over the last 30-50 years.[61] Outside of the military, relatively few people receive the shot each year.[62]

Indeed, the Defense Department's inoculation of 150,000 servicemen during the Gulf War with the anthrax vaccine, knowledge of which was withheld from most individuals, was the first major use of the vaccine in any significant quantity. In one year, nearly six times the number of people were inoculated by the Pentagon than had been in the prior 30 years combined. Despite lacking sufficient tests surrounding the vaccine, particularly regarding its long-term effects, the current AVIP represents a tremendously expanded inoculation program which has never been seen before in the history of the anthrax vaccine - literally one hundred times more people, each of whom are involuntarily being subjected to the vaccine.[63]

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[61]James W. Crawley, *Military Seeks To Ease Fear Of Anthrax Vaccine*, San Diego Union-Tribune, Feb. 9, 1999 ("Crawley").

[62]Dr. Bradford Smith, a veterinary professor at UC-Davis, was interviewed by CNBC-TV, the airing of which occurred March 22, 1999, and stated he knew of few veterinarians that were taking the vaccine. Contrary to the Pentagon's repeated assertions, he expressly denied that it was used by the veterinarian community on a routine basis.

[63]Interestingly, despite likely having the second largest force in the Gulf region, the British government's anthrax vaccination program is entirely voluntary. See Warren Richey, *A vaccination war erupts in military*, The Christian Science Monitor, Jan. 28, 1999 (noting that 70 percent of British military personnel have declined the vaccine).

Repeatedly, my colleagues and myself have submitted requests for supporting documentation of the Pentagon's assertions that the vaccine is widely used and lacking any long-term ill effects. Invariably a deliberate non-responsive answer is provided with a mere standard citation to the long history of the vaccine with no known reported serious adverse reactions. Another favorite line is that it would be unethical to conduct such tests on humans.[64] Such a response misses the point entirely.

Whether use of the vaccine has caused serious adverse reactions immediately following or shortly after the actual inoculation is a separately valid issue. And one that should be properly explored. But no one is calling for the initiation of actual human tests to be conducted to determine long-term effect. It has been the Pentagon's position that the FDA-approved vaccine has been widely used for nearly three decades among veterinarians and live-stock workers. A form of the anthrax vaccine has, in fact, existed in this country for nearly half-a-century. How difficult would it be then to locate several hundred or thousand individuals who once took the vaccine and, after taking into account all appropriate variables, examine their health? Do any now suffer from cancer, or leukemia, or Alzheimer or any significant medical malady? When 2.4 million lives are at stake, is it not worth the effort to try? Indeed, is it not the lawful or moral responsibility of the Pentagon to undertake such an effort? Yet the Defense Department has not, nor has it shown any willingness to do so. Instead, it offers excuses as it cannot answer the question.

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[64]These assertions were espoused as recently as March 22, 1999, by Lt. General Kevin Kiley, Assistant Surgeon General, USAF, when he appeared on a nationally-television program on CNBC.

The most revealing aspect of the VIG FOIA lawsuit was what was not disclosed: no studies regarding the long-term safety of the anthrax vaccine have been conducted.[65] This fact alone unequivocally destroys the Pentagon's assertions that the vaccine has no known long-term health affects. What is amazing is that the Pentagon has seen fit to implement the AVIP based on very limited information. Its own documents repeatedly refer not to studies that support its assertions that the vaccine is safe and effective, but that none state otherwise.[66] That is a dangerous way to operate, particularly when millions of lives are at stake. Indeed, the manufacturer's label itself reveals that "[s]tudies have not been performed to ascertain whether Anthrax Vaccine Adsorbed has

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[65]The only document released that discusses long-term safety was a two page Information Paper dated November 23, 1994 that merely glosses over the potential future risks posed by the vaccine. It summarily concludes "[t]here is no scientific data to indicate a long term safety-risk associated with the use of the Anthrax vaccine." See Exhibit "9A". Of course, this conclusion is to be expected given that no such data has ever been collected. One would think the Pentagon would be responsible enough to concern itself with the collection of such data given the breadth to which it is implementing the AVIP over vocal objections. Nor have any relevant studies concerning the anthrax vaccine presumably been withheld due to classification concerns. VIG was notified that the only studies withheld on grounds of national security dealt with vaccine production and technological issues. Should other classified documents exist, they were illegally withheld.

[66]Aside from the potential long-term effects, another concern that has arisen is the effect of the anthrax vaccine when combined in close proximity with other vaccines. Concerns over "vaccine soup" have been of particular interest to those researching potential causes of Gulf War Syndrome. A limited study conducted at Fort Bragg and Fort Detrick revealed that the combination of the anthrax and botulinum vaccines did produce "mild and moderate reactions", as well as a "few serious side effects." Memorandum for Dr. Edward Martin, Principal Deputy to the Assistant Secretary of Defense (Health Affairs) from BG Russ Zautchuk, U.S. Army Medical Research and Materiel Command, July 19, 1995, at 2 (copy on file with the Subcommittee and the author). But once again the Army was more willing to rely on the fact that computer databases searches and telephone inquiries revealed that "no studies have reported on interactions between anthrax vaccine and other pharmaceuticals" rather than actually perform such studies. Id. at 1.

carcinogenic action, or any effect on fertility."[67] Nor is even the FDA aware of any clinical studies on the long term health effects of the vaccine.[68]

Documentation obtained from the Army through the VIG lawsuit highlights the significant problems facing any real study of the vaccine. In furtherance of the Army's desire to change the dose and usage of the vaccine to protect against inhalation, it was noted that:

- It is questionable whether anthrax occurs with sufficient regularity in humans anywhere in the world to allow for meaningful studies to be practically undertaken.[69]
- Presently there are no precise serological or other immunological correlates of protection to enable conclusions to be drawn from immunization studies in man.[70]
- The demonstration in some animal models that protection with the present vaccine varies across challenge strains further complicates studies and limits the breadth of efficacy claims that can be made.[71]
- The potency test required for the present vaccine has not been well correlated to efficacy in humans and it is doubtful that it can be.[72]

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[67]"Anthrax Vaccine Adsorbed", F-483 100M 10/90 (rev. 10/87), attached at Exhibit "10" ("Manufacturer's Label").

[68]See Letter dated April 28, 1998, to Patrick G. Eddington, Executive Director, Veterans for Integrity in Government, from Kathryn C. Zoon, Ph.D., Director, Center for Biologics Evaluation and Research, FDA, at 2, attached at Exhibit "11" ("Zoon Letter").

[69]Undated briefing page, U.S. Army (copy on file with the Subcommittee and the author).

[70]Id.

[71]Id.

[72]Id.

There can be no dispute that there is a dearth of studies examining any potential long-term effects of the anthrax vaccine. The important question is why the Pentagon will not admit this fact.[73]

D. Pending IND Application To Modify The Number Of Shots And Intended Use Of The Vaccine Calls Into Question The Necessity Of The AVIP

Withheld from the public's knowledge until VIG's FOIA lawsuit and, for the most part, until this hearing today, the Pentagon has ascertained that the current AVIP requiring a series of six shots is outdated, unnecessary and perhaps not as effective as a second generation anthrax plan that has been known for years.

On September 20, 1996, Michigan Biologic Products Institute ("MBPI"), the manufacturer of the vaccine, submitted, with the support and encouragement of the Department of the Army, an initial Investigational New Drug ("IND")[74] application for Anthrax Vaccine Adsorbed.[75] "The ultimate purpose of this IND is to obtain a specific indication for inhalation anthrax and a reduced vaccination schedule. The new schedule

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[73]In addition to the concerns regarding potential long-term ill-effects, this Subcommittee should explore the problems associated with contamination at the manufacturing processing plant. Evidence beyond the scope of my statement suggests that contaminated vaccine lots were re-dated and shipped to various military units. Eddington, *supra* note 32.

[74]An IND is "required for the clinical evaluation of an unlicensed product or for an unapproved use of a licensed product, such as a new indication, dose, or route of administration." Anthony, Bascom F. and Sutton, Ann, *The Role of the Food and Drug Administration in Vaccine Testing and Licensure*, NEW GENERATION VACCINES 1188 (2d ed. 1997).

[75]According to Dr. Walter Brandt, Science Applications International Corporation (SAIC), amending the license is the responsibility of MDPH [MBPI] since it currently holds the license and interacts with FDA. Although the Defense Department may actually develop the scientific data to support the amendment, "MDPH must agree with and present the plan to the FDA for their concurrence...the DoD must fully support the MDPH in this effort through a formal agreement." November 13, 1995 Meeting, *supra* note 17, at 3.

may be two initial doses with annual booster doses, as compared to the licensed six-dose series over 18 months."[76] Despite ample proof from its own studies that the six series shot was essentially redundant[77], the Pentagon nevertheless initiated the current AVIP in an attempt to inoculate all personnel, even those who realistically will never be at risk, and knowing full well that not enough vaccination lots presently exist to accomplish the purpose of the mission. Obviously, of course, by not waiting for the FDA's approval of the IND, the Pentagon's current program has cost taxpayers at least an additional $32 million dollars.[78]

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[76]Investigational New Drug Application, "Anthrax Vaccine Adsorbed (AVA)", submitted by Michigan Biologic Products Institute, September 20, 1996, at 001, attached at Exhibit "12" ("IND Application")(complete copy on file with the Subcommittee and the author). Additionally, the interval between immunization may be changed as well from two weeks to four weeks. Why the Army waited until 1996 to have MBPI pursue FDA approval for a reduced series program is unknown. The Pentagon has stated that it was experimenting with a second generation anthrax vaccine of this nature prior to 1990. See "Department of Defense Responses to Questions From Mr. Mark S. Zaid, Attorney At Law" at 3-4, attached at Exhibit "4" ("DoD Responses").

[77]Nearly four years ago, Colonel Arthur Friedlander, Chief, Bacteriology Division, U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID), commented at a meeting to discuss the planned vaccination dose schedule change that "there is no evidence to indicate that six does are necessary to protect humans against anthrax infection." November 13, 1995, Meeting, *supra* note 17, at 2 (emphasis added).

[78]In April 1998, the cost of a single dose of the vaccine was $4.44. Memorandum from General William W. Crouch, U.S. Army, Vice Chief of Staff, dated April 28, 1998 with Questions and Answers Appendix at E-26 ("Crouch Memo")(copy on file with the Subcommittee and the author). If implemented the IND would appear to require only three shots within an 18 month period. The $32 million dollar figure is derived from the cost per single shot (3x) multiplied by the 2.4 million servicemen. Of course, this figure does not take into account that additional transportation, storage and administration costs would also be saved.

What actions the Pentagon or FDA have taken on this IND is unknown.[79] No other documentation post-dating the IND was obtained through the VIG FOIA litigation. The IND does indicate that its "Comparative Study To Determine the Best Two-dose Schedule and Route of Administration of Human Anthrax Vaccine" was to have begun in Winter 1996 and completed in Winter 1998.[80]

Therefore, this Subcommittee should require the FDA and the Army to provide information concerning the status of the IND and any relevant studies undertaken in support thereof.

Curiously, in a 1990, article entitled "*Military Immunizations: Past, Present, and Future Prospects*", which was co-written by Drs. Ernest T. Takafuji and Philip K. Russell, both former Commanders of the U.S. Army Medical Research and Development Command at Fort Detrick, it was stated that:

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[79]Internal Army documentation obtained through the VIG FOIA lawsuit intimates that the FDA will take 5-6 years to make a final decision on modifying the vaccine. November 13, 1995, Meeting, *supra* note 17, at 4 (statement of COL Hurst, Office of the Deputy Assistant to the Secretary of Defense - Chemical/Biological Matters). Given the alleged seriousness, according to the Pentagon, of the impending threat posed by potential use of an anthrax weapon, one must question why perhaps a waiver was not sought as during the Gulf War as well as why the approval process would take so long under the circumstances. More importantly, the extreme length of time apparently necessary to merely change the vaccination schedule and projected use - nothing that effects the actual composition or production of the vaccine itself - raises serious questions concerning whether the original vaccine would be approved were it submitted today. In fact, licensure of the vaccine was approved by the FDA in 1970, based merely on one clinical efficacy trial published in 1962. See Zoon Letter, *supra* note 68, at 1. Unfortunately, evidence of efficacy was not required for licensure of biologics until after 1972. See Anthony, Bascom F. and Sutton, Ann, *The Role of the Food and Drug Administration in Vaccine Testing and Licensure*, NEW GENERATION VACCINES 1186 (2d ed. 1997).

[80]IND Application, *supra* note 12, at 021. The study, which was to have been undertaken in Ward 200, Medical Division, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland, was to involve at least two hundred military and/or civilian volunteers. Id. at 030A-032.

> Limited use vaccines and products are defined as those *unlicensed experimental vaccines*, toxoids, and immunoglobulins that have been developed against specific military threats associated with high morbidity. These products would be used in specific contingency situations. Some of the limited use vaccines could be considered to be *experimental deployment vaccines* since they are directed against serious region-specific endemic diseases. Limited use vaccines include ... *anthrax*.[81]

This characterization of anthrax as "unlicensed" and "experimental" is, of course, in contradiction to the current literature and present posture of the Pentagon and FDA. In response to my request for elaboration as to what this article was referring to, the Defense Department stated:

> According to COL Takafuji, a co-author of the referenced article and a previous Commander at the U.S. Army Medical Research and Development Command, the anthrax vaccine referred to in the article is not the FDA-licensed anthrax vaccine, but an experimental second generation anthrax vaccine under development at USAMRIID. The experimental anthrax vaccine is being developed utilizing emerging technologies that should require fewer doses and be more cost-effective to produce and administer.[82]

The Defense Department's response would seem to indicate that the anthrax vaccine referenced in the article refers to the second generation vaccine proposed in the IND, but is it? Setting aside the stringent FDA-requirements now required to obtain a vaccine license or even to affect a change to an existing license, one must question what is truly afoot here. The purpose of the IND is not to change the composition of the vaccine. It is not an attempt to make the vaccine itself stronger. Apparently studies have demonstrated that the six dose regiment now in place is unnecessarily excessive. Therefore, a mere modification of the dose schedule will apparently enable an individual to develop greater

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[81]4 Infectious Disease Clinics of North America 156 (1990)(emphasis added).

[82]See DoD Responses, *supra* note 4, at 4.

immune protection to the anthrax spores. Was the dose modification truly what was being referenced in the article that led two distinguished military medical commanders to term the anthrax vaccine as "unlicensed" and "experimental"? Or has the composition of the vaccine now in use been modified in some way?

The Subcommittee should require the Army to provide a more detailed explanation.

E. Adverse Side Effects Have Been Significantly Higher Than Reported

According to the Manufacturer's Label:

> Mild local reactions occur in approximately thirty percent of recipients and consist of a small ring of erythema, 1-2 cm in diameter, plus slight local tenderness(1). This reaction usually occurs within 24 hours and begins to subside by 48 hours....
>
> Moderate local reactions which occur in 4 per cent of recipients of a second injection are defined by an inflammatory reaction greater than 5 cm diameter....
>
> More severe local reactions are less frequent and consists of extensive edema of the forearm in addition to the local inflammatory reaction....
>
> Systemic Reactions: Systemic reactions which occur in fewer than 0.2 per cent of recipients have been characterized by malaise and lassitude. Chills and fever have been reported in only a few cases. In such instances, immunization should be discontinued.[83]

The truth, however, has been that systemic reactions have been two to nearly seven times greater than reported by the manufacturer. Although the evidence for these alarming figures arises directly from the Pentagon's own studies, it appears not to have created the type of concern one would normally expect. Indeed, it has been completely ignored and/or intentionally downplayed by military officials. Consider these figures derived from government data obtained through the VIG FOIA lawsuit:

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[83]Manufacturer's Label, *supra* note 67, at 2-3. I have received reports from servicemen and their families of experiences involving adverse effects, such as fever, following inoculation with the vaccine, but that military medical personnel refused to discontinue the vaccinations or even report the incident.

Systemic Reaction Rates	Source of Information
First Shot (1.33%)	USAMRIID, Fall 1990-Spring 1991[84]
First Shot (0.9%)	USAMRIID, 1977-1994[85]
Second Shot (0.6%)	USAMRIID, Fall 1990-Spring 1991[86]
Second Shot (0.4%)	USAMRIID, 1977-1994[87]
Third Shot (0.2%)	USAMRIID, 1977-1994[88]
Boosts (0.5%)	USAMRIID, 1977-1994[89]
MDPH Vaccine (0.7-1.3%)	USAMRIID, 1998[90]

Despite ample evidence that the systemic reaction rate far exceeds the manufacturer's stated limit, the Pentagon nevertheless maintains that only one possible case of a severe systemic reaction has occurred thus far.[91] This is obviously demonstrably false. Indeed, reports of systemic reactions, such as fever and prolonged muscular weakness, have been occurring since the AVIP began. However, military medical officers have been reluctant or have even refused to file adverse reaction reports. In fact, they have attempted to convince servicemen that the effects they were encountering had little or nothing to do with the anthrax vaccine.[92]

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[84]Anthrax Vaccine Reaction Rates, USAMRIID, Fall 1990-Spring 1991, attached at Exhibit "13" ("Anthrax Rates I").

[85]Anthrax Vaccination Reactions, Primary Series, Special Immunizations Clinic, USAMRIID, Ft. Detrick, MD, 1977-94, June 1994 (Unpublished Data), attached at Exhibit "14" ("Anthrax Rates II").

[86]Anthrax Rates I, *supra* note 84.

[87]Anthrax Rates II, *supra* note 85.

[88]Id.

[89]Id.

[90]USAMRIID Briefing Slide, 1998, attached at Exhibit "15".

[91]Executive Summary dated 11 June 1998, "Possible Anthrax Vaccine Related Reaction", attached at Exhibit "16".

[92]These are all reports I have received from servicemembers and their families.

It is vitally important to understand the significance of the systemic reaction rates. These reactions are potentially extremely harmful and possibly fatal. While a percentage rate of 0.7% to 1.33% may not seem high, when applied to the fact that 2.4 million servicemen will be receiving the vaccine under the AVIP, this means that from 16,800 to 31,920 servicemen may suffer serious or fatal reactions to the vaccine; a far cry from the 4,800 individuals who might suffer according to the manufacturer's label. Yet the Pentagon has offered no comments about this alarming and significant discrepancy.

The Department of Defense in its effort to downplay the significance of the number of systemic reactions experienced during their studies simply geared up their public affairs machine. Suddenly, systemic reactions of 0.2% or more were now labeled as "very rare" and fever and chills became re-categorized as a "severe local reaction".[93] As I do

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[93]In its brochure "What Every Soldier, Sailor, Airman and Marine Should Know About The Anthrax Vaccine", attached as Exhibit "17" ("Anthrax Informational Brochure"), which is made available to servicemen in each branch, the Defense Department attempts to minimize the concerns of the anthrax vaccine by comparing adverse reaction rates with the typhoid and influenza vaccines. The document notes that less than 1% of those who receive the anthrax vaccine should experience fever. Thus it would clearly appear fever is to be considered a systemic reaction. Indeed, in an apparently unpublished report, obtained through VIG's FOIA lawsuit, in which Dr. Phillip R. Pittman, Chief, Special Immunizations Branch, USAMRIID, served as the Principal Investigator, even *low-grade* fever was characterized as a "[m]oderate systemic reaction". "Anthrax and Botulinum Vaccines: Antibody Prevalence and Immune Response to Boost(s) in Military Personnel Initially Vaccinated During Operations Desert Shield/Desert Storm", March 21, 1995, at 9 (copy on file with the Subcommittee and the author). Furthermore, in response to concerns raised by the Vice Chairman, Joint Chiefs of Staff, over the safety of the anthrax vaccine, the Assistant Secretary of Defense (Health Affairs), Dr. Stephen C. Joseph, submitted a memorandum dated July 25, 1995, that described systemic reactions as being "characterized by chills, fever, and general malaise." Memorandum for Vice Chairman, Joint Chiefs of Staff, "Anthrax Vaccine", July 25, 1995, at 1, attached at Exhibit "18". Finally, in a Program Review prepared for the Deputy Secretary of Defense in August 1998, it was noted that four systemic reactions to the vaccine had occurred, and that systemic was defined to encompass malaise, chills and fever and anaphylaxis. See AVIP, Program Review for the Deputy Secretary of Defense, August 1998, attached at Exhibit "19".

not possess sufficient medical expertise on whether fever or chills are more properly labeled as a "severe local reaction" or "systemic", I can not provide further comment on this aspect. However, it is quite obvious that the manufacturer of the vaccine considers these types of reactions as systemic and this calls into question the actions and motivations of the Defense Department to assert otherwise.[94]

F. Public Remarks Of Pentagon Officials Have Fueled The Debate

The fault for the growing hysteria that is spreading throughout the military branches must also lie with several Defense Department and military officials whose public comments have not only been inaccurate or insensitive, but also raise additional concerns. Examples include:

"*The side effect percentage is something like .00002 percent, which makes it many times safer, for example, than the diphtheria shots we give our children.*" Rear Admiral Michael Cowan, medical readiness director on the Joint Staff.[95]

"*No third eye has emerged.*" Secretary of Defense William S. Cohen.[96]

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[94]At the initial trials that led to FDA approval of the anthrax vaccine, "four cases resulted in systemic reactions, defined as chills and fever (2 cases), fever only (one case), and illness with general aching for 24 hours (1 case)." Memorandum for Deputy Secretary of Defense from Stephen C. Joseph, M.D., M.P.H., Assistant Secretary of Defense (Health Affairs), undated, at 8 (copy on file with the Subcommittee and the author). In light of the clear evidence that fever constitutes a systemic reaction, the obvious effort by the Defense Department to convince its personnel and the public otherwise is deplorable.

[95]GulfNEWS, November 1998, at 3 (copy on file with the Subcommittee and the author). Perhaps the diphtheria vaccine is not an appropriate model for the Pentagon to rely upon. Since 1989, $830 million dollars has been paid out to 1100 diphtheria claims under a special no-fault federal vaccine court. Washington Post Magazine, Aug. 30, 1998, at 14.

[96]Washington Post, Oct. 30, 1998.

"People are petrified that their penis is going to fall off, yet it is the safest vaccine ever given to American citizens. The polio vaccine was far more dangerous, yet the public lined up for it." General Charles Krulak, MC.[97]

"It just increases your sex drive." Unidentified military doctor to reserve officer.[98]

"It's safe and reliable...It works and has no side effects." Pentagon Spokesman Ken Bacon.[99]

Despite realizing at the outset the many problems and criticisms that would arise from a total force inoculation program, the Pentagon nevertheless still has a great deal of work to do and lessons to learn.

G. Implementation Of The AVIP Raise Significant Policy Questions

The decision to openly publicize the total force inoculation of American troops with the anthrax vaccine should raise questions in many people's minds. What exactly does this program serve to accomplish? Certainly one can genuinely argue that the policy may serve to ensure that our troops are not impeded by any nation or force that chooses to utilize the dangerous anthrax spores, although the Pentagon admits that no nation has ever used anthrax as a weapon.

Then again, one can argue that the public revelation of our force's protection merely serves to encourage the production of a different strain of anthrax that would not be thwarted by our vaccine, or the use of an entirely different biological or chemical weapon (certainly enough choices exist) for which no adequate vaccine is available. Or, perhaps the Pentagon's decision is intended to merely deflect the weakness of our detection capability and inherent lack of research and development in that area.

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[97]San Diego Union Tribune, date unknown. On what basis General Krulak asserts the anthrax vaccine is the safest vaccine ever is unknown. The VIG FOIA lawsuit certainly failed to reveal any such supporting documentation.

[98]This quote was conveyed to me by a former reserve officer who refused the anthrax vaccine.

[99]Pentagon Press Conference, date unknown.

As a layperson to military affairs, but one who does routinely become emerged in issues of national security as a result of my law practice, I am particularly perplexed by the absence of an existing explanation justifying why it was so vital during Desert Storm/Desert Shield to maintain an extremely high-level of secrecy surrounding the inoculation of our troops with certain vaccines. Indeed, the program was so secret that many servicemembers still do not know what they were injected with, particularly due to poor record keeping.[100] But yet, now, the Pentagon believes it appropriate to establish an entire public relations protocol to ensure the world knows our troops have been vaccinated against anthrax.

The purpose, as I understand it to have been, of the secrecy during the Gulf War regarding certain experimental inoculations - several of which were permitted only through the acquisition of a highly questionable FDA waiver - was to provide our forces a tactical advantage should Iraq choose to utilize a particular biological weapon. In fact, one could reasonable presume that if Iraq were to have used any of its known biological weapons, the Defense Department was hoping it would be one of those for which troop vaccinations had been given, rather than one that was not. Following this rationale to its logical conclusion, have we not set ourselves up for potential defeat before even entering battle?

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[100]According to recently declassified documents obtained through VIG FOIA lawsuit, the Defense Department believed in 1991, that the release of any information under FOIA concerning the use of vaccine for botulinum on servicemembers stationed in the Persian Gulf during Desert Shield and Desert Storm "would be very valuable to present and potential adversaries. The disclosure of detailed information such as the number of individuals vaccinated, quantities of vaccine produced, etc., would interfere with our ability to respond rapidly in the future to the now identified chronic shortages in the industrial base." See Joint Staff Action Processing Form, Freedom of Information Request #3106 (91-FOI-1267), August 1, 1991, at 2 (copy on file with the Subcommittee and the author). The document concluded that "[d]isclosure of the information requested, in the detail requested, would not be in the DOD's best interest and could be expected to *cause serious damage in the future.*" Id.

In responding to the objections and questions that have been raised by servicemembers, their families and concerned Americans regarding the anthrax vaccine, the Pentagon has attempted to label such individuals as part of a "paranoid Internet craze". This unfounded categorization by Defense Department officials to deflect their perceived and apparent lack of adequate response has resulted in the one humorous aspect of this entire issue. While the Pentagon derides those who received their so-termed "misinformation" about the vaccine from the Internet, at the same time it directs those who wish to be responsible researchers to examine the real truth which, of course, is posted on the Defense Department's Internet site.[101]

Indeed, at this Internet site one will find an elaborate effort to provide answers to the many, many questions raised concerning the safety and effectiveness of the anthrax vaccine. One section in particular deserves mention - Fact vs. Myth. This section represents the Defense Department's attempt to dissuade potential refusers. Based on my research, however, I have developed my own Fact vs. Myth section on the vaccine, one that undoubtedly will not find its way to the Pentagon's website.

MYTH: "Although the manufacturer, Michigan Biologic Products Institute, has had some production problems, mostly due to an aging facility, the FDA has inspected and approved every lot of anthrax vaccine produced there since it was licensed in 1970, according to Deputy Secretary of Defense John J. Hamre and military medical officials."[102]
FACT: The FDA does not routinely physically inspect samples.[103]

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[101]The website can be viewed at http://www.defenselink.mil/specials/Anthrax.

[102]Air Force Policy Letter, Anthrax Update, August 1998 Edition at 1, attached at Exhibit "21".

[103]Eddington, *supra* note 32.

MYTH: "A safe and effective vaccine is available that will protect our forces."[104]
FACT: New spores have already been developed that will not be effected by the present vaccine.[105]

MYTH: "There have been no long term side effects from this vaccine."[106]
FACT: Totally unsupportable conclusion. The Defense Department has never attempted to research whether or not use of the vaccine has led to long-term side effects or other health consequences. In fact, no studies appear to exist, even from the private sector, that examine the potential long-term consequences of the vaccine.

MYTH: "This vaccine has been routinely used in the US since 1970, when it was licensed by the Food and Drug Administration."[107]
FACT: With the exception of the military, no industry *routinely* uses the vaccine. Some use can be found among veterinarians or livestock workers, but no evidence exists demonstrating widespread usage. Only about 30,000 individuals have received the vaccine since 1970, compared with the Pentagon's plan to inoculate over 2.4 million servicemembers.[108] In fact, documentation obtained from the Army through the VIG

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[104]News Release, Office of Assistant Secretary of Defense (Public Affairs), December 15, 1997, "Defense Department to Start Immunizing Troops Against Anthrax, at 3, available at http://www.defenselink.mil.

[105]Deb Riechmann, *Russian Version Of Anthrax Can Thwart U.S. Vaccine/Unknown If Iraq Has Deadly Strain*, Navy Times, Mar. 2, 1998; Bradley Graham, *Dose of Explanation comes with Anthrax Shots*, Washington Post, Oct. 30, 1998. Additionally, military experiments upon guinea pigs demonstrated that the present anthrax vaccine provided little or no protection against certain strains of anthrax. See MDPH-PA Vaccine Efficacy Data, USAMRIID, 1992 (copy on file with the Subcommittee and the author).

[106]Crouch Memo, *supra* note 78, at E-24. Documents distributed throughout the services also assert that "no long term consequences have been demonstrated. Anthrax Informational Brochure, *supra* note 93, at 2. While accurate on its face, the statement is misleading. Not one study has been conducted to determine the long-term effects of the anthrax vaccine.

[107]Id. at 1. See also News Release, Office of Assistant Secretary of Defense (Public Affairs), December 15, 1997, "Defense Department to Start Immunizing Troops Against Anthrax, at 2, available at http://www.defenselink.mil ("It has been widely used in the United States since the early 1970s....").

[108]Crawley, *supra* note 61. This low number is likely due to the fact that "human anthrax is rare in the United States, with only four cases between 1979 to 1988." Operational Requirements Document for Improved Anthrax Vaccine, U.S. Army Med. Materiel Develop. Activity, Mar. 1995, at 1 (copy on file with the Subcommittee and the author).

FOIA litigation reveals that "private sector use of the vaccine is between 400-500 doses per year."[109] Given that the approved FDA dosage schedule is 6 shots, this amounts to less than 100 people per year using the vaccine; a far cry from the perception intentionally created by the Defense Department.

MYTH: The anthrax vaccine is effective against inhalation anthrax.
FACT: The Defense Department bases its assertion purely on limited and predominantly unpublished and non-peer reviewed studies. The anthrax vaccine presently being produced was never specifically designed to protect against inhalation anthrax, although that is not to say it is ineffective.[110] The still-pending IND which was submitted in 1996 seeks to change the label of the vaccine to include inhalation protection as an intended use. Obviously it would be unethical to conduct experiments on humans in order to demonstrate effectiveness of the vaccine. However, one would hope the military would at the very least seek independent and more detailed reviews of its experiments on non-human primates, or other appropriate animals, before relying on such a conclusory assertion.

One thing is clear. Sometimes the lines between myth and fact are blurred. Substantive information regarding the anthrax vaccine represents just such a line.

CONCLUSION

Mr. Chairman, it is a sad fact that we regulate industries, such as machinery and automobiles, far better than we do those industries that affect what may be placed within our own bodies. The anthrax vaccine currently in use for the military probably would not withstand FDA scrutiny were it submitted for approval today. Yet no one seems concerned that various unknowns exist that go to the heart of whether this vaccine is actually a safe product over the long term. And no one seems alarmed that the adverse reaction rates far exceed the figures supplied by the vaccine manufacturer itself, or that

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[109]Crouch Memo, *supra* note 78, at E-23.

[110]Nevertheless, according to a staff report prepared for the Senate Committee on Veterans' Affairs, the "vaccine should ... be considered investigational when used as protection against biological warfare." Is *Military Research Hazardous To Veterans' Health? Lessons Spanning Half A Century*, Staff Report, Committee on Veterans' Affairs, U.S. Senate, 103d Cong., 2d Sess. 15 (1994).

the Defense Department has sought to masquerade these ill effects through questionable wording changes.

To be sure anthrax is an intensely dangerous biological weapon. It is imperative that we seek out ways to adequately detect the spores before contact and protect ourselves after. But the Defense Department's anthrax program represents nothing more than an easy out from the hard task of devoting time and money to develop adequate detection equipment and, if possible, efficient vaccines that are truly safe and effective.

The Defense Department has knowingly misled the American people concerning this vaccine. Whether twenty years from now advanced medical technology will demonstrate that the anthrax vaccine was, in fact, dangerous or perhaps safe is anyone's guess. But until we know the full facts surrounding the safety, effectiveness and necessity of the anthrax vaccine, 2.4 million people are potentially being placed in harm's way for possibly no legitimate reason. Until then the United States should follow the lead of the United Kingdom, and restore some semblance of our cherished constitutional rights to our brave and honorable servicemembers and implement the vaccination program as voluntary.

If continued unchecked and unchallenged, the Defense Department's actions to involuntarily vaccinate its total force may serve as a prelude to forced civilian vaccinations, and the stripping of many of our protected civil liberties. This specific debate is best left to another day and another hearing, but the potential repercussions of what is now transpiring merits our immediate attention.

Thank you for the opportunity to present my views on this matter.

(32)

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STATEMENT ON ANTHRAX VACCINE IMMUNIZATION PROGRAM (AVIP)
Redmond H. Handy, Colonel, USAFR

PREPARED FOR THE HOUSE OF REPRESENTATIVES
Committee on Government Reform
Subcommittee on National Security, Veterans Affairs, and Intn'l Relations
March 24, 1999

INTRODUCTION

Mr Chairman, I sincerely thank the committee for inviting us to discuss the Pentagon's mandatory anthrax vaccine policy. It is truly a privilege for us to participate in this matter of critical importance to our national security.

I believe this policy is harmful to our national defense capabilities. I believe that common sense and logic must prevail in addressing biological warfare threats. I do not believe this policy meets those criteria. I have spent a significant amount of time during the past year giving thought to the impacts of this policy on our hard-working and dedicated volunteer force. The more I researched the more uncomfortable I became. The objectionable issues with this policy are many, and I would like to simply outline them for the committee in the form of preliminary findings.

EFFECTS OF MISGAUGING THE BIOWARFARE THREAT

Produces Fear Out Of Proportion To Actual Threat
- Daniel Greenberg wrote recently "While a gullible press echoes its frightening warnings, there are no independent assessments of the potential for terrorist attacks."
- Literature reviews indicate the potential for biological attack remains small and incalculable
- DOD descriptions of biowarfare as "not a matter of if, but when", suggests 100% probability
- Vaccine package indicates routine immunization is not recommended; low risk in population

Other National and International Effects
- Vaccine policy erodes 1972 Biological Weapons Convention; encourages biological arms race
- Sends message that US expects anthrax to be used
- Deemphasizes massive retaliation response threat which worked in Desert Storm
- Vaccine failure threatens unit effectiveness and survival and risks public outrage

VACCINE EFFECTIVENESS

Vaccines are Useless Against Bioterrorist Threats
- Bill Patrick, probably the nation's foremost expert on germ warfare who directed offensive biological programs at Ft Detrick in the 1960s, has **no confidence in vaccines as a defense**
  - -- He says it takes only 18 months to develop a germ, but 10 years to develop a vaccine
  - -- Smart adversaries choose a different germ or modify an old one to defeat the vaccine
- **Vaccines could never keep up** with the possible anthrax permutations, variations of other biological agents, combinations of agents, stronger doses, and genetically-engineered germs.

Anthrax Vaccine Already Proven Ineffective By The Army's Own Tests

- Ft Detrick guinea pig experiments in 1986 and 1998 showed dismal efficacy results.
  - -- In the 1998 study, the anthrax vaccine failed to provide survival rates of 50% (the military definition of unit effectiveness) in 27 of 33 different anthrax isolates. **(an 82% failure rate!)**
  - -- Even worse, 12 of those isolates killed 75-96% of the vaccinated pigs.
  - -- Similar **mice studies indicate a 90-100% failure rate** for this vaccine.

DOD Discarding Relevant Reports and Data To Claim AVIP Effectiveness

- DOD basing use of the vaccine on rhesus monkey and rabbit trials showing 90%+ survival
  - -- DOD states pig and mice studies are less relevant
- Are these studies thrown out for a myriad of other medical assessments for similar reasons?
- Journal of the American Medical Association says **data is lacking** for inhalation efficacy claim
- Senate Staff Report 103-07 says ***efficacy against inhaled anthrax is "unknown".***

HEALTH AND SAFETY

Although I understand a separate hearing is scheduled by the committee to address this area with medical professionals, I would like to relate discoveries to the level of my understanding gained from research and discussions with several civilian and medical professionals familiar and directly involved with this issue.

Anthrax Vaccine Parallels Government Swine Flu Vaccine Mistakes

- Several analyses of swine flu vaccine shows **disturbing similarities** to anthrax vaccine
  - -- 1 Ft Dix swine flu death caused scare because of 1918-19 pandemic (450K died)
  - -- Inoculation decision made regardless antibiotics (also suggested for anthrax, but not available in '18-'19 to fight the actual bacterial pneumonia cause of many deaths)
  - -- Center for Disease Control unable to estimate probability of epidemic occurrence
  - -- Severity could also not be predicted
  - -- No serious side effects anticipated for the swine flu vaccine, even though untested
  - -- 3-24-76 meeting to decide program implementation characterized as a "staged event"
  - -- Field trials yielded depressing efficacy results, many adverse reactions
  - -- Swine flu program vaccinated 2X as many as ever before for a single season virus **(2.5 million military receiving anthrax vaccine is 17X as many as in the Gulf War)**
  - -- Military reactions to the shot were reported at substantially and suspiciously lower rates
  - -- **Deaths/severe reactions halted program; 4,000 nerve damage claims over 12 years**

Relevant Gulf War Illness Information

- Senate Staff Report 103-97 indicates **43% of Gulf War troops had vaccination side effects**
- Same report indicates **anthrax vaccine is possible contributor to Gulf War Syndrome**

FDA Vaccine Approval Process, Inspection Reports And Warning Letters to Manufacturer

- Approved in 1970 based on study of only 26 textile workers in the 1950s
- Approved 2 years before FDA began requiring efficacy demo—**wouldn't be approved today**
- FDA Warning Letters sent to the manufacturer in 1995 & 1997 **(threatened to revoke license)**
- Feb 20, 1998, scathing FDA report lists 53 categories of discrepancies, 31 subcategories

FDA Vaccine Approval Process, Inspection Reports & Warning Letters to Manufacturer (Con't)

- The plant is now shut down for renovation, but DOD is still using the current vaccine supply
- Retests of all lots only overseen by DOD contractors—manufacturer actually did the retesting
- **Initially, 22 of 30 lots failed retest; those cleared are still causing serious reactions**

Problems with Systemic Reactions to the Vaccine (Requiring Shots be Discontinued)

- **DOD figures**--.0002% systemic reaction (**5 out of 2.5M** service members should stop the shot)
- Vaccine package insert claims a .2% reaction rate (5000 out of 2.5M members should stop)
- Two Ft Detrick studies show up to a 1.3% reaction rate (**32,500 members could be affected**)
- Documented cases exist of shots continuing after systemic reactions--violates insert instructions
- **Documented reactions to the anthrax vaccine** from the FDA's Vaccine Adverse Event Reporting System include the following: Tremors -- trembling or shaking; Somnolence -- state of being drowsy); Syncope -- loss of consciousness resulting from insufficient blood flow to the brain; Bradycardia -- slow heart rate; Dyspnea - difficult or labored breathing; Pharyngitis – inflammation of the throat; Rhinitis -- inflammation of the mucous membrane of the nose (allergy-type); Cellulitis -- inflammation of connective tissue; Purpura/Thrombopenia – hemorrhage of blood into the skin/decrease in the number of blood platelets; Stomatitis – inflammation diseases of the mouth; Angioedema -- an allergic skin disease; Photophobia – painful sensitiveness to strong light; Meningitis -- life threatening illness caused by bacterium Urticaria – hives; Paresthesia -- a sensation of pricking, tingling, creeping on the skin associated with injury of a sensory nerve; Pruritis -- localized or generalized itching due to irritation of sensor nerve endings from organic or psychogenic causes; Edema -- an abnormal excess accumulation of serous fluids in connective tissue or in a serous (thin, watery constitution) cavity; Vasodilation -- widing of the lumen (blood vessels); Alopecia -- loss of hair (baldness); Arthralgia -- Pain in one or more joints; Asthenia -- loss or lack of strength Lymphadenoma -- (1) lymphoma (2) Hodgkin's Disease; Myalgia -- pain in one or more muscles; Hypokinesia -- decreased muscular movement
- **Other reactions that don't need translation**: Agitation, Amnesia, Diarrhea, Dizziness, GI Distress, Headache, Insomnia, Chest pain, Sweating, Weight loss, Injection Site Reaction, nausea, rash, vomiting, pain at injection site, chills, fever, mass at injection site, headache, cough, allergic reaction, visual field defect, abdominal pains, abnormal stool, previous reaction, ulcer in mouth. **Nearly 50 different types of reactions have occurred.**

ALLIES EXPERIENCE WITH THE VACCINE

- French: Didn't vaccinate in the Gulf War; their military members don't have GWS
- British: Admit mistakes in Gulf; offered a voluntary vaccine; program stopped
- Israelis: Don't have a mandatory vaccine policy either; relying on antibiotics
- Canadians: Had mandatory vaccine policy; recently stopped because of supplies/controversy

SUPPORT FOR THE PROGRAM

- U. S. TalkSpot Radio Program Survey shows 83% AGAINST this forced vaccination program
- Army Times Publishing Company poll showed 77% AGAINST
- British voluntary anthrax vaccine program - 73% DECLINED

REACTIONS AND IMPACTS ON THE GUARD AND RESERVE

Background
- Reservists couldn't turn to military facilities, the VA or their civilian health care providers for accurate diagnosis or treatment of vaccine side-effects from shots administered in the Gulf War
- Thousands of Gulf War shot records were lost or did even not reflect shots were administered
- The Reserve Officer's Association challenged DOD on Gulf War Syndrome (GWS) in 1997
  -- Their resolution urged Congress to provide appropriations to pay for GWS problems
- **This vaccine is creating fresh wounds and deep resentment less than a decade after GWS**

Medical Issues
- Reservists personally know people who contracted Gulf War Syndrome
- Even severe health problems occurring on active duty are sometimes treated with skepticism
- **Both civilian and military doctors seem to lack accurate/important information, especially on how the vaccine might generate the 50 different side-effects and how to treat them.**

Personal, Family and Women's Issues
- Reservists are concerned about what they might pass on to nursing babies or future children
- Reserve women might be concerned they can't start a family during 18 month initial shot series
- Are pregnant reservists going to be kept out of theater or deployed "exposed" without shots **(Active duty pregnant women are not reassigned back to states - unprotected in theater?)**
- Reservists are concerned that everyone is given the vaccine regardless of individual medical conditions (such as allergies which might trigger an immune system response) or interactions with other medications they are taking (package insert does not address)
- **Health risks jeopardize civilian income; reservists can't afford vaccine side-effects!**

Professional Objections/Issues
- Strategic Lift aircrews especially take a myriad of shots already, what's next?
- Senior aircrew inclined to retire; loss of leadership (5000 flying hours, instructor pilots)
- *Younger pilots have less to lose with the military, a lot to lose when just signing on with airline*
- Policy is creating tension in units
- Increases turnovers (one unit had 50% turnover in past 3 years, hadn't had in previous 10 years)

CIVILIAN ISSUES

Administration Won't Use Current Vaccine on Civilian Population Which Is Also At Risk
- Oklahoma City, Atlanta Olympics and New York City Trade Center bombings—civilian targets
- 50+ anthrax threats across country in last several months; *None* against the military
  -- Who are the hoaxers? Who's behind them?
- Administration official has said **"Vaccinating civilians is another thing entirely and we don't think we want to do that with the vaccines currently available."**
- All military will absorb a risky product, while most of America *may* get better protection
- What sense does it make to allow civilians and contractors to remain "exposed" while working side by side with "protected" military members

LIMITATION ON FREEDOM OF RELIGION

- DOD provides a religious reason for not taking the vaccine, implying ethical and moral issues
- Policy requires religious objection based on recognized church doctrine against ALL vaccines
- No religion, unless it is a self-destructive cult, would approve injecting questionable substances
- This limitation is a step too far in limiting freedom of religion and could evoke a public outcry
- Doesn't allow for private religious beliefs; must be recognized church-going individual
- **National survival is not dependent on religious objections to questionable vaccines**

FINANCIAL INTERESTS IN VACCINES WARRANT FURTHER INVESTIGATION

- Vaccine market potential increased with recent tax, patent and litigation changes
- Allegations of corruption over the vaccine plant sale; Michigan lawmakers outraged
- Administration meeting on vaccine stockpiling plan included those who would gain financially

IMPLICATIONS FOR THE FUTURE

- $322M budgeted for new biological vaccines compared to $115M for 121 GWS Studies
- DOD has requested FDA waivers in handling civilian disasters; wants greater involvement
    - -- Plans to use some of the same experimental drugs and vaccines used in Gulf War
    - -- Seeking broad authority waive requirements such as keeping track of who gets what drugs, proper labeling, monitoring side effects, and informing patients of complications before they give consent

CONCLUSION

As you can see, I believe there are many disturbing issues here. Lawful orders must not include controversial policies created from waivers to medical standards established at such great cost by the Greatest Generation. I urge continued focus on this vaccine until a voluntary policy is established which is respectful of the legitimate concerns of the men and women who pledge their lives to this nation's freedom. I thank the committee for this opportunity to testify.

(33)

CMAT Control #
1999085-0000014

WRITTEN TESTIMONY
AVIP HEARING
3/24/99
LORENE GREENLEAF

Testimony of Lorene Greenleaf
AVIP Hearing 3/24/99

I begin this written testimony by thanking the Committee for giving me the opportunity to express my concerns regarding the Anthrax Vaccination Policy. I write this statement on behalf of thousands of concerned military troops and family members.

As the mother of an Honorably discharged Navy veteran who was coerced into taking anthrax inoculations in the spring of 1998, we have serious concerns related to the safety, efficacy, and necessity of the anthrax vaccine. My son was inoculated with vaccines that were in violation on the FDA inspection report of 2/98 as being "expired" and only tested for potency rather than safety and sterility. (See attachments 1, 2)

Out of fear for my son's health, I began searching for information on the anthrax vaccine, submitting Freedom of Information Act requests to the FDA, Dept. of the Army, and the Michigan production facility. (See attachment 3) After reviewing information obtained, I made several phone calls to the DOD, FDA, and MBPI regarding statements made by FDA inspectors in some reports, (See attachment 4) and found these conversations very troubling. (See attachment 5)

I then became very active speaking with the media, therefore my name has become familiar among military troops as someone to contact for factual information regarding the vaccine. In the past year, I have responded to thousands of requests for information from military troops and family members. (See attachment 6)

These brave young men and women have been accused of gathering false information from the Internet, when in fact, most are obtaining information I have accumulated through FOE requests. This information is forwarded via email upon their request. When this information hits a military base or ship, it spreads like wildfire.

These concerns are justified however, these troops are being punished (in many cases more than once for the same offense), (See attachment 7) financially strapped due to reduction in rank, (See attachment 8) discharged under less than honorable conditions, harassed, and threatened. Some have gone as far as going AWOL to avoid forced inoculation. Most have impeccable service records, and are not looking for a way out of the military, they are only looking out for their health. The military is losing some of America's finest. (See attachment 9)

Unfortunately, I have also had several reports of soldiers who have become ill shortly after receiving anthrax inoculations. (See attachments 10,11) In most cases these symptoms are tightness in chest, severe headaches, bloody diarrhea, rashes and vomiting. Some more severe than others, and these symptoms reportedly worsen with each dose. In reviewing the Vaccine Adverse Event Reporting System report obtained from the FDA, I find these reactions have not been reported. (See attachment 12) Many of these sick soldiers have requested that an adverse event report be filed, only to be turned down by

the military medical facility. (See attachment 13) I have responded to several requests to mail VAERS forms to soldiers suffering what they believe to be adverse reactions to the vaccine. The military medical facilities are not following this critical procedure, and most are unaware that this can be done themselves.

Studies show that anthrax vaccine alone is not sufficient if exposure occurs, anti-biotic treatment must begin immediately. Is our military prepared for a situation like this, and would our soldiers be able to seek medical treatment immediately if exposure occurred in the middle of a battlefield?

Many are receiving 1 or 2 inoculations before the expiration of their active duty enlistment term. These soldiers do not have the opportunity to complete the inoculation series while on in-active status. Is it necessary to partially inoculate these troops? And, would they need to begin the series again if called back to active duty in a wartime situation?

Finally, in my communications with thousands of service members, I expect the refusal and resigning numbers to continue growing. Is our military prepared for this kind of loss?

Thank you very much for your time.

ATTACHMENT 1

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4 - 20/98	C. F. NUMBER 1873896
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Services & Vaccine Mfg	
FIRM NAME MICHIGAN BIOLOGIC PRODUCTS INSTIT	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. MARTIN LUTHER KING JR BLVD.	STREET ADDRESS OF PREMISES INSPECTED Same	
CITY AND STATE (Zip Code) LANSING, MI 48909	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

ANTHRAX Vaccine

1. The manufacturing process for Anthrax Vaccine is not validated. For example,

a. The formulation tank has not been qualified for long term storage of formulated bulk Anthrax. Storage times have varied from one week to four months between formulation and filling. Lot FAV033 was formulated on 8/27/96, however it was not filled until 12/23/96.

b. The formulation tank has not been qualified for mixing time, demonstrating homogeneity of the suspension. Mixing time is not specified in the batch record prior to filling and during the filling operations. The product is [redacted] and settles quickly in the tank.

c. The firm did not perform media fill challenges to validate aseptic manufacturing after harvest from the holding tank. These operations include the transfer of the sublots from building [redacted] to building [redacted] for formulation.

Media fills are performed on fermentation and harvest trains, however not on a scheduled basis.

d. There is no validation of [redacted] as a sporicide in anthrax production and potency testing facilities.

e. The analytical methods for determination of [redacted] and [redacted] in Anthrax Vaccine are not validated with respect to accuracy, precision, linearity, specificity and limit of detection.

f. There is no validation of the length of time sublots are held until they are used in a lot. Sublots have been held longer than 3 years prior to use. There is no stability data to support this hold time.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type) Linda A. Yuan, Investigator Jeffrey A. Stamm, Investigator Donald E. Jeska, Investigator Christine U. Mack, Investigator	DATE ISSUED 2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4-20/98
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivatives & Vaccines
FIRM NAME Michigan Biologic Products Institute	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. Martin Luther King Jr. Blvd.	STREET ADDRESS OF PREMISES INSPECTED Same
CITY AND STATE (Zip Code) Lansing MI 48909	CITY AND STATE (Zip Code) Same

DURING AN INSPECTION OF YOUR FIRM I (WE) OBSERVED:

-- For example, sublot AV370 was produced and placed in coldroom ~~~ of building ~~~ (further referred to as ~~~ in 2/94 until 7/97 at which time it was used to produce lot FAV040.

-- Sublot AV450 was produced and placed in ~~~ in 5/95 until 8/97 at which time it was used to produce lot FAV039.

-- Sublot AV456 was produced and placed in ~~~ in 5/95 until 8/97 at which time it was transported to the formulation room of building ~~~ with ~~~ other sublots to make FAV039. Here it was discovered that AV456 was contaminated with mold, and it was destroyed.

g. The reference standard used for potency testing is lot FAV009, produced March 1991.

h. There are no expiration dates for the working spore concentrations (virulent or avirulent strains). For example, the production strain, ~~~ was used to produce sublot AV216 as early as 3/92 and sublot AV450 as late as 4/95.

i. ~~~ testing for Anthrax sublots used sublot AV462, with a ~~~ content of 23ppm. The specification for ~~~ in Anthrax vaccine is 15-30ppm. There is no BF testing at 15ppm or 30ppm.

k. Prior to August 1997, the ~~~ filters used for harvest of Anthrax vaccine were neither validated nor integrity tested. This filter is the only sterile filtration step in the Anthrax manufacturing process.

l. Validation of microbial retention by the ~~~ filters used for harvest of Anthrax vaccine was performed only with ~~~ media, which is used in tetanus production. Studies were not performed using Anthrax product or media.

"M" M/SS1/06

n. WFI used in the production of Anthrax sublots in

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			2/20/98

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4 - 2/9/98
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivative & Vaccine Mfg
FIRM NAME MICHIGAN BIOLOGIC PRODUCTS INSTITUTE	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. MARTIN LUTHER KING BLVD.	STREET ADDRESS OF PREMISES INSPECTED Same
CITY AND STATE (Zip Code) LANSING MI 48909	CITY AND STATE (Zip Code) Same

DURING AN INSPECTION OF YOUR FIRM I (WE) OBSERVED:

building [redacted] is transported from building [redacted] in a stainless steel tank. There is no validation to assure that the WFI retains it's critical quality attributes.

c. There is no completed cleaning validation of product contact equipment.

2. There are no written procedures, including specifications, for the examination, rejection, and disposition of sublots of Anthrax and Rabies.

a. Sublots are tested at the time of production, and are not retested prior to formulation. For example, sublot AV450 was produced in 5/95 and then used in formulation of lot FAV039 in 3/97.

b. Quarantined materials are held for extended periods.

-- For example, sublot AV216 was placed in [redacted] on quarantine in 3/92 and was not destroyed, for low antigen content, until 5/97.

-- Sublot AV222 was placed in [redacted] in 4/92 and was removed and destroyed in 5/97 due to mold.

-- Sublot AV493 was manufactured in 8/95 and is still in quarantine in [redacted] for low antigen content.

3. Potency testing of Anthrax Vaccine requires either testing 1 finished product vial, an aliquot from the formulated bulk tank, or a pilot bulk sample. There is no data demonstrating that these samples are representative of the lot.

In addition, expiration dates are assigned based on the latest valid potency test. There is no correlation between this date and formulation of bulk or filling of the finished product.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type) Jeffrey A. Stamper, Investigator Edward E. Lowell, Investigator	DATE ISSUED 2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. FOOD & DRUG ADM.-N 1401 ROCKVILLE PIKE ROCKVILLE, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4 - 2/20/98
	C. F. NUMBER 1873816
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Bldg. Sanitation & Vaccine Mfg.
FIRM NAME MICHIGAN BIOLOGIC PRODUCTS INSTIT	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. MARTIN LUTHER KING	STREET ADDRESS OF PREMISES INSPECTED JR. BLVD. Same
CITY AND STATE (Zip Code) LANSING, MI 48909	CITY AND STATE (Zip Code) Same

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

4. There is no written justification for redating lots of Anthrax vaccine that have expired. "Redating" testing consists only of a potency test. There is no documentation of testing for container/closure integrity or container/closure compatibility for periods up to 7 years. In addition there is no analytical testing identifying and demonstrating the absence of degradants.

There is no written SOP for redating, including when redating will be performed in order to extend the expiration period.

-- Lot FAV023 was tested for redating 2 times in 1997 and failed. It also failed twice on stability in 1997. It is scheduled to be retested for redating on 4/21/98.

Anthrax lots that are submitted for redating are released by CBER with alternate lot numbers to indicate the redate. However product is not labeled with the alternate lot number.

-- Lot FAV020 (initial date of potency 4/13/93) was submitted for redating as FAV020-1 and was labeled on 2/6/98 as FAV020.

For Anthrax Vaccine lots #FAV008 through #FAV016, the firm unpacked the vials from the cartons and removed the labels (the labels were removed by soaking in alcohol). The firm does not have a written procedure for performing unpackaging of vials and removal of labels. Also, the firm does not have documentation of performing reconciliation of the vials before and after this operation.

5. Regarding the firm's stability program for Anthrax:

a. The firm's stability program did not start until 1997. Stability testing consists only of performing release tests at various intervals and does not address product degradation. There is no justification for placing lots manufactured as early as 1991 into the stability program.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Jeffrey A. Stewart, IPM Donald W. Lebel, CBER	2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4 - 20/98
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivatives + Source Plasma
FIRM NAME Michigan Biologic Products Inst	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. Martin Luther King	STREET ADDRESS OF PREMISES INSPECTED Jr Blvd. Same
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) Same

DURING AN INSPECTION OF YOUR FIRM I) (WE) OBSERVED:

b. . The firm does not have a system in place to investigate and report stability failures. (All results noted below are from samples stored at 2-8°C. Accelerated stability test results are not included.) For example,

-- Lot FAV010 was filled on 7/1/91 and submitted for redating on 10/11/94, having passed all potency testing. It was placed in the stability program (zero time) on 10/7/97, and tested for potency. The "zero time" potency for this lot is recorded as "unsatisfactory". There is no investigation into this result nor is there any additional potency testing.

-- Lot FAV011 was filled on 10/17/91 and submitted for redating on 10/11/94, having passed all potency testing. It was placed in the stability program (zero time) on 10/27/97, and tested for potency. The "zero time" potency for this lot is recorded as "No Test" having not met the ~~~ dilution criteria. Test records indicate it was tested for potency 11/24/97. There is no investigation into this result nor is there any additional potency testing. In addition, the test result for p~~~~~~~~~~~~~~~~, dated 10/30/97 is 11 ppm. (Specification is 25-30 ppm.) This lot was not rejected nor placed in quarantine.

-- Lot FAV013 was filled on 10/25/91 and submitted for redating on 11/22/94, having passed all potency testing. It was placed in the stability program (zero time) on 11/12/97, and is recorded as "No test", having an invalid test. Test records indicate it was tested for potency on 12/5/97. There is no investigation into this result nor is there any additional potency testing.

-- Lot FAV018 was filled on 7/28/92 and submitted for redating on 6/11/96, having passed all potency testing. It was placed in the stability program (zero time) on 6/10/97, and is recorded as "Unsatisfactory". Test results dated 7/7/97 indicate it failed potency specifications. There is no investigation into

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		Paul Parker, Investigator Jerry A. Sinnett, Investigator Donald E. Lebet, Investigator Marlene V. Pruss, Investigator	2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. FOOD & DRUG ADM. 1701 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers DVM	PERIOD OF INSPECTION 2/4-20/98	C. F. NUMBER 1873RK
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivatives + Recombinant Prods	
FIRM NAME MICHIGAN BIOLOGIC PRODUCTS INSTIT.	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. MARTIN LUTHER KING JR BLVD.	STREET ADDRESS OF PREMISES INSPECTED Same	
CITY AND STATE (Zip Code) LANSING, MI 48909	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

this result nor is there any additional potency testing.

-- Lot FAV022 was filled on 2/9/93 and submitted for redating on 10/15/96, having passed all potency testing. It was placed in the stability program (zero time) on 10/7/97, and is recorded as having an "Unsatisfactory valid test". Test results dated 10/31/97 indicate it failed potency specifications. There is no investigation into this result nor is there any additional potency testing.

-- Lot FAV023 was filled on 12/13/93 and passed a potency test on 3/29/94. It was submitted for redating on 4/2/97 and was placed in the stability program (zero time) at the same time. It is reported as failing potency on 4/2/97, and is reported as having an "invalid test" on 5/14/97. It was tested again on 8/12/97 and is reported as failing potency. A fourth potency test conducted on 10/6/97 is listed as passing by 0.01. There is no investigation into the original result and justifying the additional testing.

-- Lot FAV040 was filled on 11/13/97 and placed in the stability program (zero time) on 11/19/97. It is reported as having an "invalid" potency test on 11/19/97. There is no investigation into this result nor is there any additional potency testing.

c. The firm's SOP(s) for handling manufacturing deviations/departures does not address when a lot should be monitored on stability.

6. There has been no investigation into numerous "invalid" potency test results for lots. For example:

-- Lot FAV021 was filled on 11/24/92, having a passing potency test. It was tested again on 10/15/96 and failed potency. It was tested again on 1/28/97 for redating and passed. There is no investigation into the test failure nor justification

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type) Jeffrey A. Stamper, IPA Douglas A. Usher, Investigator Richard U. Mueller, Investigator	DATE ISSUED 2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Adm. 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Hyers DVM	PERIOD OF INSPECTION 2/4-20/98
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Donation & Vaccine Mfg
FIRM NAME Michigan Biologic Products Instit	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. Martin Luther King	STREET ADDRESS OF PREMISES INSPECTED Jr Blvd. Same
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) Same

DURING AN INSPECTION OF YOUR FIRM I (WE) OBSERVED:

for retesting the lot.

-- Lot FAV025 was filled on 4/24/94, having a passing potency test. It was tested again on 4/22/97 and failed potency testing. There is no investigation into the test failure.

-- Lot FAV028 was filled on 6/2/95. It was not tested for potency until 7/3/96 when it failed the test. It was tested again on 8/27/96 and passed. There is no investigation into the test failure nor justification for retesting the lot.

-- Lot FAV041 was filled on 11/18/97. It had an "invalid" potency test on 9/30/97. There is no investigation into this invalid test.

-- Lot FAV042 was filled on 11/21/97. It had an "invalid" potency test on 10/29/97. There is no investigation into this invalid test.

-- Lot FAV043 was filled on 12/25/97. It had an "invalid" potency test on 11/18/97. There is no investigation into this invalid test.

-- Lot FAV044 was filled on 1/7/98. It had an "invalid" potency test on 12/8/97. There is no investigation into this invalid test.

7. The firm's SOP dated 9/3/96, requires that vials discarded as rejects be counted, however, it does not specify limits for when a lot should be investigated or rejected as a result of this lot reconciliation. For example:

-- Lot FAV016 had 6579 vials rejected due to particulates during post filling inspection. These particulates were not identified, nor was an investigation conducted. The batch was released.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Jeffrey A. Stewart, Inv. David E. Lesar, Investigator	2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin. 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C Myers DVM	PERIOD OF INSPECTION 2/4-20/98
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivative & Vaccine Mfg
FIRM NAME Michigan Biologic Products Inst.	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. Martin Luther King Jr Blvd.	STREET ADDRESS OF PREMISES INSPECTED Same
CITY AND STATE (Zip Code) Lansing, MI 48908	CITY AND STATE (Zip Code) Same

DURING AN INSPECTION OF YOUR FIRM I (WE) OBSERVED:

-- Lots FAV028, FAV031, FAV033 and FAV038 had 3323, 2441, 2509, 1347 vials rejected respectively for low volume during post filling inspection. There was no investigation conducted.

-- Lot FAV035 had 409 vials rejected for faulty closure during post filling inspection. There was no investigation conducted.

8. The firm does not have specifications for time limits at which the product can be exposed to room temperature conditions during filling, labeling and packaging operations (repeat observation).

-- Lot FAV036 was at room temperature for .. hours and then the filling operation was aborted, it was placed back in the refrigerator (deviation report #97DAV34).

In addition, there is no stability information regarding product exposure to room temperature. Prior to 1996 the firm did not monitor the length of time at which the product was exposed to room temperature conditions during the filling operations (FAV009-FAV015).

9. The firm's procedures for Environmental Monitoring of critical production areas do not require that additional cleaning and increased sampling be performed when environmental action limits are exceeded. When environmental monitoring action limits are exceeded during filling, investigations do not consider environmental monitoring results during production of sublots, sterility test results of sublots and sterility test results of final product. In addition, when a sterility retest is performed during stability testing, no investigation is performed. For example:

-- Lot FAV029 was filled on 8/21/95 and passed sterility testing. On 9/23/97, during stability testing w/

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			2/20/98

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Hyer DVM	PERIOD OF INSPECTION 2/4 - 20/98	C. F. NUMBER 1K7388K
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivative & Vaccine Mfg	
FIRM NAME Michigan Biologic Products Instit	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. Martin Luther King	STREET ADDRESS OF PREMISES INSPECTED Jr Blvd. Same	
CITY AND STATE (Zip Code) Lansing, MI 48908	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

it required a sterility retest. The contaminant was identified as Penicillium species. The product passed a retest. Production records for sublots used to produce FAV029 indicate [redacted] were bulked to produce the lot. Sublot AV383 had an initial sterility failure on 5/17/94 (Rhodococcus species); Sublot AV390 had an initial sterility failure on 7/19/94 (Propionibacterium acnes). Both sublots passed sterility retest. There is no environmental monitoring data from preparation of the sublots. On 8/11/95, during filling of lot FAV029, environmental monitoring testing found the following on critical surfaces: Cladosporium species, Alternaria species, Micrococcus species, Bacillus subtilis, Staphylococcus saprophyticus, Staphylococcus epidermidis, and Staphylococcus capitis.

-- Lot FAV032 was filled on 10/26/95. On 7/28/97, during stability testing [redacted] it required a sterility retest. The contaminant was identified as Penicillium species. The product passed a retest. The lot was formulated on 9/21/95. Two operators performing the formulation exceeded action limits on viable monitoring. Four CFU were sampled from one of the operator's gloves and identified as Penicillium species.

-- Lot FAV035 was filled on 2/5/97. On 8/11/97, during stability testing [redacted] it required a sterility retest. The contaminant was identified as Bacillus cereus. The product passed a retest. The lot was formulated on 1/9/97. Environmental monitoring exceeded action limits in the gowning area prior to formulation identifying the following: Staphylococcus capitis, Micrococcus species, Bacillus coagulans, and Corynebacterium species. In addition, photohelic gauges were out of range during this time indicating insufficient air pressure in critical areas.

-- The firm does not trend multiple contaminations with microorganisms in sublots. For example, between 4/94 and 2/95, [redacted] were produced of which 23 were discarded due to some kind of microbial contamination. Lots FAV029, FAV030 and FAV031

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C Myer DVM	PERIOD OF INSPECTION 2/4 - 20/98
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivatives & Vaccines
FIRM NAME MICHIGAN BIOLOGIC PRODUCTS INSTT	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. MARTIN LUTHER KING	STREET ADDRESS OF PREMISES INSPECTED Jr Blvd. Same
CITY AND STATE (Zip Code) LANSING, MI 48909	CITY AND STATE (Zip Code) Same

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were whole or partially formulated from those sublots not discarded in this time period. In January and February 1997 of 12 consecutive sublots produced, 5 were discarded for microbial contamination. The others were included in lot FAV039. In September and October 1997, of ~~~~ produced, 6 had contamination and two of those were retested and released for formulation. The remaining sublots were formulated into FAV045 or FAV046.

10. Recording of data in building ~~ from room ~~~ log books in room ~~ is accomplished by viewing the results through the UV pass box and is not checked for accuracy prior to discarding the original data.

11. Specifications for the release of sublots were not formally established until 1995.

12. The firm does not have a current SOP for environmental monitoring in the Anthrax production facility. The firm has replaced it's previous environmental monitoring SOP with a centralized procedure that references area specific monitoring plans. However, the Anthrax specific plan has not been finalized.

Anthrax Building Facilities Conditions:

13. In Room ~~~~~~~~~~ of the Anthrax production facility, we observed peeling paint, exposed duct and pipe work, insulation peeling off the pipes, and rusty steam and gas lines.

14. Compressed air used to perform positive pressure transfers of sterile products (Anthrax and Rabies) is central plant air and is not monitored. The ~/~ micron filters used at the point of use are not integrity tested.

15. Rooms ~~~~~~~~~~ are not environmentally controlled. There was no active environmental monitoring of aseptic

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	[signature] David Hoenig	Lynn Poole, Investigator Jeffrey A. Jenkins, IOA Donald N. Leask, IOA Mark W. Milnes, Dist. Director	2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C Myers, DVM	PERIOD OF INSPECTION 2/4-20/98	C. F. NUMBER 1873846
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Plasma Derivatives + Vaccines	
FIRM NAME Michigan Biologic Products Instit	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. Martin Luther King	STREET ADDRESS OF PREMISES INSPECTED Jr Blvd. Same	
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

manufacturing activities until 1996. During the 1996 production of sublots, more than half of the sublots had environmental monitoring excursions. There was no tracking of these events and no significant corrective action taken until 10/96.

16. Plant steam is used for sterilizing production vessels and glassware in buildings [redacted] and is not monitored or controlled.

17. Poor facility arrangements exist for aseptic processes in building [redacted], room [redacted] in that media is made, dishes washed, equipment and glassware autoclaved, as well as the production processes of fermentation, inoculation, and harvest all occur in this one room simultaneously.

18. Regarding cold storage of critical seed stock:

a. In the Anthrax production suite the logs for the refrigerator/freezers [redacted] are incomplete. The logs do not match the refrigerator/freezer contents. The Anthrax refrigerator/freezer contained unlabeled vials.

b. There is no segregation of the master spore concentrations and the working spore concentrations of both the virulent and [redacted] strains in [redacted] Anthrax production and potency testing facilities.

c. The keys for all refrigerator/freezers in building [redacted] and building [redacted] were found on top.

19. There is no SOP for change over in building [redacted] Anthrax Biosafety Cabinets (BSC). Both inoculum preparations and aseptic sublot formulation occur in these hoods.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Type or Print) Kyle Fraser, Investigator Jeffrey A. Stegeman, Investigator Donald G. Lenz, Senior Investigator Marsha L. Mueller	DATE ISSUED 2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers DVM	PERIOD OF INSPECTION 2/4-20/98
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivative & Vaccine Mfg
FIRM NAME MICHIGAN BIOLOGIC PRODUCTS INSTIT	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. MARTIN LUTHER KING JR BLVD.	STREET ADDRESS OF PREMISES INSPECTED Same
CITY AND STATE (Zip Code) LANSING, MI 48908	CITY AND STATE (Zip Code) Same

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

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21. fol:

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23.

24.

25.

RABIES Vaccine

26. The manufacturing process for Rabies Vaccine is not

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C Myers DVM	PERIOD OF INSPECTION 2/4 - 2/20/98	C. F. NUMBER 1873886
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivative & Vaccine Mfg.	
FIRM NAME Michigan Biologic Products Institute	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. Martin Luther King Jr. Blvd.	STREET ADDRESS OF PREMISES INSPECTED Same	
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

validated.

-- Media fills have not been performed to validate the aseptic preparation of sublots and hold times prior to filling. The product does not pass through a [redacted] micron filter during production.

-- There has been no determination or identification of environmental organisms present during the manufacturing process.

-- There is no validation of the length of time sublots are held until they are used in a formulation. Sublots have been held as long as 14 months prior to use. There is no stability data to support this hold time.

-- The autoclave used to sterilize glassware used in the preparation of sublots and formulated vaccine is supplied with ~~city water~~ plant steam and has no vent filter.

-- Glassware used in production is not depyrogenated. In addition, glassware/tubing assemblies used for harvesting the product are autoclaved and then placed on a shelf for up to 90 days. This storage time has not been validated.

-- WFI supplied to [redacted] used to prepare sublots and rinse glassware, is filled from the point of use in building [redacted] into glass bottles and transported to building [redacted] These bottles are used, rinsed with tap water, rinsed with WFI from another transport bottle, dried in an incubator at [redacted] covered with blue paper wrap, and placed on a shelf until filled again. There is no assurance this water meets WFI specifications.

-- The analytical method for determination of [redacted] in Rabies vaccine has not been validated.

-- Reagents used in the preparation of the product are prepared in building [redacted] and assigned an expiration date of [redacted]

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print) Paul A. Schaefer, ISO Jeffrey A. Jenkins, ISO Donald E. Lewis, CBER Barbara U. Mack, ISO	DATE ISSUED 2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C Hyslop DVM	PERIOD OF INSPECTION 2/4-20/98
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Donating & Source Plasma
FIRM NAME Michigan Biologic Products Instit	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. Martin Luther King	STREET ADDRESS OF PREMISES INSPECTED Jr Blvd. Same
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) Same

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months. There is no documentation that the bottles used to store the reagents are sterile when filled, nor has the expiry period been validated. Potency testing is not performed on the reagents.

27. The specification for potency is the average of [illegible] test results and shall be >/= [illegible] This allows out-of-specification results to be averaged with in-specification results to obtain a passing final average. In addition potency tests have been conducted more than [illegible] times, [illegible] results selected and a passing average reported with no justification for the additional testing. For example:

-- Rabies Vaccine, lot #150, was tested for potency 13 times in October and November, 1995 (2.06, 3.08, 2.62, 0.94, 1.01, 0.92, 1.86, 1.74, 1.94, 0.92, 2.52, 1.93 5.09 IU/ml). [illegible] results [illegible] were averaged and a potency result of 2.6 IU/ml reported.

-- Rabies Vaccine, lot #152, was tested for potency 6 times in March, 1996 (5.09, 3.18, 1.86, 2.27, 1.40, 3.49 IU/ml) with an average of 2.6 IU/ml reported.

-- Rabies Vaccine, lot #158, was tested for potency 5 times in July and August, 1997. (0.84, 4.45, 3.40, 2.73, 1.68). Two of the results are marked "Invalid test" (0.84, 1.68). There is no documentation justifying the invalidation of these two results. An average of 3.46 IU/ml was reported.

28. SOP # [illegible] dated 10/11/97, states [illegible] will be placed on stability each year. Two samples were placed on stability in 1996 and no samples for 1997.

Lots #152 manufactured 3/7/96 and #153 manufactured 4/26/96 were placed on stability (zero time) on 8/27/96.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type) Jeffrey A. Siegert, Dir. Devel. Manuf. Douglas W. Leslie, Chief Investigator Marlene L. Swanz	DATE ISSUED 2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C Myers, DVM	PERIOD OF INSPECTION 2/4 - 2/20/98
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivatives & Vaccine Mfg
FIRM NAME Michigan Biologic Products Institute	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. Martin Luther King Jr. Blvd.	STREET ADDRESS OF PREMISES INSPECTED Same
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) Same

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The initial stability test for Lot #152, initiated 9/6/96, is classified "Invalid" with only 2 of 3 results reported (2.11 IU/ml; 1.69 IU/ml), with no investigation. The results were not reviewed until 11/12/97. The 3 month stability test results (11/26/96) were reported 11/12/97 (1.12; 4.99; 3.14 IU/ml).

The initial stability test results for Lot #153, initiated 9/6/96, are 2.11 IU/ml. The 12 month stability test results, dated 8/28/97, are listed as "Invalid", and reported 12/4/97 (1.86; 2.03). There was no investigation.

29. On 9/16/97 samples of Rabies cell lines were sent to ~~~~~ for evaluation of their ability to form colonies in soft agarose. There is no documentation of review, particularly by Senior Quality management of the results received from this company which were inconclusive. There is no written justification for the continued use of this cell line in production. There are no written procedures for the notification of Senior Quality management of product rejections, investigations and failures.

30. Rabies Vaccine sublots #RSL902 and RSL903 contained errors, yet these batch records were released by QA, without any correction.

31. Cells, ~~~~~ used for rabies manufacturing (ie. lot #155 to current) have not been qualified.

Diphtheria-Tetanus Vaccine, Lot DT4176:

32. There is no environmental monitoring data for production, formulation and filling of the product in 1994.

33. There are no finished product specifications for release of Diphtheria-Tetanus vaccine.

34. There is no procedure for redating of the vaccine including

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FORM FDA 483 (5/85) PREVIOUS EDITION MAY BE USED. INSPECTIONAL OBSERVATIONS PAGE 15 OF 19 PAGES

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4 - 20/98	C. F. NUMBER 1873116
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivatives + Vaccines	
FIRM NAME MICHIGAN BIOLOGIC PRODUCTS INSTIT	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. MARTIN LUTHER KING	STREET ADDRESS OF PREMISES INSPECTED Jc Blvd. Same	
CITY AND STATE (Zip Code) LANSING MI 48909	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

release testing specifications.

35. Diphtheria-Tetanus vaccine lot DT4176 is not on stability.

36. The analytical methods for ~~~~ is not validated.

37. Bacteriostasis/Fungistasis testing and preservative effectiveness testing have not been performed on DT vaccine.

Blood Derivative Products:

38. Training of employees performing examination of incoming plasma does not include examples of defects including: excess red blood cells; hemolysis; microbial contamination; and examination of product labels.

39. Media fills do not represent all product manipulations after sterile filtration. Immune Globulin and Albumin (Human) are sterile filtered in Building ~~ and may be stored in bulk for up to 90 days prior to being moved to building ~~ for filling. There has been no media challenge of this storage period.

40. There is no SOP defining the actions to take, including when the Quality Unit is to be notified, when the following situations occur in production:

a. the sterile filter fails in building ~~

b. the filling line is stopped and product must be stored and moved to another tank in building ~~

c. when the product requires refiltration.

41. There has been no investigation into out of specification pressure differential readings in Building ~~~~ for the time period of 6/97 to 1/98. The current SOP #2303.300 for monitoring air pressure differentials

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		Jeffrey A. Stanniti, Dir. Donald E. Baer, Director	2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Admin 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4 - 2/20/98	F. E. NUMBER 1873886
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Fractionator & Source Plasma	
FIRM NAME Michigan Biologic Products Instit	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. Martin Luther King	STREET ADDRESS OF PREMISES INSPECTED Jr Blvd. Same	
CITY AND STATE (Zip Code) Lansing, MI 48908	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM I (WE) OBSERVED:

does not require notification of the Quality Unit when differentials are OOS.

42. The analytical method for determination of [redacted] in Immune Globulin has not been validated.

43. Bacteriostasis and Fungistasis (BF) testing for Immune Globulin was performed on product with a [redacted]. The specification for [redacted] in the product is [redacted] There is no BF testing at 85 or [redacted] ppm. There is no information that the antimicrobial effectiveness of [redacted] is effective through the expiration date of the product.

44. SOP #5431, [redacted] does not include reporting incidents that may occur while transporting tanks and vials between Building [redacted]

45. Contract testing labs are used for HBsAg, HCV, HTLV-1, HIV1/2 anti-HBc, HIV-1 Ag testing. Samples of Fraction I supernatant or pooled Recovered Plasma are sent to the lab for analysis. No qualification of the contract lab, nor tests performed has been conducted.

46. A [redacted] is used to monitor temperature and humidity of production rooms in building [redacted] Calibration documentation of this instrument indicates it can not be calibrated because it lacks accuracy of measurement. No other instrumentation is used to monitor these parameters in these areas.

GENERAL:

47. The procedures (#6108 and 6107) for routine sampling of the WFI loop at a point of use (POU) require a [redacted] of the POU prior to collecting the sample. There is no requirement for this [redacted] prior to production. (Building [redacted]

48. Pressure differential readings are recorded in each batch...

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Type or Print)	DATE ISSUED
	[redacted]	[redacted]	2/20/98

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Adm. 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4-20/98
	F. E. NUMBER 1873846
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivatives & Vaccine Mfg
FIRM NAME Michigan Biologic Products Instit	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same
STREET ADDRESS 3500 N. Martin Luther King	STREET ADDRESS OF PREMISES INSPECTED Jr Blvd. Same
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) Same

DURING AN INSPECTION OF YOUR FIRM I (WE) OBSERVED:

record. There is no written procedure for monitoring pressure differentials, including instructions for follow-up of pressure differentials that are out of limits in Building [redacted]

49. No annual review of [redacted] (repeat observation).

50. Training of employees performing visual inspection of finished product containers does not include examples of types of particulates and discoloration they are to look for. Finished containers are not held up against a black and white background during inspection. In addition, there is no requirement that employees performing the inspection demonstrate their ability to detect defects.

51. According to the firm's SOP #6430, [redacted] raw materials that do not have an expiration date will be automatically assigned a [redacted] year expiration date by the firm. The firm does not have data to support a [redacted] year expiration date on raw materials including:

a. [redacted] used in the manufacture of Rabies vaccine.

b. [redacted] used in the manufacture of Anthrax vaccine.

c. [redacted] used in the manufacture of

d. [redacted] used in the manufacture of Plasma Derivatives.

This SOP does not indicate when a supplier will be requalified.

This procedure does not address raw material monographs updates. For example, during certification of the vendor for [redacted]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. FOOD & DRUG ADMIN 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4 - 20/98	F. E. NUMBER 1873886
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Derivatives & Vaccine Mfg	
FIRM NAME Michigan Biologic Products Institute	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. Martin Luther King	STREET ADDRESS OF PREMISES INSPECTED Jr Blvd. Same	
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED,

USP, in 1989, the firm did not perform microbial testing. The USP XXIII requires microbial testing of this raw material which has not been performed by the firm.

52. The _____ scale inside the hood in the raw material warehouse has not been calibrated and is not included in the equipment calibration schedule.

53. The system for investigating out-of-specification (OOS) results:

a. Allows a test to be invalidated when equipment or analytical error is documented. It does not require the subsequent repair or correction of the equipment or retraining of the analyst.

b. Allows a retest on a valid initial test result and subsequent invalidation of the original result if the retest passes. It does not require notification of production of the OOS.

c. Does not require corrections be made and actions be taken to prevent recurrence.

SOPs for both the Deviation System (QA07-001-00) and Out-of-Specification Results (AL00-021-00) do not specify time limits in which to complete investigations.

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ATTACHMENT 2

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Bethesda MD 20892

November 14, 1996

To: File

Robert C Myers
Michigan Biologic Products Institute
3500 North Martin Luther King, Jr., Blvd
P.O. Box 30035
Lansing MI 48909

Report on action taken on product submitted:

Released - Extension of Dating
Based on potency test of 24-SEP-96

Anthrax Vaccine Adsorbed

Lot No.(s)
FAV020-1

Notified by transceiver

Sincerely,

Kathryn C. Zoon, Ph.D., Director
Center for Biologics Evaluation and Research

ATTACHMENT 3

Lori Greenleaf
4494 S. Cole Court
Morrison, CO 80465
Fax (303) 697-9822
Home Phone (303) 697-0508
Email david.greenleaf@gte.net

October 09, 1998

Department of the Army
Freedom of Information and Privacy Act
7798 Cissna Road #205
Springfield, VA 22150-3166

Attn: Rose Marie

Dear Rose Marie,

Per our conversation 10/7/98, please accept this letter as a request under the Freedom of Information Act for all inspection reports done by the Dept. of the Army at the Michigan Biologic Products Institute in Lansing, Michigan on the anthrax vaccine line.

I have been informed by Dr. Robert Myers at the Michigan Biologic Products Institute, and by the FDA, that all inspections on the anthrax vaccine line prior to 2/98 have been done by the Dept. of the Army.

This issue is critical, please do what you can to expedite this request. If you should have any questions, please feel free to contact me.

Sincerely,

Lori Greenleaf

Lori Greenleaf

cc: Mark Zaid, Attorney
Dr. Sushil Sharma, GAO
Dr. Meryl Nass
Etta Dewey

ATTACHMENT 4

JAN 14 1997

Michigan Biologic Products Institute
1911 N. Martin Luther King Jr. Blvd.
Lansing, MI 48909

11/18-27/96/FAR/LPN/PR/WDT
FOI/MI/73886Y96.E27
Page 1

SUMMARY OF FINDINGS

This was a compliance followup inspection of a biologics manufacturer, according to a 10/31/96 CBER Office of Compliance memo and DET-DO workplans (WATS #103826). The firm is licensed by CBER to manufacture blood derivative products, including albumin and immune globulin, as well as toxoids and vaccines.

The previous inspection, in April and May 1995 was classified OAI due to GMP and other deficiencies. At that time Michigan Biologic Products Institute (MBPI) was the Michigan Department of Public Health, Biologic Products Division, license #0099. The firm submitted a 6/9/95 written response to the FDA 483. They also held a meeting with CBER on 6/15/95 to discuss planned renovations to the vaccine production building 15.

CBER issued an 8/31/95 Warning Letter to the firm, who in turn submitted a 9/30/95 response (with a copy dated 12/16/95 sent to DET-DO). Subsequent correspondence occurred between CBER and the firm, to clarify specific issues. The latest was a 5/2/96 CBER response to a 3/22/96 MBPI letter.

Currently we covered the manufacture of blood derivatives and rabies vaccine, and corrections to previous deficiencies. The firm is renovating facilities for manufacture and testing of diphtheria, tetanus and pertussis vaccines. In addition, anthrax vaccine was not covered, since it comes under military inspection.

The firm has corrected many of their previous deficiencies, and has an active validation program in place. However, they lack an adequate quality assurance program for oversight of activities, and there are still significant GMP deficiencies.

An FDA 483 was issued for deficiencies in validation, environmental monitoring, preventive maintenance, water systems, cleaning, product protection, record review, employee practices, stability, facilities, equipment, and other areas. In addition, some of the 1995 FDA 483 items remain uncorrected or corrections have not been completed. The management promised corrections and a written response to DET-DO and CBER.

Complaint CIN-6281, for rabies vaccine was also covered. The firm did not have any significant complaints for blood derivatives or other products, which would indicate a sterility or container/closure integrity problem.

3/14/97

ATTACHMENT 5

Lori Greenleaf

4494 S. Cole Court
Morrison, CO 80465
Fax (303) 697-9822
Home Phone (303) 697-0508

Dr. Sushil Sharma
General Accounting Office
441 G Street NW Room 4T43
Washington DC 20548

Dear Dr. Sharma,

Per our conversation 10/5/98, I would like to bring to your attention a paragraph in a Summary of Findings report on an FDA inspection done at the Michigan Biologic Products Institute in November 1998, regarding the anthrax vaccine.

This paragraph reads "currently we covered the manufacture of blood derivatives and rabies vaccine, and corrections to previous deficiencies. The firm is renovating facilities for manufacture and testing of diphtheria, tetanus, and pertussis vaccines. In addition, anthrax vaccine was not covered since it comes under military inspection".

I find this statement troubling as I have been informed several times by the FDA and the Dept. of Defense that this vaccine is FDA licensed and approved since 1970. After reviewing this I phoned Joanne Bankley at the FDA to question this statement, and was put on a speaker phone conversation with Joanne, and an employee by the name of Lori Harrison. It was very obvious to me that these employees were both shocked and concerned when I questioned the vaccine being inspected by the military. They both assured me that this statement was made in error, and the FDA does in fact inspect the anthrax vaccine. I asked who would have written this document with this statement and was told "the inspector". Lori Harrison and Joanne Bankley told me they would like to have someone higher up call me on Monday. I never received a call from anyone at the FDA.

After speaking with the FDA, I called Mr. Gary Christopherson at the Dept. of Defense, Health Affairs Office, and asked him about the statement made on the Summary of Findings. Mr. Christopherson also claimed someone had made a very big mistake, the FDA inspects the anthrax vaccine line at MBPI, not the military.

Monday, October 5, 1998, I phoned Mr. Robert Myers, the responsible head of Michigan Biologic Products Institute, asked Mr. Myers about the inspecting being done on the anthrax vaccine, Mr. Myers stated "the Army does inspect the anthrax vaccine line several times per year, however the FDA has not relinquished authority to the Dept. of Defense". I questioned why in all reports from 1992-1997 the anthrax vaccine is not mentioned, Mr. Myers stated absence of comment does not necessarily mean it was not inspected, it could mean that all items inspected were in compliance. Dr. Sharma, I find this a little hard to believe given the fact that there were 15 pages of observations not in compliance in the 2/98 inspection report which was done by the FDA. I am especially concerned that the FDA inspection done in 2/98 was the only one done by the FDA per documentation received prior to the inoculations beginning.

Tuesday, October 6, 1998, I phoned JoAnne Bankley at the FDA to inform her that I had not received a call from anyone yet, she stated they have been very busy. I informed Ms. Bankley that Mr. Myers had confirmed that the military does inspect the anthrax vaccine line at MBPI, she said "he said what?". I

went on to ask Ms. Bankley if the anthrax vaccine given to veterinarians and livestock workers was also inspected by the Army or the FDA, she simply stated she did not know. I asked Ms. Bankley for the phone number of Mr. William Tingley the inspector who signed the report of 11/96, she said she is not a liberty to give out telephone numbers. I then asked her to transfer me to personnel. I was able to obtain Mr. Tingley's telephone number.

October 8, 1998, I phoned Mr. Tingley and once again was informed that until recently the inspecting of the anthrax vaccine line was done by the military. I began asking questions regarding the vaccine that veterinarians get, he referred me to his immediate supervisor Mr. John Dempster. I phoned Mr. Dempster, was told the same thing. The anthrax vaccine line at MBPI until very recently was only inspected by the military. He stated he does not know if the vaccine given to veterinarians is in a separate place at MBPI, or if the military is also inspecting this.

As requested, I am forwarding all documentation regarding these inspections which I obtained under the Freedom of Information Act in a request dated May 1998. You will find an annual biologics inspection done 4/24-5/5/95 which has no mention of the anthrax vaccine. You will also find in the Summary of Findings report that there has been a sentence removed, which I suspect states the same as the report of 11/96, "anthrax vaccine was not covered, since it comes under military inspection".

If you should need additional information, please do not hesitate to contact me.

Sincerely,

Lori Greenleaf

cc: Mark Zaid, Attorney at Law
Patrick Eddington
Meryl Nass, MD
Etta Dewey
Senator Wayne Allard, CO

ATTACHMENT 6

Lori Greenleaf

From: BOYNAZZ25@aol.com
To: david.greenleaf@gte.net
Subject: Re: Fw: gulf-chat Expired Anthrax vaccine used in Gulf
Date: Thursday, October 01, 1998 5:49 PM

I wanted to write to you and let you know that I have found your E Mail materials helpful and informative. I have a son on board the Eisenhower which is presently in the Med, and have advised him to refuse to take the shots and to continue to refuse them until the uncertainty is straigtened out (if ever). I would prefer to have him home, general discharge or otherwise, rather than regret matters in years to come.

I intend to initiate a barrage of letter writing. I intend to write to the Editorial Boards of most of the major newspapers, to our reps in Congress, TV people, etc.

This matter is important to our family and a day does not go by now without some thought to the pressures and military reaction to a young sailor (or any sailor) who refuses to take the vaccine.

I am an attorney in the Chicago area and would appreciate knowing the Case Number of the civil action filed in DC. If the pleadings are available, I would like to review them. Anything I can do, let me know.

Agent Orange, LSD, radiation, Gulf War syndrome and a President who discussed military matters on the phone with Congressmen while the Pres. is otherwise engaged in the Oval Office.

Thanks again.

ATTACHMENT 7

Lori Greenleaf

From: Steve Anderson <piano@nwi.net>
To: david.greenleaf@gte.net; Boynazz25@aol.com; MeChall66@aol.com; david.coffey@owlx.com; patrickhall@Juno.com; Katie.Bettendorf@cheerful.com; piano@nwi.net; bears317@aol.com; mnass@igc.apc.org; rhafemeister@bnd.com; gulfwar@flash.net; prabe@mediaone.net; ddnew@bigfoot.com
Subject: Re: Update on anthrax refusal
Date: Thursday, November 12, 1998 2:16 AM

Dear All,

As most of you know, my husband, Hunter Brisel serving aboard the USS Abraham Lincoln has been refusing the anthrax inoculations. I just wanted to give you all an update on what has been happening in his situation....

For those of you who don't know already, Hunter and his colleague (Gerry) were put on restriction again for the third time on Nov. 1. They were both given another 60 days restriction, reduction in pay and rank, and were told again by their CO that they would be on restriction until they took the vaccine or until their EAOS. For their third Captain's Mast they were charged again under article 90, which is disobeying a lawful order from a superior commissioned officer. (That being their XO). As many of you may know... the UCMJ explicitly states under Non Judiciary Punishment procedures that double and multiple punishments for the same offense are prohibited under article 15 (which is a captain's mast hearing) What has happened, is that these two men have been punished three times for the same offense!

On November 6th, I spoke at a small Town Meeting/Press Conference, regarding my husband's situation. Many of you were there. There have been some very interesting new developments since that time.

On the morning of Nov. 8th, I received a phone call from my father. Hunter had called him late the night before to tell my father to tell me that he and Gerry had been taken off of restriction! This is no small matter! When I finally talked to my husband on Monday night, he told me the whole story. Apparently Hunter and Gerry were summoned up to the CDC to speak with their Senior Chief. When they arrived, the Senior Chief shook their hands and said " Congratulations, you're officially off of restriction ". Needless to say, both men came close to having a heart attack! They couldn't believe what they were hearing. Of course they asked the Senior Chief how this sudden change had come about. He said that. Legal on board had received a call from Legal in San Diego. San Diego had received a call from somebody very high up in Washington D.C. who told them to get a hold of the ship and get Hunter and Gerry off of restriction ASAP! Both men were able to get off of the ship in Perth, Australia for the first time in 142 days.

I realize that it is very simple for Washington D.C. to get a hold of the ship if they need to. But I don't think I have to tell you all that getting them to actually make that call is no small thing! I can

tell you right now that if it were up to the CO both men would have been on restriction until their EAOS. He apparently had taken this matter very personally. I am quite sure that he is very upset that he had to reverse his punishment decision. I received an email from a friend of Hunter's this morning. It said "Thought I would let you know that Hunter will more than likely be out of the Navy before the ship leaves Hobart. The Captain wants him and Gerry off the ship by then. I'll let Hunter give you the details on it, but I thought I'd let you know." I don't quite know what to make of that! The ship will be in Hobart tomorrow. I am expecting to hear from my husband within the next couple of days. I will be sure to keep you all posted.

I mostly wanted to tell you all what is going on and update you. I do not know what will happen from here, but progress is being made so don't give up! I think that the Town Meeting in San Francisco probably played a part in all of this. In addition, we have a formal congressional inquiry filed, as well as a request for a formal court of inquiry on the part of the Navy under Article 135. I want to thank you all for all of the help and support you have showed for my husband and his situation. I assure you that even if my husband is discharged we will not stop this battle. The DoD MUST make a formal policy on this issue soon! For those of you that are fighting this first hand, do not give up. We have prayed long and hard about this situation. And I believe that God is opening doors for us.

I will continue to keep you posted. You are all in our prayers. For those of you that I met in San Francisco it was wonderful meeting you all. Mr. Coffey: thank you so much for lunch! You shouldn't have.

Take Care and God Bless

Your Friend,
Deborah Bried.

ATTACHMENT 8

Lori Greenleaf

From: JEAN SKOGLUND <jeanskoglund@hotmail.com>
To: david.greenleaf@gte.net
Subject: My current statis
Date: Saturday, March 20, 1999 2:34 PM

Dear Lori,

Hi. This is Jean Skoglund. I live in San Diego, CA. I am stationed at the Naval Amphibious Base in Coronado. My command is Amphibious Conctruction Battalion One. I refused the anthrax in late January. I was conseled three times before I went to X.O.I. From there, I was sent to Captain's Mast. I was sentenced to 30 days restriction, 30 days extra duty, and I was reduced from E-2 to E-1. I served my time on the Naval Air Station, North Island. I talked to my legal officer when I returned to get a "heads up" on my situation. I asked her if I could be punished again for not taking the anthrax and she said no. I asked her what the captain's plans were for me. She said that the captain did not plan to do anything with me; that I had served my time and that was it. I asked myself, "How can that be?"

This whole Anthrax situation has made me very angry, to the point where I don't want anything to do with the Navy at all! They punished me for looking out for my own health, standing up for what I believe in. They hurt me not only emotionally, but financially as well. I was less than a month away from E-3. I was suppose to take the September '99 exam. Now I have to start all over. It will be 9 months before I even make E-2 again, and from E-2 to E-3 is another 9 months. Then you have to be an E-3 for 6 months before you're even elegible for the third class exam. I want nothing more than to go home. I just can't see myself working for people that I can't trust. The beliefs they have reguarding the anthrax are so opposite of my own. I don't want to be here. This is a waste of my time. My life has been nothing but hell the past few months. I have been tremendously stressed out. I haven't slept one night through in so long. I usually wake up at least 3 times a night. I have even lost weight. Of course there's always people who are curious about what is going on and I land up having to defend myself time and time again. I hate that. I just want it to end. I'm tired of the stress. I want out! I have requested to have a closed Captain's Mast(that is where I just go and talk to the Captain one on one. Anytime you go to see the Captain, good or bad, it's called a Mast). I should be seeing him the beginning of next week. Please, if you know of anyone who can help me, give them my phone number or even give them this letter. Thank you!

Sincerely,
Jean Skoglund

ATTACHMENT 9

Lori Greenleaf

From: Dan Hlavac <sheehanw@stennis.navy.mil>
To: david.greenleaf@gte.net
Subject: Daniel Hlavac - USS John C. Stennis
Date: Saturday, May 16, 1998 8:24 PM

Dear Lori,

here is some of the information you requested. This is information pulled directly from my service record. I sent this letter to Senator Rockefeller. He did not respond. However, the information about my naval carrer is in it.

The following is a letter to inform Senator John Rockefeller of my current situation and to see if we may assist each other in anyway. The situation I speak of is my refusal to receive the Anthrax Inoculations. I am currently aboard the USS John C. Stennis deployed to the Arabian Gulf. On March 19th the first of six shots of the Anthrax vaccine was administered. Due to the information I received in regarding the safety and efficacy of the Anthrax vaccine verses the information provided by senior personnel aboard the USS John C. Stennis, I made the decision not to receive the shots. It is important for you to know that this decision was not an easy one. My name is Daniel Lee Hlavac and I am from Houston, Texas. Before joining the Navy I completed one year of college and worked a variety of jobs around the United States. I exceeded at all places of employment and decided to challenge myself further by voluntarily enlisting in the United States Navy as a Naval Intelligence Specialist. I left for the Navy on April 9th 1995 to fulfill my desire of proudly serving my country as my Grandfather and Father had done before me. I currently have ten months left of my enlistment and completed a six-month deployment aboard the USS George Washington in 1996. I say this because I do not want you to think I am looking for an easy way out of the Navy, as most seem to feel.
I am concerned for my future in the Navy and the possibility of receiving a dishonorable discharge. I have been a member of Seaconron Three One (VS-31) out of Jacksonville, Florida since November 28th 1995. In the time serving in this Command I earned many awards and Commendations, including receiving many privileges for my outstanding performance. After my refusal of the Anthrax shots my Commanding Officer has verbally banned me from all squadron work centers and prohibited me from associating with other squadron personnel. I no longer feel I will receive fair treatment or be informed of all of my rights and options concerning my situation. I understand that my future is in the hands of the Chief of Naval

Operations and the Secretary of the Navy. Your position on the Veterans Affairs Committee is the reason I have written you. I am hoping you can shed some light on my options or share with me your opinion on the Anthrax Inoculations. I have many questions and much more to tell of my situation. I am sorry if I have asked too much or wasted your time. The following I have pulled from my Military service record. I have not left out any acts of misconduct or counseling because I have never had any. If you wish to E-mail me my address is: sheehanw@stennis.navy.mil Please notify me if you receive this. I appreciate your time and am looking forward to your response, thank you.

Sincerely,

Daniel Lee Hlavac

The following is a list of all Medals and Ribbons I have received:
National Defense Service Medal
Armed Forces Expeditionary Medal
Armed Forces Service Medal (twice)
Sea Service Deployment Ribbon
Battle "E" Ribbon
NATO Medal
Navy and Marine Corps Achievement Medal
I have also received:
A Letter of Commendation from Captain, USN K.M. Jan
A Letter of Commendation from Rear Admiral, USN Henry C. Giffin, III
I was nominated for Intelligence Specialist of the Year (1997) Navy wide. This package was submitted about four months ago and has since been pulled by my Commanding Officer.
My last Evaluation Report rated me a 4.43 with the max being a 5.0. This is much higher than the average given out in the Navy. I was also submitted as an early promote. This means the Command recommended me to be promoted to the next senior rank, this being E-5/Petty Officer 2nd Class.

Special Training I have received:
Survival, Evasion, Resistance and Escape (SERE)
Cold Weather Environmental Survival Training (CWEST)
Antiterrorism Awareness
Aviation Physiology and Water Survival (this was to become back seat qualified to fly in the S-3B Viking Aircraft, which I flew in several times.

Punishments for refusing the Anthrax Vaccination:
We were given an Administrative Counseling/Warning on 28 March 1998

(NAVPERS 1070/613 (rev. 10-81))
This form states:
1. You are being retained in the naval service, however, the following deficiencies in your performance and/or conduct are identified: Commanding Officer's non-judicial punishment of 24 March 1998 for Violation of the UCMJ, Article 90, Willful disobedience of a superior commissioned officer by not receiving the anthrax vaccination.
2. The following are recommendations for corrective action: Familiarize and comply with existing regulations and the UCMJ. Maintain a positive attitude; review directives on basic military requirements.
3. Assistance is available through: Chain of Command, Chaplain, Command Judge Advocate, CMC, CMAA, CAAC/DAPA.
4. Any further deficiencies in your performance and/or conduct will terminate the reasonable period of time for rehabilitation that this counseling and warning entry implies and may result in disciplinary action and in processing for administrative separation. All deficiencies or misconduct during your current enlistment, occurring before and after the date of this action will be considered. Subsequent violation(s) of the UCMJ or conduct resulting in civilian conviction(s) could result in an administrative separation Under Other Than Honorable Conditions.
5. This counseling and warning entry is made to afford you an opportunity to undertake the recommended corrective action. Any failure to adhere to the guidelines cited above, which is reflected in your future performance and/or conduct, will make you aligible for administrative separation action.
6. This counseling and warning entry is based upon known deficiencies or misconduct. If any misconduct, unknown to the Navy, is discovered after this counseling and warning is executed, this letter of counseling and warning is null and void.

Additional Punishments:
-We were placed on Restriction until 22 April 1998, a period of 30 days.
-Assigned extra duty until 22 April 1998, a period of 30 days.
-Loss of half a months pay for 1 month.
-Reduction in rank from a E-4 to E-3 Naval Intelligence Specialist
-Loss of my security clearance. I had a Top Secret / SCI clearance.
-Temporarily assigned to work for the Mess Decks(cleaning food trays, taking out trash and wiping down tables)
-Pulled my test for E-5
-Also, canceled my Intelligence Specialist of the year package. I was the only Intelligence Specialist in the entire battle group who was nominated to compete for this award which is navy wide.
Thanks for your time Lori.

ATTACHMENT 10

Lori Greenleaf

From: Lori Greenleaf <david.greenleaf@gte.net>
To: Richard Debeauclair <Richard.Debeauclair@ha.osd.mil>
Cc: lori <david.greenleaf@gte.net>; CTC1 <jonhome@swbell.net>; teresaj@cyprstech.com
Subject: Joseph Jones
Date: Monday, March 01, 1999 10:04 AM

To: Dept. of Defense, Health Affairs
Attn: Richard Debeauclair
From: Lori Greenleaf
Re: Joseph Jones, Ft. Benning, GA
SS # 459-97-3373
(706) 561-2232

Dear Rick,

As you requested this morning, the following is information regarding Joseph Jones who is active duty Army, stationed at Ft. Benning, GA.

Joseph Jones, a 22 year old male stationed at Ft. Benning, GA while serving in the Persian Gulf received an anthrax vaccine 3/17/98. He immediately began suffering flu-like symptoms, headaches, bloody diarrhea, tightness in chest, and rash over arms, back, and chest. He received dose two on 3/31/98 and again began suffering the same type symptoms only worse. Joseph went to the medical facility on base, and was given antibiotics to take. On 4/14/98, Joseph was given dose three while still taking antibiotics for symptoms related to dose number two. Once again, the same type symptoms occurred each time worsening. Joseph was given dose number four on 9/22/98, and began having blackouts. Joseph has since suffered 21 blackout spells, the worst happening Thursday, 2/25/98 when medics were unable to detect a pulse during the blackout. Joseph was taken by ambulance to the hospital, where he was checked then released approximately 40 minutes later.

Joseph has been diagnosed with a mass behind the sinus cavity, and is currently scheduled to have a liver biopsy. The medical facility is claiming Joseph has an undiagnosed illness, has stated that he is currently 10-15% disabled, and will be medically boarded out of the Army in the very near future. Joseph and his mother believe these symptoms began immediately after receiving anthrax inoculations. Until his first inoculation, Joseph was a very healthy young man. Joseph has been unable to even drive since 9/98.

The anthrax vaccine doses that Joseph received came from Lot FAV020, which I'm sure you are well aware, were in violation on an FDA inspection report of 2/98. The violation reads as follows:

"There is no written justification for redating lots of anthrax vaccine that have expired. "Redating" testing consists only of a potency test. There is no documentation of testing for container/closure integrity or container/closure compatibility for periods up to 7 years. In addition there is no analytical testing identifying and demonstrating the absence of degradants."

---Lot FAV020 (initial date of potency 4/13/93) was submitted for redating as FAV020-1 and was labeled on 2/6/98 as FAV020.

Unless Joseph is considered 30%+ disabled, he has been told that he will leave the military without medical benefits. I am forwarding the Vaccine Adverse Event Reporting System report of 9/98, which you will find to state 17 adverse reactions similar to what Joseph suffers from have been reported on Lot FAV020, and Lot FAV030. As you will see, the military did not report Joseph's reactions! I have forwarded a VAERS form to Joe's mother, this will be filed in the next day or so.

We are convinced that Joseph's illnesses are caused from the anthrax inoculations. Please do what you can to help Joseph get the medical attention he needs and deserves, and help to see that when Joseph is discharged, he qualifies for his military benefits.

You may reach Joseph at the number listed above, and you may reach his mother Teresa Jones at
(512) 258-9165 or (512) 267-9973.

I look forward to hearing that you have taken the proper steps to help this young man. Time is of the essence here, as Joseph will be medically boarded out in the next few weeks. I have advised Joseph to see a civilian physician before he is discharged from the Army.

Thank you for your assistance in this matter.

Lori Greenleaf
(303) 697-0508

ATTACHMENT 11

LAW OFFICES OF
Jacobs, Grudberg, Belt & Dow, P.C.

360 ORANGE STREET
POST OFFICE BOX 606
NEW HAVEN, CONNECTICUT 06503-0606

TELEPHONE (203) 772-3100
FAX (203) 772-1691

OUR FILE NUMBER
C98-1594R

HOWARD A. JACOBS
IRA B. GRUDBERG
DAVID L. BELT
WILLIAM F. DOW, III
JONATHAN KATZ
SUSAN H. BARTHOLOMEW
CHARLES B. PRICE, JR.
WILLIAM M. BLOSS
SHIRLEY V. HOOGSTRA
MARA R. SOBOSLAI
DAVID T. GRUDBERG
DAVID A. LEFF
STEVEN J. DEFRANK
ALINOR C. STERLING
PHILLIP A. ESCOBEDO
MARYBETH D. GAUTHIER
TRISHA MORRIS PORTO
PERRY ZINN-ROWTHORN

ISRAEL J. JACOBS (1918-1982)

March 22, 1999

Honorable Christopher Shays, Chairman
House Subcommittee on National Security,
[illegible] and International Relations
United States Capitol
Washington, D.C. 20515

Re: Anthrax vaccine

Dear Representative Shays:

Our office represents David Fredette in a serious criminal case in New Haven, involving an assault on two police officers during an apparently delusional episode. Until shortly before the incident, he was a respected member of the United States Merchant Marine, a graduate of the U.S. Merchant Marine Academy, with a spotless record. The incident followed, by a matter of weeks, Mr. Fredette's having been given an anthrax vaccine. At this time, I can do no more than recite the undisputed factual record. Conclusions will need to be drawn by others.

1. Fredette is a 29-year old graduate of the U.S. Merchant Marine Academy, receiving his degree in 1994, and is employed by the American Maritime Officers Union. The U.S. Coast Guard licensed him in 1994 as a 3rd assistant engineer, as a 2nd assistant engineer in 1996, and as a 1st assistant engineer in 1998. He is also licensed as a maritime officer by the Republic of the Marshall Islands and the Republic of Liberia. He received an Associate in Arts degree from the State University of New York at Morrisville in 1990. From 1994 through 1998, he was assigned to various shipping companies, including those serving as part of the Military Sealift Command. His personnel ratings were consistently above average.

2. On May 12, 1998, Fredette was given the anthrax vaccine –apparently from lot FAV 020 -- while serving in the Middle East. On June 6, 1998, his superiors ordered him to seek medical attention for "behavioral changes- past 3-1/2 weeks." The medical request noted that he had received the anthrax shot. A doctor in Dubai

pronounced Fredette unfit for duty due to a "psychiatric disturbance," and recommended a further psychiatric evaluation. He was sent to London, where he was diagnosed with "delusional disorder," unspecified, as defined in the DSM-IV 297.1. He was ordered to return to the United States, with an escort. His employer discharged him from duty.

3. While traveling through Connecticut on July 7, 1998, he apparently stopped his automobile on the shoulder of I-95 near New Haven for no apparent reason. Two police officers approached his car to see whether he needed help. Certain aspects of what happened next are uncertain, but it is clear that a violent incident resulted in both officers being hurt, one seriously. According to police reports, when police approached him, Fredette glared at the officer with teeth clenched and body tensed. Although police ordered him to remain in his car, he left the car, although eventually he returned. Because of bizarre behavior, police ordered him to step out of the car and stand at the back of the car. Reports say that Fredette refused, staring angrily, again with clenched teeth. Police say that because they were concerned for his safety, they attempted to lead him to the back of his car, away from the road, but Fredette began fighting. Fredette yelled a variety of nonsensical sayings, including "raise the gates and we shall be set free." Reportedly he tried to grab one officer's gun, and tried to push one or both into traffic (along with himself). Both officers were injured in the fighting, one seriously (he is still out of work, and is likely to be for many more months). Fredette was taken to a local hospital for treatment of physical and psychiatric injuries.

4. There is nothing in Fredette's background even remotely resembling this incident. He has no past criminal record. The preeminent forensic psychiatrist in New Haven has concluded that Fredette was legally insane at the time of the incident.

5. Since July 8, 1998, Fredette has been in psychiatric treatment, both in-patient and out-patient. Various delusions have been reported. One psychiatrist has diagnosed his condition as severe bipolar affective disorder. Suffice it to say that lengthy treatment will be required.

Mr. Fredette had no history of mental illness prior to May 12, 1998, when he received the anthrax vaccine. Almost immediately thereafter, his superiors reported "behavioral changes" and delusions, serious enough to make him unfit for duty less than one month later. It is not my place to offer conclusions, and I would not presume to do so. However, the timing of the vaccination and the subsequent problems -- which have led to two police officers being injured and a promising career as a Merchant Marine officer in tatters – strongly suggest that this Committee ought to review the

evidence carefully in order to determine any possible effect of the anthrax vaccine on those receiving it. Please do not hesitate to contact me if I may provide further information.

Respectfully Submitted,

JACOBS, GRUDBERG, BELT & DOW, P.C.

By _____
William M. Bloss

ATTACHMENT 12

VAERSID	Age	Sex	Vaccines	Dates	Vaccine	Onset	Days	Status	Birth	ST	MFR Report ID
51014	41	0	M	ANTH CHOL MEM TYP	01-JAN-1991	PAR NULL	1	05-APR-1991	07-SEP-1952		NULL
SERIOUS:			DISABILITY HOSPITALIZD	10 days							
SYMPTOMS:			ARTHRALGIA/ASTHENIA/DYSPNEA/LAB TEST ABNORM/RASH/								
51015	18	F	M	ANTH CHOL MEM TYP	01-JAN-1991	SAR NULL	1	05-APR-1991	08-MAR-1973		NULL
SERIOUS:			HOSPITALIZD	14 days							
SYMPTOMS:			ASTHENIA/DYSPNEA/RES INCR/LAB TEST ABNORM/RASH/								
51016	28.3	M	ANTH CHOL MEM TYP	NULL	SAR NULL	1	05-APR-1991	01-FEB-1955		NULL	
SERIOUS:			HOSPITALIZD	6MM days							
SYMPTOMS:			ARTHRALGIA/ASTHENIA/LAB TEST ABNORM/PAIN ABDO/								
51021	38M	M	ANTH CHOL MEM TYP	25-DEC-1990	UNK NULL	1	05-APR-1991	NULL		NULL	
SYMPTOMS:			ARTHRALGIA/ASTHENIA/LAB TEST ABNORM/LYMPHADENOPAT/RASH/								
107870	31.3	M	ANTH	20-JAN-1990 Rec'd 21-JAN-1990		31	17-FEB-1991	06-JUN-1960	TX	NULL	
DIEDDATE:			BODY INJECT SITE/HEAD INJECT SITE/MASS INJECT SITE/								
110544	35.1	M	ANTH	02-APR-1990 Rec'd 11-APR-1990		31	11-MAY-1990	13-MAR-1955	MD	NULL	
SYMPTOMS:			RASH INJECT SITE/PAIN INJECT SITE/PSE RECTAL/								
111115	30.4	M	ANTH	17-MAY-1990 Rec'd 18-MAY-1990		31	18-JUN-1990	13-JAN-1960			
SERIOUS:			HOSPITALIZD	13 days	CAPR THERAPY						
SYMPTOMS:			CAIN ABNORM/GUILLAIN BARRE SYND/HYPOKINESIA/LAB TEST ABNORM/MYASTHENIA/MYOPATHY/NEUROPATHY/PARESTHES OOC								
112153	24.8	M	ANTH	23-APR-1990 Rec'd 25-APR-1990		31	25-JUN-1990	25-APR-1970	HS	NULL-E0901222	
SYMPTOMS:			ASTHENIA/DEARN-ZA DE PLOPSA/DIZZINESS/HYPERHIDROSIS/PSE RECTAL/								
112856	24.4	M	ANTH	15-APR-1990 Rec'd 15-APR-1990		01	15-JUN-1990	15-APR-1970	SD	NULL-E0901222	
SYMPTOMS:			DIZZINESS/SYNCOPE/VERTIGO/								
113330	32.0	M	ANTH	31-MAR-1990 Rec'd 01-APR-1990		-21	11-AUG-1990	31-MAR-1970	CC	NULL	
SYMPTOMS:			HEADACHE/								
113339	32.1	M	ANTH	30-APR-1990 Rec'd 19-APR-1990		11	11-AUG-1990	31-MAR-1970	CC	NULL	
SYMPTOMS:			HEADACHE/PSE RECTAL/								
113360	32.1	M	ANTH	24-MAY-1990 Rec'd 24-MAY-1990		01	11-AUG-1990	31-MAR-1970	CC	NULL	
SYMPTOMS:			HEADACHE/PSE RECTAL/								
113347	UNK	M	ANTH	31-MAR-1990 Rec'd NULL		1	18-AUG-1990	18-FEB-1977	PA		
SYMPTOMS:			BODY INJECT SITE/								
113360	UNK	M	ANTH	17-APR-1990 Rec'd NULL		1	16-AUG-1990	31-MAR-1977	PA		
SYMPTOMS:			BODY INJECT SITE/PSE RECTAL/								
113369	21.2		ANTH	26-APR-1990 Rec'd 29-APR-1990		11	18-AUG-1990	28-FEB-1977	PA		
SYMPTOMS:			CHILLS/FLU SYND/								
113513	UNK		ANTH	25-MAR-1990 Rec'd 26-MAR-1990		11	30-AUG-1990	NULL		NULL	
SYMPTOMS:			DRUGS/PARALYSIS/HEADACHE/								
113517	UNK		ANTH	24-MAY-1990 Rec'd 26-MAY-1990		01	25-AUG-1990	NULL		NULL	
SYMPTOMS:			BODY INJECT SITE/HEAD INJECT SITE/PAIN INJECT SITE/								
113518	UNK		ANTH	11-MAY-1990 Rec'd 17-MAY-1990		01	26-AUG-1990	NULL			PUB
SYMPTOMS:			ALLERG REACT/PROSTATUS/RASH/								

VAERSID	Age	Sex	Vaccines	Dates	Vaccine	Onset	Days	Status	Birth	(ST)	VERS Report ID
113515	11.2	F	MMR	14-JUL-1999	MMR	25-JUL-1999	11		15-AUG-1987	17-MAY-1971	(N) (MIL)
COMMENTS:	DIZZINESS/VOMIT/										
113710	13.6	F	MMR	29-AUG-1996	MMR	05-AUG-1998	341		23-SEP-1984	08-APR-1969	(UNK) (MIL)
COMMENTS:	PARESTHESIA/										
113742	17.5	M	MMR	14-AUG-1998	MMR	15-AUG-1998	1		01-SEP-1981	03-FEB-1971	(UNK) (MIL)
COMMENTS:	MYALGIA/MUSCULR SKIN/PAIN/RASH/VASCULITIS/										
113743	21.7	M	MMR HEP	25-JUN-1998	MMR	15-AUG-1998	51		01-SEP-1998	16-NOV-1974	(UNK) (MIL)
COMMENTS:	ANGIOEDEMA/DIZZINESS/HEADACHE/HYPOTENSION/ INJECT SITE/VISUAL FIELD DEFECT/										
113744	21.8	M	MMR VAR	01-AUG-1998	MMR	01-AUG-1998	0		01-SEP-1998	11-JUL-1975	(UNK) (MIL)
COMMENTS:	PAIN CHEST/SYNCOPE/										
114318	21.7	M	MMR	01-AUG-1998	MMR	31-AUG-1998	30		21-SEP-1998	16-DEC-1974	( ) (MIL)
COMMENTS:	ASTHENIA/EDEMA INJECT SITE/EDEMA PERIPH/HYPOTENSION/ INJECT SITE/NAUSEA VOMIT/VASCULITIS/										
114352	21.7	F	MMR	10-MAR-1998	MMR	30-MAR-1998	20		24-SEP-1998	23-JUL-1976	( ) (MIL)
COMMENTS:	EDEMA INJECT SITE/FEVER/MYALGIA/										
114391	17.7	F	MMR	24-MAR-1998	MMR	14-APR-1998	21		24-SEP-1998	23-JUL-1979	( ) (MIL)
COMMENTS:	EDEMA INJECT SITE/FEVER/HEADACHE/NAUSEA/PAIN INJECT SITE/SOMNOLENCE/										
114516	21.1	M	MMR	15-SEP-1998	MMR	19-SEP-1998	4		26-SEP-1998	31-JUL-1977	(UNK) (MIL)
COMMENTS:	REACT ADVERSE/										
114613	14.1	F	MMR	15-SEP-1998	MMR	16-SEP-1998	1		01-OCT-1998	19-NOV-1983	(UNK) (MIL)
COMMENTS:	PEDIATRICS/RASH/										
114614	14.1	M	MMR	14-SEP-1998	MMR	15-SEP-1998	1		30-OCT-1998	05-AUG-1984	(UNK) (MIL)
COMMENTS:	HEADACHE/MYALGIA/MUSCULR SKIN/PAIN/RASH/										
114721	13.5	F	MMR FLU	15-SEP-1998	MMR	28-SEP-1998	13		07-OCT-1998	21-APR-1975	(UNK) (MIL)
COMMENTS:	EDEMA INJECT SITE/HYPH INJECT SITE/MASS INJECT SITE/PAIN INJECT SITE/PRURITUS/VASCULITIS/										
114722	15.9	F	MMR FLU	15-SEP-1998	MMR	25-SEP-1998	10		07-OCT-1998	14-SEP-1973	(UNK) (MIL)
COMMENTS:	EDEMA INJECT SITE/HYPH INJECT SITE/PAIN INJECT SITE/										
114723	22.7	F	MMR FLU	22-SEP-1998	MMR	25-SEP-1998	3		07-OCT-1998	06-JAN-1976	(UNK) (MIL)
COMMENTS:	DIARRHEA/PAIN ABDO/STOOL ABNORM/										
115329	21.8	M	MMR	01-APR-1998	MMR	NULL			23-OCT-1998	17-DEC-1987	(UNK) (MIL)
COMMENTS:	DIARRHEA/FEVER/MALAISE/RESPIR DISORDER NOS/ PROV REACT/										
115374	25.3	M	MMR	15-SEP-1998	MMR	02-OCT-1998	17		14-OCT-1998	17-NOV-1973	(UNK) (MIL)
COMMENTS:	MYALGIA/PARESTHESIA/PARESTHESIA/TREMOR/										
115375	23.0	M	MMR	23-SEP-1998	MMR	23-SEP-1998	0		14-OCT-1998	NULL	(UNK) (MIL)
COMMENTS:	ARTHRALGIA/CHILLS FEVER/DYSPNEA/MYALGIA/PAIN CHEST/										
115376	18.3	F	MMR	21-SEP-1998	MMR	24-SEP-1998	3		14-OCT-1998	12-JUN-1980	(UNK) (MIL)
COMMENTS:	EDEMA INJECT SITE/EDEMA PERIPH/HYPOT INJECT SITE/MALS INJECT SITE/MYALGIA/PAIN/PRURITUS/										
115537	24.7	F	MMR	25-AUG-1998	MMR	25-AUG-1998	0		01-NOV-1998	NULL	( ) (MIL)
COMMENTS:	ALLERG REACT/COUGH INC/EDEMA INJECT SITE/HEADACHE/HYPOT INJECT SITE/PAIN CHEST/PAIN INJECT SITE/PRURITUS/										
115540	42.7	F	MMR	14-SEP-1998	MMR	14-SEP-1998	0		01-NOV-1955	07-JAN-1965	( ) (UNK)
COMMENTS:	ADRENYL/BRADYCARDIA/DIZZINESS/DYSPNEA/HYPOTENS/HYPOTENSION/NAUSEA VOMIT/RASH XXC FAX/										

115541 50 F ; ANTH ; 25 AUG-1990 Exp 27 AUG-1550 ; 3| 05-NOV-1990 11 FEB-1944 ; ; (NULL)
COSTARTS: DYSPNEA/HYPOTENSION?/OTHER?/N/A,SKIN/PAIN/CHEST/PHARYNGITIS/RHINITIS/

115581 41 M ANTH ; 25-AUG-1990 Exp 25-AUG-1550 ; 3| 05-NOV-1990 24-SEP-1956 ; ; (NULL)
COSTARTS: DYSPEPSIA/FLU SYND/HEADACHE/MYSTH INJECT SITE/MALAISE/PARESTHESIA/

115581 32 M ANTH ; 15-AUG-1990 Exp 25-AUG-1990 ; 3| 05-NOV-1990 28-APR-1966 ; ; (NULL)
COSTARTS: ARTHRALGIA/ASTHENIA/CHILLS/FEVER/MALAISE/RHINITIS/

115604 32.5 F ANTH ; 23-SEP-1990 Exp 23-SEP-1550 ; 3| 05-NOV-1990 17-MAR-1966 [CA] (NULL)
COSTARTS: FEVER/FLU SYND/PROD REACT/RHINITIS/

115703 34 F M ANTH ; 04-OCT-1990 Exp 04-OCT-1550 ; 3| 05-NOV-1990 25-JUN-1956 ; ; (NULL)
COSTARTS: ARTHRALGIA/CHILLS/HEADACHE/NAUSEA/PROD REACT/SWEAT/

115895 25.1 M ANTH ; 16-OCT-1990 Exp 16-OCT-1990 ; 6| 13-NOV-1990 31-DEC-1973 [CA] (NULL)
COSTARTS: PAIN/PROSTATIS/SMALL ERY/VASCULAT/

116158 54 F M ANTH ; 17-OCT-1990 Exp 19-OCT-1990 1| 16-NOV-1990 NULL ; ; (NULL)
SERIOUS. HOSPITALIZN ; 3 days)
COSTARTS ALLERG REACT/CHILLS/ITIS/EDEMA INJECT SITE/EDEMA FACE/FEVER/HYPOKINESIA/MYSTH INJECT SITE/VASCULAT/

116078 32 M F ANTH ; 25-SEP-1990 Exp 25-SEP-1990 3| 13-NOV-1990 29-MAR-1967 ; ; (NULL)
COSTARTS: ALLERG REACT/ARTICHOKE/

116081 54 F F ANTH ; 25-SEP-1990 Exp 25-SEP-1990 3| 12-NOV-1990 23-FEB-1944 ; ; (NULL)
COSTARTS: DYSPNEA/EDEMA FACE/EDEMA INJECT SITE/EDEMA FACE/HEADACHE/HYPESTHES/POS RECHAL/PROV REACT/

116093 35.1 M ANTH ; 24-SEP-1990 Exp 25-SEP-1990 3| 12-NOV-1990 02-OCT-1963 ; ; (NULL)
COSTARTS: MYSTH INJECT SITE/INJECT SITE REACT/VASCULAT/

117043 22.1 F ANTH ; 19-SEP-1990 Exp 19-SEP-1990 1| 12-NOV-1990 31-DEC-1973 ; ; (NULL)
COSTARTS: EDEMA INJECT SITE/PAIN INJECT SITE/

112004 30.1 F ANTH ; 15-OCT-1990 Exp 16-OCT-1990 1| 15-NOV-1990 04-SEP-1960 ; ; (NULL)
COSTARTS: EDEMA INJECT SITE/EDEMA FACE/INCONTIN INJECT SITE/MASS INJECT SITE/PROSTATIS/VASCULAT/

116085 24 M M ANTH ; 27-SEP-1990 Exp 27-SEP-1990 3| 12-NOV-1990 19-DEC-1973 ; ; (NULL)
COSTARTS: HYPOKINESIA/MYSTH INJECT SITE/VASCULAT/

116086 43.1 F ANTH 21-SEP-1990 Exp 23-SEP-1990 1| 13-NOV-1990 07-NOV-1956 ; ; (NULL)
COSTARTS: ALLERG REACT/EDEMA/EDEMA INJECT SITE/MYSTH INJECT SITE/POS RECHAL/PROV REACT/RHINITIS/RASH/

116106 25.1 M M ANTH ; 05-OCT-1990 Exp 07-OCT-1990 1| 15-NOV-1990 NULL ; ; (NULL)
COSTARTS: EDEMA INJECT SITE/MYSTH INJECT SITE/MASS INJECT SITE/THROMBOPEN/

116116 22.1 M M ANTH ; 06-OCT-1990 Exp 09-OCT-1990 1| 13-NOV-1990 28-NOV-1975 ; ; (NULL)
COSTARTS: MYSTH INJECT SITE/MASS INJECT SITE/

116135 24.1 M ANTH PCP) 14-OCT-1990 Exp 17-OCT-1990 1| 13-NOV-1990 01-JUL-1970 ; ; (OTH)
SERIOUS: HOSPITALIZN ; 2 days)
COSTARTS: EDEMA INJECT SITE/MYSTH INJECT SITE/PAIN INJECT SITE/VASCULAT/

116135 29K M ANTH ; 15-MAR-1990 Exp 31-MAR-1990 ?| 12-NOV-1990 NULL ; ; (NULL)
COSTARTS: ARTHRALGIA/ASTHENIA/CHILLS FEVER/COUGH INC/HEADACHE/INJECT SITE REACT/MYALGIA/SINUSITIS/

116143 35 M M ANTH) 23-APR-1990 Exp 25-MAY-1990 1| 15-NOV-1990 20-DEC-1962 [CA] (NULL)
COSTARTS: ACNE/ANOREXIA/ARTHRALGIA/ASTHENIA/CONFUS/CONSTIP/CONVULS/DIARRHEA/DIZZINESS/EDEMA FACE/ERUCTATION LACRIM/ECH DIS/FEBRILE R
EC MALE/HEADACHE/HYPERKINESIA/HYPOKINESIA/HYSTERIA/MIGRAINE/MYALGIA/MYASTHENIA/PAIN/PAIN CHEST/PARESTHESIA/PERIS DIS/PHARYNGITIS/RECTA
L DIS/SKIN DISCOLOR/SWEAT/SYNCOPE/THINKING ABNORM/TREMOR SKIN/VASCULAT/

VAERS ID# Age Sex (Vaccines) Dates Vaccine Onset S days) Status Birth (ST) (NPR Report ID)

1186935 23.5 M (ANTH) 16-NOV-1998 Acc 16-NOV-1998 (0) 07-DEC-1958 29-MAY-1975 ( ) (MIL)
COSTARTS: RASH?

1187027 23.6 M (ANTH FLU) 28-SEP-1998 Acc 28-SEP-1998 (0) 09-DEC-1998 15-FEB-1975 (HO) (MIL)
COSTARTS MUCOUS MEM DIS/PHARYNGITIS/PERI REACT/SOCIAL WORKER

1187056 23.6 M (ANTH) 19-NOV-1998 Acc 19-NOV-1998 (0) 09-DEC-1998 15-APR-1975 ( ) (MIL)
SERIOUS: HOSPITALIZ (days)
COSTARTS: ANGIOEDEMA/EDEMA/POS RECHAL/PREV REACT/

1187113 23.5 F (ANTH) 21-NOV-1998 Acc 21-NOV-1998 (0) 15-DEC-1998 26-MAY-1975 (HO) (MIL)
COSTARTS: EDEMA FACE/PAIN SYE/PHOTOPHOBIA/POS RECHAL/PREV REACT/PRURITUS/

1187115 23.5 M (ANTH) 23-NOV-1998 Acc 24-NOV-1998 (1) 15-DEC-1998 19-MAR-1961 (HO) (MIL)
COSTARTS: POS RECHAL/PREV REACT/PRURITUS/RASH/

1187141 22.1 F (ANTH) 14-NOV-1998 Acc 18-NOV-1998 (4) 16-DEC-1998 24-NOV-1976 ( ) (MIL)
COSTARTS: GENERAL SKIN/RASH/RASH VESIC NEC/

1187187 19.7 M (ANTH HERA TO TYP) 25-NOV-1998 Acc 26-NOV-1998 (1) 10-DEC-1998 20-MAR-1979 (DA) (MIL)
SERIOUS: HOSPITALIZ (days)
COSTARTS: CHILLS/FEVER/HEADACHE/MYALGIA/PAIN BACK/SWEAT/

1187231 22.2 F (ANTH) 01-DEC-1998 Acc 01-DEC-1998 (0) 23-DEC-1998 11-SEP-1976 (RS) (MIL)
COSTARTS DYSPNEA/PRURITUS/RASH/

1187561 30.1 M (ANTH) 11-DEC-1998 Acc 11-DEC-1998 (0) 11-DEC-1998 26-FEB-1968 (DO) (MIL)
DUPLICATES: 1187561 ——— Dup Of -> 1187831
COSTARTS: EDEMA INJECT SITE/EDEMA PERIPH/VASODILAT/

1187604 36.0 M (ANTH) 11-DEC-1998 Acc 11-DEC-1998 (2) 04-JAN-1999 16-FEB-1962 (DO) (MIL)
DUPLICATES: 1187561 ——— Dup Of -> 1187604
COSTARTS: EDEMA/EDEMA PERIPH/HYPERSENSITIV/

1187881 36.0 M (ANTH) 13-NOV-1998 Acc 13-NOV-1998 (0) 06-JAN-1999 28-JUN-1978 ( ) (MIL)
COSTARTS: FEVER/HEADACHE/NAUSEA/POS RECHAL/PREV REACT/

1188571 36.0 M (ANTH) 13-JAN-1999 Acc 21-JAN-1999 (11) 04-FEB-1999 02-APR-1962 (PL) (MIL)
COSTARTS: RASH/

1188614 28.2 M (ANTH) 12-MAY-1998 Acc 04-JUN-1998 (373) 11-FEB-1999 19-MAY-1978 ( ) (MIL)
SERIOUS: HOSPITALIZ (30 days)
COSTARTS: EXTRACTING ABNORMAL

1188710 34.9 M (ANTH) 21-JAN-1999 Acc 26-JAN-1999 (5) 17-FEB-1999 18-DEC-1964 (CA) (MIL)
COSTARTS: EDEMA INJECT SITE/PAIN INJECT SITE/PAIN INJECT SITE/PRURITUS/

1188756 35.1 M (ANTH) 14-OCT-1998 Acc 21-OCT-1998 (7) 17-FEB-1999 18-JUN-1963 (HO) (PUB)
COSTARTS: EDEMA/LYMPHADENO/PAIN/POS RECHAL/PREV REACT/

1188771 36.1 M (ANTH FLU EDEMA DEV TOP) 15-JAN-1999 Acc 18-JAN-1999 (3) 18-FEB-1999 16-SEP-1972 (HO) (MIL)
COSTARTS /PARAMYOCLONUS/CONVULSION/

1188814 21.1 M (ANTH) 15-JAN-1999 Acc 16 JAN-1999 (1) 18-FEB-1999 16-NOV-1977 (AZ) (MIL)
COSTARTS: PRURITUS/RASH/

1188838 37.5 F (ANTH) 15-JAN 1999 Acc 06 JAN-1999 (1) 21-FEB 1999 01-AUG-1961 (NC) (MIL)
COSTARTS: FEVER/MASS INJECT SITE/POS RECHAL/PREV REACT/PRURITUS/

VAERS ID	VAX LOT
51414	
51415	
51416	
51431	
107470	FAV016
110504	FAV020
111835	FAV020
112155	FAV020
112156	FAV020
113338	FAV020
113339	FAV020
113340	FAV020
113367	FAV020
113368	FAV020
113369	FAV020
113512	FAV020
113513	FAV020
113514	FAV020
113595	FAV017
113740	FAV030
113742	FAV030
113745	FAV030
113746	FAV030
114290	FAV020
114292	FAV020
114293	FAV020
114365	FAV030
114513	FAV030
114514	FAV030
114721	FAV030
114722	FAV030
114723	FAV030
115329	FAV020
115374	FAV017
115375	FAV017
115376	FAV017
115537	
115540	FAV017
115541	
115560	
115561	
115614	FAV019
115722	FAV017
115895	FAV034
116058	
116078	FAV017
116081	
116082	FAV017
116083	FAV017
116084	
116085	FAV017
116086	
116116	FAV017

116118 FAV017
116125 FAV017
116135 FAV020
116443 FAV020
116975 FAV030
117077 FAV030
117106 FAV030
117113 FAV034
117115 FAV034
117143 FAV030
117197 FAV034
117321 FAV030
117561 FAV030
117684 FAV030
117881 FAV034
118527 FAV036
118650 FAV020
118714 FAV034
118756 FAV030
118777 FAV017
118818 FAV034
119038 FAV030
119084 FAV017
119279
119382 FAV030
119383 FAV030
119698 FAV030
119752 FAV033
119753 FAV033
119781 FAV020
120109 FAV020

IVEC W/ Vaccine Adverse Event Reporting System Database Line List |
Total Distinct Records (excluding duplicates): 86

Thu Sep 17

VACCINE ADVERSE EVENT REPORTING SYSTEM (VAERS)
LINE LISTING OF VACCINE ADVERSE EVENT REPORTS
RECEIVED BETWEEN 01-JUL-98 AND 17-SEP-98
VAERSTOI

VAERS ID NUMBER	VACCINES GIVEN /MFR CNTRL	LOT	AGE AT ILLN S. YRS	BIRTH DATE	S E X	CONSULT DATE	ONSET DATE	DAYS BTW	DAYS THRU	S E R	HOSP	D A S	L I F E	D I E D
107170	ANTH MICHIGAN D FAV016		33.7	06-JUN-1964	M	TX 20-JAN-1998	22-JAN-1998	2						Y

CONTACT TERMS (EVENTS):
MTSN INJECT SITE EDEMA INJECT SITE MASS INJECT SITE

REPORT TEXT:
12cm x 4cm x 4cm red swollen nodule to lt deltoid;no discharge, +redness, +tenderness, negative streaking;no tx;

113595	ANTH MICHIGAN D FAV017		24.2	27-MAY-1974	M	AZ 16-JUL-1998	23-JUL-1998	7						Y

CONTACT TERMS (EVENTS):
DIZZINESS VOMIT

REPORT TEXT:
pt recv vax 16JUL98 AM & seen @ clinic 23JUL98 645PM for c/o dizziness & vomiting x3 episodes;exam by MD concluded NL results;no tx given;

110504	ANTH MICHIGAN D FAV020		39.1	30-MAR-1959	M	MB 02-APR-1998	11-APR-1998	9						Y

CONTACT TERMS (EVENTS):
MTSN INJECT SITE PAIN INJECT SITE FOR RECALL

REPORT TEXT:
severe red, painful arm @ site of inj;

111835	ANTH MICHIGAN D FAV020		24.4	13-JAN-1974	M	17-MAY-1998	18-MAY-1998	1	Y	Y	Y	13		U

CONTACT TERMS (EVENTS):
MYASTHENIA MYOPATHY GUILLAIN BARRE SYND HYPOKINESIA

REPORT TEXT:
pt recv vax & noted weakness of feet-over next 24hr worsens to include knees & hands;pt adm to hosp EMG showed conduction abn of leg
s & hands;dx GBS;pt able to walk small distances & fine motor of hands improving;

112155	ANTH MICHIGAN D FAV020	ID98022	24.0	26-APR-1974	M	ID 29-APR-1998	29-APR-1998	3	Y					N

CONTACT TERMS (EVENTS):
DIPLOPIA DIZZINESS NAUSEA ASTHENIA DIARRHEA FOR RECALL

REPORT TEXT:
double vision;dizziness;nausea;fatigue;diarrhea;tx w/rest/phenergan/antivert;

112156	ANTH MICHIGAN D FAV020	ID98022	24.0	26-APR-1974	M	ID 15-APR-1998	15-APR-1998	0	Y					N

CONTACT TERMS (EVENTS):
SYNCOPE VERTIGO DIZZINESS

REPORT TEXT:
pt recv vax & passed out, exp vertigo & dizziness;

VACCINE ADVERSE EVENT REPORTING SYSTEM (VAERS)
LINE LISTING OF VACCINE ADVERSE EVENT REPORTS
RECEIVED BETWEEN 01-JUL-90 AND 17-SEP-98
VAERSTDI

VAERS ID NUMBER	VACCINES GIVEN	LOT NUMBER	AGE AT VAX	BIRTH DATE /MFR CNTRL	S E X	ONSET DATE	INT DAYS	LIFE THRT	S DATE RECVD	S C I D E P	L V D

CONTARY TERMS (EVENTS)

REPORT TEXT

113368 ANTH 19-FEB-1977 M PA 17-APR-1998 Y
MICHIGAN D FAV020
EDEMA INJECT SITE POS RECHAL

pt exp swelling in arm whot was given;

113369 ANTH 21.2 19-FEB-1977 PA 28-APR-1998 29-APR-1998 1 Y
MICHIGAN D FAV020
CHILLS FLU SYND

pt recv vax & devel severe cold, felt like the flu (4 days);

113512 ANTH 25-MAR-1998 26-MAR-1998 1 T Y
MICHIGAN D FAV020
MALAISE MYALGIA FEVER

pt recv vax 4 4hr later exp malaise, myalgias & T102.2 w/o any preceding;viral-like sx & no localizing source of infect;

113513 ANTH 24-MAY-1998 24-MAY-1998 0 T Y
MICHIGAN D FAV020
NYSN INJECT SITE EDEMA INJECT SITE PAIN INJECT SITE

pt had redness, swelling & pain from inj site (upper tricep) to lower forearm;thi occured w/in 2 days p/vax;pt adm for 24hr of ATB
& arm elevation w/good results;pt switched 6 day course to ATB;

113514 ANTH 17-MAR-1998 17-MAR-1998 0 Y
MICHIGAN D FAV020
ALLERG REACT RASH PRURITUS

systemic potentially allerg rxn to last vax;pt had rash & itchy trunk & face 17MAR98;

113740 ANTH 29.4 08-APR-1969 F NM 25-AUG-1998 25-AUG-1998 0
MICHIGAN D FAV030
PARESTHESIA

approx 35min p/vax pt c/o numbness & tingling to rt side of face, back, shoulder, & arm;

113742 ANTH 27.5 03-FEB-1971 M MM 14-AUG-1998 15-AUG-1998 1
MICHIGAN D FAVO30
PAIN VASCULITIC MODULE SKIN MYALGIA RASH

tender, red lump w/soreness in muscle;inc in redness, soreness;erythema >= 5cm w/redness;

113745 ANTH REP 23.7 16-NOV-1974 M MM 29-JUN-1998 03-AUG-1998 35 Y
MICHIGAN D FAVO30
AMBLYOPIA VISUAL FIELD DEFECT DIZZINESS HEADACHE MTSN INJECT SITE

5 days p/vax 83 pt c/o blurred vision, tunnel vision, lightheadedness, h/a (pinpointed in back of head);local sun inj site erythema
1-5cm (diameter);

113746 TYP ANTH 23.0 31-JUL-1975 M MM 04-AUG-1998 04-AUG-1998 0 Y Y
MICHIGAN D FAVO30
SYNCOPE PAIN CHEST

appox 5min p/vax pt sat down in waiting area & passed out;when pt came to a few seconds later, c/o tightness in chest;pt was seen b
y MD & released;

51414 TYP MEN CHOL AN 41.0 07-SEP-1952 M 01-JAN-1991 Y 10 Y N
UNCLASSIFI

INT=INTERVAL (ONSET DATE - DATE GIVEN), HT = STATE, ER = EMERGENCY ROOM VISIT, DSBL = DISABLED, RCOV = RECOVERED

Thu Sep 17

VACCINE ADVERSE EVENT REPORTING SYSTEM (VAERS)
LINE LISTING OF VACCINE ADVERSE EVENT REPORTS
RECEIVED BETWEEN 01-JUL-90 AND 17-SEP-96
/VAERSPOI

VAERS ID NUM	VACCINES GIVEN	LOT NUMBER	AGE AT VAX	BIRTH DATE	SEX M/F	STATE GIVEN	ONSET DATE	INT DAYS	LIVE ER	DAYS HOSP	DIED	L.T.D.	BIRTH DEFECT

COMPANY TERMS (EVENTS)

REPORT TEXT

TH

ARTHRALGIA ASTHENIA RASH DYSPNEA LAB TEST ABNORM

joint pain, fatigue & rash feet, dyspnea hosp FEB93 to MAR93;

51415 TYP MEN CHOL AN 43.0 06-MAR-1950 F 01-JAN-1991 Y 14 N
UNCLASSIFI
TH

RASH DYSPNEA ASTHENIA ESR INC LAB TEST ABNORM

rash feet & rt hand dyspnea & fatigue;

51416 TYP MEN CHOL AN 34.0 03-FEB-1959 M Y U
UNCLASSIFI
TH

PAIN ABDO ASTHENIA ARTHRALGIA LAB TEST ABNORM

abdo pain, fatigue, joint pain; hosp 18MAR93;

51431 TYP MEN CHOL AN M 05-DEC-1990
UNCLASSIFI
TH

RASH ARTHRALGIA ASTHENIA LYMPHADENO LAB TEST ABNORM

rash hands, joint pains, fatigue, lymph node swelling;

INT-INTERVAL (ONSET DATE - DATE GIVEN), ST = STATE, ER = EMERGENCY ROOM VISIT, DISBL = DISABLED, RECOV = RECOVERED

23 rows selected.

113338 ANTH 22.0 31-MAR-1976 M 31-MAR-1998 01-APR-1998 1 Y
MICHIGAN D FAV020
HEADACHE

h/a for approx 2wk p/vax;started one day p/vax given;

113339 ANTH 22.1 31-MAR-1976 M 28-APR-1998 29-APR-1998 1 Y
MICHIGAN D FAV020
HEADACHE POS RECHAL

h/a for approx 2wk p/vax;started 1 day p/vax;

113340 ANTH 22.1 31-MAR-1976 M 14-MAY-1998 14-MAY-1998 0 Y
MICHIGAN D FAV020
HEADACHE POS RECHAL

h/a for approx 2wk p/vax;started one day p/vax given;

113367 ANTH 19-FEB-1977 M PA 31-MAR-1998 Y
MICHIGAN D FAV020
EDEMA INJECT SITE

pt exp swelling in rt arm where the shot was given;

INT-INTERVAL (ONSET DATE - DATE GIVEN), ST = STATE, ER = EMERGENCY ROOM VISIT, DSBL = DISABLED, RCOV = RECOVERED

ATTACHMENT 13

Lori Greenleaf

From: thomas nolan <twista69@hotmail.com>
To: david.greenleaf@gte.net
Subject: Anthrax
Date: Monday, September 14, 1998 12:11 AM

Lori,
I recieved my first anthrax shot on 9 Sep, 98. I experienced flu symptoms and after worked used the bathroom and noticed blood in my stool. I told my chain of comand and they sent me to the doctor (military) and he said it was an ulcer. My stomach still is feeling upset and i have been having migrain headaches. Do you think these symptoms can be related to the first shot I recieved? If so what should I do to go about getting it anitated on my medical records because the doctor insists that it is an ulcer. Thank you
Tommy
USA Army

Lori Greenleaf

From: thomas nolan <twista69@hotmail.com>
To: david.greenleaf@gte.net
Subject: Re: Anthrax
Date: Monday, September 14, 1998 3:52 PM

Lori,
I have never had ulcer problems in the past. My stomach pain and bloody stool started that night after I recieved the shot. I havent had any bloody stools since then but ever time i eat i get really bad cramps and its hard to hold food down. same as my roommate he was dry heaving the day after the shot and still has stomach prblem through out the day. the doctor also insisted to him it was an ulcer. there are also others with diarea, headaches, and numbness in extremeties. certain people have only been feeling certain ways and others it didnt even effect. I will let you know as soon as possible what the doctor says when I return today. because my second shot is due very soon. thanks
Tommy

2000033-0000002

(34)

Congressional

SECRETARY OF DEFENSE CORRESPONDENCE ROUTING SLIP

Action Agency: GWI
Action Required: **REPLY DIRECT (Forward copy of reply to CCD, Room 3A948)**
Coordinate With: **LA**

Remarks:

Special Instructions:

Suspense Date: **February/22/2000**	Routing Date: **January/31/2000**	OSD CONTROL #: **U01329-00**

INFORMATION DISTRIBUTION

OFFICE

ASD (LEGISLATIVE AFFAIRS)

CMAT Control #
2000033-0000002

SECRETARY OF DEFENSE CORRESPONDENCE ACTION REPORT

This form must be completed and forwarded to the Correspondence Control Division (CCD), WHS Room 3A948. Suspense Desk: (b)(6) FAX Number: (b)(6) Email: (b)(6)@osd.pentagon.mil

Action Agency	GWI
Suspense Date	02/22/2000

1. ACTION TAKEN (Check one)

- [X] a. ACTION HAS BEEN COMPLETED (Copy attached)
- [ ] b. REQUEST EXTENSION OF SUSPENSE DATE TO _____ *(Justify below)*
- [ ] c. INTERIM REPLY HAS BEEN SENT (Copy attached) EXTEND SUSPENSE TO _____ *(Justify below)*
- [ ] d. REQUEST CANCELLATION *(Justify below)*
- [ ] e. REQUEST TRANSFER TO _____ *(Justify below /include POC Name & Phone Number)*
- [ ] f. REQUEST DOWNGRADE TO _____ *(Justify below)*

2. JUSTIFICATION

Reply direct to MOC Norm Dicks (Cheri Williams - Bremerton office) attached

3. REPORTING AGENCY

a. ACTION AGENCY: GWI

b. NAME OF ACTION OFFICER: (b)(6)

c. TELEPHONE NO.:

d. DATE:

e. APPROVING AUTHORITY (Service Secretary/Under Secretary/ASD/Military/Executive Assistant Level)

Signature: [signature]

Date Signed: 2-14-00

4. CCD CONTROL

U01329-00

5. ACTION TAKEN (For EXSEC/ Correspondence Control Division Use Only)

a. EXT	[ ] Approved	[ ] Disapproved
b. CANX	[ ] Approved	[ ] Disapproved
c. DWNGRD	[ ] Approved	[ ] Disapproved
d. TRANSFER	[ ] Approved	[ ] Disapproved
e. OTHER (Specify)		

Signature: _____ Date Signed: _____

SD FORM 391, JAN 2000

NORM DICKS
6TH DISTRICT, WASHINGTON
COMMITTEE:
APPROPRIATIONS
SUBCOMMITTEES:
INTERIOR
RANKING DEMOCRATIC MEMBER
NATIONAL SECURITY
MILITARY CONSTRUCTION

OFFICE OF THE SECRETARY OF DEFENSE
JAN 31 AM 8:17

2467 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-4706
PHONE: (202) 225-5916
DISTRICT OFFICES:
SUITE 2244
1717 PACIFIC AVENUE
TACOMA, WA 98402-3234
PHONE: (253) 593-6536
SUITE 301
500 PACIFIC AVENUE
BREMERTON, WA 98337
PHONE: (360) 479-4011
http://www.house.gov/dicks/

Congress of the United States
House of Representatives

OSAGWI

December 15, 1999

FEB 01 2000

Office Of the Chief Legislative Liaison
1600 Army Pentagon
Washington, D.C. 20310-1600

Re: (b)(6)

Dear Colonel Jones:

I have been contacted by one of my constituents, (b)(6) concerning symptoms he is experiencing as a result of serving in Operation Desert Strom.

I would appreciate your looking into this matter and providing me with a reply that will assist me in addressing the concerns raised by my constituent. Please send your response to Cheri Williams at my Bremerton office.

Thank you for your prompt attention and consideration of this matter. Your assistance is appreciated.

Sincerely,

Norm Dicks

NORM DICKS
Member of Congress

NDD:cfw

Enclosure(s)

U01329 /00

91204566

DOC HASTINGS
4TH DISTRICT, WASHINGTON

ASSISTANT MAJORITY WHIP

COMMITTEE ON RULES
SUBCOMMITTEE ON
LEGISLATIVE AND BUDGET PROCESS

1323 LONGWORTH BUILDING
WASHINGTON, DC 20515
(202) 225-5816

2715 ST. ANDREWS LOOP
PASCO, WA 99301
(509) 543-9396

302 E. CHESTNUT
YAKIMA, WA 98901
(509) 452-3243

Congress of the United States
House of Representatives

December 9, 1999

The Honorable Norman Dicks
500 Pacific Avenue
Suite 301
Bremerton, WA 98310

Dear Congressman Dicks:

(b)(6) has contacted my office on behalf of her grandson, (b)(6) (b)(6) regarding health problems he is experiencing as a result of having served during Operation Desert Storm. I note that (b)(6) resides within the district that you represent. Therefore, I am forwarding their correspondence to your attention.

If you have any questions, please contact my staff assistant, Anna Kane, at 2715 Saint Andrews Loop, Suite D, Pasco, WA 99301, phone (509) 543-9396, or FAX (509) 545-1972.

Thank you for your attention to (b)(6) concerns.

Sincerely,

Doc Hastings
Member of Congress

DH:AK

NORM DICKS
6TH DISTRICT, WASHINGTON
COMMITTEE:
APPROPRIATIONS
SUBCOMMITTEES:
INTERIOR
RANKING DEMOCRATIC MEMBER
NATIONAL SECURITY
MILITARY CONSTRUCTION

Congress of the United States
House of Representatives

2467 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-4708
PHONE: (202) 225-5916
DISTRICT OFFICES:
SUITE 2244
1717 PACIFIC AVENUE
TACOMA, WA 98402-3234
PHONE: (253) 593-6536
SUITE 301
500 PACIFIC AVENUE
BREMERTON, WA 98337
PHONE: (360) 479-4011
http://www.house.gov/dicks/
RECYCLED PAPER

December 15, 1999

National Personnel Records Center
Congressional Liaison Office
9700 Page Avenue, Room 2077
St. Louis, Missouri 63132

Re: (b)(6)

Dear Director:

I have been contacted by one of my constituents, (b)(6) concerning symptoms he is experiencing as a result of serving in Operation Desert Strom.

I would appreciate your looking into this matter and providing me with a reply that will assist me in addressing the concerns raised by my constituent. Please send your response to Cheri Williams at my Bremerton office.

Thank you for your prompt attention and consideration of this matter. Your assistance is appreciated.

Sincerely,

NORM DICKS
Member of Congress

NDD:cfw

Enclosure(s)

DOC HASTINGS
4TH DISTRICT, WASHINGTON

ASSISTANT MAJORITY WHIP

COMMITTEE ON RULES
SUBCOMMITTEE ON
LEGISLATIVE AND BUDGET PROCESS

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WASHINGTON, DC 20515
(202) 225-5816

2715 ST. ANDREWS LOOP
PASCO, WA 99301
(509) 543-8386

302 E. CHESTNUT
YAKIMA, WA 98901
(509) 452-3243

Congress of the United States
House of Representatives

December 9, 1999

(b)(6)

Dear (b)(6)

I received the privacy waiver from your (b)(6) regarding the symtoms he is experiencing as a result of having served during Operation Desert Storm.

I note that your (b)(6) resides in the Sixth Congressional District, an area represented by Congressman Norm Dicks. Therefore, as a courtesy, I have forwarded your correspondence to his office in Bremerton.

For your information, you or your grandson may contact Congressman Dicks at 500 Pacific Avenue, Suite 301, Bremerton, WA 98310, or call (360) 479-4011.

Sincerely,

Doc Hastings
Member of Congress

DH:AK

DOC HASTINGS
4TH DISTRICT, WASHINGTON

ASSISTANT MAJORITY WHIP

COMMITTEE ON RULES
SUBCOMMITTEE ON
LEGISLATIVE AND BUDGET PROCESS

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WASHINGTON, DC 20515
(202) 225-5816

2715 ST. ANDREWS LOOP
PASCO, WA 99301
(509) 543-9396

302 E. CHESTNUT
YAKIMA, WA 98901
(509) 452-3243

Congress of the United States
House of Representatives

November 23, 1999

(b)(6)

Dear (b)(6)

Thank you for contacting me on behalf of your (b)(6) However, due to the provisions of the Privacy Act of 1974, all federal government agencies and departments are strictly prohibited from releasing information about anyone without that individual's written permission. This protection of the person's right to privacy means that I can do nothing to help until I have written authorization from (b)(6)

I am enclosing a privacy waiver form that will give me the authorization I need to be of assistance in this matter. Please have (b)(6) complete the form and return it to my staff assistant, Anna Kane, at 2715 Saint Andrews Loop, Suite D, Pasco, WA 99301, phone (509) 543-9396, or fax (509) 545-1972. Then I will be able to follow up on the matter by contacting the appropriate government officials.

I appreciate your interest and concern in this matter.

Sincerely,

Doc Hastings
Member of Congress

DH:AK

Enclosure

DOC HASTINGS
4TH DISTRICT, WASHINGTON
COMMITTEE ON RULES
SUBCOMMITTEE ON
LEGISLATIVE AND BUDGET PROCESS

DEC 08 1999

1323 LONGWORTH BUILDING
WASHINGTON, DC 20515
(202) 225-5816

2715 ST. ANDREWS LOOP
SUITE D
PASCO, WA 99301
(509) 543-8396

302 E. CHESTNUT
YAKIMA, WA 98901
(509) 452-3243

Congress of the United States
House of Representatives

PLEASE DESCRIBE THE SITUATION WITH WHICH YOU ARE REQUESTING ASSISTANCE:

Symptoms undiagnosed Incurred During Operations
Desert Storm

(If you need additional space, please use the back of this page.)

"I hereby request the assistance of the office of Congressman Doc Hastings in resolving the matter described above and authorize Congressman Hastings and his staff to receive any information which they may need in order to provide this assistance."

This information may also be released to the following person (spouse, parent, attorney, etc.) (b)(6)

Please print

Name (b)(6)

Address (b)(6)

City, State, ZI (b)(6)

Telephone Home: (b)(6) Work:

Social Security Number (b)(6)

Claim, alien, ID or other numbers

Military Personnel Only: Home of Record

Currently my case _____ is or X is not pending before a federal, state, or local court. (please check one)

SIGNED (b)(6) DATE: 11-30-99

Please return this completed form to: Anna Kane
2715 Saint Andrews Loop, Suite D
Pasco, WA 99301
(509) 543-9396
(509) 545-1972 (FAX)

NOV 17 1999

NOV 23 1999

(b)(6)

November 7, 1999

Hon. Doc Hastings
1323 Longworth H.O.B.
Washington, D.C. 20515

RE: (b)(6)

Dear Representative Hastings,

My (b)(6) needs your help. As indicated above he served his country for 90 plus days in Operation Desert Storm during the height of the campaign. He is now suffering from the ill effects of his service. Please let me explain:

1. He received Anthrax injections prior to entering the Operation Desert Storm Theater.
2. He received and ingested PB pills every day to reduce the immediate effect of nerve agents.
3. He was subjected to an intense oil cloud, which hung over the area where he was stationed. He literally inhaled gallons of oil by-product vapors stemming from this oil cloud. These vapors interfered with his concentration and disoriented his thinking processes..
4. He received phosphorous burns on his back due to exploding ordinance.

The Following are symptoms (b)(6) is now experiencing:

(a) Severe stomach cramps or spasms.
(b) Excessive diarrhea one or two days a week even though he eats a normal diet.

(c) Several round, bald spots on his head. His VA doctors feel this is an indication of an immune disorder. He is being treated for this but the treatment is not working.

(d) He has extreme fluctuations in his energy levels. His sleep requirements are excessive for someone his age.

(e) At times he has difficulty articulating his thoughts and his speech becomes garbled indicating possible chemical and organic brain damage due to chemical warfare exposure.

(f) He tends to have a short temper with high frustration levels and his eyes have large dark circles around them, which become worse when his symptoms are flaring.

When (b)(6) received his medical records, all records relating to his Operation Desert Storm duty were missing. These missing medical records included the events and treatment regarding the phosphorous burns on his back.

(b)(6) is proud to have served his country. Prior to his duty in Operation Desert Storm, had none of the above-described symptoms. He was a healthy young man serving and defending his unit and his country.

While he recently has received a small disability package for his back injury, it simply is not enough. He is obviously suffering effects from chemical warfare exposure, which will effect him for the rest of his life. I am concerned these symptoms will become worse as time goes by leaving him 100% disabled.

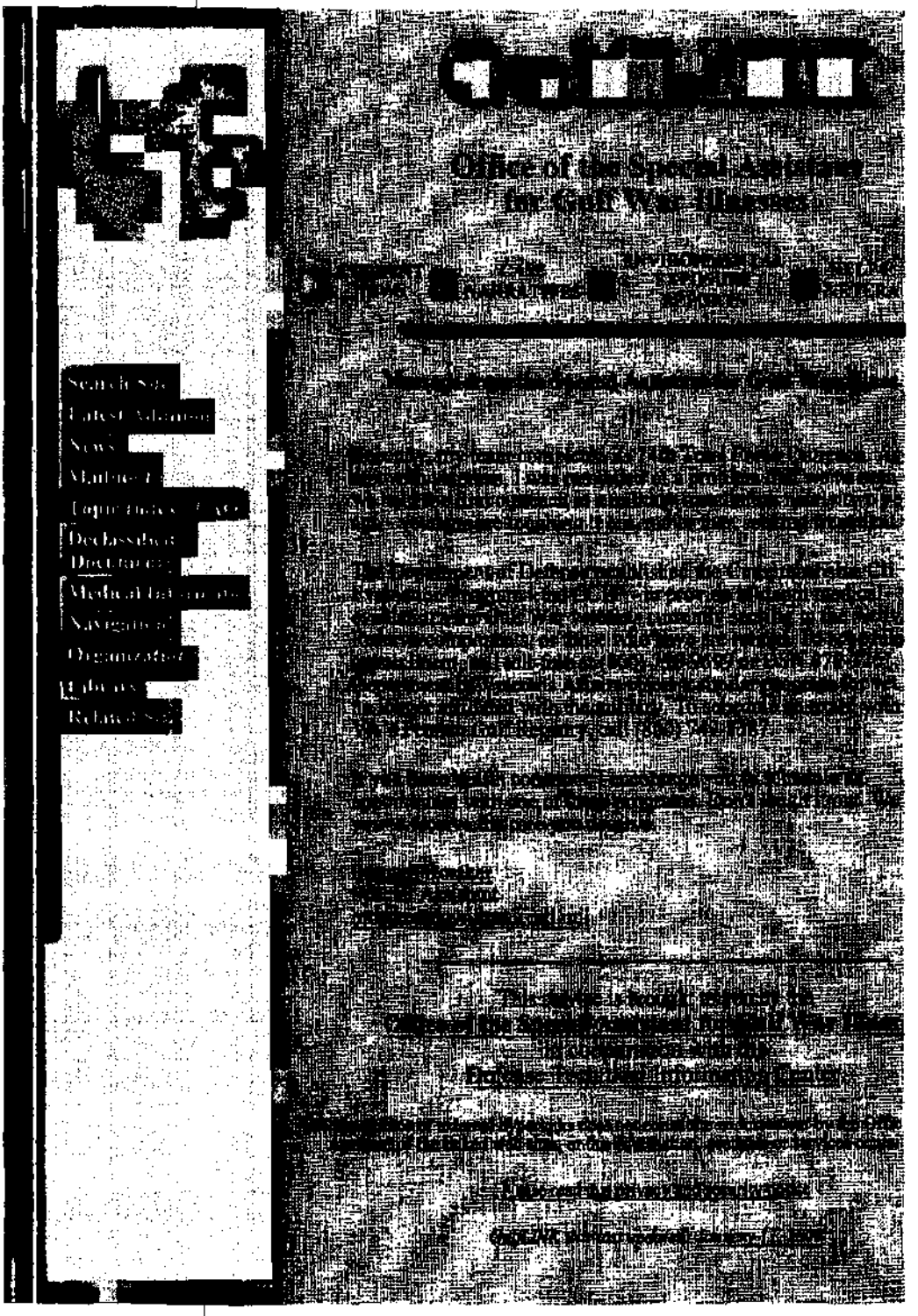
(b)(6) is a husband and father who needs to be assured that he will be living a long and normal life. He needs to be supported by his Country and the citizens who he served by getting the best medical treatment this country has to offer. He is not asking for a handout, but a chance at a normal life.

This is where you can assist (b)(6) You can ask for an investigation of his circumstances and begin the process of proper medical treatment for his conditions. The best doctors, medications and treatments are the least my country can do for (b)(6) who served her well. I am asking this for my (b)(6)
(b)(6

Thank you for your assistance in this matter. I look forward to hearing from you soon.

Very truly yours,

(b)(6)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DEPARTMENT OF THE ARMY
OFFICE OF THE CHIEF OF LEGISLATIVE LIAISON
1600 ARMY PENTAGON
WASHINGTON DC 20310-1600

REPLY TO ATTENTION OF

January 11, 2000

The Honorable Norman D. Dicks
Representative in Congress
500 Pacific Avenue
Great Northwest Building, Suite 301
Bremerton, Washington 98337

Dear Congressman Dicks:

This replies to your inquiry on behalf of (b)(6) concerning medical concerns that he believes are related to his service during the Gulf War.

This matter comes under the jurisdiction of the Office of the Special Assistant to the Secretary of Defense for Gulf War Illness. Accordingly, I have referred your inquiry to that agency for appropriate action and further response to you. Additional information may be obtained from the enclosed information or directly from the following Web address: http://www.gulflink.osd.mil/.

I trust this information will be of assistance.

Sincerely,

Teresa T. Ray
Congressional Coordinator
Congressional Inquiry Division

Enclosure

C*O*N*G*R*E*S*S*I*O*N*A*L

CHIEF OF LEGISLATIVE LIAISON
CONGRESSIONAL INQUIRY DIVISION
ROOM 2C600
1600 ARMY PENTAGON
WASHINGTON, D.C. 20310-1600

January 14, 2000

OSD CORRESPONDENCE CONTROL DIVISION
ROOM 3A948, ATTN: ED HAWLEY
WASHINGTON DC 20310

Control ID: 91204566 Task Officer: (b)(6)

Tasked Agency: **OSDC** Action: **Necessary Action/Info**

Suspense Date:

Constituent: (b)(6)

Subject:

Member of Congress: Congressman Norman D. Dicks

Remarks:

Keyword: MYSTERY ILLNESS

24-hour FAX Service:
(b)(6)

If there is a problem with this FAX, please call (b)(6)

*DSN: (b)(6)
E-Mail Address: (b)(6) @hqda.army.mil
REMINDER: Direct replies require a courtesy copy be provided to OCLL

FAX

Date : 01/28/00

Total number of pages : 12

To : OCLLCC OSDC

Company :

Department :

Fax number (b)(6)

From : Rozmeski, Suzanne D Ms OCLL

Headquarters, Department of the Army

Subject: Congressional, (b)(6) Rep Dicks

CONGRESSIONAL or SPECIAL CORRESPONDENCE

CMAT: 0033-002

Date: FEB 14 2000

Office of Special Assistant for Gulf War Ill[redacted]
Internal Routing/Tasking Sheet

Coord/ Routing	Position/Organization		Action	Info	Comments
8	Special Assistant	(SA)			signature
6	Deputy Special Assistant	(DSA)	VSF dr.		
7	Executive Assistant to SA	(EA)			
	Executive Assistant to DSA	(EADSA)			
4	☐ Director, Investigation & Analysis _____ (IAD) ☐ DepDir _____ ☐ MED _____ ☐ VDM _____ ☐ C/B _____ ☐ ENV _____ ☐ PAG _____				
	Dir Lessons Learned Implementation	(LLI)			
2	Dir Public Affairs & Outreach	(PA)			
	Dir Legislative Outreach	(LA)			
3	Dir Medical Outreach & Issues	(MOI)			
	Legal Advisor	(LGL)			
5	PM, Gulf War Illnesses Support	(PM)			
1	Editorial Review ☒ AMB _____ ☒ Editors	(ER)			
	CMAT	(CMAT)			
9	Action Management Call 845-8369 ☐ COMEBACK COPY TO: _____ ☐ GET CMAT NUMBER WHEN SIGNED & SENT ☐ READING FILE ☐ THANK YOU FILE ☒ CHRON FILE ☐ ADD TO GulfNEWS				

SUSPENSE:

Prepare reply for signature of:
☐ SA/GWI ☐ SD ☐ DSD ☐ DepSA/GWI

MOC Norm Dicks Response

☐ Congress	☐ Oversight	☐ FOIA	☐ OSD	☐ WBM	☐ VSO/MSO	☐ Outgoing
☐ Ltr to SA	☐ IR	☐ E-Mail	☐ OGA	☐ Other		☐ Veteran

KEYWORDS:

01/12/00 Issuance

OFFICE OF THE SECRETARY OF DEFENSE
1000 DEFENSE PENTAGON
WASHINGTON, DC 20301-1000

SPECIAL ASSISTANT
FOR
GULF WAR ILLNESSES

Honorable Norm Dicks
500 Pacific Avenue, Suite 301
Bremerton, Washington 98337

16 FEB 2000

Dear Congressman Dicks:

This is in reply to your recent inquiry on behalf of your constituent, (b)(6) and her (b)(6) Your letter was forwarded to my office for response in my capacity as the Special Assistant to the Deputy Secretary of Defense, appointed to oversee the Department of Defense investigation of Gulf War illnesses. In December, (b)(6) sent a similar request to Senator Slade Gorton. We responded to her inquiry last month and since that time, there have been no further changes.

In her letter, (b)(6) asked for information related to the Department of Defense's effort to investigate the possible causes and treatment strategies for the illnesses of Gulf War veterans. A collaborative effort by the Departments of Defense, Veterans Affairs, and Health and Human Services currently funds more than 140 scientific studies to determine the causes of the undiagnosed illnesses experienced by some Gulf War veterans. These studies are conducted by government and independent researchers and focus on multiple, potential factors. Twenty-six of these projects look for possible adverse effects of pyridostigmine bromide. In addition to pyridostigmine bromide, other research projects include exposures to environmental hazards, neuro-psychological and neurological research, depleted uranium, chemical exposures, and reproductive outcomes.

In checking our records, we know that (b)(6) unit was one of those positioned within the potential exposure area of a plume created by the Khamisiyah munitions demolitions. His unit was identified as under the plume for at least part of the day on March 11, 1991. Given that, if he was with his unit at the time, he may have been exposed to extremely low levels of the nerve agent sarin. We notified (b)(6) of this possible exposure by letter in July 1997.

Although little is known about the long-term effects from a brief, low-level exposure to nerve agents, the current medical evidence indicates that long-term health problems are unlikely. However, because the scientific evidence is limited, the DoD and the VA have initiated research into the possible health effects of brief, low-level nerve agent exposures. These studies are currently underway.

We have continued to attempt to piece together the events at Khamisiyah. Since the publication of our first report in 1997, we have subjected our initial hazard models and analyses to rigorous scientific review. The Central Intelligence Agency also announced that it has completed a separate analysis and will soon release its findings. When this analysis is correlated with our improved data, our 1997 report will be updated. We realize this information is important to Gulf War veterans and their families.

(b)(6) also wrote that her (b)(6) had received anthrax injections before entering the Gulf War theater. It is possible he may have received an anthrax inoculation after he deployed to the Gulf, but not before. The anthrax program was carried out in-theater, beginning in January, 1991 and ending with the start of hostilities in February. If (b)(6) did not receive any inoculations in theater, he most likely did not receive the anthrax vaccine.

It is regrettable that some personal medical records were not kept current during the Gulf conflict. We have taken steps to correct such problems in the future. For those who served in the Gulf and were treated as inpatients at hospitals there, some medical information has been found in records maintained by the hospitals. Our office has assisted in the recovery of more than 25,000 of these records from various sources. We checked our database of recovered records for (b)(6), but he is not listed. It is still very possible that his records are somewhere in the National Personnel Records Center in St. Louis, Missouri, the VA system, or possibly still on file with the unit that operated the particular field hospital that treated him in theater. We are making every attempt to recover missing records.

Unfortunately, we do not have any easy answers for veterans like (b)(6) (b)(6) However, by seeking medical care through the VA, he is pursuing the correct course. The VA is on the front lines when it comes to medical issues related to Gulf War veterans. The most recent examples are the antibiotic and exercise and cognitive behavioral treatment trials being conducted at 28 VA sites nationwide, including Seattle. If (b)(6) is interested in participating, he should call the trial coordinator at (206) 764-2205. I have enclosed a recent news story about the program.

Another option available to (b)(6) is the VA's Persian Gulf Registry. If he hasn't yet registered, this program will provide him with a medical screening and physical exam free of charge. To schedule an appointment, he should call the VA Helpline at (800) 749-8387. We encourage all veterans to enroll in the registry.

I have enclosed a copy of our last annual report that describes the activities of this office and the research supported by the Department of Defense. If (b)(6) and her (b)(6) have Internet access, they can also check out the latest information, as well as everything else we've published, at the GulfLINK website (*http://www.gulflink.osd.mil*). If they have any questions, I encourage them to call our toll-free number, (800) 497-6261, and speak with a member of my staff. There is someone there from 7:00 a.m. to 10:00 p.m., Eastern Standard Time, every weekday.

We also forwarded a copy of (b)(6) letter and my original response to Dr. Mark Brown, Director, Environmental Agent Service at the VA. (b)(6) health and the health of all Gulf War veterans is extremely important to us. The DoD and VA are committed to providing the best possible medical care to all veterans and are equally committed to gaining a full understanding of the possible health effects of service during the war. As we learn more about the events of the Gulf War, we will continue to keep veterans informed.

Sincerely,

Bernard Rostker

Enclosures

Questions & Answers for Congressman Shays' 29 April 1999 Hearing on Anthrax Vaccine

Question #15:

What lots were shipped during the Gulf War?

Answer:

Information provided recently to JPOBD by BioPort indicates that doses were shipped from the following lots on the dates provided:

Lot	Doses	Date Shipped
18	250	5 Jul 89
19	750	14 Nov 89
19	1000	16 Aug 90
19	1000	20 Aug 90
19	1000	22 Aug 90
19	3000	28 Aug 90
FAV001	68630	5 Sep 90
FAV002	70450	22 Oct 90
FAV003	68430	18 Dec 90
FAV004	51830	19 Dec 90
FAV005	70840	22 Jan 91
FAV006	72600	22 Jan 91
FAV007	68740	10 Jan 91
FAV008	10000	15 Jan 92

(36)

Congressional

CMAT Control #
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Remarks: PER C&D (MAJ (b)(6)), ADD GWI COORDINATION.

103 VF 1

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SENATE ARMED SERVICES COMMITTEE
HEARING ON THE
DEPARTMENT OF DEFENSE ANTRAX VACCINE IMMUNIZATION PROGRAM
APRIL 13, 2000

QUESTION 37

Senator McCain.

Currently the vaccine label does not specify that the vaccine is safe and effective against anthrax spores that are inhaled. Are you concerned that this means that the vaccine was not designated, or has not been adequately tested against inhalation?

Lieutenant General Blanck.

No. Efficacy is based in part on the Brachman study and further substantiated in Rhesus monkey trials. The original Brachman and CDC studies of anthrax vaccine in textile workers proved that the vaccine protected against anthrax. The calculations performed in that study combined the cutaneous (skin) and inhalation forms of anthrax infection that occurred. No inhalation anthrax occurred among the vaccinated workers, while five cases of inhalation anthrax occurred among workers who had not been vaccinated. The total number of cases was judged too few to show statistically conclusive proof of protection for inhalational anthrax as a separate analysis. However, results from several animal studies provide additional evidence that the vaccine protects against anthrax challenge with more than 500 times the lethal dose of anthrax by inhalation. This information coupled with the results of the effectiveness and immune response in humans assures us that the vaccine will greatly increase the chances of soldiers surviving exposure to inhalation anthrax. When full immunization is combined with proper use of protective masks, detection devices, surveillance and post-exposure treatment with antibiotics, the threat is even further reduced.

Congressional

CMAT Control # 2000081-0000002 (38)

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JUDICIARY
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Subcommittee on Criminal Justice, Drug Policy, and Human Resources
VICE CHAIRMAN

March 9, 2000

The Honorable William S. Cohen
Secretary of Defense
United States Department of Defense
1000 Defense Pentagon
Washington, D.C. 20301-1000

IN RE: Anthrax Vaccine Immunization Program (AVIP)

Dear Secretary Cohen:

A report released today by the House Government Reform Committee raises serious questions about the Anthrax Vaccine Immunization Program (AVIP) being administered to our military personnel. In light of these questions -- which relate to the integrity of the vaccine itself, as well as the immediacy of any threat sufficient to justify pressing forward with the vaccine program at this time -- I urge you in the strongest terms to suspend mandatory anthrax vaccinations pending further study.

Addressing the dangers posed by the AVIP is not a theoretical issue. Rather, it is an issue on the minds of citizens, armed forces personnel (active, reserve, and National Guard) and military and medical experts, as a very real and immediate problem with both short and long-term ramifications for individual servicemen as well as our entire force structure. In my district, this is an issue regularly brought to my attention.

In addition to possibly threatening the health of soldiers, the Department of Defense policy of making this vaccine mandatory -- especially for reservists -- is harming recruitment and retention efforts, at the very time we are already facing great difficulty filling our ranks and keeping them filled.

Until the safety of the vaccine can be fully evaluated by independent experts, I ask you to end mandatory inoculation for all troops immediately.

With kind regards, I remain,

very truly yours,

BOB BARR
Member of Congress

cc: The Honorable Dan Burton
The Honorable Chris Shays
The Honorable Floyd Spence

U03681 /00

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(39)

Congressional

CMAT Control #
2000102-0000006

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Congress of the United States

House of Representatives

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March 27, 2000

OSAGWI

APR 07 2000

The Honorable William S. Cohen
Secretary
Department of Defense
Washington, D.C. 20301-1155

Dear Secretary Cohen:

We continue to be concerned over the impact of the Anthrax Vaccine Immunization Program (AVIP) on the readiness, retention and morale of U.S. forces. In particular, it appears enforcement of the mandatory program has been inconsistent, leading to unfair and harsh punishments for some who made a personal health decision to decline the vaccine.

We estimate that at least 350 active duty service members have refused the vaccine, and more than 500 reservists and national guard members have quit or transferred because of the AVIP. We believe it imperative that each service compile and track the number of refusals attributable to the anthrax program so it can be determined whether punishments are being meted out justly, and to determine the effect of refusals on individual unit readiness.

It appears that punishments have varied widely between service branches, between officers and enlisted, and between active duty and reserve component members. With no standards to guide commanders in applying the range of disciplinary options, from non-judicial punishment to a court martial, the same offense has drawn very different verdicts. Some, whose only desire is to be of service to their nation, have been branded with a federal felony conviction, while others committing more numerous or more flagrant offenses received far more lenient treatment. The Marine Corps appears to have been particularly harsh, and arbitrary, threatening refusers with multiple orders to be vaccinated, multiple disciplinary actions and bad conduct discharges. Additionally, the Navy saw fit to transfer a sailor to Okinawa to carry out his court martial. It also appears, at times, that individuals who have blemish-free records are still given the most severe punishments available.

The true impacts of the AVIP, and the fairness of the program, remain in doubt because the Pentagon has not tracked the disposition of anthrax refusals in any force-wide, systematic way. In October 1999, the General Accounting Office recommended that DOD "routinely

collect and report, among other program performance measures, data on the number of service members refusing to take the vaccine." (GAO/NSIAD-00-39) To date, we have seen only half-hearted efforts to implement that important recommendation.

In the absence of that data, both Congress and the Department must rely on anecdotal and circumstantial evidence in assessing the success, or failure, of the program. While DOD may at times find the lack of hard facts convenient in defending the program, we find the consistent failure to assess AVIP impacts and performance very troubling. Good intentions and a firm belief in the need for the program are important, but they are no substitute for empirical data in meeting our mutual obligation to be sure defense programs operate effectively, efficiently and fairly.

Therefore, we request that the Department provide the following;

1. The number of individuals who who have refused the vaccine, by service and year.

2. A list of all disciplinary actions initiated to date attributable in whole or in part to anthrax vaccine refusal. The data should include service branch, unit, and rank of each individual subject to administrative punishment or court martial, the exact charge(s), a chronology of the action and a detailed description of the disposition of the matter, if any. (To the extent the list contains personal-identifying information, you may be sure it will be handled appropriately and used only for official purposes.)

3. A list (as described above) of all disciplinary actions initiated from 1991 to the present attributable in whole or in part to refusal to take any mandatory vaccine (other than anthrax).

4. A description of the process to be used by DOD in the future to track anthrax vaccine refusals and other AVIP performance measures, including any guidance to commanders on disciplinary standards.

Thank you for your prompt attention to our request. If you have any questions or concerns, please have your staff contact S. Elizabeth Clay at 202-225-5074.

Sincerely,

Dan Burton
Chairman
Government Reform Committee

Christopher Shays
Chairman
Subcommittee on National Security,
Veterans Affairs and International Relations

cc: The Honorable Henry Waxman

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON GOVERNMENT REFORM
WASHINGTON, DC 20515-6143

OFFICIAL BUSINESS

Dan Burton
M.C.

The Hon. William S. Cohen
Secretary
Department of Defense
Washington, D.C. 20301-1155

(40)

Congressional

CMAT Control #
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CONGRESS OF THE UNITED STATES
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website: www.house.gov/filner

March 24, 2000

OSAGWI

APR 07 2000

The Honorable William S. Cohen
Secretary of Defense
Department of Defense
The Pentagon, Room 3E880
Washington, DC 20301-1000

Dear Secretary Cohen:

I am attaching a list of questions about the anthrax vaccination. I would appreciate receiving an answer to these questions as quickly as possible.

Thank you for your attention to this matter.

Sincerely,

BOB FILNER
Member of Congress

BF/ss
268017

cc: John Veroneau, Assistant Secretary of Defense for Legislative Affairs

U04821 /00

1. Given the apparent correlation between systemic and/or chronic symptoms and anthrax (healthy before the shots, unhealthy after the shots based on Dover AFB testimonies), why is the burden of proof in favor of proving the symptoms were caused by the shots instead of caused by something other than the shots?

2. Given that FDA approval is only applicable when following the prescribed shot regimen and its strict schedule, how can deviations from the schedule be justified? (There is a deviation checklist posted at our unit which tells among other things how to get back on schedule as well as saying that you can be sent into Phase 1 regions with only 1 shot (at least 3 preferred))

3. How can DOD state that they have found no evidence of long term effects when they also admit that there are no studies of long term effects?

4. Please explain the administrative lapses that occured during the Gulf War which conveniently deleted shot and medical record information pertaining to anthrax and other vaccinations recieved.

5. If no correlation between GWS and the anthrax vaccine exists, explain why troops who were vaccinated but did not deploy show signs of GWS and French troops who deployed but were not vaccinated do not show signs of GWS. Also, British and Canadian troops who received US anthrax vaccine have sufferers of GWS.

6. Dr. Pam Asa recently released a report in which she found conclusive evidence of squalene antibodies in GWS and anthrax vaccinees, but not in control groups. If we assume that DOD's statements that they never used squalene as an adjuvant, shouldn't DOD at least investigate whether the anthrax vaccine (possibly combined with other vaccines received at the same time) causes natural production of squalene antibodies?

7. Anthrax is apparently among the first vaccines to combat biowarfare or bioterrorism. I understand that there are dozens of additional vaccines under development. Does this mean that service members will be receiveing dozens more vaccination shots and are they being investigated for interrelated side effects caused by receiving multiple injections at the same time?

8. Given DOD's track record with regards to radioactive testing, Agent Orange, Swine Flu, nerve agent and chemical agent testing during the 50's and 60's, etc., why should anyone believe DOD's claims of product safety? Why should service member concerns get them labeled as a troublemaker?

9. Why did DOD stop independent testing of the vaccine?

10. Why doesn't DOD destroy anthrax vaccine that failed supplemental testing? Secretary of defense William Cohen referred to approxomately 1 million doses that failed testing but were still being stored.

11. If very few of the severe reactions are judged by the AVEC to be caused by anthrax vaccine, what are the rest of the reactions caused by?

12. In some pilot's units, up to 30% of members have quit or transferred - leaving manpower critically short. The costs to train new pilots exceeds 1 million dollars each. Probably more costly is the loss of combat experience with 10 to 20 years of service. Why continue a program that threatens military readiness and negatively impacts morale and retention so much more than the perceived threat of anthrax.

13. It was disclosed recently that all of the military's chemical warfare suits are being recalled for defects, however this has been known for more than 5 years. Why the lapse in action and how long to secure new suits for all military personnel? Shouldn't this be the first line of defense?

14. Why is DOD allowed to redate vaccine that has expired?

15. Didn't the DOD testing, which only shows effectiveness in animals and not humans, only use a single strain of the approximately 2 dozen naturally occuring strains and none of the bio-engineered strains? In some follow-up independent testing, some of the other strains killed virtually all of the vaccinated animals. Any comments?

16. DOD is finalizing exemptions based on previous reactions to the vaccine. What are the proposed thresholds for the exemptions?

17. Initially, VAERS forms were only accepted for review if the service member was hospitalized or missed more than 24 hours of duty time. After severe criticism of these extreme requirements, the VAERS policy was amended to allow anyone to file a VAERS report for any reason. Are there current statistics showing more accurate reaction rates after the threshold was reduced that exclude the previous skewed data?

18. The Nuremburg Code requires informed consent prior to being injected with experimental or investigational new drugs. Why the need for Executive Order 13139, which allows for experimental and investigational new use drugs to be used without informed consent under the guise of Force Protection?

19. In 1990, a DOD threat report stated that there were 9 or 10 countries with the ability to wage biowarfare. This is the same number of countries in the report represented as the impetus for the AVIP program. Why the change in attitude to the same level of threat?

20. Didn't the US supply Iraq with a significant portion of its biowarfare equipment during its war with Iran?

21. Why is DOD ignoring the Congressional Reform Committee's report urging the AVIP program to be suspended until a safer vaccine is developed?

22. What happens to AVIP if Bioport is unable to gain FDA certification before current stockpiles run out?

23. The Japanese cult Aum Shinriyko has released anthrax as a terrorist act at least 8 times, yet no illnesses or deaths have been reported. This doesn't seem to substantiate DOD's claims of anthrax toxicity.

24. Life magazine reported in November 1995 that Gulf War vets in both US and

England were having babies with severe unexplainable birth defects at a rate exceeding 4 times the national average. No studies have been done on the reproductive side effects for anthrax vaccine. Comments?

25. Secretary Cohen has repeatedly likened the use of the anthrax vaccine as sending a soldier into battle with a helmet. Would you be willing to wear a helmet 24 hours a day for the rest of your life? What if the helmet mysteriously swelled to 6 times its normal size 20 years later?

26. If both vaccinated and unvaccinated are exposed to anthrax, why do both have to undergo the same intensive antibiotic treatment?

27. Army Surgeon General Ron Blanck stated in Senate Report 103-97, 8 Dec. 1994 that "although the anthrax vaccine had been considered approved prior to the Persian Gulf War, it was rarely used. Therefore, its safety, particularly when given to thousands of soldiers in conjunction with other vaccines, is not well established. Anthrax vaccine should continue to be considered as a potential cause for undiagnosed illnesses in Persian Gulf military personnel because many of the support troops received the anthrax vaccine, and because DOD believes that the incidence of undiagnosed illnesses in support troops may be higher than in combat troops."
Why the change of heart by General Blanck and has he annouced his reasons for retiring earlier than expected?

28. The production plant MBPI was not examined by the FDA from 1970 until 1993. In 1996 FDA found significant quality control problems. In 1997, FDA issued a 'Notice of Intent to Revoke' due to continued problems and in 1998 finally halted production. Bioport took over and built a larger facility on site. This new facility was inspected in November 1999 and the FDA found more than 30 significant problems including quality control, sterility, potency, temperature monitoring and other issues. How can service members be assured that every dose isn't contaminated, doesn't cantain too much protective antigen (testing indicated as much as 4000% variation between samples) , hasn't previously expired, hasn't at some point exceeded its storage temperature, is given following the proper protocols (shaking the bottle before each dose, swabbing the bottle cap, asking questions before giving the shot, etc.), etc., given the fact that all Phase 1 doses were manufactured during the time of the quality control problems. Can you understand the aprehension service members have about the shot? It reminds me of the scene in the movie Dirty Harry, only instead of Clint Eastwood and his .44 magnum, it's William Cohen holding a syringe saying,
"This shot is the safest vaccine in the world. It will blow any anthrax attack clean off. You're probably asking yourself 'is this my fifth shot or my sixth?' Well, tell me soldier, are you feeling lucky?"

(41)

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House of Representatives

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Statement of Rep. Christopher Shays
February 2, 2000

In November, 1997, after extensive hearings on Gulf War veterans' illnesses, this Committee found "current approaches to research, diagnosis and treatment unlikely to yield answers to veterans' life-or-death questions in the foreseeable, or even far distant, future." We called for an aggressive, well coordinated research effort, independent from institutional inertia and bureaucratic self-interest, to support the goals of accurate diagnosis, effective treatment and fair compensation for all Gulf War veterans.

Since 1997, the Departments of Defense, Veterans Affairs, and Health and Human Services have spent more than $121 million trying to meet basic research goals to better understand the extent, the causes and the cures of Gulf War veterans' illnesses. More than 150 studies have been funded. The Office of the Special Assistant for Gulf War Illnesses contracted for additional studies and surveys.

To assess the productivity of this substantial research program, we asked the General Accounting Office (GAO) to examine the extent to which the agenda is being managed effectively, efficiently and with an appropriate sense of urgency. Their findings validate our initial assessment, and confirm our worst fears, about the pace and prospects of the search for answers for sick Gulf War veterans.

The group charged to coordinate the research effort has not even assessed how well the current portfolio is meeting established objectives. More than half DOD's total expenditures took place outside the multi-agency coordination framework designed to focus research and avoid costly duplication. Nine years after the Persian Gulf War, basic questions remain unanswered. We still don't know how many veterans are suffering unexplained illnesses; we still don't know how their illnesses progress; and we still don't know if they are getting any better.

We are, of course, mindful of the incremental nature of scientific inquiry. Many Gulf War veterans' illnesses are difficult to diagnose, can only be treated symptomatically, and may be impossible to associate with a wartime exposure or event. But patience is no excuse for a lack of vigilance. We must be certain all federal research into Gulf War illnesses is well designed, vigorously pursued and keenly focused on the most promising hypotheses.

Our witnesses today represent the GAO, the federal departments and agencies conducting Gulf War studies, and private researchers who have made some of the most significant findings in this area, often without federal funding. We look forward to their testimony.

United States General Accounting Office

GAO

Testimony

Before the Subcommittee on National Security, Veterans' Affairs, and International Relations, Committee on Government Reform, House of Representatives

For Release on Delivery
Estimated at
10:00 a.m., EST
Wednesday,
February 2, 2000

GULF WAR ILLNESSES

Basic Questions Unanswered

Statement of Kwai-Cheung Chan, Director, Special Studies and Evaluations, National Security and International Affairs Division

Mr. Chairman and Members of the Subcommittee:

We are pleased to be here today to discuss our recently completed report on the research and investigations conducted on Gulf War veterans' illnesses.[1] Many of the approximately 700,000 Gulf War veterans have complained of illnesses since the war's end in 1991, and over 10 percent have completed health examinations through the Department of Veterans' Affairs (VA) or Department of Defense (DOD). Some are concerned they are suffering from chronic disabling conditions because of exposures during the war to agents with known or suspected effects on health. In response to this concern, the government has funded research, investigation, and information activities through various agencies, including DOD, VA, and the Department of Health and Human Services (HHS). These agencies participate in an interagency group, the Persian Gulf Veterans' Coordinating Board, which was established in 1994 to coordinate these activities. The Coordinating Board's Research Working Group, currently chaired by the Department of Veterans' Affairs, focuses on research planning, review, and dissemination, but it is not authorized to manage or distribute the Departments' research funds. In 1996, DOD established the Office of the Special Assistant for Gulf War Illnesses to oversee DOD's efforts regarding illnesses being experienced by Gulf War veterans.

As requested, today we will discuss the expenditures on these efforts by the Departments of Defense, Veterans' Affairs, and Health and Human Services and our work to evaluate their results. Specifically, we determined

[1] Gulf War Illnesses: Management Actions Needed to Answer Basic Research Questions (GAO/NSIAD-00-32, Jan. 6, 2000).

- the amount of money that these three departments spent in fiscal years 1997 and 1998 on research and investigation into Gulf War veterans' illnesses and health concerns,

- the results of the research and investigation spending,

- the extent of coordination between the Coordinating Board's Research Working Group and DOD's Office of the Special Assistant for Gulf War Illnesses, and

- the management of contracts supporting DOD's Office of the Special Assistant.

SUMMARY

I will briefly summarize our four principal findings before providing more detail.

- First, during fiscal 1997 and 1998, the Departments of Veterans' Affairs, Health and Human Services, and Defense spent more than $121 million for research and investigation into Gulf veterans' illnesses. The Defense Department spent $112 million of this total, mostly through its Office of the Special Assistant for Gulf War Illnesses.

- Second, results of the research and investigation activities are accruing slowly and basic questions about the causes, course of development, and treatments of Gulf War veterans' illnesses remain unanswered.

- Third, the activities of the Office of the Special Assistant are not effectively coordinated with those of the Research Working Group.

- Finally, work was improperly awarded to the Office's support contractors for tasks worth more than $20 million.

DOD SPENT MOST OF THE RESEARCH AND INVESTIGATION FUNDS

DOD spent most of the $121 million used for Gulf War research and investigation by the three agencies in fiscal 1997 and 1998. The Department of Health and Human Services reported it spent less than $2 million, the Department of Veterans' Affairs $7 million, and DOD $112 million. These amounts exclude expenses for examinations and clinical care of ill veterans. Within DOD, the Office of the Special Assistant spent the largest amount, $65 million, while other activities, such as the medical research efforts catalogued by the Research Working Group, accounted for $47 million.[2]

Representatives of the Office of the Special Assistant told us that the Office had projected spending $36 million in fiscal 1999 and $30 million in fiscal 2000. These officials told us in 1998 that they were seeking the guidance of the President's Special Oversight Board on DOD Investigations of Chemical and Biological Incidents to determine what portion of the Office's investigative work should continue and how it should reduce the role of the Office. However, funding for the Office is included in DOD's budget through fiscal 2005.

[2] The expenditures for VA's studies do not include overhead costs because indirect costs are included under VA's medical care appropriation. Similarly, the majority of HHS' expenditures represent direct costs only. DOD's spending does not include overhead costs for internal studies run by the Department but does for external ones financed by the Department. In addition, the numbers reported for the Office of the Special Assistant include overhead costs and some spending on veteran outreach.

BASIC QUESTIONS ABOUT VETERANS' ILLNESSES REMAIN UNANSWERED

Regarding the results to date of the three Departments' research and investigations, we have several observations. First, as of November 30, 1999, the Research Working Group of the Persian Gulf Veterans' Coordinating Board had not published an assessment of the extent to which the research agenda has satisfied the objectives it identified in 1995. These objectives include questions about the prevalence of specific health problems and exposures among the veteran population and the way the prevalence differs between Gulf War veterans and appropriate control populations. We recommended, and agency officials agreed, that a date should be established in 2000 for publication of this assessment.

Also, while findings from research are beginning to accumulate, most of the sponsored studies are ongoing or in review. By mid-1999, of the 151 research projects monitored by the Research Working Group, 70 percent were still ongoing, including 19, or about 30 percent of the 62 that were scheduled for completion by then. Group officials attributed the extended completion dates either to efforts to collect or incorporate additional data or to unanticipated delays, such as difficulties in securing approval to collect data or problems in locating and recruiting veteran participants.

In addition, DOD's Office of the Special Assistant for Gulf War Illnesses had received 19 of the 20 reports due from its major research contractors. However, only 6 had been publicly

released; the remainder was largely in various stages of interagency review. Fourteen of these reports had remained in draft or review status for a year or longer.[3]

While federally sponsored studies have resulted in some descriptive information concerning veterans' symptoms, many basic questions remain. Identification of the potential causes of veterans' unexplained symptoms has been difficult because researchers are faced by persistent problems in ascertaining veterans' specific exposures. In addition, the Research Working Group has not endorsed any case definition or set of such definitions that might focus federal research. These difficulties led us to conclude in our 1997 report that the many epidemiological studies being sponsored would not provide definitive information on the causes of veterans' illnesses.[4] In particular, difficulty in accurately classifying veterans by the levels of their exposure to specific agents makes it hard to detect associations between exposures and health outcomes.

Other basic questions remain unanswered 9 years after the veterans returned home. As early as 1994, a National Institutes of Health Work Group that met to consider research needs on Gulf War veterans' illnesses, observed that better estimates of the prevalence of symptoms were desirable. In 1997, we noted – as did the Special Investigative Unit of the Senate Veterans' Affairs Committee – that open questions included how many of the veterans who had been examined had unexplained illnesses or symptoms. However, a

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[3] For a review of the Office's investigatory activities, see Gulf War Illnesses: Improved Monitoring of Clinical Progress and Reexamination of Research Emphasis Are Needed (GAO/NSIAD-97-163, June 23, 1997).

[4] Epidemiology is the study of the distribution of illness. Epidemiological studies generally first describe patterns of illness, environmental factors, and exposures. Researchers then form hypotheses based on patterns seen in such descriptive data and conduct analytic epidemiological studies to test these hypotheses, often by comparing the exposures of persons who fit specific illness criteria to those who do not or by comparing rates of illness among persons with different levels of specific exposures.

September 1999 report of the Institute of Medicine noted that no systematic evaluation has been done to determine whether or how veterans' health status is changing.[5] Also, in its 1998 report to Congress, the Research Working Group acknowledged that no government research is specifically directed toward understanding the progress of Gulf War veterans' illnesses over time and that research should assess the long-term health of these veterans.[6]

Some data that might be helpful in answering such questions are being collected as part of a national health survey of Gulf War veterans being conducted by VA, but an analysis of these data was not available at the close of our review. In addition, an HHS-sponsored project, which began in 1997, is assessing the persistence and stability of veterans' symptoms over time. This study is planned to end in 2000.

We recommended that steps be completed to compile data on the number of Gulf War veterans with unexplained illnesses, the treatments they were receiving, and the success of these treatments. DOD partially concurred with this recommendation and VA did not concur. Neither agency opposed the collection of information on the number and health status of Gulf War veterans with unexplained illnesses. However, VA stated that it could not implement the recommendation as worded without specific case definitions (that is, criteria to identify distinct illnesses). DOD objected that veterans' illnesses were not amenable to a single, unifying case definition. Although consensus on a single definition

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[5] Institute of Medicine, Gulf War Veterans: Measuring Health (Washington, D.C.: National Academy Press, Sept. 1999), p. 3, 35.
[6] Persian Gulf Veterans' Coordinating Board – Research Working Group, Annual Report to Congress – 1998 (Washington, D.C.: PGVCB RWG, June 1999), p. 53.

would simplify this task, it is not essential. Nonetheless, we agree that some categorization scheme or set of working case definitions will be useful in counting the numbers of veterans that have unexplained illnesses of some type and we revised our recommendation to reflect this. In September 1999, the Institute of Medicine issued a report to VA which recommended a methodology for measuring veterans' health status. This approach is consistent with our recommendation that VA and DOD select a strategy for answering this question and compile the appropriate data.

ACTIVITIES ARE NOT EFFECTIVELY COORDINATED

The Office of the Special Assistant's activities have not been effectively coordinated with those of the Research Working Group to maximize the efficient use of resources. Group and Office representatives stated that the Office's activities involve investigations, not research, and were therefore not subject to coordination. However, in a 1997 letter to the Office of the Special Assistant, the Research Working Group clearly regarded some of the Office's activities as research. Regardless of whether the work of the Office is considered research or not, it describes the extent and nature of veterans' possible exposures to hazardous materials. Characterizing veterans' exposures is the focus of several of the research objectives the Group established in 1995, and the Office's investigations of potential exposures should be germane to researchers trying to identify the consequences of such exposure.

The lack of effective coordination between the Group and the Office also increases the potential to miss opportunities to take advantage of ongoing and completed work by other

agencies. For example, in January 1998, the Institute of Medicine presented a proposal to VA, which was funded under a congressional mandate, to pursue studies at a projected cost of $1.25 million to review, evaluate and summarize the available scientific and medical information regarding the association between Gulf War veterans' exposures and the adverse health effects they had experienced. However, in 1997, the Office of the Special Assistant contracted with RAND at a cost of more than $1.5 million to conduct a similar review.[7] In addition, the three Departments separately funded reviews of the health effects of depleted uranium. Better coordination of these efforts might have saved both time and money.

To prompt these offices to work more closely on behalf of all veterans, we have recommended that the three Department secretaries direct the Executive Director of the Research Working Group to effectively coordinate the efforts of the Office of the Special Assistant for Gulf War Illnesses with related activities of DOD, VA, and HHS to prevent duplication and improve the efficiency of resource use. We believe that greater cooperation, exchange of information, and coordination will help expedite the process and help find solutions the veterans need.

CONTRACTING FOR THE OFFICE'S SUPPORT SERVICES WAS FLAWED

With regard to the management of contracts supporting the Office, we reviewed four support agreements, which accounted for more than 91 percent of the $47 million the Office spent for support services. We found that two task orders worth over $20 million were awarded improperly, and the Office discouraged competition for another task order by

[7] The Office eventually authorized RAND work valued at $3.2 million.

specifying a preferred vendor. Because the Office is likely to continue to spend a significant part of its budget on support contracts, the Office needs to ensure that its contracts fully comply with applicable requirements.

We recommended that the Secretary of Defense direct the Office of the Special Assistant to replace an improperly awarded task order with a proper contracting arrangement as soon as practicable. Finally, we recommended that the Secretary direct the Office that all future support contracts should comply fully with applicable laws and regulations. DOD did not concur with these recommendations, stating that the Office of the Special Assistant does not have its own contracting officers and relied on the judgment of contracting professionals outside the office, who did not object to the Office's contract actions. We recognize that the Office of the Special Assistant relies on contracting professionals outside the office to execute its support contracts. Nevertheless, the office is, at a minimum, responsible for determining its requirements for support, a process that in one instance resulted in naming a preferred vendor and in another led to an overly broad statement of work. The effect of these practices is to discourage competition. It is important that both requiring agencies, such as the Office, as well as agencies that execute contracts, adhere to the statutes and regulations designed to maximize competition.

Mr. Chairman, this concludes my statement. I would be happy to answer any questions you may have.

Contacts and Acknowledgments

For future questions regarding this testimony, please contact Kwai-Cheung Chan at (202) 512-3652. Individuals making key contributions to this testimony included Dr. Sushil K. Sharma and Dr. Betty Ward-Zukerman.

(713045)

Statement of

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Before the National Security, Veterans Affairs, and

International Relations Subcommittee

House Committee on Government Reform

Research on Gulf War Veterans' Illnesses

February 2, 2000

*

Mr. Chairman and members of the Subcommittee, thank you for this opportunity to discuss the status of the current and projected federal research program on Gulf War veterans' illnesses. I serve as the Department of Veterans Affairs' (VA) Chief Research and Development Officer and the Chairperson of the Research Working Group (RWG) of the Persian Gulf Veterans Coordinating Board (PGVCB).

In your invitation to this hearing, you indicated that the purpose of the hearing was to examine the pending report of the General Accounting Office (GAO): ***Gulf War Illnesses: Management Actions Needed to Answer Basic Questions.*** Indeed, VA commented on the draft report last summer; until today we have not seen the final report. Nevertheless, as I update your Subcommittee on our research concerning Gulf War veterans' illnesses, I have attempted to incorporate appropriate references and sensitivity to the GAO's work. While we did not agree with everything the draft report contained six months ago, we do agree that we should continue reviewing these matters as we develop future plans and studies.

Mr. Chairman, the primary charge to the RWG is to assess the state and direction of research; identify gaps in factual knowledge and conceptual understanding; identify testable hypotheses; identify potential new research approaches; review research concepts as they are developed; collect and disseminate scientifically peer-reviewed research

information; and ensure that appropriate peer review and oversight are applied to research conducted and sponsored by the federal government.

An important function of the RWG is programmatic review of, and recommendation to, funding agencies on research proposals that have been competitively and scientifically reviewed. The RWG continues to work diligently to foster the highest standards of competition and scientific review for all research on Gulf War veterans' illnesses.

As an operational policy, the RWG works through the line management authority each department maintains over its intramural scientists, extramural research program managers, and budgets.

By drawing together the three Departments (Defense, Health and Human Services, Veterans Affairs), the RWG has been able to develop an overall research strategy, serve as a common forum for researchers to present ideas and findings, and collectively respond to emerging research issues and problems.

The RWG has guided the federal research portfolio using a number of different sources of input. These sources include results from ongoing research; various expert panels and oversight committees, such as the Institute of Medicine (IOM), the National Institutes of Health (NIH); the Senate Veterans' Affairs Committee Special Investigations Unit; several Congressional committees including this Subcommittee; the Presidential Advisory Committee on Gulf War Veterans' Illnesses; independent scientists; and Gulf War veterans themselves. The RWG has used advice and information from these sources in developing and implementing a research strategy embodied in ***A Working Plan for Research on Persian Gulf Veterans Illnesses***. This strategy was first released in August 1995 and revised in November 1996. These documents resulted in twenty-one research objectives. The RWG is currently developing summary updates of these research objectives, work, which should be finalized prior to the end of this fiscal year. This plan is responsive to the draft recommendation of GAO that we publish an assessment of progress on the 1995-96 research objectives stated in the working plan.

Mr. Chairman, other notable activities and accomplishments of the RWG include:

- Production and dissemination of annual reports to Congress on progress and results of federal research activities;

- Secondary programmatic review of research proposals submitted to funding agencies;
- Presentations by federal and non-federal researchers before the RWG;
- Organization of annual meetings for federally-funded researchers;
- Organization of an international symposium in conjunction with the Society of Toxicology on the health effects of low-level exposure to chemical warfare nerve agents;
- Development of a strategy for research on the health effects of exposure to low levels of chemical warfare nerve agents;
- Follow-up investigation of preliminary reports of positive experimental serological tests for leishmaniasis; and
- Development of treatment trials for Gulf War veterans.

To date, the federal government is projecting cumulative expenditures of $159 million for Gulf War research from FY 1994 through FY 2000. There are over 150 projects at various stages of completion in the research portfolio on these veterans' illnesses. In the past two years alone, 30 projects have been added to this portfolio. Research projects have been funded in the categories of basic research and applied research such as clinical epidemiology and population-based epidemiologic research. Thus far, the overall emphasis of research has been in the areas of the brain and nervous system and in symptoms and general health of Gulf War veterans. After these, the greatest research emphasis is in diagnosis. To date, 47 federally funded projects have been completed resulting in a total of 98 peer-reviewed publications in the scientific literature. Government and non-government researchers conduct research on Gulf War veterans' illnesses. There are currently a total of 116 principal investigators, including 25 from DoD, 38 from VA, 4 from HHS, 32 who are university-affiliated, 5 non-U. S. counterparts, and 12 from non-government organizations other than universities. All projects and their categories are described in complete detail in the ***Annual Report to Congress*** for 1998. The next annual report will include research updates through calendar year 1999. We believe that this kind of collaboration within the federal medical and research communities is consistent with that which was recommended in the GAO's draft report.

Other highlights of the ongoing research efforts on Gulf War veterans' illnesses include the following:

In early 1997, VA and DoD tasked the Medical Follow-up Agency (MFUA) of the Institute of Medicine to undertake a feasibility study on the potential to do follow-up of individuals at Aberdeen Proving Ground to examine for potential long-term health effects of exposure to chemical warfare nerve agents. This work is focusing on MFUA's access to cohorts of veterans exposed at Aberdeen as a part of their research on the health effects of low-level exposure to nerve agents dating back to the 1950s. The MFUA completed the pilot study in 1998 and determined that the full study could be completed. DoD funded the MFUA (#DoD-93) to proceed with the full-scale study, which is currently underway.

Shortly after the June 1996 announcement of the events at Khamisiyah, Iraq, the RWG recommended that DoD fund three scientifically-meritorious projects in the areas of (1) dosimetry research on exposure to sulfur mustard that will enable quantitative determinations of sulfur mustard exposure at short and long-term intervals; (2) research on the toxicokinetics of the nerve agent VX in three species of animals. The results of this research will facilitate animal to human extrapolation of observed effects in animals resulting from controlled low-level nerve agent exposure; and (3) research on the role of genetic expression of cholinesterases in protecting against anticholinesterase nerve agents. Each of these is described in more detail in the ***Annual Report to Congress on Federally Sponsored Research on Gulf War Veterans' Illnesses*** (Projects DoD-49 through 51). We expect that these studies will be completed this year.

The DoD published a four-part broad agency announcement (BAA) to amplify research on low-level chemical warfare nerve agent effects, as well as research on the health effects of other exposures including insecticides, the nerve agent prophylaxis pyridostigmine bromide (PB), and stress. The BAA resulted in funding recommendations for 12 new projects, valued at approximately $12 million, and covering such exposures as Sarin, PB, insecticides, psychological and heat stress, alone and in various combinations.

As part of the BAA, the scientific community was asked for proposals for a feasibility study on the conduct of epidemiological research on the possible health

outcomes among troops potentially exposed to Sarin at Khamisiyah, Iraq in March 1991. Unfortunately, there was no response from the scientific community to this request. The DoD subsequently asked MFUA to develop a protocol for conducting such a study. MFUA designed a protocol that was peer-reviewed by a panel of experts assembled by the American Institute of Biological Sciences. The proposal was deemed meritorious by an independent scientific peer-review panel and the RWG recommended to DoD that this project be funded. This project (#DoD-69) is anticipated to be completed this year.

Although issues around the potential health impacts on our troops of potential low-level exposures to nerve agents are very important to us, there are other exposures and health outcomes of concern as well. For example, musculoskeletal conditions among Gulf War veterans are clearly evident based on the frequency of these conditions among veterans reporting to the VA and DoD registries, and on results of a number of research studies, including CDC's study of Iowa Gulf War veterans. The federal government sponsors a significant amount of research to better clarify the pathophysiology and clinical significance of musculoskeletal conditions in Gulf War veterans.

Because of the importance of ensuring appropriate and effective treatment for Gulf War veterans' illnesses, my office formed a planning group and charged it with developing a Program Announcement (a type of invitation for applications) requesting proposals within the VA system, or in collaboration with DoD, for multi-center trials for candidate treatments of clearly defined medical syndromes or illnesses among subgroups of Gulf War veterans. This Program Announcement was issued in January 1998.

As a result of epidemiological findings to date, subgroups of ill Gulf War veterans have been identified for whom trials of potential treatment are appropriate. In the spring of 1998, the VA Cooperative Studies Program initiated planning for two treatment trials, subsequently known as the "ABT" (antibiotic treatment) and "EBT" (exercise-behavioral therapy) trials. Both trials underwent thorough scientific review and were approved for funding only after rigorous external review provided by the Cooperative Studies Evaluation Committee. Patient characteristics for entry into both trials are similar. All veterans who served in the Gulf between August 1990 and August 1991 are eligible for the studies. Patients are considered to have Gulf War Veterans' Illnesses (GWVI) if they have at least two of three symptoms (fatigue, musculoskeletal pain, neurocognitive

dysfunction) that began after August 1990 and that have lasted for more than six months up to the present.

The ABT trial seeks to study 450 Gulf War veterans at 28 sites throughout the U.S. The study initiated patient accession in May of 1999. The primary hypothesis of the study is that antibiotic treatment directed against mycoplasma species will improve functional status of patients with GWVI who are tested as mycoplasma positive at baseline. The total cost of this treatment trial is approximately $13 million. The trial will be completed about one year from now. Preliminary demographic information indicates that 15% of the study participants are women, nearly 20% represent minority groups, 37% have attained an educational level of college or higher, and about 70% are employed. Nearly 85% of patients currently enrolled in the study exhibit all three symptoms of fatigue, pain, and neurocognitive difficulties. Recruitment of Gulf War veterans into the antibiotic trial is proceeding ahead of schedule.

The EBT trial seeks to study 1,356 Gulf War veterans at 20 sites throughout the U.S. The study initiated patient accessions in April of 1999. The primary hypotheses of the study is that both aerobic exercise and cognitive behavioral therapy (CBT) will significantly improve physical function in veterans with GWVI, and that the combination of CBT and exercise will be more beneficial than either treatment would be alone. The cost of this treatment trial is approximately $9.3 million. The trial will be completed on or about December 2001. Thus far, nearly 500 veterans have joined the study.

Both VA and DoD have undertaken new initiatives that are focused on the neurobiology of stress and stress-related disorders. In addition, other new research efforts include:

- A total of 14 new projects were initiated in FY 1998/99 as part of the 1997 DoD BAA request for proposals for studies of post conflict illnesses that extend beyond the Persian Gulf War. These studies will address aspects of the wartime experience that create a confluence of cognitive, emotional, and physical factors to produce chronic, non-specific symptoms and physiological outcomes.
- A total of nine new projects were funded in July 1998 as a result of VA and DoD's request for intramural proposals valued at $5 million for research on the neurobiology

of stress. Expected completion dates for these studies range from the year 2000 through 2002.

Mr. Chairman, I will now provide you with an update of the VA National Survey of Persian Gulf Veterans authorized by Public Law 103-446.

As you may recall, the National Survey is designed to determine the prevalence of symptoms and illnesses among a national random sampling of Gulf War veterans. The Survey is being conducted in three phases. Phase I was a population-based mail survey of the health of 30,000 randomly selected veterans from the Gulf War era (15,000 Gulf War veterans and 15,000 non-Gulf War veterans, males and females). The data collection phase is complete and analysis of the data continues. Phase II consisted of a telephone interview of 2,000 non-respondents from Phase I (1,000 from each group) to determine if there are any response differences between respondents and non-respondents. Phase II is complete. In Phase III, 2,000 of the veterans who responded to the postal survey and underwent a telephone interview will be invited, along with their family members, to participate in a comprehensive physical examination protocol. These examinations are being conducted at 16 VA medical centers and involve specialized examinations including neurological, rheumatological, psychological, and pulmonological evaluations. When the National Survey is complete we will have a much clearer picture of the prevalence of symptoms and illnesses among Gulf War veterans.

The VA's Office of Research and Development awarded funds for Phase III of the National Health Survey of Persian Gulf Veterans in November 1998. Currently, 16 sites are participating in these physical examinations. A subcommittee of the Cooperative Studies Evaluation Committee (CSEC, a federally chartered advisory committee) scientifically reviewed the protocol for Phase III and recommended funding. This study is scheduled to examine approximately 2,000 veterans, plus 3,000 of their spouses and children. To date, over 1,000 veterans have joined this observational study, and another 1,230 spouses and children have been examined. The study will cost approximately $12 million and will complete patient recruitment in May of 2001.

The medical evaluations in Phase III are designed to determine:

- Whether Gulf War veterans have an increased prevalence of the following conditions frequently reported in the literature, compared to a control group of non-deployed

veterans: Chronic Fatigue Syndrome (CFS); Fibromyalgia (FM); neurologic abnormalities, including peripheral neuropathy and cognitive dysfunction; post-traumatic stress disorder (PTSD); and measures of general health status.

- Whether the specific medical conditions of arthritis, dermatitis, hypertension, bronchitis, and asthma that have been reported as more frequent among Gulf War veterans compared to non-deployed veterans are of greater prevalence among deployed Gulf War veterans upon objective clinical examination.
- Whether the prevalence of any of these conditions is greater among the spouses of Gulf War veterans than among spouses of non-deployed veterans.
- Whether the prevalence of medical conditions and major birth defects found on a pediatric physical examination in the children conceived after the war is greater for Gulf War veterans than for non-deployed veterans.

Mr. Chairman, one of the GAO draft report's recommendations addressed the need to compile data on Gulf War veterans, track their health problems and map the care they receive. We believe that our work in implementing the survey required under Pub. L. 103-446 is responsive to the intent of GAO's draft recommendation.

This research program, as well as research outside of the government, has yielded important new information. Some of the highlights of recent research findings include:

- Ongoing analysis from the Iowa epidemiologic study of Gulf War veterans using standard measures of health status indicate that nearly 90% of Gulf War veterans reported their health status as "good" to "excellent," while the remainder rate their health status as "poor" to "fair." Interim analysis of this population-based cohort of Gulf veterans also indicates that a minority of them (14%) experienced a significant decline in their health status. Declines were noted in physical functioning and social functioning, while mental health scales showed improvement.
- Population-based epidemiological studies are showing that Gulf War veterans self-report more symptoms and exposures than non-deployed veterans of the same era. Ongoing and newly-funded projects are directed toward determining whether a causal connection may exist.
- Based on VA and DoD mortality studies there does not appear to be more deaths from disease-related causes among Gulf veterans when compared to non-deployed

veterans of the same era. VA plans to continue following the mortality trends of these veterans.

- A study of military hospitalizations has shown that, at least among active duty personnel, the rate of hospitalizations of Gulf War veterans did not exceed that of their non-deployed counterparts. This suggests that Gulf War veterans, who remain on active duty, are not experiencing more illnesses of an acuity or severity that would lead to hospitalization. To account for potential bias from restricting this study to military hospitals, the investigators are extending their study to include civilian health care facilities.
- A sub-study of the hospitalization study shows that infants of Gulf War veterans have not experienced a greater prevalence of birth defects compared to the infants of non-deployed era veterans. A more focused examination of the rare birth defect known as Goldenhar Syndrome also failed to find any difference in prevalence in infants of Gulf War veterans compared to non-deployed era veterans. Further studies of birth outcomes continue to explore this concern.
- The Baltimore VAMC Depleted Uranium Program team recently published results showing elevated urine uranium excretion by soldiers who had been wounded by uranium shrapnel. The Baltimore VAMC has an ongoing medical surveillance program that is following a cohort of 33 U.S. soldiers wounded while on or in vehicles struck by depleted uranium penetrators during the Gulf War. The presence of retained shrapnel was identified by x-ray. Urine uranium concentrations were measured. The presence of uranium in the urine can be used to determine the rate at which embedded depleted uranium fragments are releasing biologically active uranium ions. Importantly, there is no evidence of a relationship between urine uranium excretion and kidney function. While we have seen no definitive evidence of adverse clinical outcomes associated with uranium exposure, these veterans will remain under continuing medical surveillance.
- Recent research studies have provided important information on the interactions of neurotoxins and other exposures. One study indicates that exercise stress can increase the penetration of pyridostigmine (PB) across the blood-brain barrier in mice suggesting the possibility that PB could cause a central nervous system effect.

Another published study, however, suggests that PB does not cross the blood-brain barrier in guinea pigs exposed to extreme heat stress. These inconsistent results with different stressors, in different rodent species, suggest that any extrapolation of such results to humans would be premature. Still another research project has reported on the effects of two weeks' exposure to low doses of PB on the neuromuscular junction. Although ultra-structural examination of the nerve terminal showed degeneration after two weeks of exposure, the effects were reversed following cessation of exposure. The RWG will continue its research on the toxicology of such interactions.

- Neurobehavioral studies of Gulf War veterans and control populations suggest that some Gulf War veterans have brain function abnormalities in such areas as memory, cognition, and motor control. The current RWG research portfolio includes seven studies using methods of sophisticated brain imaging such as conventional and functional magnetic resonance imaging (fMRI), magnetic resonance spectroscopy, and "SPECT" imaging. In addition, four studies are currently under contract review.
- A study conducted at the National Cancer Institute examined blood samples drawn from deployed veterans who went to the Gulf immediately after the end of hostilities. Blood samples were collected in Germany and in the Gulf and tested for a marker of exposure to polycyclic aromatic hydrocarbons (PAH) (a carcinogenic product of partial combustion of petroleum products). The researchers found more markers for PAH exposure in the samples taken in Germany than in the Gulf.
- Recently, Gulf War veterans have voiced concerns about a possible association between amyotrophic lateral sclerosis (ALS) and service in the war. Although there is no clear indication of an excess rate of ALS among Gulf veterans, the available data could represent an underestimate of the actual rate. Furthermore, preliminary data suggested that the age distribution of cases of ALS in Gulf veterans appeared to be younger than the age distribution of cases of ALS in the general U.S. population. Accordingly, VA is leading a research effort to identify all cases of ALS, or other motor-neuron diseases, occurring among Gulf War veterans. VA is collaborating with DoD, CDC, and various university disease experts to determine the veterans' health status and to describe their exposures to potential causal and risk factors for ALS, based on clinical examinations at VA or non-VA centers of excellence in

neurologic diseases. This initial case-finding effort will take approximately one year and will provide the most definitive information about the rate of ALS among Gulf veterans, and the age distribution of the diagnosed patients.

As the federal research program continues to provide more results, we will substantially increase our understanding of Gulf War veterans' illnesses, which, in turn, will enhance our ability to diagnose and treat them. In addition, this newly gained knowledge will enhance prevention of, and intervention in, illnesses in participants of future deployments.

Mr. Chairman, thank you again for permitting me this opportunity to summarize our work to date so that, using science, we may better understand the health problems of Gulf War veterans. You have my assurance that we will continue this effort to resolve or ameliorate health problems in this population to the greatest extent possible.

Mr. Chairman, I will conclude my testimony here and am happy to answer any questions you or other Committee members may have.

DEPARTMENT OF DEFENSE

WRITTEN STATEMENT OF

JOHN F. MAZZUCHI, Ph.D.
DEPUTY ASSISTANT SECRETARY
OF DEFENSE
(CLINICAL AND PROGRAM POLICY)

BEFORE THE

COMMITTEE ON GOVERNMENT REFORM
SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS
AND INTERNATIONAL RELATIONS

FEBRUARY 2, 2000

NOT FOR PUBLICATION
UNTIL RELEASED BY THE
COMMITTEE ON GOVERNMENT REFORM
SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS
AND INTERNATIONAL RELATIONS
UNITED STATES HOUSE OF REPRESENTATIVES

Mr. Chairman and members of the Committee, I am pleased to be here today to provide testimony before this subcommittee on our current clinical and research efforts to understand and treat illnesses among Gulf War veterans.

I am Dr. John F. Mazzuchi, Deputy Assistant Secretary of Defense, Clinical and Program Policy, Office of the Assistant Secretary of Defense for Health Affairs. Within the Department of Defense, the primary role of Health Affairs is to ensure medical services and support to members of the Armed Forces during military operations, and to provide medical services and support to members of the Armed Forces, their dependents, and others entitled to DoD medical care. Our interface with the Departments biomedical research programs derives primarily from our role as Co-chair, along with the Director, Defense Research and Engineering, of the Armed Services Biomedical Research Evaluation and Management Committee, which facilitates consideration of DoD biomedical research.

The Assistant Secretary of Defense for Health Affairs also serves as the principal alternate member and primary DoD liaison official to the Military and Veterans Health Coordinating Board and is a voting member of the Research Working Group, along with the Director, Defense Research and Engineering.

The Gulf War in 1991 was the last critical test of military medicine during full-scale ground and air combat operations. By nearly all measures, this war was a victory not only for United States combat troops and its allies but also for the military health care system. The Department of Defense (DoD) was able to deploy an extensive clinical care and preventive medicine infrastructure rapidly to a distant, desert environment. As a result of these efforts and prevention programs established before the war, the disease and non-battle injury rate among deployed U.S. forces was lower in this war than in previous major conflicts.

Despite the success of military medicine in the Arabian Gulf, the general perception almost ten years later is considerably different because of unresolved questions about the health of Gulf War veterans. In particular, veterans have experienced fatigue, joint pains, sleep problems and other diverse symptoms that have not been definitively explained. Gulf War health questions have resulted in substantial controversy over potentially hazardous exposures during the deployment, the possibility of adverse affects from preventive health measures, and the role of stress in causing chronic illness.

Deployments present unique and difficult challenges. Through many years of research and progress in military medicine, tremendous strides have been made in the medical protection and care provided to soldiers, sailors, airmen, and marines. The medical consequences of the Gulf War made it clear, however, that some threats remain poorly understood and inadequately addressed. Despite few combat causalities and low rates of disease and non-battle injuries

during both the build-up to the war and the war itself, many veterans have since reported health problems, including medically unexplained symptoms, that followed their service in the Gulf War. These unexplained illnesses have proved to be frustrating to diagnose and treat.

Although further research is in progress, much information on veterans' health already has been provided by an extensive research effort. Systematic clinical examinations have not identified a unique syndrome or a characteristic organic abnormality among over 100,000 U.S., British, and Canadian Gulf War veterans. Additionally, the overall mortality rate of Gulf War veterans has been less than half that of the civilian population (adjusted standardized mortality ratio of 0.44), and deaths due to medical causes have not increased. Only deaths due to accidents have been higher, as similarly observed after previous wars. Moreover, there has been no overall increase in hospitalizations among Gulf War veterans or birth defects among their children.

Efforts within the Department to care for Gulf War veterans have reinforced our appreciation of the seriousness of their health complaints, and military physicians fully recognize that these veterans require careful evaluations and appropriate therapeutic programs.

The Comprehensive Clinical Evaluation Program (CCEP) has provided an in-depth medical evaluation to Department of Defense beneficiaries who are experiencing illnesses which may be related to their service during the Gulf War. The clinical protocol of the CCEP currently involves a three-phase evaluation process developed in close coordination with the Department of Veterans Affairs (VA). The initial phase of the protocol consists of a physical examination, supplemental baseline laboratory tests, and clinically directed specialty consultations available at the local MTF. Patients with unexplained symptoms who lack definitive diagnoses are referred to one of fourteen TRICARE Regional Medical Centers (TRMCs) where they progress to the second phase for further evaluation according to an established clinical protocol. Patients with unexplained symptoms or symptoms not completely explained by the second phase diagnoses, can be referred to the Specialized Care Center at Walter Reed Army Medical Center. The CCEP protocol provides a framework for diagnostic evaluation and is not all-inclusive or restrictive.

The Specialized Care Center at Walter Reed Army Medical Center is available to members of the armed services and family members with persistent symptoms who have completed the first and second phases of the CCEP. This program is a three-week intensive outpatient program that emphasizes treatment over evaluation. The Specialized Care Center at the Walter Reed Army Medical Center continues to offer a more intensive therapeutic program for those veterans on active duty or in the reserves with more disabling health problems related to their Gulf War service.

The CCEP has highlighted the need to develop a comprehensive medical surveillance system that is capable of monitoring the health outcome of individuals upon return from deployments. On January 14, 1995 the ASD(HA) announced a medical surveillance plan for the deployment to Bosnia which reflects many of the "lessons learned" from the Department's experiences in the aftermath of the Gulf War. Guidelines for implementation of a medical surveillance system which features pre-deployment education, enhanced capability to assess health hazards in theater, standardized pre- and post-deployment health screening, and monitoring of health consequences were promulgated in August 1997, in DoD Directive 6490.2 and DoD Instruction 6490.3. A Joint Preventive Medicine Policy Group has been established to work implementation of these guidelines.

Health problems among Gulf War veterans, however, persist. Therefore the Department remains engaged in a comprehensive, coordinated effort to respond to the health concerns of Gulf War veterans; our veterans and their families deserve no less. The Departments of Defense (DoD), Veterans Affairs (VA), and Health and Human Services (HHS) are committed to finding answers to Gulf War veterans' questions. To address these complicated issues, we will continue to solicit advice from independent scientists and experts.

In response to health questions following the Gulf War and the increasing demands of a series of hazardous deployments, the military health system has undergone a fundamental reorientation. A new strategy has been developed and is being implemented to protect U.S. forces against foreseeable physical and psychological threats. DoD's "Force Health Protection" strategy balances the military's key responsibilities to: 1) promote and sustain health and wellness throughout each person's military service; 2) prevent acute and chronic casualties; 3) rapidly stabilize, treat, and evacuate casualties; and, 4) perform medical surveillance, longitudinal health studies, and ensure adequate medical records documentation and clinical follow-up for deployed forces. The Force Health Protection strategy has played a key role in further reductions in illness and injury rates since the Gulf War.

The development of sound health policy for Force Health Protection has to rely on a rigorous standard of scientific proof to improve clinical care and preventive medicine practices. Preferably, such proof should be based on peer-reviewed science published in leading medical journals; because of the limitations of individual studies, research findings require expert review and confirmation before conclusions are adopted. Multiple and sometimes conflicting hypotheses and suggested changes are continually being advanced by clinicians, scientists, advocates, and concerned citizens, both in and out of the military and federal government. These diverse ideas have to be evaluated by rigorous scientific methods to provide the best possible health care for military service members and veterans.

The Department of Defense is committed to an aggressive program of Force Health Protection. A comprehensive approach to health care and prevention has been implemented that will coordinate the activities within DoD and among multiple federal agencies. New DoD and VA deployment health clinical and research centers are being established that will actively investigate potential health risks and medical, psychological, and reproductive outcomes. DoD has recognized the need for proactive health risk communication as an essential part of the force health protection strategy. Specific Force Health Protection initiatives include:

- Documentation of health status, including mental health assessments, blood sample collections, and health threat briefings before deployment.
- Improvement in medical record keeping, including tracking of immunizations and other preventive countermeasures, during deployment.
- Assessment of health status -- individual and force - after deployment.
- Improvement of health risk communication efforts.
- Prospective cohort studies of deployed military personnel.

The Department and our Federal partners are committed to resolving Gulf War veterans' health concerns and preventing similar occurrences among our service men and women as a consequence of future deployments. The challenges are great and while there may be no quick solutions, we are committed to responsible and aggressive pursuit and resolution of these problems.

The lack of predeployment health and deployment exposure data is recognized as a chief limitation in evaluation of Gulf War veterans' illnesses. Numerous improvements have or are being made to document and analyze health data regarding future US military deployments. These efforts include capturing better service-entry health data, pre- and post-deployment health data, environmental and morbidity data during deployments, improved communications to troops regarding deployment risks, and focused clinical evaluation and epidemiological research programs of deployed populations.

In the 1998 report to Congress, *Effectiveness of Medical Research Initiatives Regarding Gulf War Illnesses,* DoD identified the need for a coordinated capability to apply epidemiological research to determine whether deployment-related exposures are associated with post-deployment health outcomes. Subsequent to this report, Congress authorized the Secretary of Defense to establish a center devoted to "...longitudinal study to evaluate data on the health conditions of members of the Armed Forces upon their return from deployment..." On 30 September 1999, Dr. Sue Bailey, the Assistant Secretary of Defense for Health Affairs directed establishment of DoD Centers for Deployment Health, creating a research center at the Naval Health Research Center, San Diego, with the mission of "...longitudinal study to evaluate data on the health conditions of members of the Armed Forces upon their return from

deployment..." A clinical center was established at the Walter Reed Army Medical Center, to oversee the Departments clinical evaluation programs for deployed service personnel.

One of the many lessons of the Gulf War is that the lack of ongoing population-based longitudinal health studies has limited our capabilities to identify deployment-related health outcomes. Additionally, the only way to determine health status change is through prospective monitoring of health and health outcomes. Recognizing the challenges of conducting such studies, DoD and VA asked the National Academy of Sciences, Institute of Medicine, to establish a committee to consider these questions and suggest appropriate scientific and practical methodologies. In response, the Institute of Medicine recommended in the report *Gulf War Veterans: Measuring Health*, that DoD and VA initiate longitudinal cohort studies of both Gulf War and deployed veterans.

DoD and VA have initiated planning to develop a research program of ongoing longitudinal studies with the specific aim of determining how the health of US military veterans changes over time. This study - the Millennium Cohort Study - will focus upon US military cohorts of the future, yet be constructed so as to enable comparisons to military cohorts of the recent past. A concurrent program will use similar data collection methods to study a comparable Gulf War veteran population.

Our goal for the two studies is to determine how the health of several veteran cohorts changes over time. The specific goal of the Millennium Cohort Study is to identify and prospectively follow health outcomes in future US military cohorts beginning in the year 2001. In this study we intend to adapt and coordinate the numerous dynamic medical information systems that are currently being developed such that future investigators will not have to rely as much on special investigative studies to determine the effects on health of military deployments.

We appreciate the interest this Committee and others have shown in the health of the men and women who serve and have served this nation in our armed forces. The health and fitness of military personnel have long been concerns of those responsible for ensuring troop readiness and effectiveness. The Military Health System wants to achieve its goal to take care of those men and women and their families, and protect their health. We recognize that our commitment to keeping our veterans healthy does not end when they leave active service. We will maintain a strong post deployment evaluation and care program in coordination with the VA and continue to move forward to strengthen our Force Health Protection Program as well as the total Military Health System.

Again, we appreciate the opportunity to testify before this Committee, and look forward to answering your questions.

DEPARTMENT OF DEFENSE

STATEMENT OF

DR. ROBERT FOSTER
DIRECTOR, BIOSYSTEMS
OFFICE OF THE DEPUTY UNDER SECRETARY OF DEFENSE
(SCIENCE AND TECHNOLOGY)

BEFORE THE
COMMITTEE ON GOVERNMENT REFORM
SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS
AND INTERNATIONAL RELATIONS

FEBRUARY 2, 2000

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SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS
AND INTERNATIONAL RELATIONS
UNITED STATES HOUSE OF REPRESENTATIVES

Mr. Chairman, thank you for the opportunity to review with you and the members of this subcommittee the Department of Defense's (DoD's) science and technology program addressing multiple aspects of Gulf War Veterans' Illnesses (GWVI) and general deployment health concerns.

I am Dr. Robert Foster, Director for BioSystems, Office of the Deputy Undersecretary of Defense (Science and Technology) (ODUSD(S&T)). My office is a component in the organization managed by the Director of Defense Research and Engineering (DDR&E). As the Director for BioSystems, I oversee the Defense biomedical science and technology program.

Today I will focus my testimony on a research program that was initiated with the Fiscal Year 1999 Defense appropriation for Research Development Test and Evaluation (RDT&E). At that time the Department established a dedicated program element to support basic research into Gulf War Illnesses and related deployment health concerns. I also will address research activities funded with special Defense RDT&E appropriations over the period of Fiscal Years 1994 to 1998 and focused on GWVI. I will begin by briefly reviewing our processes for initiation and oversight of these research efforts.

Department of Defense Oversight of Research

In February 1998, my predecessor, Dr. Anna Johnson-Winegar, provided a detailed overview of the processes that the Department uses for establishing research priorities and for selecting proposals for contract and grant awards. The processes have not materially changed since that testimony. Hallmarks of the process include independent scientific review for technical merit and programmatic review for relevance. This process is further augmented through assistance with defining research scope from the interagency Research Working Group (RWG) of the Persian Gulf Veterans Coordinating Board (PGVCB). The assistance of this interagency RWG is essential in order for this program to focus on the most vexing health care issues in GWVI and deployment health. Dr. Feussner and Dr. Mazzuchi have already provided more detailed information on the role of the DoD and Veterans Administration's clinical systems in defining research needs. In many ways the success of our research program depends on insights from medical practitioners, from the results of clinical epidemiological studies, and from the process of defining the clinical characteristics of disease.

The RWG plays the essential role of providing the linkage between medical practitioners both inside and outside the Department and the scientists doing the basic research and allows each individual Department's scientific strengths to be unified into a productive, responsive and fully integrated national research effort.

The Department is committed to a coordinated and scientifically meritorious research program that accomplishes the following:

- Furthers the fundamental understanding of illnesses relevant to service during conflict including the Gulf War deployments;
- Provides enhanced diagnostic capabilities and effective treatments for these illnesses; and
- Supports the establishment of policies and preventive measures that minimize the risk of such illnesses during future military operations.

The Department and our Federal partners are committed to answering basic science questions related to Gulf War Veterans' health concerns and any emerging health concerns associated in general with military deployments. The challenges to the scientists supported by this program are great and, while there may be no quick solutions, all concerned have devoted their energy to responsible, aggressive pursuit and resolution of the problems. Dedication to partnership is an essential element of the scientific community that is engaged in this effort. The clinical and research components of the Veterans Administration, the military health care community led by the Office of the Assistant Secretary of Defense for Health Affairs, and the basic scientists of our in-house laboratories and from the independent science community all intersect. I believe that this research program can address the breadth of issues related to GWI and deployment health. A broad spectrum of hypotheses concerning illnesses in Gulf War veterans have been or are being pursued through this program of basic science research. I will highlight some specific examples later in this testimony.

We are steadfast in ensuring that our research program is of the highest quality. We use competition and independent review for scientific merit to secure the best research performers, hypotheses, and experimental designs, from all possible sources, including the Federal, civilian, national and international communities. This commitment follows an appreciation at all levels within the Department of our responsibility to achieve an optimal investment of this research appropriation. It also reflects our desire to quickly transfer knowledge derived

from the research into a form that can assist Gulf War veterans to secure diagnoses and treatments for their disabilities and illnesses, and to prevent such disabilities and illnesses as a consequence of future deployments.

Research Solicitations and Awards

The majority of all appropriations to date (1994-1999) for GWVI research have been executed as part of a technically meritorious, competitive research program. The U.S. Army Medical Research and Materiel Command (USAMRMC) is the program management agency for this DoD research program. The processes and procedures of USAMRMC are utilized to solicit, review, award, monitor, and close out all research projects. The majority of the contract and grant awards have resulted from DoD solicitations using "specific purpose announcements" issued under a USAMRMC Broad Agency Announcement (BAA).

Seven GWVI special-topic BAAs were issued for RDT&E appropriations from 1994-1998. To date, these seven announcements have resulted in 43 contract or grant awards. A summary of this activity is provided in the following Table.

GWVI BAA SUMMARY (FY94 – FY98)

Date of Announcement	Special Solicitation Subject Area	Proposals Received	Awards/ Completed	Funding*	Reports
29 Apr 94	Low-level chemical sensitivities	5	1/1	375,000	GL:1 OL:6
29 Apr 94	Depleted uranium	2	2/1	1,916,214	GL:3 OL:5
24 May 95	Gulf War Illness, 3 subtopics	117	14/3	8,922,100	GL:3 OL:17
10 Dec 96	Low-level chemical exposures (includes open BAA submissions)	22	8/1	6,722,000	GL:1 OL:16
29 Jan 97	Gulf War Illnesses (non-Federal) (includes addition of DoD $3M)	36	9/2	12,198,516	GL:3 OL:23
29 Jan 97	Historical War Syndromes	14	3/0	1,915,687	GL:0 OL:1
20 Nov 97	Gulf War Illnesses (non-Federal, U.S. universities)	41	5/0	7,432,791	GL:0 OL:0

Key: Funding* – amount provided to contractors/grantees and does not include other Defense RDT&E program costs

GL: - government technical literature publication

OL: - open source technical literature publication

Numerous insights have resulted from the research projects initiated with the RDT&E funding from 1994-1998, and work on some efforts has been extended. Following are five examples:

1. Development of an effective skin test for Leishmania was expanded to include New World antigens as well as a diagnostic capability for the type of Leishmania encountered in the Persian Gulf. This product provides important new diagnostic capabilities for future deployment, and it is expected to enter Food and Drug Administration approved Phase I clinical trials this year. Further Leishmania research supported with Fiscal Year 2000 GWVI funding is expected to improve prevention and treatment capabilities.

2. Results from a study with Dr. Garth Nicolson that evaluates his mycoplasma assay in Gulf War veterans who have health problems compared to a group in good health will be forthcoming. At our last briefing to this committee, it was noted that we had provided funding to Dr. Nicolson to provide the training in his assay technique for other investigators involved in this validation study. After delays associated with selection of an appropriate test population, an additional contract for more than a half million dollars was awarded to collect and manage blood samples and to fund the participation of Dr. Nicolson and other independent mycoplasma investigators. Collection of the needed blood samples will be completed this calendar year. In addition, we have initiated an antibiotic treatment trial that will test if treatment of mycoplasma infection results in improvement of symptoms.

3. Our cooperative research agreement with Dr. Robert Haley was extended to permit analysis of the large amount of data that he has collected in tests of a Seabee veteran population. He recently reported finding a significant neurochemical difference between symptomatic veterans and his healthy group. Although this was only one test from a large battery of tests applied in the study and, of course, needs to be confirmed in further studies, this may contribute to objective measures which can be linked to specific subjective symptom reports. Dr. Haley's work has already advanced our

knowledge of disease variables in GWVI that should be examined with basic research in neurobiology.

4. At the last hearing, Dr. Dan Clauw presented research on hard-to-diagnose conditions such as chronic fatigue syndrome (CFS), fibromyalgia (FM), and chemical sensitivities, conditions with symptom complexes very similar to those of undiagnosed problems in Gulf War veterans. Since then, he has shown that Gulf War veterans have many similarities to patients in the general population with these diagnoses, such as changes in pain sensitivity and other changes in nervous system activity. Dr. Clauw has demonstrated the importance of health habits as simple as exercise frequency, following up on the finding that modest exercise is an effective treatment for some patients with CFS and FM. Subjects who experimentally ceased their regular exercise routines developed symptoms common to these conditions and with similarities to those of undiagnosed Gulf War veterans. In addition, Dr. Clauw will be participating with colleagues from the DoD and DoVA in a treatment trial investigating the potential benefits of exercise and cognitive behavior therapy. We expect that Dr. Clauw's work will substantially advance understanding and treatment of these illnesses.

5. Finally, Dr. Simon Wessely at King's College in London has explored hypotheses similar to those of Dr. Haley and Dr. Clauw using a population of British veterans of the Gulf War. His findings of undiagnosed symptoms are similar to ours. Although physical symptom measures were reported more frequently in their Gulf War veterans, the pattern of symptoms was also present in Bosnia and non-deployed groups of soldiers. His project was extended to permit completion of objective clinical tests of symptomatic and healthy veterans.

I now will turn to the research program established in Fiscal Year 1999 in the basic research account of the Defense-wide RDT&E appropriation.

<u>New Gulf War Illnesses and Force Health Protection Research Funding</u>

In 1999, DoD established a new program element within the basic research budget to provide stable funding for systematically tackling research gaps in our understanding of GWVI and Force Health Protection issues. The appropriated amounts for this Program Element were $22.588 million in FY 1999 and $24.543 million in FY 2000. The overall strategy is to deal with relevant research issues in five thrust areas, with periodic evaluation of progress resulting in an annual, tailored solicitation for research proposals. The five thrust areas are, as follows:

- Health-hazard assessment methods for toxic industrial and agricultural chemicals and mixtures;
- Force Health Protection – epidemiological studies and deployment health monitoring methods;
- Safety of medical materiel in operational environments;
- Prevention and treatment of undiagnosed persistent stress symptoms; and
- Leishmania diagnosis methods, treatments, and vaccine.

Funding also will be available to continue research in the original portfolio to permit follow up on emerging findings. This plan has been carefully developed in coordination with the RWG. As mentioned before, the role of the RWG is to provide an essential linkage and communications path to the interagency research effort, to health care communities, and to Veterans.

In comparison to the 1994-1998 program, the most important distinction of this new, dedicated program funding is the ability to plan and implement a long-term strategy of deployment health research. In response to health questions following the Gulf War and the increasing demands of a series of hazardous deployments, the Department has undergone a fundamental reorientation. A new strategy has been developed and is being implemented to protect U.S. forces against all foreseeable physical and psychological threats. DoD's "Force Health Protection" strategy balances the military's key responsibilities to: 1) promote and sustain health and wellness throughout each person's military service; 2) prevent acute and chronic casualties; 3) rapidly stabilize, treat, and evacuate casualties; and, 4) perform medical surveillance, longitudinal health studies, and ensure adequate medical records documentation and clinical follow-up for deployed forces. The establishment of a dedicated research program is a key enabler for this new strategy on deployment health.

New Research in FY99

In 1999, tailored research solicitations were advertised to pursue significant areas of research under most of the GWVI and force health protection thrusts. The topics of the four solicitations were, as follows:

- Force health protection and deployment health;
- Innovative biologically-based toxicology methods and models for assessing mixed chemical exposures with potential neurotoxicological and other health effects;
- Interactions of drug, biologics and chemicals in service members in deployment environments; and
- Integrated psychosocial and neuroscience research on stress and somatic consequences.

In addition, the Leishmania thrust area is being addressed by in-house research at the Walter Reed Army Institute of Research and the Naval Medical Research Center.

The solicitations elicited 81 proposals. From this group of proposals, there have been or will be approximately 17 awards for research work. A summary of this solicitation will be included in the Annual Report to Congress. I will briefly highlight four of the awards as representative of the breadth and quality of the research we are pursuing, and will describe some anticipated benefits of this work to past, current, or future military members:

1. Motor-vehicle crashes are the leading cause of death among active-duty Army personnel, and are the only cause of death significantly higher for GW veterans compared to non-deployed veterans. Potential risk factors for fatal motor vehicle accidents will be studied in a large population of current and former military personnel.

2. The role that deployment experiences play in Army National Guard soldiers' health will be examined. This establishes baseline health parameters and follows changes when soldiers are deployed and after they leave the military, considering also the effect of job strain associated with National Guard service as a "second job."

3. The metabolism of chemicals important in military deployments and that were also important in the Gulf War will be studied. Using animal studies, effects of these chemicals on activation of the enzyme systems important in humans for disposal of toxic chemicals will be investigated. This will lead to identification of populations at special risk for health consequences from exposure to these toxic chemicals and may provide methods to determine exposures after the fact.

4. We will reexamine the question of whether or not physical and biochemical stressors can modify access to the brain of chemicals that would normally be prevented from reaching the brain. This study will help determine whether normal assumptions about the safety of drugs need to be reconsidered in the context of use in military settings.

New Research Solicitations in FY00

With the Fiscal Year 2000 Defense RDT&E appropriation, a new round of research solicitations will be developed and issued. In fact, the USAMRMC proposal for the Fiscal Year 2000 topics has been reviewed and approved by the RWG. The topics are in the following key areas:

- Biochemical and physiological markers to assess toxic chemical exposures and health effects in deployed military personnel;
- Epidemiological investigations of deployment health monitoring methods;
- Toxicity of militarily-relevant heavy metals; and
- Deployment stress health and performance consequences.

It should be apparent that these topics carry forward some concerns identified in previous years. Projects that result from successful proposals, together with additional funding for Fiscal Year 1999 research projects on health behavior interventions and improved monitoring of the health of deployed soldiers, will contribute to our goal of ensuring that many health problems encountered in the Gulf War will not be repeated in future deployments.

Additionally, the DoD and VA are acting on the recommendations from the recent Institute of Medicine (IOM) report, *Gulf War Veterans: Measuring Health.* In response to questions from Congress and the GAO, the DoD and VA asked the IOM to recommend strategies and methodologies to answer the following questions: 1) how many Gulf War veterans are suffering from health problems that affect their ability to function; 2) whether the prevalence of such problems among gulf War veterans is consistent with their prevalence among the general public or among other veterans groups; and 3) whether the health of veterans is getting better, staying the same, or deteriorating with time. The IOM noted in this report that many veterans, active-duty personnel, governmental agencies, and non-governmental scientists and physicians have a strong interest in finding answers to the numerous and complex questions regarding the health of Gulf War veterans, and that various types of research and health measurement are needed to address these diverse issues.

To address these questions, the IOM stated that it will be necessary to measure not only the health status of those who served in the Gulf War, but also to compare Gulf War veterans with other groups through time to determine whether the groups differ in the way their health status is changing. The IOM committee quickly realized that such a study could have important implications for understanding not only the health of Gulf War veterans, but also the health of veterans of other conflicts.

The IOM Committee recognized that the recommended study will be challenging and that it will require a sustained commitment of resources by Congress, VA and DoD, and of time and cooperation by study participants. Nevertheless, the Committee felt that these commitments are important and worthwhile if the nation is to adequately understand and respond to the health needs of not only Gulf War veterans, but veterans of any conflict in which significant U.S. military forces are committed. The IOM recognized that if study began immediately upon return from participation in a conflict, many of the problems we face in attempting to resolve Gulf War veterans health issues, several years removed from the end of that conflict, could be mitigated. The IOM, DoD and VA agreed that such efforts would contribute greatly to our understanding of the impact of military conflict on the health of the men and women who serve in those conflicts.

The DoD and VA are currently working on a research strategy to implement the recommendations of the IOM and conduct longitudinal cohort studies on military forces including follow-up of Gulf War veterans. These studies will be national in scope, based on probability sampling, and used to collect a broad range of morbidity data related to health outcomes among deployed military forces. The study design will permit estimation of the distribution within the population of a broad variety of health-related measurements, including psychological measurements. The study design will capitalize on existing and planned DoD and VA infrastructure and resources to track and measure health of military forces and veterans. The stable nature of the new program funding will provide for consistency in the research component of this study approach.

Summary of Oversight Initiatives and the Research Investment

In the presentation to this committee in 1998, you heard about several actions to be taken by the DDR&E to increase visibility and oversight of Defense research efforts on GWVI. Those initiatives have paid significant dividends in terms of program quality, and it is appropriate to provide an update at this time:

1. The first action was the establishment of a single Defense Program Element for dedicated research into GWVI and deployment health. As you have heard, this has been completed. In fact, program accomplishments, plans and resource information will appear as a single program on the RDT&E Budget Item Justification Sheet (R-2 Exhibit) in the future submissions for the Defense-wide Science and Technology program.

2. For the second, we chartered a Working Integrated Process Team (WIPT) on Deployment Toxicology in November 1997 and their work has been completed successfully. This team was established to review current toxicology research initiatives and to develop appropriate recommendations for the Defense biomedical research oversight body, the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee. The issues addressed by the WIPT originated from a concern that DoD research on long-term health consequences,

such as from low level chemical exposures, may have less visibility and priority in comparison to more immediate health and performance issues facing deployed soldiers. Indeed, greater attention to these types of issues is one of the positive changes produced by the public dialogue on GWVI. The WIPT has identified a timely, proactive process for bringing operational, occupational, and environmental health issues to the research community. The process has been implemented with productive interactions between the Joint Environmental Safety Working Group (JESWG) (health-care requirements) and the Military Operational Medicine (MOM) Joint Technology Coordinating Group (medical research).

3. The third and last initiative concerned outside review of research. We have incorporated review of DoD-sponsored GWVI science and technology in the Technology Area Review and Assessment (TARA) process. This subjects the program to scrutiny by recognized experts in biomedical science and technology who assess its objectives, scientific rigor, resources, and output. The Biomedical TARA Panel reviewed the program in March 1999, rating it positively and looked forward to a report of continuing success when the review is held again in 2001.

These initiatives are indicative of the Department's determination to invest in an aggressive, coordinated program of basic research into Gulf War Illnesses. In doing so, we are following the general procedures for conducting a quality program as mandated by the Deputy Under Secretary of Defense (Science and Technology). It is important to recognize that each specific RDT&E program has its own detailed, tailored approach under the Department's broader policy guidance for science and technology programs. In the case of the GWVI and Force Deployment Health program, USAMRMC serves as program manager. A unique aspect of this program is that USAMRMC utilizes the members of the RWG in developing the investment strategy and in assessing proposals. This interagency coordination mechanism is essential and has been successful.

One indicator of that success is that the investment in GWVI has been highly effective in providing new information on the impact of military service in the Gulf War on health-related problems, in providing new areas of research

exploration, and in prompting new force-protection initiatives that provide for medical surveillance during future operations. With specific reference to GWVI, the investment and findings have highlighted the need for improved prevention, intervention, and treatment approaches, and the national program has responded to these needs both in its approaches for veterans' health care and in the RWG emphasis on its research investment strategy.

Although the investment in GWVI research has already provided meaningful results, the true impact of this research cannot be fully assessed for years after awards are made. Once initiated, studies usually take between 3 and 5 years to complete. The final results are normally published in the scientific literature several months after completion of the contract or grant. Over time, these individual studies eventually merge into a body of knowledge that may be used for definitive prevention and treatment of an illness, as well as for advancing related scientific hypotheses for subsequent work. Nonetheless, progress in this research area will be evident in the summaries provided in the annual interagency report. Indeed, the details of the RWG-coordinated and -integrated research efforts of DoD, VA, and DHHS will be provided in the Annual Report to Congress that the Secretary of Veterans Affairs will submit this calendar year. When you review that report, I believe you will see ample evidence of a high-quality, carefully planned research program.

Conclusion

The organizations testifying before you today share a genuine concern for and recognition of the magnitude and consequences of the medical and scientific challenges before us. Our sense of shared responsibility is reflected in our commitment to work in a productive and cooperative manner that exploits our respective Departments' scientific strengths and unifies them into a productive, responsive and fully integrated research effort. As you are aware, the path of science is difficult, challenging, expensive, and time-consuming. Easy and complete solutions to complex health problems are exceptionally attractive but extremely rare. This truth is especially obvious to those who suffer the consequences of prolonged, often incapacitating, illnesses of uncertain or unknown origins and for whom current medical science offers little in the way of long-lasting relief or a cure.

While there may be no quick solutions to the health problems experienced by Gulf War veterans, we are committed to responsible and aggressive pursuit and resolution of those problems and to the prevention of similar illnesses following future deployments. We appreciate the continuing interest in this important topic shown by members of the committee.

Mr. Chairman, I am prepared to answer your questions.

Statement
of
LTG (Ret) Dale A. Vesser
Deputy Special Assistant to the
Deputy Secretary of Defense for Gulf War Illnesses

House Committee on Government Reform
Subcommittee on National Security, Veterans Affairs,
and International Relations
February 2, 2000

Mr. Chairman, I appreciate the opportunity to appear before the Subcommittee on National Security, Veterans Affairs, and International Relations to review with you and the members of the subcommittee the support the Office of the Special Assistant for Gulf War Illnesses provides to the ongoing research into the potential causes of Gulf War illnesses.

As you know, the Office of the Special Assistant for Gulf War Illnesses does not directly undertake medical research and, with a few exceptions, does not directly sponsor medical research. When the office was established, the then-Deputy Secretary of Defense, Dr. John White, reconfirmed the Department's policy that the Assistant Secretary of Defense for Health Affairs was responsible for the Department's medical programs. In that regard, the Assistant Secretary of Defense for Health Affairs and the Deputy Under Secretary of Defense for Science and Technology represent the Department on the Research Working Group of the Persian Gulf Veterans' Coordinating Board, which coordinates pertinent medical research for DoD, Veterans Affairs, and Health and Human Services.

Over the last three years, the Office of the Special Assistant has been instrumental, however, in funding or impacting the funds of several medical research programs that, for one reason or another, were not being supported by the traditional medical research funding process. Generally speaking, these did not receive sufficiently high evaluation scores in the competitive medical review process, but had become of great concern with a significant number of Gulf War veterans. We recognize that sometimes exceptions need to be made to the competitive medical review process. Specifically, we believe that in the case of Gulf War illnesses, it is important to listen to our veterans and provide any assistance we can by researching claims to the potential cause and cure for the unexplained illnesses that are affecting many of them. Frankly, we have a credibility problem with some veterans who believe that we are not funding promising research because we either don't care about their health or that we have something to hide. In such cases, we can demonstrate that neither is the case. We owe it to our veterans to apply accepted medical research standards to determine if the theory being proposed can help either explain why veterans are ill or help in their treatment.

Let me highlight for you the projects that we have either directly funded or have been instrumental in making sure that funds were provided. This is in addition to the general work of our office. Specifically, we have funded or impacted the funding of the work of Dr. Garth Nicolson (Tests for Mycoplasma fermentans [incognitus strain] in human blood) and Dr. Robert Haley (Multi-

Disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes). We have also funded a review of the medical records of the Saudi Arabian National Guard by the Uniformed Services University of the Health Sciences and the Naval Health Research Center.

As you know, we have commissioned a number of medical literature review papers prepared by the RAND Corporation. These papers are not medical research in the traditional sense, but were important to inform and direct the work of our office. These papers, case narratives, information papers, and our environmental exposure reports are available on the Internet at GulfLINK, and have been reviewed by the Presidential Special Oversight Board headed by former Senator Warren Rudman.

We also helped to coordinate for DoD funds to be provided to the Department of Veteran's Affairs program in Baltimore to monitor the health of veterans exposed to depleted uranium. I am pleased to say that the last published results for this program, and I quote, "show no evidence of adverse clinical outcomes associated with uranium exposure at this time in these individuals."

Again, thank you Mr. Chairman for giving me the opportunity to put the work of the Office of the Special Assistant into the proper context, I stand ready to answer any question you or the Subcommittee may have.

TESTIMONY OF

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NATIONAL CENTER FOR ENVIRONMENTAL HEALTH

CENTERS FOR DISEASE CONTROL AND PREVENTION

U.S. PUBLIC HEALTH SERVICE

BEFORE THE

SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS AND

INTERNATIONAL AFFAIRS

COMMITTEE ON GOVERNMENT REFORM

U.S. HOUSE OF REPRESENTATIVES

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Mr. Chairman, thank you for the opportunity to update the Subcommittee on the Centers for Disease Control and Prevention's (CDC) research programs pertaining to Gulf War veterans' illnesses and to discuss the General Accounting Office's (GAO) report, "Gulf War Illnesses: Management Actions Needed to Answer Basic Research Questions." I am Dr. Drue Barrett, Chief of the Veterans' Health Activity Working Group in the Division of Environmental Hazards and Health Effects of the National Center for Environmental Health (NCEH). I serve as CDC's liaison to the Department of Health and Human Services (HHS) on Gulf War issues and I am a member of the Research Working Group of the Persian Gulf Veterans Coordinating Board. NCEH has been designated as the lead Center at CDC for addressing Gulf War veterans' health concerns, however other Centers within CDC have also been involved in this effort, most notably, the National Center for Infectious Diseases.

The purpose of my testimony is to update the Committee on the extent of CDC's Gulf War research activities, the productivity of our research efforts, and how our research has been coordinated with the research being conducted by other Federal agencies.

Completed CDC-funded Gulf War Studies:

Before describing our current studies, I would like to review the results from two completed CDC-funded studies because these studies are pertinent to questions raised by the GAO regarding the success of the federal government in documenting the symptoms of Gulf War veterans. The Iowa study, conducted in collaboration with the Iowa Department of Public Health and the University of Iowa, was one of the first population-based epidemiologic studies to document that Gulf War veterans are reporting more medical and psychiatric conditions than their non-deployed military peers. In fact, this study was recently described by the Institute of

Medicine as "perhaps the strongest study on Gulf War veterans' experience of symptoms related to deployment in the Gulf." The 3,695 subjects who completed this study were selected from a larger population of almost 29,000 military personnel who listed Iowa as their home of record. Furthermore, the subjects in this study were specifically selected to represent individuals from all four branches of the military, and include both regular military personnel and National Guard and reservists. Seventy-six percent of the eligible study subjects completed the detailed telephone interviews. This study is also one of the first controlled epidemiological studies to evaluate the health consequences of the Gulf War. The study included a carefully selected comparison group of military personnel who were not deployed to the Persian Gulf but who served during the time of the Gulf War. The Iowa study found that the Gulf War military personnel were more likely than those who did not serve in the Gulf War to report symptoms suggestive of cognitive dysfunction, depression, chronic fatigue, post-traumatic stress disorder, and respiratory illness (asthma and bronchitis). The conditions identified in this study appear to have had a measurable impact on the functional activity and daily lives of these Gulf War veterans. Among Gulf War veterans, minimal differences were observed between the National Guard or reserve troops and the regular military personnel.

The results of the Iowa study were published in the *Journal of the American Medical Association* in 1997. In addition, a number of other manuscripts from the Iowa study have been published, are in press, or are currently in the process of peer review. These include an article on quality of life and health service utilization among military personnel reporting multiple chemical sensitivities, published in 1999 in the *Journal of Occupational and Environmental Medicine*, and an article on symptom prevalence and risk factors of multiple chemical

sensitivities, in press in the *Archives of Internal Medicine*. Manuscripts are currently being considered at peer-reviewed journals on the topics of defining a Gulf War syndrome, the relationship between post-traumatic stress disorder and physical health status, and self-reported injuries among Gulf War veterans.

Likewise, the CDC Air Force study has significantly contributed to our understanding of the health consequences of the Gulf War. This study organized symptoms reported by Air Force Gulf War veterans into a case definition, characterized clinical features, and evaluated risk factors. The cross-sectional questionnaire was sent to 3723 currently active volunteers from four Air Force populations. Clinical evaluations were performed on 158 Gulf War veterans from one unit, irrespective of health status. A case was defined based on reporting one or more chronic symptoms from at least 2 of 3 categories (fatigue, mood-cognition and musculoskeletal) and was further characterized as mild-to-moderate or severe depending on the severity of the reported symptoms. The prevalence of mild-to-moderate and severe cases were 39% and 6%, respectively, among 1155 Gulf War veterans versus 14% and 0.7% among 2520 non-deployed veterans. Fifty-nine (37%) clinically evaluated Gulf War veterans were non-cases, 86 (54%) were mild-to-moderate cases and 13 (8%) were severe cases. The key observation of the study was that Air Force Gulf War veterans were significantly more likely to meet criteria for severe and mild-to-moderate illness than were non-deployed personnel. There was no association between the chronic multisymptom illness and risk factors specific to combat in the Gulf War (month of season of deployment, duration of deployment, duties in the Gulf War, direct participation in combat, or locality of Gulf War service). The finding that 15% of non-deployed veterans also met illness criteria was equally important and suggests that the multisymptom

illness observed in this population is not unique to Gulf War service. The clinical evaluation component of the study found that neither mild-to-moderate nor severe cases were associated with clinically significant abnormalities on physical examination or routine laboratory tests. However, Gulf War veterans classified as having mild-to-moderate and severe illness had a significant decrease in functioning and well-being compared with non-cases.

The results from this study were published in CDC's *Morbidity and Mortality Weekly Report* in 1995 and in the *Journal of the American Medical Association* in 1998. In addition, an article from the Air Force study examining the relationship between deployment stressors and chronic multisymptom illness is currently in press in the *Journal of Nervous and Mental Disorders.*

Current CDC-funded Gulf War Studies:

CDC is currently funding a follow-up to the Iowa study focusing on evaluating self-reported symptoms of asthma. This study involves a detailed clinical evaluation of a sample of subjects who completed the initial telephone survey. This evaluation includes a physical examination; tests of lung functioning; questions regarding medical, occupational, and exposure history; assessment of functional status and quality of life; and assessment of psychiatric history and personality functioning. The examinations are being conducted at the University of Iowa Hospitals and Clinics in Iowa City, Iowa. This study is in its final phases of data collection and we anticipate that results should be available later this year.

The University of Iowa has also been funded by the Department of Defense (DoD) to conduct validation studies of additional health outcomes among participants of the telephone survey. These include validation of depression, cognitive dysfunction, and fibromyalgia. CDC is

providing technical assistance to DoD and the University of Iowa for this study.

We are also funding the Boston University School of Public Health to conduct a study examining the relationship between cognitive function and symptom patterns among Gulf War veterans. In one component of this study, functional magnetic resonance imaging (fMRI) is being used to examine possible differences in brain activation patterns between Gulf War veterans and era controls with different levels of symptoms. A second component of the study is using a new data-driven mathematical technique, Logical Analysis of Data, to examine how Gulf War veterans' symptoms cluster together. This may provide useful information for determining etiology or for developing a case definition. Finally, this study also includes a component examining the neuropsychological functioning of a sample of Danish Gulf War troops. Investigators are currently in the data collection phase for the fMRI component of this study and in the data analysis phase for the other two components. We anticipate that this study will be complete by the end of this year.

Finally, CDC is funding the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School to conduct a study examining case definition issues. The study will assess the persistence and stability of Gulf War veterans symptoms over time, compare the performance of data-driven case definitions to existing definitions for medically unexplained symptoms, and examine the role of psychiatric conditions in Gulf War veterans' unexplained illnesses. We originally expected that this study would be completed in late 2000, however the process of protocol development and clearance took somewhat longer than we anticipated. Thus, we expect that this study will require an additional year to complete.

Research Collaborations:

CDC is collaborating with DoD and the Department of Veterans Affairs (VA) on a number of projects including a study of health outcomes among Saudi Arabia National Guard members and a study of Amyotrophic Lateral Sclerosis (ALS) among Gulf War veterans. This collaboration has included providing input on study protocols, reviewing human subjects issues, and assisting in laboratory assessments.

Future Gulf War Research Planning:

In addition to these current research projects, CDC, in collaboration with other HHS agencies, recently sponsored a conference to develop future Gulf War research recommendations. On February 28 through March 2, 1999, CDC brought together scientists, clinicians, veterans, veterans' service organizations, Congressional staff, and other interested parties to discuss and make recommendations regarding the direction of future research on undiagnosed illnesses among Gulf War veterans and their links with multiple chemical and environmental exposures.

Concurrent workgroups were convened in order to develop research recommendations in four areas: pathophysiology, etiology, and mechanisms of action; assessment and diagnosis of illnesses; treatment; and prevention of illnesses in future deployments. This conference highlighted the importance of including veterans in the process of planning and implementing research. Veterans and scientists alike expressed that they found the process useful and that future similar efforts should be encouraged. A report is soon to be released that summarizes the outcome of each of the four workgroup sessions. It is anticipated that this report will be of interest to a broad range of individuals and organizations and may provide the basis for development of new research collaborations and exchanges. Recommendations for new research

will need to be considered in light of the existing research portfolio of the Research Working Group in order to avoid unnecessary duplication of efforts.

Coordination of Federal Research Efforts:

Finally, I would like to address the issue of coordination of federal research efforts. There has been HHS representation on the Persian Gulf Veterans Coordinating Board Research Working Group since its inception. In addition to CDC, the Office of the Secretary, the National Institutes of Health, and the Agency for Toxic Substances and Disease Registry are represented. Through its membership, HHS has been involved in providing guidance and coordination for DoD, VA, and HHS research activities relating to Gulf War veterans. Specifically, this has included assessing the state and direction of research, review of government research concepts as they are developed, identification of gaps in factual knowledge and conceptual understanding, and providing recommendations regarding research direction.

The Research Working Group also serves as a forum for research data exchange among the three departments and among federally funded investigators. CDC's role in this area has included providing information on the status of projects for a research database of all VA, DoD, and HHS research activities, input on the Annual Report to Congress on federally sponsored Gulf War Veterans' Illnesses research, and participation on the planning committee for the federal investigators meeting where new research results are shared.

Conclusions:

An intensive research effort to address Gulf War veterans' health concerns has been mounted by federal agencies and non-governmental scientists. As of 1999, there have been 145 federally-funded research projects on Gulf War veterans' illnesses with a cumulative expenditure

of $133.5 million for research from FY94 through FY99. These projects represent a broad spectrum of research efforts, ranging from small pilot studies to large-scale epidemiology studies addressing mechanistic, clinical, and epidemiological issues. Similar efforts have been initiated in other coalition countries, most notably in the United Kingdom and Canada. In addition, numerous review panels and expert committees have evaluated the available data on Gulf War veterans' illnesses. As noted in the GAO report, despite these extensive research and review efforts, many questions remain regarding the health impact of the Gulf War. However, these remaining questions do not reflect scientific indifference; instead they reflect the complexity of assessing and predicting the health impact of military deployments. Despite this complexity, the federal research effort continues in an effort to uncover the causes of illnesses among Gulf War veterans so that effective treatment approaches can be developed and similar illnesses in future deployments can be prevented.

Mr. Chairman, this concludes my testimony. I would be happy to answer any questions the Subcommittee may have.

Committee on Government Reform
Subcommittee on National Security, Veterans Affairs, and International Affairs
United States House of Representatives
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Invited Testimony by

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I have been asked to give my views about the Government's Gulf War research programs and to summarize my own research related to Gulf veterans' illnesses, with a focus on the direction medical science is taking or should be taking, to address the issue. I am currently a VA-funded researcher investigating an area termed neural sensitization as a possible mechanism for development of heightened responsivity to low levels of environmental chemicals in Gulf veterans. I have also been involved in research on possible mechanisms of illness from low level chemicals, primarily funded by private foundations, for almost 25 years. I have published numerous peer-reviewed papers on this subject in civilians, as well as several book chapters and a scientific monograph. Our research group published results of a preliminary study on elevated prevalence of self-reported chemical intolerance in chronically ill Gulf veterans compared with controls in the journal *Military Medicine* in 1998. My work is interdisciplinary, influenced by clinical training in psychiatry and research training in the neurosciences and in multifactorial health outcomes research. I am speaking today as an individual researcher, not as an official representative of the VA or any other agency.

With regard to the issues for medical science and Gulf-related illness, my points are as follows:

- As noted in the GAO report (p. 13), data from several studies on Gulf veterans with unexplained illness suggest convergent themes of multiple, non-specific symptoms in multiple systems of the body ("fatigue, neurocognitive complaints, and musculoskeletal complaints..."). Collectively, these symptoms have pointed to a potentially increased prevalence of controversial, phenomenologically overlapping set of conditions that have, to date, fallen at the outskirts of conventionally-accepted diagnoses. These conditions include chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity (Buchwald and Garrity 1994).

- Civilian research, including our own studies of chemical intolerance, suggests that varying degrees of these conditions may be common in the general population, without reaching a level of severity that merits a clinical diagnosis (Bell et al. 1998b; Jason et al. 1999). Some research on ill Gulf veterans indicates a similar type of continuum. In other words, these may not be conditions that are fully a "case" or not a "case" to the examining physician. Rather, they may be present *to a degree*. This type of problem poses significant, though not insurmountable challenges to epidemiological research approaches, which, as the GAO report indicates, rely on case-ness or non-case-ness. Other, sophisticated statistical approaches are available to deal with this problem (e.g., Mulaik 1998).

- It is likely that most Gulf veterans who have non-controversial, even if rare, diagnoses at a clinical degree of severity have received and/or could receive effective medical care within the VA, DoD, or civilian health care systems. The ability to make some progress in studies of leishmaniasis would be an example of this point.

- However, typically in medicine, when a patient is "subclinical" in severity or appears to have a controversial diagnosis of which the average physician is skeptical or unfamiliar, conventional care has little to offer. This is especially the situation when there is no standardized, widely-available laboratory test to assist in confirming a diagnosis (as in unexplained Gulf-related illnesses in veterans). Overt, diagnosable diseases, not lesser levels of wellness, are the usual domain of conventional medicine.

- If the above argument is valid, then it follows that one factor accounting for the delays in progress with Gulf-related illness research is that the problem may be challenging the field of medicine and medical research in general, which the VA and DoD approaches reflect, to change its prevailing beliefs now, not some time in a distant future, i.e., much sooner and more abruptly than it otherwise would do.

- Studies on unexplained illnesses in Gulf veterans are generating scientific data that logically tell us to take polysymptomatic patients and the controversial conditions of chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity more seriously than ever before, even though the long-standing debates over the validity of the multiple complaints and of the existence of the conditions in civilians remain intense and emotional. Those of us who have worked in this area for many years are well aware of the illogic and frequent lack of objectivity in these debates. This situation could reflect an appropriate conservatism on the part of medicine against accepting every "odd" idea put out for consideration. However, in my view, given the growing weight of evidence, it is more likely a current example of resistance by scientists, even to new ideas with reasonable merit (Barber 1961). This resistance is partly a reflection of social nature of science and scientists in making and acknowledging discoveries.

- The fact that a subset of veterans, who likely were more fit at the time of deployment than the average civilian, nonetheless became ill, offers us an opportunity to understand how these types of health problems can develop. The possibility of multi-causal factors in etiology adds complexity but also may be the appropriate approach to understanding the emergence of illness in veterans with different experiences and different exposures in the Gulf War theater.

- What is crucial to note here, is that much research has previously focused on identifying the original etiological factors in initiating the Gulf illnesses. This work is limited by a myriad of indeterminate variables relating to exposures. It assumes that we must know some specific "cause" if we are to find the appropriate treatment. This is a very reasonable assumption, but it might be limiting our vision in the area of Gulf War treatment research. If these illnesses were classical toxicant-induced processes, research would be showing clearer linkages by now between specific symptoms and possible Gulf exposures. However, most of the polysymptomatic symptoms are not those usually associated with a specific toxicant in the field of toxicology. We are fairly certain that every ill Gulf veteran did not have exactly the same exposures as every other veteran with similar symptoms. A straightforward linkage is not emerging from the available data.

- Even without knowledge of initiating factors, it is still possible to examine the eliciting factors that make a given veteran susceptible to illness, e.g., *current* triggering variables in veterans' illness. My own research on ill Gulf veterans is attempting to test for one possible mechanism by

which polysymptomatic conditions and enhanced susceptibility to environmental chemicals, foods, drugs, and stress could now be elicited, even though we do not know with certainty the possible initiating factors (see below).

- Unfortunately, even assuming that the medical profession were to accept the validity of these subclinical polysymptomatic conditions and controversial diagnoses tomorrow, we then still face the question of treatment. Conventional psychiatry often has effective tools to treat depression and anxiety disorders with which some Gulf veterans have been diagnosed. However, conventional psychiatry has no effective tools with which to treat patients that it labels as having a "somatoform disorder" (a non-etiological, descriptive label for multiple symptoms in multiple systems with no known conventional diagnosis) or, worse, a subclinical collection of symptoms in multiple systems from which many Gulf veterans suffer. Conventional medicine and psychiatry have not made significant advances in understanding the nature of or the treatment for these types of chronic health problems in civilians, let alone Gulf veterans.

- Interventions such as cognitive-behavioral therapy or exercise therapy, which are under study for Gulf veterans with chronic fatigue syndrome-like conditions, are a good start and may prove helpful, but not likely definitive, in resolving the health problems. Even those with treatable psychiatric diagnoses also may have significant persisting chronic symptoms that impair function and quality of life for Gulf veterans, as my VA psychiatric colleagues have previously told me, in their experience. Such anecdotal observations are testable by outcomes research and deserve evaluation. If supported by systematic research, this means that psychiatric treatment will not be a sufficient answer by itself.

- It is far too limited a perspective to focus as much as has been done in various panels on Gulf-related illness on "stress" per se. Stress can interact with many different medical conditions to bring out worse outcomes, but in itself is generally insufficient to explain these conditions as a whole.

- The illogic of emphasizing stress or psychological factors emerges in considering the research finding of increased mortality rates in depressed as opposed to nondepressed heart attack patients (Carney et al. 1999). If depression were believed sufficient as a cause of heart disease mortality, then we should have no reason to study the multiple biological mechanisms of heart disease now under investigation. I doubt that most physicians or cardiac patients would want us to study depression to the exclusion of these other mechanisms. In the least, researchers would probably hypothesize that depression exerts its effects in part by acting via specific biological mechanisms to worsen outcomes. And some heart patients are not depressed, making depression a highly unlikely factor in their outcomes.

- Similarly, not all ill Gulf veterans or civilians with chronic fatigue syndrome, fibromyalgia, or multiple chemical sensitivity have evidence for psychiatric problems (Aaron et al.1996; Fiedler et al. 1996). Furthermore, previous studies on chronic fatigue syndrome even suggest that it is the patients *without* concomitant psychiatric problems who have the poorest neurocognitive function (DeLuca et al. 1997). If this turns out to be the case for Gulf veterans with cognitive difficulties, it will be especially inappropriate to focus on stress and stress-related interventions to the exclusion of other possible treatments.

- How do civilians deal with this situation? A large proportion (e.g., over 80% of fibromyalgia patients - Pioro-Boisset et al. 1996; Schuman et al. 1996) resort to various forms of complementary and alternative medicine (CAM). Even in the general American population, the estimates of utilization rates fall in the range of 40%% (Eisenberg et al. 1998). To my knowledge, it is not

known at what rate ill Gulf War veterans are utilizing CAM, but that alone is worthy of investigation.

- In qualitative research as part of our ongoing VA-funded study of veterans with all types of health problems enrolled in primary care clinics, we have found that veterans seek CAM treatments of many types outside the VA system. They appear generally satisfied with the conventional care, *as measured by their expectations of conventional care*, that their VA primary care providers (PCP) offer, but they describe problems with the limited benefits and unpleasant side effects of pharmaceutical-based medicine. When they perceive limits to the help they can obtain from conventional care, they add various types of CAM to their total program, generally without informing their PCP.

- As you can see, the controversies then compound in complexity. Not only do we have conditions that mainstream medicine as a field does not recognize, but we also have proposed treatments that conventional medicine considers unproven and even potentially unsafe.

- At this moment, we cannot simply declare that ill veterans should obtain particular CAM treatments. There is no body of evidence at this time that any of those are in fact safe or effective for Gulf veterans. As a nation, we are facing the collective dilemma that an individual, desperate patient faces all the time – stop hoping for help and "live with it" indefinitely in a debilitated state or resort now to trying treatments that mainstream medicine largely ignores or rejects.

- At a national level, we can go about this task with scientific rigor, however. We can take a patient-centered rather than disease-centered approach to treatment research for veterans with Gulf War-related illnesses. It is now time to start looking systematically at a range of CAM interventions as possible resources for helping Gulf veterans with their conditions. The scope of CAM, as defined by the NIH National Center for Complementary and Alternative Medicine (NCCAM), includes not only the many controversial interventions that fall under the label of "environmental medicine" or treatments for multiple chemical sensitivity (e.g., comprehensive chemical avoidance with challenge testing, rotation diets – see Miller 1997), but also numerous other nutritional, lifestyle, botanical, mind-body, and energy medicine (e.g., acupuncture) modalities.

- In turn, physicians working in environmental medicine may object to being lumped with some CAM modalities that they themselves consider very strange and beyond rational consideration. Nonetheless, these methods fall into a broad category of treatments considered controversial and unproven by mainstream medicine. Whatever the label, it is time to take a look at these treatments.

- At the CAM conferences and web sites that I have encountered in recent years, it is common to hear claims of major benefit for Gulf veterans made. We need to test those claims. We need to find out what Gulf veterans and civilians with similar health problems are choosing and finding helpful. Then we also need to test those claims for effectiveness in real world situations as patients actually use CAM, i.e., with blended packages of CAM and conventional care, not single interventions in isolation, using appropriate scientific controls.

- With the NCCAM, NIH is fostering a cohort of serious medical researchers around the country who could perform this type of research. I respectfully suggest that it is time to move forward with establishing funding channels to set studies of CAM treatments for veterans with unexplained polysymptomatic Gulf War-related illnesses into motion. Given the methodological difficulties of doing good CAM research (Levin et al. 1997), it is likely that this work will require new collaborations. These would be between VA/DoD and non-VA/DoD investigators, partnering with

CAM providers and researchers, after the model used by the NCCAM to insure that the research team understands all of the parameters with which it must deal to do a good study, i.e., nature of the patient population, the philosophy and features of the CAM intervention(s), and proper scientific design.

- In summary, we should not abandon our current research efforts toward finding the original, albeit multifactorial, etiologies and treatments related to those etiologies. This work is important for avoiding adverse health outcomes after future military operations. However, we can and should invest much more concerted effort toward testing the many CAM treatment possibilities now available (but unproven) for persons with polysymptomatic conditions, including veterans with Gulf War-related illnesses. Without this patient-oriented research, a) mainstream medicine, as reflected in VA and DoD care, will continue to see the patients' multiple symptoms as outside its domain of treatable problems and CAM treatments as outside the scope of "accepted" practice; and b) the ill Gulf veterans will continue to wait in frustration for the availability of properly-studied treatment options.

With regard to my own research on Gulf-related illness, my points are as follows:

- In addition to my emphasis on patient-centered approaches to treatment research, my approach to mechanism research for Gulf War-related illnesses is also patient-centered. We focus on the patient's susceptibility to the environment more than on the environment itself.

- Preliminary research in our own laboratory and in other Gulf War investigators' laboratories suggests that a subset of chronically ill Gulf veterans report newly acquired intolerances for low levels of environmental chemicals that they attribute to their military service (Fiedler et al. 1996). Our data on a randomly chosen, though small, sample Tucson VA-enrolled Gulf veterans revealed that 86% (12/14) of ill Gulf veterans, vs 30% (3/10) of healthy Gulf veterans and 30% (3/10) of healthy era veterans considered themselves "especially sensitive to certain chemicals" (Bell et al. 1998e). The 30% rates in the control groups were similar to those we have observed in general civilian populations (Bell et al. 1998b). In the ill vs healthy Gulf veterans, we also found increased rates of reported multiple chemical exposures (oil well smoke, pesticides, diesel exhaust, raw fuels, insect repellent, paints) during military service (odds ratio 18.7, confidence interval 1.6-223), especially to insect repellents (odds ratio 12.0, confidence interval 1.1-137) and pesticides (odds ratio 12.0, confidence interval 1.3-111). These elevated exposure reports were obtained without asking veterans to attribute health problems to exposures.

- Notably, Miller several years ago found not only similarly high rates of newly acquired chemical intolerance in 59 ill Gulf veterans from Texas (e.g., 78%), but also high rates of newly acquired intolerances to alcoholic beverages, tobacco, foods, and medications. In other words, the intolerances may involve multiple substances with very different chemical structures and different degrees of inherent toxicity. This type of history is similar to those obtained in civilians who report multiple chemical intolerances.

- Conventional toxicology has no easy explanation for this diversity of eliciting factors or for the enhanced low dose reactivity.

- However, the field of pharmacology has studied a phenomenon extensively which can accommodate precisely this diversity of eliciting factors and the enhanced reactivity, i.e., neural sensitization (Antelman 1994; Bell et al. 1992).

- Sensitization is the progressive amplification of response in a host to repeated, intermittent exposures to an initiating stimulus. Once the sensitization is initiated, re-exposures to the same or to other cross-sensitizing stimuli can elicit a heightened response. This process of amplification may reflect changes in the functioning of cells, especially nerve cells, and it does not require immune system involvement.

- As in clinical observations of chemical intolerance, neural sensitization involves separate steps – 1) initiation; 2) elicitation.

- Of note, a sensitized individual at rest in the absence of an eliciting stimulus can function and appear just like a normal, non-sensitized individual. This means that proper studies testing for sensitization must examine subjects not only at rest, but also under stimulus exposure conditions. Furthermore, this research requires at least two testing sessions separated in time by days, not minutes or hours.

- Importantly, stress can cross-sensitize with drugs; drugs can cross-sensitize with chemicals. Endogenous mediators of inflammation or pain can also initiate or foster sensitization. In other words, the sensitized host can experience many diverse stimuli as initiators and as triggers for hyper-reactivity. In some sense, sensitization is a response of the whole organism to the whole environment; it avoids the conceptual and practical limitations of splitting mind from body or one body part from another.

- Mainstream research is looking at sensitization as a possible model for craving in substance abuse, for stimulus hyperreactivity in posttraumatic stress disorder, for development of chronic pain syndromes including fibromyalgia and somatization (Ursin 1993, 1997), and for recurrent episodes in chronic mood disorders (Antelman 1988, 1994).

- Our past research on civilians with multiple chemical intolerances showed that such persons, even though psychologically distressed, are different physiologically in their brain waves from controls with similar types of psychological distress but no concomitant chemical intolerances (e.g., women with depression – Bell et al. 1998d; women with sexual abuse histories – Fernandez et al. 1999). "Somatization" scores (rating multiple symptoms in multiple systems) correlate with a blood biomarker of inflammation called neopterin in women with chemical intolerance in a pattern not seen in depressed or normal controls (Bell et al.1998c). When tested over repeated sessions, persons with chemical intolerances also exhibit sensitization (progressive increases over time) in brain waves (electroencephalographic alpha frequency activity, EEG), heart rate, and blood pressure, i.e., a capacity for sensitization (Bell et al. 1997, 1998a,d; Fernandez et al. 1999) not seen in controls without chemical intolerance.

- We have also found evidence for individual difference susceptibility factors in civilians parallel to those in sensitizable animals. These factors include: female gender, certain genetic strains (i.e., family histories of substance abuse including alcoholism), spontaneous preference for sucrose (sugar), and baseline hyperreactivity to novel environments (Bell et al. 1998b, 1999).

- Several groups of basic neuroscientists, e.g., vonEuler et al. (1994); Sorg et al. (1996, 1998), have developed animal models of sensitization to environmental chemicals. Low level formaldehyde, for example, cross-sensitizes with cocaine (Sorg et al. 1998). Thus, the methodology also exists to test the sensitization model for Gulf War illnesses in animals using various complex combinations of agents and factors that may have been present during the Gulf War.

- If sensitization and/or cross-sensitization were etiological factors in certain Gulf War-related illnesses, then they could account for veterans with different exposure histories and different stress histories during military service ending up with similar polysymptomatic conditions. This mechanism could also help explain the ability of interventions with different emphases to benefit various patients. Removing eliciting stimuli of any class (e.g., chemical or stress) might reduce the frequency and severity of currently sensitized symptoms, without proving a role for the stimulus in the initiation of the illness.

- In our VA-funded study, we are testing the possibility that chronically ill Gulf veterans are persons who are now more sensitizable than are healthy veterans. We are using extremely low level chemical exposures as our probe at levels below olfactory detection (no obvious smell) to avoid patient expectation confounds and to limit symptom provocation. Our outcome measures over three exposure sessions spaced over 3 weeks are more sensitive and objective than symptom reports, i.e., we are looking at physiological responses of the heart and eyeblink to acoustic startle stimuli.

- Preliminary analyses of our interim dataset on approximately 60 veterans suggest that we are seeing sensitization over sessions in ill Gulf vs healthy Gulf and era veterans in the time intervals between heartbeats, as a function of receiving undetectable levels of jet fuel JP-8 versus clean compressed air in the sessions. This is occurring without apparent provocation of subjective symptoms. Earlier analyses controlling for emotional state suggested that anxiety and psychological distress do not explain these findings. Once we have completed a thorough check for more possible confounding variables in our statistical analyses, we plan to submit the data for peer-reviewed publication.

- If our sensitization hypothesis is supported and eventually tested in terms of symptom generation, it would provide a plausible model of mechanism by which Gulf War-related illnesses might have developed. Chemical intolerance, for which there are now validated self-report scales, may be a subjective, clinical indicator of susceptibility to sensitization.

- In conclusion, the phenomenon of neural sensitization is well-documented in basic neuroscience research (Antelman 1988; Ferger et al. 1993; Yoshida et al. 1993). It depends on time-related changes in the functioning, not the structure, of nerve cells in response to repeated, intermittent stimuli. The stimuli capable of initiating and eliciting sensitized responses are diverse in nature, ranging from chemicals to stress, and can cross-sensitize. Some individuals sensitize more readily than do others. Sensitization deserves further study as a possible host mechanism by which a subset of Gulf veterans may have become ill.

Thank you very much for this opportunity to express my views on this important topic.

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Committee on Government Reform
Subcommittee on National Security, Veterans Affairs and International Affairs
United States House of Representatives
February 2, 2000
Invited Testimony by

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There's an old parable: For want of a nail, the horseshoe was lost; for want of a shoe, the horse was lost; then the rider was lost; then the battle; the war; and finally the kingdom—all for want of a nail.

This is precisely the situation we find ourselves in today. For want of a paradigm, our veterans are—lost in a sea of inconclusive reports, redundant studies, expanding budgets, programs and committees, and cries of conspiracy—all for want of a paradigm, something to explain the relationship between the exposures they experienced during the Gulf War and the multi-system symptoms that now plague them.

Different specialists apply different monikers to their symptoms.

—The rheumatologist observing diffuse muscle pain diagnoses myalgias.

—The neurologist hearing head pain and nausea diagnoses migraine headaches.

—The pulmonologist finding airway reactivity diagnoses asthma.

—The psychiatrist seeing chronic malaise diagnoses depression.

—The gastroenterologist noting GI complaints diagnoses irritable bowel syndrome.

Most ill veterans have symptoms involving several organ systems simultaneously. For them there is no unifying diagnosis, no known etiology, and no identified disease process.

This is not the first time doctors have found themselves baffled by wartime disease. One hundred and thirty years ago, during the Civil War, doctors were faced with a similarly mysterious "syndrome" characterized by fever. Hundreds of thousands of soldiers died. The doctors did what good epidemiologists do today. They classified the cases. Since the hallmark symptom was fever, they classified the cases by fever type—remittent, intermittent, or relapsing. In doing so, they unknowingly lumped together dozens of

unrelated illnesses—everything from typhus and typhoid to malaria and tuberculosis (Sartin, 1993). Who would have dreamed it—this germ theory of disease? This war going on between invisible invaders and the body's immune defenses, with the only outward sign being—literally—the heat of battle.

Today we face this same situation with Gulf War veterans, only this time the hallmark symptom is not as simple as fever. It's the newly acquired intolerances these veterans have been experiencing since the War. Like the mechanic who before the war used to "bathe" in solvents and now becomes ill after one whiff of gasoline. Or the young woman soldiers who recalls how she used to be able to drink any man in her company under the table, but since the war she can't take even one drink without becoming violently ill. The vast majority of sick veterans report these newly acquired intolerances which date from their experiences in the Persian Gulf.

During the past seven years I have served as the environmental medical consultant to the Houston VA's regional referral center. Approximately 90% of veterans interviewed described new-onset intolerances to everyday chemical exposures which set off their symptoms: 78 percent were intolerant of fragrances, tobacco smoke, gasoline vapors, etc.; 78 percent described food intolerances; 66 percent reported alcohol intolerance; 25 percent were intolerant of caffeine; and nearly 40 percent reported adverse reactions to medications—all since the Gulf War. These intolerances, resulting in flare-ups of symptoms, including fatigue, headaches, gastrointestinal problems, mood changes, cognitive impairment and diffuse musculoskeletal pain, are like the fevers experienced by the Civil War soldiers—they are the outward manifestation of the underlying disease process.

This is not the first time this illness pattern has appeared on the medical landscape. Researchers have described these same new-onset intolerances and multi-system symptoms in demographically diverse groups in more than a dozen countries—sheep dippers exposed to organophosphate pesticides in the United Kingdom; radiography workers exposed to Xray developers containing glutaraldehyde, etc. in New Zealand; U.S. aerospace workers on the West Coast exposed to solvents and plasticizers; and environmental scientists exposed to indoor air contaminants at the EPA's own headquarters in Washington, D.C., to name a few (Ashford and Miller, 1998).

What ties all these groups together is the common experience of an initiating toxic exposure followed by newly acquired intolerances and multi-system symptoms. These observations provide compelling scientific evidence for a shared underlying disease mechanism—one involving a *fundamental breakdown in natural tolerance*. This two-step process—an initiating toxic exposure followed by newly acquired intolerances that trigger multi-system symptoms—has been referred to with the acronym "TILT," or Toxicant-induced Loss of Tolerance (Golomb, 1999; Newlin, 1997; Miller, 1999, 1997; Miller et al, 1997).

This two-step process is the key to understanding Gulf War illness. It doesn't matter so much which exposure caused the breakdown in tolerance—be it pesticides, smoke from

the oil fires or pyridostigmine bromide pills; those things have long since left these veterans' bodies. It's the aftermath of these exposures—the new-onset intolerances to low-level chemical exposures—which appear to be perpetuating their symptoms. In some cases, it may be difficult to sort out individual intolerances, or "triggers," because of a phenomenon called "masking." This occurs when individuals are reacting to so many exposures that they become a confusion of overlapping symptoms.

But the confusion clears for both the patient and the physician when the underlying paradigm is understood. And questions that could not be answered, are answered.

Like why some veterans became ill and others didn't—because individuals react differently to toxic exposures; some have no response at all.

Or why researchers have been unable to isolate a single culprit exposure—because the answer to the question "What caused Gulf War illness?" is more likely to be "all of the above."

It explains why veterans remain sick almost a decade after the War, long after their initiating exposures.

It explains why symptoms wax and wane unpredictably—as daily exposures wax and wane.

What can be done to diagnose and treat the chemically intolerant? There is evidence that removing them from the exposures that are affecting them by putting them in an environmental medical unit (EMU), will cause their symptoms to subside. The EMU is an environmentally controlled in-patient hospital unit designed to help patients avoid common, low-level exposures. Previous experience shows that within days of entering the EMU, patients will arrive at a "clean baseline," and their exposure-related symptoms will disappear. During the next two weeks, each patient is exposed to potential triggers—such as caffeine, gasoline, perfume, various foods, medications, and tobacco smoke—one at a time, to determine what is setting them off.

Epidemiological data and literature reviews can only go so far in determining the nature of a new disease process. New paradigms require new approaches, and new tools. EMU studies will enable doctors to witness this disease mechanism firsthand and understand Gulf War illness for what it is, while providing a built-in treatment component—one that enables veterans to understand their disease and emerge less confused, less hopeless, and more in control of their lives.

A validated questionnaire (attached) is available in the medical literature which VA and military doctors could use as a first step toward introducing physicians and patients to this paradigm so they can begin to see it for themselves.

If we are going to help these veterans, what is needed is not more epidemiologic studies or literature reviews, but, rather, a Manhattan Project-style approach consisting of EMU studies and other patient-oriented diagnostic and treatment studies.

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Figure 1. Exposures that may initiate TILT or trigger symptoms

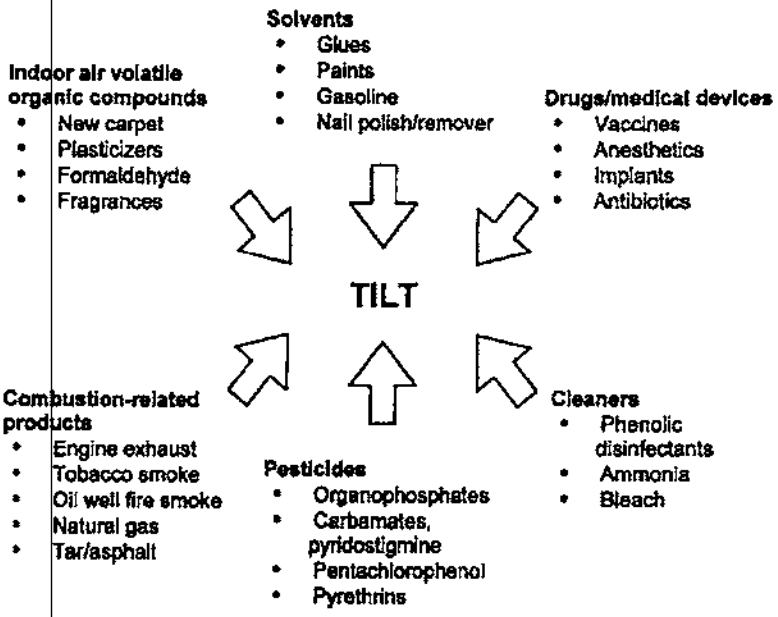
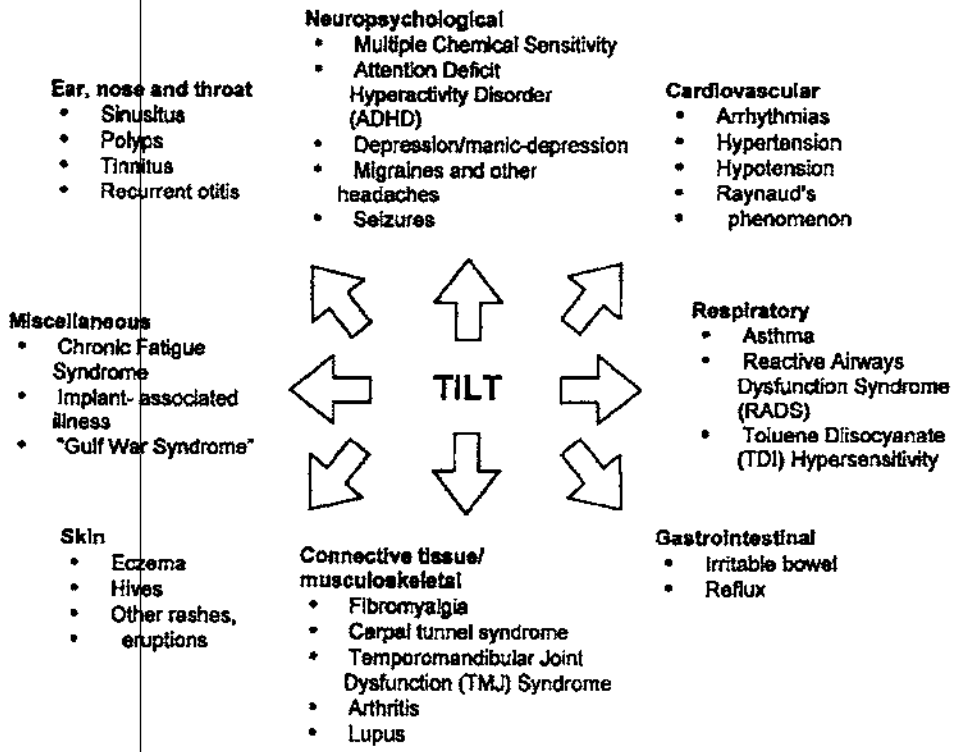


Figure 2. Conditions that may have their origins in TILT



The QEESI©

The Quick Environmental Exposure and Sensitivity Inventory (QEESI©) was developed as a screening questionnaire for multiple chemical intolerances (MCI). The instrument has four scales: Symptom Severity, Chemical Intolerances, Other Intolerances, and Life Impact. Each scale contains 10 items which are scored from 0 = "not a problem" to 10 = "severe or disabling problem." A 10-item Masking Index gauges ongoing exposures that may affect individuals' awareness of their intolerances as well as the intensity of their responses to environmental exposures. The QEESI© can be used for:

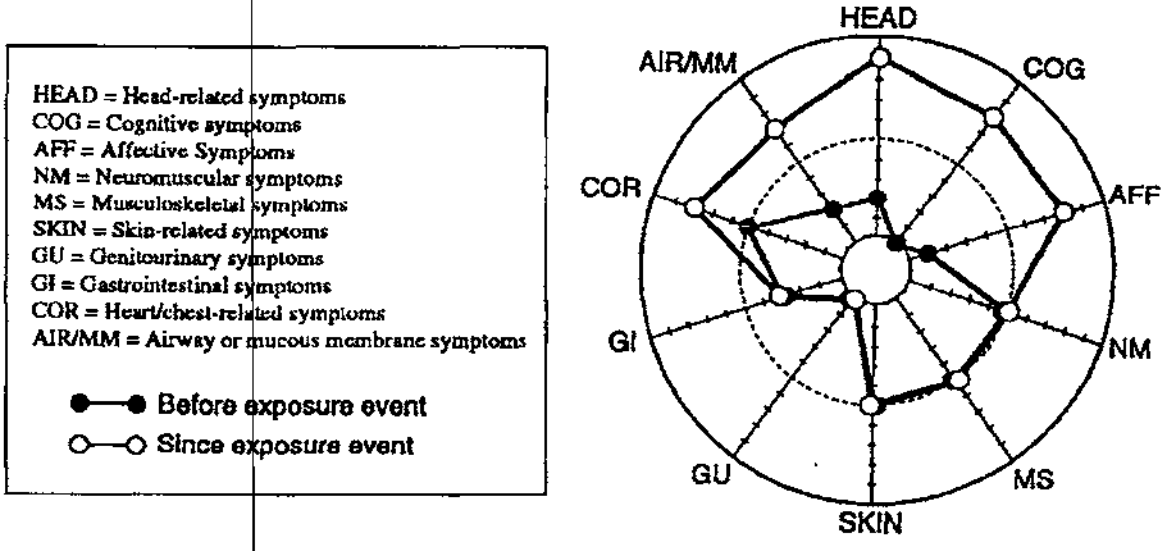
(1) Research, to characterize and compare study populations and to select subjects and controls.

(2) Clinical evaluations, to obtain a profile of patients' self-reported symptoms and intolerances. Patients can be asked to complete a QEESI© at intervals in order to follow the course of their illness over time or in response to treatment or exposure avoidance.

(3) Workplace or community investigations, to identify and provide self-assessment information to individuals who may be more susceptible or who report new intolerances. Affected employees should have the option to discuss the results with investigators or their personal physicians.

Individuals whose health problems began or became worse following a particular exposure event can fill out the QEESI© using one color of ink to illustrate how they were before the event, and a second color to illustrate how they have been since the event. On the cover of the QEESI© is a "Symptom Star" (Figure 1) which provides a graphical representation of patients' responses on the Symptom Severity Scale.

Figure 1. QEESI Symptom Star illustrating symptom severity in an individual before and after an exposure event (e.g., pesticide application, indoor air contaminants, chemical spill)



For additional copies of the QEESI©, contact Claudia S. Miller, M.D., M.S., University of Texas Health Science Center at San Antonio, Department of Family Practice BCT 150, 7703 Floyd Curl Drive, San Antonio, Texas 78229-3900. Phone: (210) 567-7760; fax: (210) 567-7764; email: millercs@uthscsa.edu. For further information see Chemical Exposures: Low Levels and High Stakes by Nicholas A. Ashford and Claudia S. Miller, John Wiley & Sons, 1998 (1-800-225-5945).

Interpreting the QEESI©

In a study of 421 individuals, including four exposure groups and a control group, the QEESI© provided sensitivity of 92% and specificity of 95% in differentiating between chemically intolerant persons with multiple chemical intolerances (MCI) and the general population (Miller and Prihoda 1999).

Cronbach's alpha reliability coefficients for the QEESI©s four scales—Symptom Severity, Chemical Intolerances, Other Intolerances and Life Impact—were high (0.76-0.97) for each of the groups, as well as over all subjects, indicating that the questions on the QEESI© form scales showing good internal consistency. Pearson correlations for each of the four scales with validity items of interest, i.e., life quality, health status, energy level, body pain, ability to work and employment status, were all significant and in the expected direction, thus supporting good construct validity.

Information on the development of this instrument, its interpretation, and results for several populations have been published (Miller and Prihoda 1999a,b). Proposed ranges for the QEESI©'s scales and guidelines for their interpretation appear in Tables 1 and 2 below:

Table 1. Criteria for low, medium, and high scale scores

Scale/Index	Score		
	Low	Medium	High
Symptom Severity	0-19	20-39	40-100
Chemical Intolerance	0-19	20-39	40-100
Other Intolerance	0-11	12-24	25-100
Life Impact	0-11	12-23	24-100
Masking Index	0-3	4-5	6-10

Table 2. Distribution of subjects by group using "high" cutoff points for symptom severity (≥ 40) and chemical intolerances (≥ 40), with masking low or not low (< 4 or ≥ 4)

Degree to Which MCI is Suggested[2]	Risk Criteria[1]			Percentage of Each Group Meeting Risk Criteria				
	Symptom Severity Score	Chemical Intolerance Score	Masking Score	Controls n=76	MCS - No Event n=90	MCS – Event n=96	Implant n=87	Gulf War Veterans n=72
Very suggestive	≥ 40	≥ 40	≥ 4	7	16	23	39	45
Very suggestive	≥ 40	≥ 40	< 4	0	65	66	36	4
Somewhat suggestive	≥ 40	< 40	≥ 4	3	1	2	16	26
Not suggestive	≥ 40	< 40	< 4	0	0	2	3	6
Problematic	< 40	≥ 40	≥ 4	7	3	1	1	0
Problematic	< 40	≥ 40	< 4	3	13	4	2	0
Not suggestive	< 40	< 40	≥ 4	68	1	0	2	18
Not Suggestive	< 40	< 40	< 4	12	1	2	1	1
				100	100	100	100	100

[1] Subjects must meet all three criteria, i.e., Symptom Severity, Chemical Intolerance, and Masking scores, as indicated in each row of this table.
[2] "Very suggestive" = high symptom and chemical intolerance scores.
"Somewhat suggestive" = high symptom score but possibly masked chemical intolerance
"Not suggestive" = either (1) high symptom score but low chemical intolerance score with low masking, or (2) low symptom and chemical intolerance scores.
"Problematic" = low symptom score but high chemical intolerance score. Persons in this category with low masking (<4) may be sensitive individuals who have been avoiding chemical exposures for an extended period (months or years).

References:

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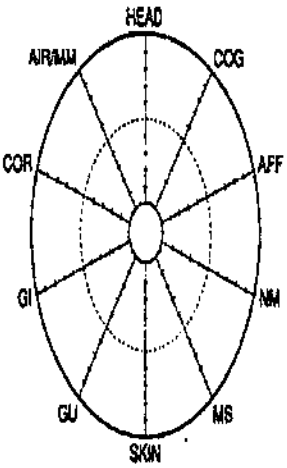
Quick Environmental Exposure and Sensitivity Inventory V-1

(QEESI)©

The purpose of this questionnaire is to help identify health problems you may be having and to understand your responses to various exposures. If your health problems began suddenly or became much worse after a particular exposure event, such as a pesticide exposure or moving to a new home or office building, complete pages 1-3 describing how you are now, then go back through these same questions a second time, and identify how you were before the exposure event. After you have completed all of the items on pages 1-5, fill in the "target" diagram below.

Symptom Star



Instructions: After completing pages 1 through 5, unfold page 3 so that it lies just to the right of this page. Place a small dot on the corresponding spoke for each symptom item on page 3. Connect these points. For "before and after" scores (described above), use two different colors.

Chemical Exposures

The following items ask about your responses to various odors or chemical exposures. Please indicate whether or not these odors or exposures would make you feel sick, for example, you would get a headache, have difficulty thinking, feel weak, have trouble breathing, get an upset stomach, feel dizzy, or something like that. For any exposure that makes you feel sick, on a 0-10 scale rate the severity of your symptoms with that exposure. For exposures that do not bother you, answer "0." Do not leave any items blank.

0 = not at all a problem
5 = moderate symptoms
10 = disabling symptoms

For each item, circle one number only:

1.	Diesel or gas engine exhaust	0 1 2 3 4 5 6 7 8 9 10
2.	Tobacco smoke	0 1 2 3 4 5 6 7 8 9 10
3.	Insecticide	0 1 2 3 4 5 6 7 8 9 10
4.	Gasoline, for example at a service station while filling the gas tank	0 1 2 3 4 5 6 7 8 9 10
5.	Paint or paint thinner	0 1 2 3 4 5 6 7 8 9 10
6.	Cleaning products such as disinfectants, bleach, bathroom cleaners or floor cleaners	0 1 2 3 4 5 6 7 8 9 10
7.	Certain perfumes, air fresheners or other fragrances	0 1 2 3 4 5 6 7 8 9 10
8.	Fresh tar or asphalt	0 1 2 3 4 5 6 7 8 9 10
9.	Nailpolish, nailpolish remover, or hairspray	0 1 2 3 4 5 6 7 8 9 10
10.	New furnishings such as new carpeting, a new soft plastic shower curtain or the interior of a new car	0 1 2 3 4 5 6 7 8 9 10

Total Chemical Intolerance Score (0-100): ____

Name any additional chemical exposures that make you feel ill and score them from 0 to 10: _____ _____

_____

_____

_____

_____

Other Exposures

The following items ask about your responses to a variety of other exposures. As before, please indicate whether these exposures would make you feel sick. Rate the severity of your symptoms on a 0-10 scale. Do not leave any items blank.

0 = not at all a problem
5 = moderate symptoms
10 = disabling symptoms

For each item, circle one number only:

1.	Chlorinated tap water	0 1 2 3 4 5 6 7 8 9 10
2.	Particular foods, such as candy, pizza, milk, fatty foods, meats, barbecue, onions, garlic, spicy foods, or food additives such as MSG	0 1 2 3 4 5 6 7 8 9 10
3.	Unusual cravings, or eating any foods as though you were addicted to them; or feeling ill if you miss a meal	0 1 2 3 4 5 6 7 8 9 10
4.	Feeling ill after meals	0 1 2 3 4 5 6 7 8 9 10
5.	Caffeine, such as coffee, tea, Snapple, cola drinks, Big Red, Dr. Pepper or Mountain Dew, or chocolate	0 1 2 3 4 5 6 7 8 9 10
6.	Feeling ill if you drink or eat less than your usual amount of coffee, tea, caffeinated soda or chocolate, or miss it altogether	0 1 2 3 4 5 6 7 8 9 10
7.	Alcoholic beverages in small amounts such as one beer or a glass of wine	0 1 2 3 4 5 6 7 8 9 10
8.	Fabrics, metal jewelry, enemas, cosmetics, or other items that touch your skin	0 1 2 3 4 5 6 7 8 9 10
9.	Being unable to tolerate or having adverse or allergic reactions to any drugs or medications (such as antibiotics, anesthetics, pain relievers, x-ray contrast dye, vaccines or birth control pills), or to an implant, prosthesis, contraceptive chemical or device, or other medical, surgical or dental material or procedure	0 1 2 3 4 5 6 7 8 9 10
10.	Problems with any classical allergic reactions (asthma, nasal symptoms, hives, anaphylaxis or eczema) when exposed to allergens such as: tree, grass or weed pollen, dust, mold, animal dander, insect stings or particular foods	0 1 2 3 4 5 6 7 8 9 10

Total Other Intolerance Score (0-100): ____

SYMPTOMS

The following questions ask about symptoms you may have experienced recently. Rate the severity of your symptoms on a 0-5 scale. Do not leave any items blank.

0 = not at all a problem
1 = moderately problem
2 = moderately problem

For each item, circle one number only:

1. Problems with your muscles or joints (such as pain, aching, cramping, stiffness or weakness)?	0 1 2 3 4 5 6 7 8 9 10
2. Problems with burning or irritation of your eyes, eyelids, with your vision, or feeling as though something is in your eyes, such as a foreign body, scratching, or excessive tearing?	0 1 2 3 4 5 6 7 8 9 10
3. Problems with your heart (for example, such as a fast or irregular heartbeat, skipped beats, your heart pounding, or chest discomfort)?	0 1 2 3 4 5 6 7 8 9 10
4. Problems with your stomach or digestion (such as abdominal pain or cramping, abdominal swelling or bloating, nausea, diarrhea, or constipation)?	0 1 2 3 4 5 6 7 8 9 10
5. Problems with your ability to think, such as difficulty concentrating or remembering things, feeling unclear, or feeling trouble making decisions?	0 1 2 3 4 5 6 7 8 9 10
6. Problems with your mood, such as feeling tense or nervous, irritable, depressed, having spells of crying or anger, or loss of emotional interest in things that used to interest you?	0 1 2 3 4 5 6 7 8 9 10
7. Problems with balance or coordination, such as dizziness or vertigo (for example, a sense of spinning), or problems with bumping into walls?	0 1 2 3 4 5 6 7 8 9 10
8. Problems with your bowel or bladder (such as frequent or urgent urination, or feeling pressure or fullness in your bladder or urethra)?	0 1 2 3 4 5 6 7 8 9 10
9. Problems with your skin (such as dryness, rashes, or dry eyes)?	0 1 2 3 4 5 6 7 8 9 10
10. Problems with your sensory function or perception, such as problems with your hearing or ringing in your ears? For women, is this related to other problems with your menstrual periods?	0 1 2 3 4 5 6 7 8 9 10

*Total Symptoms Score (0-100):

MASKING INDEX

The following items relate to ongoing exposures you may be having. Circle "0" in the answer is NO or if you don't know whether you have the exposure. Circle "1" if the answer is YES, you do have the exposure. Do not leave any items blank.

Circle "0" or "1" only:

1. Do you have a strong chemical smell in your home or workplace?	NO=0	YES=1
2. Do you drink city tap water, or have you ever had a well or spring water tested?	NO=0	YES=1
3. Do you consume any artificial sweeteners (such as aspartame, Nutrasweet, Equal, saccharin, Sweet 'n Low)?	NO=0	YES=1
4. Do you routinely pump gas, work or work in a gas station, or live near a gas station?	NO=0	YES=1
5. Has either your home or your workplace been sprayed for insects or rodents in the past year?	NO=0	YES=1
6. Is your current job or hobby such that you routinely have to wear a mask, respirator, or other protective device?	NO=0	YES=1
7. Does the water in your home routinely smell chemical?	NO=0	YES=1
8. Is there a pet or pets in the house for most of the day?	NO=0	YES=1
9. Is there an attached garage with your home or does your car routinely smell of fumes when you start or drive it?	NO=0	YES=1
10. Do you currently have or receive any of the following: steroids, such as prednisone; pain medications requiring a prescription; medications for depression, anxiety, or mood disorders; medications for allergy, or inhalers or other sprays?	NO=0	YES=1

Masking Index (>2=1):
(Total number of YES answers)

IMPACT OF SENSITI

If you are sensitive to certain chemicals or foods, the degree to which your sensitivities have affected your life. If you are not sensitive at all to any of the aspects of your life, answer "0". To the best of your

How much have your sensitivities affected:

1. Your diet	0 1
2. Your ability to work or your profession	0 1
3. How you live in your home	0 1
4. Your social activities	0 1
5. Your ability to travel to other cities or other areas	0 1
6. Your choice of personal care products, such as shampoos or makeup	0 1
7. Your ability to be around others and enjoy social activities (for example, going to meetings, movies, restaurants, etc.	0 1
8. Your choice of hobbies or recreation	0 1
9. Your relationship with your spouse or family	0 1
10. Your ability to clean your house, or maintain the level of personal care or routine chores	0 1

*Total Life Impact Score (0

For more copies of the QEESI, call 1-800-[illegible]
about the questionnaire, refer to Chemical Exposure
Etiology (See Chapter by Nicholas A. Ashford and Cla
& Short, Inc., 1998. To order, call toll-free 1-800-[illegible]

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Biosketch

Claudia S. Miller, M.D., M.S., is an Associate Professor in Environmental and Occupational Medicine in the Department of Family Practice of the University of Texas Health Science Center at San Antonio. She is board-certified in Allergy/Immunology and Internal Medicine, and has a Master's degree in Public Health/Environmental Health. Her research interests include the health effects of low level chemical exposures, pesticides, indoor air pollution, and Gulf War veterans' illnesses. Dr. Miller has held appointments to several federal advisory committees, including the National Advisory Committee on Occupational Safety and Health, the National Toxicology Program Board of Scientific Counselors, and the Department of Veterans Affairs Persian Gulf Expert Scientific Advisory Committee. She is co-author of the WHO-award-winning *New Jersey Report on Chemical Sensitivity* and a professionally acclaimed book, *Chemical Exposures: Low Levels and High Stakes* (Ashford, NA and Miller, CS, John Wiley and Sons, Inc. 1998, New York).

TESTIMONY OF HOWARD B. URNOVITZ, PH.D.

FEBRUARY 2, 2000

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON GOVERNMENT REFORM

SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS' AFFAIRS AND INTERNATIONAL RELATIONS

I am grateful to the Committee for allowing me the opportunity to review the GAO report on "Gulf War Illnesses: Management Actions Needed to Answer Basic Research Questions" and for inviting me to present my views and recommendations on research directions for Persian Gulf War Related Illnesses or GWS, Gulf War Syndrome. My name is Dr. Howard B. Urnovitz. I received my doctorate degree in Microbiology and Immunology from the University of Michigan in 1979. My entire CV is submitted with my written testimony. I currently hold the position of Scientific Director of the Chronic Illness Research Foundation as well as my current position as Chief Science Officer and Director of a publicly traded biomedical company.

With respect to my views on government research programs concerning GWS, I concur with the GAO report that many of the research objectives identified by the Research Working Group of the Persian Gulf Veterans' Coordinating Board have not been reached. Some of the government-funded epidemiological studies, particularly those of the Centers for Disease Control and Prevention and the University of Texas Southwestern have been very meaningful. Most of the government-funded research conducted thus far, however, has focused on trying to quantify exposures with little or no data, identifying single exposure agents as the sole causative factor, or summarizing the research of others. The identification of the range of toxic exposures would assist greatly in determining the array of causative factors associated with GWS. Today, we already have a great deal information on the potential exposures during the Gulf War. Unfortunately, since a significant amount of the data was not collected, we will never know with any degree of certainty what the extent and combination of the exposures were in the case of each individual patient. Further, identification of these exposures alone will not reveal the disease mechanisms involved the progression of these illnesses.

Identifying the disease mechanism has been the focus of our research. I recommend that Congress strongly encourage the Department of Defense, the Department of Veterans' Affairs and the Department of Health and Human Services to fully acknowledge non-government funded, published, peer-reviewed independent research to further expand the total information base on GWS. I am concerned that we in the independent research community do not have a structure for free dialog with government agencies and researchers. To exclude these contributions to science is not productive.

The GAO report recognizes medical science's conventional approach to chronic illnesses. The paradigm continues to be a search for a *single* causative agent. The weakness in this conceptual approach is that most chronic diseases are multifactorial. This single causative agent approach was formulated long before science recognized that the human body can sustain damage at the cellular and molecular level from a variety of physical, chemical, or biological insults, and long before we

I would like to state for the record that it is my professional opinion that the clues to solving significant medical problems in the world today: cancers, AIDS, heart and liver diseases, autoimmune and neurologic disorders, vaccine safety, chemical injuries, and military associated ailments, —lie in the blood of these veterans who suffer from GWS and possibly in the blood of their families. Once we break and catalog the code of the reshuffled RNA, we may finally have a clear direction in how to treat chronic illnesses. The Gulf War veterans will become heroes again for a second time.

I ask that the full text of my statement along with a prepared statement from my colleague Professor Montagnier be submitted for inclusion in the record of the hearing.

WRITTEN TESTIMONY OF LUC MONTAGNIER, M.D.

FEBRUARY 2, 2000

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON GOVERNMENT REFORM

SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS' AFFAIRS AND INTERNATIONAL RELATIONS

Mr. Chairman, my name is Dr. Luc Montagnier. I received a medical degree from Paris University in 1960. My CV is submitted along with my written testimony. I currently hold the position of Distinguished Professor at both Queens College in New York and at the Institut Pasteur in Paris. I also serve on the Scientific Advisory board of publicly traded company along with Howard B. Urnovitz, PhD, who was invited to testify before this committee today.

I have been involved in the study of the biological properties of RNA for nearly four decades. I first published the observation of the existence of double stranded RNA in replicating viruses in 1963 and within cells in 1968. I also led the team that discovered the RNA viruses: HIV-1, HIV-2 and HIV-1 group O.

I have been following the interesting work of Urnovitz and his colleagues. They have reported on the detection of RNA molecules in the blood of veterans with Gulf War Syndrome (GWS) which seems to be specific for the disease. I am aware of their ability to detect similar blood RNA molecules in several other chronic diseases. We should remember that the role of RNA in the process of life was first recognized just 37 years ago. Since 1963, RNA has been shown to be self-replicated, spliced, edited, reverse-transcribed and to be endowed with enzymatic activity. This new observation suggests that RNA may also be involved in the process of disease. It is my opinion that the detection and identification of blood-borne RNA is an important contribution to the field of medicine that will result in our further understanding of the nature of chronic disease and chronic disease progression.

I have reviewed Dr, Urnovitz's published research and the testimony prepared for presentation to this Committee and strongly advise that future research on Gulf War Syndrome should include the study of the detected genetic material, i.e., novel RNA in the sera of these veterans. I have agreed to provide my advice, drawing upon my experience and research into RNA to assist this research team in this matter. I foresee that the study of GWS may have major consequences for other chronic diseases.

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RNAs in the Sera of Persian Gulf War Veterans Have Segments Homologous to Chromosome 22q11.2

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Reverse transcriptase PCR (RT-PCR) was used for polyribonucleotide assays with sera from deployed Persian Gulf War veterans with the Gulf War Syndrome and a cohort of nonmilitary controls. Sera from veterans contained polyribonucleotides (amplicons) that were obtained by RT-PCR and that ranged in size from 200 to ca. 2,000 bp. Sera from controls did not contain amplicons larger than 450 bp. DNA sequences were derived from two amplicons unique to veterans. These amplicons, which were 414 and 759 nucleotides, were unrelated to each other or to any sequence in gene bank databases. The amplicons contained short segments that were homologous to regions of chromosome 22q11.2, an antigen-responsive hot spot for genetic rearrangements. Many of these short amplicon segments occurred near, between, or in chromosome 22q11.2 Alu sequences. These results suggest that genetic alterations in the 22q11.2 region, possibly induced by exposures to environmental genotoxins during the Persian Gulf War, may have played a role in the pathogenesis of the Gulf War Syndrome. However, the data did not exclude the possibility that other chromosomes also may have been involved. Nonetheless, the detection of polyribonucleotides such as those reported here may have application to the laboratory diagnosis of chronic diseases that have a multifactorial etiology.

During the Persian Gulf War approximately 700,000 individuals were exposed to genotoxic hazardous materials (GHM) (42, 42a, 51). The GHMs to which these individuals were exposed included low-level chemical warfare agents, investigational drugs (including pyridostigmine bromide, which is used as a prophylactic agent against nerve agents), organophosphate, carbamate, and other pesticides and insect repellents. Other occupational and environmental contaminants included low levels of nuclear and electromagnetic radiation, toxic combustion products from oil-well fires, diesel exhaust products, and airborne particulates. A significant proportion of the Persian Gulf War veterans (GWVs) developed a pattern of symptomatic health disorders that have been referred to as Persian Gulf War-Related Illnesses (42). The pattern of illness is reasonably consistent: rash, fatigue, muscle and joint pain, headache, irritability, depression, unrefreshing sleep, gastrointestinal and respiratory disorders, and cognitive defects (22). These Gulf War Syndrome (GWS) disorders were recently defined as a clinical entity (16).

We elected to test for polyribonucleotides in the sera of GWVs on the basis of several considerations. Most GWVs received oral poliovirus vaccine before deployment to the Persian Gulf. Persistent enterovirus infection has been implicated in the chronic fatigue syndrome (18), one of the major health disorders of GWS. Clements et al. (8) reported that enterovirus-related sequences persisted in the sera of patients with the chronic fatigue syndrome. The availability of primers (14) to the nontranslated sequences of most enteroviruses and to the P2-P3 junction of oral polioviruses provided a means to test whether enterovirus sequences persisted in the sera of GWVs. We used a reverse transcriptase (RT) PCR (RT-PCR), described in this report, to detect amplicons (RT-PCR amplicons [RPAs]) in the sera tested. We report that amplicons that were 750 bp or larger occurred in the sera of GWVs but not in the sera of healthy nonmilitary controls. Two amplicons (of 414 and 714 bp) unique to GWVs were sequenced. They contained short segments homologous to regions of chromosome 22q11.2, a hot spot for genetic rearrangements and mutations.

MATERIALS AND METHODS

RT-PCR. Sera from peripheral blood specimens were obtained after the provision of informed consent from 24 veterans with GWS (Rheumatology Clinic, Veterans Affairs, Northern California Health Care System, Martinez, Calif.) who had been deployed to the Persian Gulf approximately 5 years previously. The major signs and symptoms in the 24 GWVs with GWS were rash (n = 20), muscle and joint pain (n = 20), headache depression irritability (n = 19), gastrointestinal and respiratory disorders (n = 18), chronic fatigue syndrome (n = 17), posttraumatic stress disorder (n = 12), and cognitive losses (n = 6). Combinations of these symptoms occurred in all but one veteran. Blinded serum samples from 50 healthy nonmilitary subjects were obtained from life insurance applicants (Osborn Laboratories, Lenexa, Kans.). For the most part, the subjects were matched by age, sex, and race. They ranged in age from 26 to 56 years. All sera were separated from clots immediately after blood was drawn and were used for RT-PCR within 48 h. To prevent cross contamination, separate facilities dedicated to specimen processing, PCR amplification, and amplicon detection were used. RNA from 0.25 ml of the sample was extracted in a laminar flow hood with 0.75 ml of TRIZOL LS reagent (Gibco BRL, Gaithersburg, Md.). RNA was precipitated with 10 μg of RNase-free glycogen as a carrier. Both methods were performed as specified by the manufacturer. Precipitated RNA was washed once with 70% ethanol by centrifugation at 4°C, resuspended in 10 μl of RNase-free distilled water, and added to 17 μl of the RT mixture (GeneAmp RNA PCR kit; Perkin-Elmer, Norwalk, Conn.) containing $MgCl_2$ (5 mM), 1× PCR Buffer II, RNase inhibitor (2.5 U), murine leukemia virus RT (2.5 U), random hexamer primers (2.5 μM), and 1 mM each dATP, dGTP, dCTP, and dTTP. Poliovirus Sabin type 1 RNA (National Institute for Biological Standards and Control, Hertfordshire, United Kingdom) was used as a positive control. RT was omitted from the reaction mixture for the negative control. The RT mixture was incubated for 10 min at 22°C, 30 min at 42°C, and 5 min at 95°C with a Perkin-Elmer thermocycler. The RT mixture was then added to the top of a hot-start PCR, with a melted Ampliwax bead (Perkin-Elmer) used as the barrier. The 70 μl of the top PCR mixture contained 1× PCR Buffer II and AmpliTaq (2.5 U). The 30 μl of the bottom PCR mixture contained 1× PCR Buffer II, 2 mM $MgCl_2$, and the appropriate primer pairs (15 μM). Primers from the enteroviral nontranslated region (primer PG01 [5′-AAGCACTTCTGTTTCC-3′] and primer PG02 [5′-CATTCAGGGCCGGAGGA-3′]) and the poliovirus viral protein region (P2-P3 junction of poliovirus types 1 and 2; primer PG03 [5′-GAAATGTGTAAGAA

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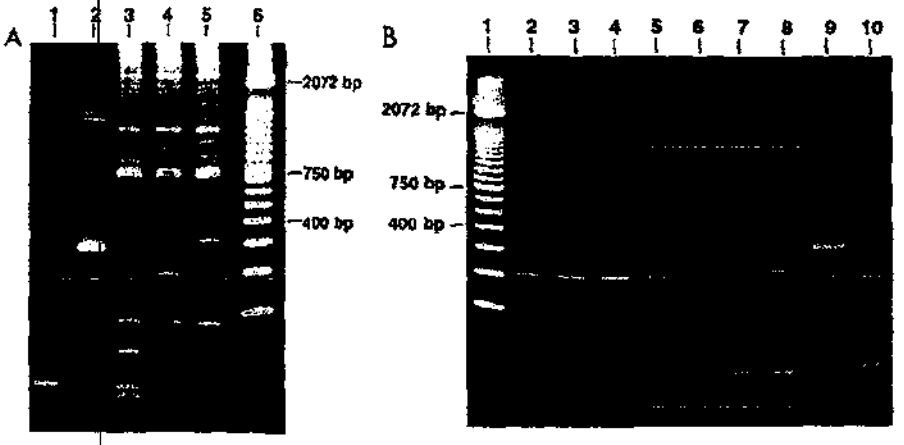

FIG. 1. Nucleotide bands (amplicons) in sera from GWVs and nonmilitary controls. (A) Results for representative samples from three different veterans. Lane 1, poliovirus without RT as a negative control; lane 2, poliovirus-positive control; lane 3, serum from veteran 1; lane 4, serum from veteran 2; lane 5, serum from veteran 3; lane 6, 100-bp ladder. (B) Results for representative samples from seven different nonmilitary controls. Lane 1, 100-bp ladder; lanes 2 to 8, sera from seven healthy controls, respectively; lane 9, poliovirus-positive control; lane 10, poliovirus without RT as a negative control.

CTGTCA-3'] and primer PG04 [5'-GTAACAATGTTTCTTTTAGCC-3']) were used as primer pairs or in a multiplex combination. After 35 cycles of amplification (1 min at 94°C, 2 min at 48°C, and 1 min at 72°C), 8 μl of the PCR mixture was electrophoresed with a precast 6% polyacrylamide gel in TBE buffer (45 mM Tris, 45 mM boric acid, 1 mM EDTA) (NOVEX, San Diego, Calif.) for 30 min at 200 V. The gels were stained for 20 min in a 0.5-μg/ml ethidium bromide solution and were photographed under UV light.

Cloning and sequencing. Sera from three different veterans were processed on three different days. The PCR products were run on and excised from a 2% NuSieve GTG low-melting-point agarose gel (FMC BioProducts, Rockland, Maine). The bands were blunt-end cloned with the Prime PCR Cloner Kit (5 PRIME-3 PRIME, Inc., Boulder, Colo.) according to the manufacturer's specifications. Sequence analysis was performed with the automated sequencer from ABI PRISM (Operon Technologies, Inc., Alameda, Calif.).

Statistical analysis. A 2-by-2 contingency analysis (see Table 1) was done by using Graphpad InStat software (Graphpad Program Software, San Diego, Calif.).

GenBank Search. All GenBank and EMBL searches were done with the DNASTAR Lasergene CD-ROM and software (release 103, November 1997; DNASTAR, Madison, Wis.). Homology searches were performed with 2 through 6 k-tuples with window sizes of 11 to 100 nucleotides (nt). Homology searches for 14 nt or higher were done by starting with position 1 and continuing through to the last 14-nt segment of each amplicon. All sequences with 100% homology were recorded and are presented in Table 2.

Nucleotide sequence accession numbers. The sequences of the 414- and 759-nt sequences derived from sera from patients with GWS were placed in the GenBank database under accession nos. AF100637 and AF100636, respectively.

RESULTS

Sera from 24 deployed GWVs and 50 serum samples from healthy nonmilitary controls were tested for RPAs. Figure 1A shows the presence of multiple bands in the sera from GWVs. The pattern was typical for most veterans, i.e., the occurrence of several bands in the 300- to 750-bp regions accompanied by discrete bands with sequences longer than 2,000 bp. These band patterns were detected by RT-PCR but not by direct PCR, implicating the presence of RNAs and not DNAs in the sera. Figure 1B shows a representative gel in which sera from seven healthy nonmilitary controls were tested. Only a few distinct bands were found. There were no bands larger than 450 bp. The results for 24 veterans and 50 healthy controls (Table 1) indicate the differences in the occurrence of RPAs in the two cohorts.

Two bands in the gel regions of ca. 400 and 750 bp that occurred only in the sera of GWVs were isolated, cloned, and sequenced. Figure 2 presents the consensus sequence data for isolates from three different veterans. Each of the 414- and 759-nt sequences from the three different isolates had approximately 99% homology. The 414 and 759-nt GWS sequences contained several initiation and stop codons (open reading frames) that could code for small polypeptides. Neither the 414- nor 759-nt sequences had direct homologies to sequences in GenBank. In analogous studies with sera from approximately 30 patients with active multiple myeloma (13), we detected RPAs that were related to chromosome 22q11.2. We therefore elected to search the chromosome 22q11.2 database for homologies to the 414- and 759-nt sequences. Several short segments of 15 nt (15mer) and 14 nt (14mer) were found. Table 2 shows that three 15mer and eight 14mer segments of the 759-nt sequence had 100% homology to sequences in chromosome 22q11.2. One 14mer segment, from positions 377 to 390 (Fig. 2 and Table 2), was identical for GWVs 2 and 3 but

TABLE 1. Occurrence of polyribonucleotide bands in sera from GWVs and nonmilitary controls

Band[a]	Band size (bp)	No. (%) positive		P value[b]
		GWVs (n = 24)	Nonmilitary controls (n = 50)	
EV NTR	297[c]	14 (58)	21 (42)	0.22
Polio P2/P3	565[d]	10 (42)	11 (22)	0.10
	200	2 (8)	15 (30)	0.043
Non-EV	350	4 (17)	0 (0)	0.0092
	450	17 (71)	19 (38)	0.0125
	750	12 (50)	0 (0)	<0.0001

[a] EV NTR, enterovirus nontranslated region; EV, enterovirus; Non-EV, nonenterovirus.

[b] See Materials and Methods for description of statistical analysis.

[c] The PG01-PG02 primer pair detects a 297-bp band from the nontranslated region of a majority of enteroviruses.

[d] The PG03-PG04 primer pair detects a 565-bp band of the P2-P3 junction of the oral poliovirus vaccine strains, Sabin types 1 and 2.

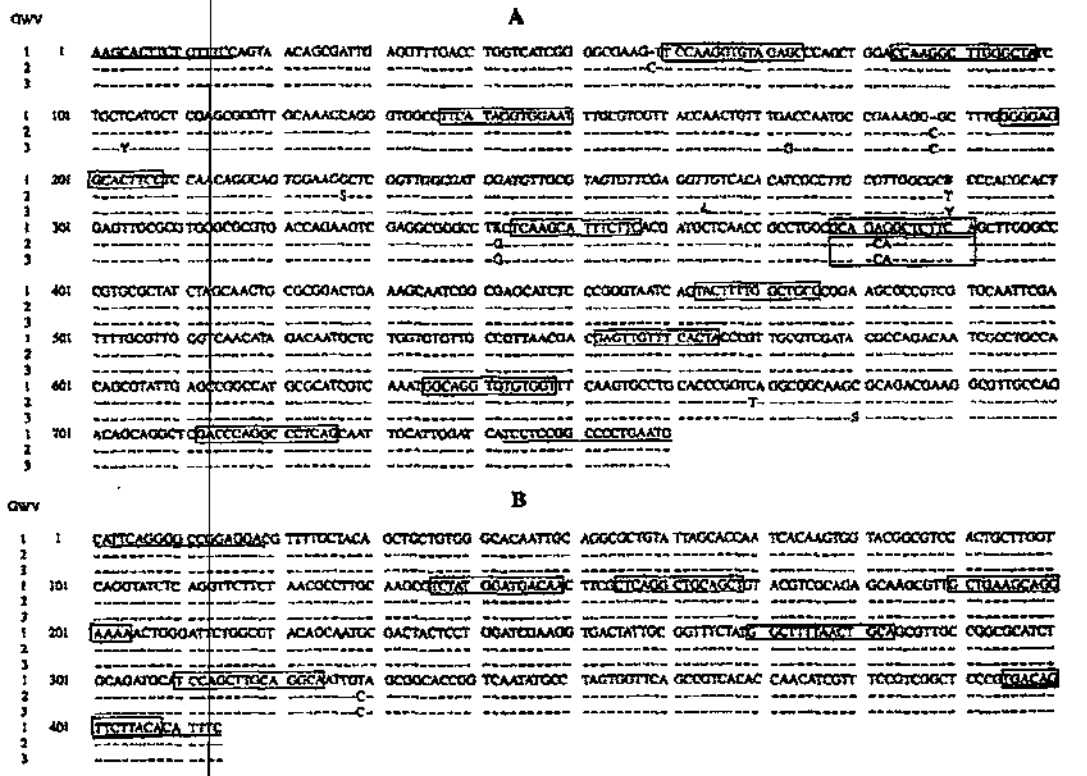

FIG. 2. Sequences of the 759-nt (A) and 414-nt (B) RPAs derived from the sera from three different GWVs. Boxed sequences denote 22q11.2 homologies (Table 2). Enteroviral primers are underlined.

differed by two nucleotides for GWV 1. The 14mer from GWVs 2 and 3 had 100% homology with a segment in the sequence with GenBank accession no. HSF4G12. The 14mer from GWV 1 had 100% homology with a segment in the sequence with GenBank accession no. HSN38E12. The gene sequences from GenBank accession nos. HSF4G12 and HSN38E12 are both located on chromosome 22q11.2. Six of 11 RPA segments were located either within an Alu region (12), between Alu and other repeat regions, or as segments flanking an Alu region. Five 759-nt segments occurred only in the chromosome 22q11.2 region. Two 14mers of the 759-nt sequence were located proximal to the immunoglobulin lambda light-chain variable-region genes. For the 414-nt sequence, there were two 15mer and four 14mer segments that also had 100% homology within the 22q11.2 region. However, these six segments also occurred at sites on other chromosomes. Interestingly, unique 15mer segments were not found in any chromosomal region other than 22q11.2.

DISCUSSION

The pattern of RPAs (polyribonucleotides) found in sera from GWVs was distinct from that found in sera from the nonmilitary cohort. Moreover, RPAs larger than 450 bp did not occur in the sera from healthy controls. The frequencies of occurrence of RPAs homologous to the poliovirus P2-P3 junction sequences and the enteroviral nontranslated region were not significantly different in the two groups (Table 1). The gels shown in Fig. 1 disclosed many bands larger than 2,000 bp in the sera of GWVs. No attempt was made to resolve or to characterize them at the molecular level. Such studies are in progress. Analysis of the 414- and 759-nt sequences showed that they are not related and that the 414-nt sequence is not a degradation product of the 759-nt sequence.

In attempting to understand the pathogenesis of GWS, the challenge has been to explain the diversity of the signs and symptoms typical of the disorder. A traditional approach of invoking a single cause is not applicable because it fails to accommodate three basic considerations. First, the etiology of the disease is multifactorial (49). Thus, different groups of signs and symptoms very likely have different causes. Second, exposure to environmental genotoxins during the Persian Gulf War likely caused an interaction among causative factors, thus affecting expression of signs and symptoms in given individuals. Third, and consistent with multifactorial diseases in general, the genetic and physiologic diversity of the affected population is in accord with the spectrum of disease expression seen. These concepts are known to be relevant to a number of chronic multifactorial diseases such as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, and insulin-dependent diabetes mellitus. For such diseases it has been essential to identify the individual causative factors, to weigh the contributions of each to the overall clinicopathologic picture, to determine how they interact in various population

TABLE 2. Segment homologies among GWS RPAs and human chromosome 22q11.2

RPA, sequence, and position	GenBank accession no.	22q11.2 GenBank sequence	Segment location	No. of other 100% matches
759-nt RPA				
15mers				
59–73	HSU07000	809–823	Between two Alu regions	0 human, 0 nonhuman
83–97	HSCN37F10	36332–36346	Between MIR and Alu	0 human, 0 nonhuman
711–725	HS322B1	45987–46001	Between AluSx and MIR	1 human, 0 nonhuman
14mers				
11–24	D86998	23151–23164	Between V2–8 and V1–3	2 human, 2 nonhuman
136–149	U30597	227965–227978	Between two Alu regions	0 human, 8 nonhuman
194–207	HSE78G1	29369–29382	Between two Alu regions	0 human, 3 nonhuman
343–356	HSN44A4	1460–1473	In AluY	9 human, 25 nonhuman
377–390 (GWV 1)	HSN38E12	19903–19916	Between AluSx and repeat region	2 human, 3 nonhuman
377–390 (GWV 2 and 3)	HSF4G12	39069–39082	Between two repeat regions	18 human, 22 nonhuman
462–475	HSN20A6	17205–17218	Near flanking repeat region	4 human, 1 nonhuman
551–564	AC000068	14136–14149	No description	0 human, 2 nonhuman
634–647	D87021	17508–17521	Between V2–7 and V2–6 light-chain genes	15 human, 7 nonhuman
414-nt RPA				
15mers				
190–204	AC002475	1301–1315	No description	23 human, 1 nonhuman
310–324	HSN74G7	10657–10671	Between Alu repeat and repeat region	3 human, 0 nonhuman
14mers				
136–149	HS65B7	4097–4110	Inside MIR repeat	4 human, 0 nonhuman
155–168	HSE78G1	35878–35891	Between repeat regions	18 human, 2 nonhuman
270–283	HSE146D10	522–535	Between repeat regions	4 human, 2 nonhuman
395–408	HSE116C6	9265–9278	Between Alu and repeat region	1 human, 14 nonhuman

[a] Sequences from a survey of consensus sequences with 100% homology to the designated RPAs from sera from GWVs with GWS (GWS RPAs) were divided into human and nonhuman categories according to the GenBank definition of the entry. MIR, mammalian-wide interspersed repeat.

groups, and to evaluate the effects of different environmental influences.

The notions outlined above reflect our approach to an analysis of GWS. First, we sought to determine whether enterovirus infection could be a contributory factor in the pathogenesis of GWS. Molecular studies that have used PCR technologies have indicated persistent enterovirus infection in myalgia and myositis (54), dermatomyositis and polymyositis (5, 43), neuromuscular disease (28, 37), and the chronic fatigue syndrome (18). The signs and symptoms of these disorders are common in GWS. Moreover, enterovirus infection is known to cause a variety of immunologic and autoimmune disorders (9, 17). Immunologic disorders appear to make up an important component of the signs and symptoms of GWS. Studies of immunologic abnormalities in GWS, similar to those done for the chronic fatigue syndrome (4), appear to offer an important approach in an analysis of the pathogenesis of the disease.

To the best of our knowledge this is the first report of the occurrence of nonviral RPAs in the sera of subjects with a multifactorial chronic disease. We consider four central questions: (i) the possible origin(s) of the polyribonucleotides (amplicons) found in sera, (ii) the possible role(s) of chromosome 22q11.2 in the pathogenesis of the GWS, (iii) whether environmental genotoxins may have played a role in its pathogenesis, and (iv) the possible diagnostic value of detecting RPAs in the sera of patients with chronic diseases.

Identification of the possible origin(s) of the RPAs in sera is an important consideration. Since the occurrence of nonenterovirus RPAs in the sera of GWVs and controls was unexpected, we were concerned that they might have been PCR artifacts. Specific steps had been taken to minimize this possibility (see Materials and Methods). Two separate lines of evidence indicate that the RPAs described here were not artifactual in origin: (i) we developed a non-PCR, total RNA assay that independently confirmed that RNA species occur in the sera of patients with chronic diseases; and (ii) studies of approximately 30 patients with active multiple myeloma and 152 healthy controls by the described RT-PCR assay disclosed the occurrence of unique RPAs, e.g., GenBank accession no. AF018254, in test sera. Accordingly, our data suggest that individual chronic diseases may be characterized by the consistent occurrence of unique RPAs in the sera of patients with the individual chronic diseases.

An explanation of how polyribonucleotides could persist in the sera without being degraded is also needed. A reasonable account comes from the work of Wieczorek et al. (52), who reported that RNAs in the sera of patients with a variety of malignancies persisted as RNase-resistant RNA-proteolipid complexes. Salmon and Seligmann (45) referred to the occurrence of RNAs in the sera of patients with multiple myeloma. We recently confirmed and extended these findings (13). We detected a 705-bp segment homologous to the flanking region of the peroxisome proliferator-activated receptor exon 4 sequence located on chromosome 22q11.2. We are testing whether RPAs found in sera were derived from diverse tissue and cellular origins. These experiments are based on the clinical observation that immunologic abnormalities appear to be commonplace in GWS. In addition, Koga et al. (25) reported that uninfected thymocytes from healthy humans contained elevated amounts of heterodisperse RNA. Such heterodisperse RNA may be released into the circulation as a result of thymocyte apoptosis. Presumably, such RNAs would be protected from RNase degradation because of a physical association with cellular debris, as described by Wieczorek et al. (52). This

hypothesis takes into consideration the evident immunologic dyscrasias that are observed in patients with GWS and that presumably occur because of underlying disorders in immune regulation.

None of the RPA sequence data disclosed homologies to enterovirus or poliovirus sequences. Since only a fraction of the RPAs observed in gels were sequenced, we do not exclude the possibility that some of them were enterovirus related. We assume that the RPAs that were sequenced are direct transcripts of recombinant sequences, although direct experimental proof is still required. Both the 414- and 759-nt RPAs, which were found only in the sera from the three GWVs tested, had short 14mers or 15mers (Table 2) that were 100% homologous to chromosome 22q11.2 segments. These findings suggest that abnormalities in chromosome 22q11.2 are involved, either directly or indirectly, in the pathogenesis of GWS. This does not mean that chromosomal regions other than 22q11.2 are not involved. Nonetheless, it appears that the GWS may be added to the list of diseases in which abnormalities in chromosome 22q11.2 are involved. These include the recently defined chromosome 22q11.2 deletion syndrome (46, 48), juvenile rheumatoid arthritis-like polyarthritis (47), idiopathic thrombocytopenic purpura (29), and hypoparathyroidism (3). In fact, deletion from chromosome 22q11 is the most common microdeletion (36). Interestingly, up to 60% of subjects (36, 53) with such deletions suffer from behavioral or psychiatric disorders. Also of note, chromosome 22 appears to be involved in the so-called Goldenhar complex (21, 24), a birth defect possibly associated with GWS (19). The mechanisms involved in embryonic development and 22q deletion disorders are now being defined at the molecular level (33).

The occurrence of hot spots for genetic deletions, translocations (6), and rearrangements, e.g., immunoglobulin lambda light chains (15, 44), in chromosome 22q11.2 is recognized widely. Such hot spots may be particularly sensitive to adverse genotoxic effects of environmental GHMs encountered during service in the Persian Gulf War. Studies with animal models (2) suggest that combined or multiple exposures to GHMs may have a synergistic genotoxic effect, thus causing some of the symptoms seen in GWS.

The juxtaposition of the detected RPA sequences with Alu sequences in chromosome 22q11.2 also may be relevant to the pathogenesis of GWS. The contemporary notion that Alu sequences are "junk DNA" is not consistent with the accumulating evidence that Alu sequences become transcriptionally active when cells are exposed to physiologic insults such as infection with DNA viruses (10, 40) or human immunodeficiency virus type 1 (23, 25) or when cells are induced to express heat shock proteins (7). Liu et al. (32) reported that cells stressed by exposure to cycloheximide or puromycin "rapidly and transiently increased the abundance of Alu RNA." We postulate that the expression of RNAs of Alu sequences, their flanking regions, and their recombinants in response to GHMs may be a supplemental mechanism for detoxification of GHMs (11, 38). Such Alu-Alu recombinants are generated by both extrachromosomal and chromosomal genetic mechanisms (20, 27, 31, 35, 39, 41). In addition, Makalowski et al. (34) described the role of Alu sequences in generating diverse proteins. Such diverse proteins may also contribute to autoimmune reactivities in patients with GWS and possibly other chronic disorders.

The possible roles of the detected RPAs in the pathogenesis of GWS are unknown. Nonetheless, their occurrence makes available markers that can be studied for possible pathophysiologic effects. The biological activities of such molecules can be significant. Krieg (26) reported that specific CpG Alu-rich DNA (30) sequences in the plasma of patients with systemic lupus erythematosus may play an important role in the pathophysiology of the disease. Interestingly, chromosome 22 is rich in CpG islands. In addition, Abken et al. (1) reported that novel mouse cytoplasmic DNA sequences immortalized human lymphocytes in vitro. Such studies provide a paradigm for GWS.

The patterns of the occurrence of RPAs in the sera of GWVs and healthy controls are sufficiently distinct to suggest possible future diagnostic applications. Sufficiently large numbers of subjects need to be studied (50) to determine the sensitivities and specificities of such tests. Our studies of patients with active multiple myeloma (13) suggest that patients with individual chronic multifactorial diseases may have unique RPAs in their sera. Validated tests for such putative surrogate markers may aid in the diagnosis of such diseases or in the evaluation of responses to therapeutic modalities.

ACKNOWLEDGMENTS

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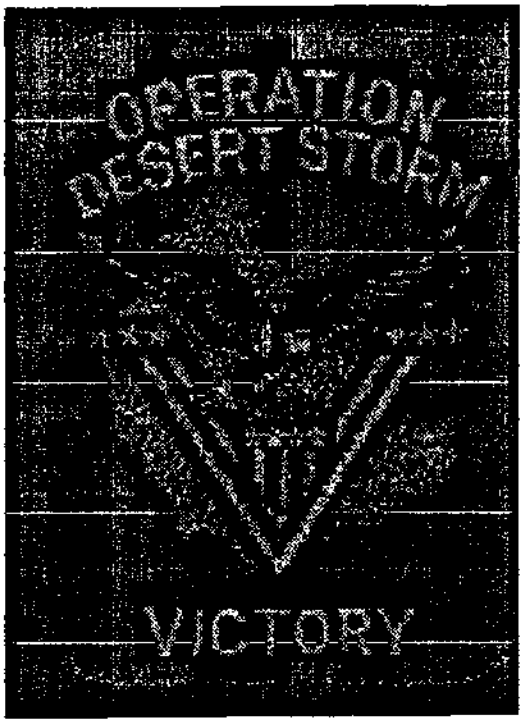
Welcome to PGEV.org

Persian Gulf Era Veterans



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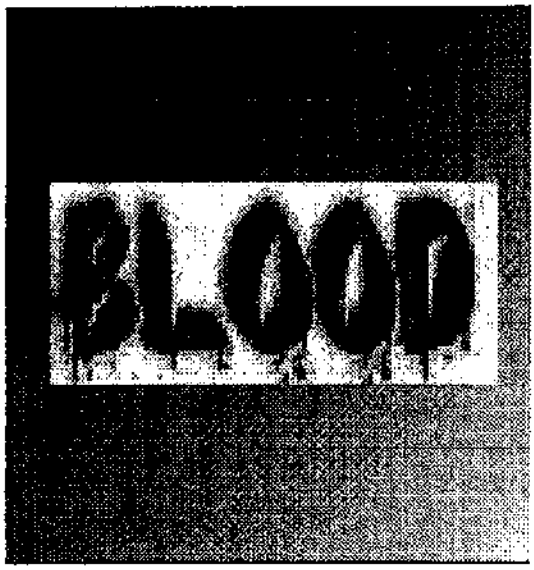
Gulf War Veteran Community

We would like you input on the attached document.

Editorial from
point of contact:
SSG Hammack
781-593-5045 voice
603-947-2138 fax

PERSIAN GULF ERA VETERANS ASK

Did this Program fail and cause the increase the abnormal number of veterans with Hepatitis C Virus ?



Subject: HCV CONSIGNEE NOTIFICATION
On March 23, 1998, the Food and Drug Administration issued Guidance for Industry: Supplemental Testing and the Notification of Consignees of Donor Test Results for Antibody to Hepatitis C Virus (Anti-HCV) which outlines requirements for HCV lookback. Each of the three Armed Service Blood Programs (Army, Navy, and Air Force) has been directed to establish a centralized database for tracking their HCV donor, recipient, and product lookback cases.

In order to adequately facilitate this program, it is requested that "all" HCV **lookback consignee** notifications be made directly to the specific Armed Service Blood Program office which represents their shipping consignee.
The following addresses are provided:
(FOR ARMY FACILITIES) Commander U.S. Army Medical Command
ATTN: MCHO-CL-R (Army Blood Program)
2050 Worth Road Ft Sam Houston, TX 78234-6000
Phone: (210) 221-6344/7989 POC: COL Gary Kagawa, MS
(FOR AIR FORCE FACILITIES) HQ USAF/SGXR Air Force Blood Program
110 Luke Ave, Rm 400 Bolling AFB, DC 20332-0750 Phone: (202) 767-5544
POC: Maj Ruth Sylvester, BSC, USAF (FOR NAVY FACILITIES)
Chief Bureau of Medicine and Surgery 2300 E Street, N.W.
Attn: MED-273 (Navy Blood Program) Washington, DC 20372-5120
Phone: (202) 762-3434/3438 POC: COL Brenda Bartley, MSC, USN

My point of contact for this action is Major L. Groshel, USAF, BSC, Deputy Director, Armed Services Blood Program Office, at 703-681-8011/8024.
Captain, Medical Service Corps United States Navy Director

HEPATITIS C INFECTION COMMON AMONG US VETERANS
STUDY INDICATES 20% MAY BE INFECTED
NEW YORK, NOV 24, 1999, REUTERS HEALTH

In a recent study, close to 20% of US veterans screened at San Francisco Veterans Affairs Medical Center tested positive for the hepatitis C virus, which can cause liver disease.

Dr. Teresa L. Wright and Megan E. Briggs announced the study results recently at the50th annual meeting of the American Association for the Study of Liver Diseases in Dallas, Texas.

The California researchers screened 791 patients. Wright reported that hepatitis C virus was most common in Vietnam-era veterans, but ``actual service in Vietnam was not identified as an independent risk factor."

Briggs told Reuters Health that, among the veterans studied, the single greatest risk factor for infection with the hepatitis C virus was intravenous drug use. At the liver disease meeting, she said that other risk factors were getting a tattoo, getting stuck with a needle while serving as a medical corpsman, and being in jail for more than 48 hours.

Wright said that the Veterans Administration has preliminary plans to conduct a larger study, which would determine how common the hepatitis C virus is among veterans nationwide.

She added that the Veterans Administration has approved the use of a combination drug therapy -- interferon plus ribavirin -- for treatment of veterans who are infected with the hepatitis C virus.

Many veterans ``do not make good candidates for this therapy because it has many side effects associated with it," Wright explained. ``But we know that we can get a 40% response with this therapy, so we think that it is important to identify those who are infected and offer treatment if appropriate."

POSTED TO NGWRC WEB Tue Nov 30 08:00:01 1999

Hepatitis C Screening

Seen Straining Resources

By Matt Pueschel

WASHINGTON—As dollars for veterans health care are squeezed ever tighter, a report released by the inspector general in mid-October shows that the impact of national guidance issued by the Department of Veterans Affairs in February calling for the screening of all veterans at risk of hepatitis C, subsequent testing, and appropriate care "is an increasing concern" to managers in VHA facilities.

"Increasingly, VHA resources will become more strained, and additional dedicated resources will be required at many VHA facilities to avoid delayed access to HCV care and treatment in the future," the IG report stated. "VAMC managers and clinicians whom we interviewed unanimously expressed their concerns to us about the anticipated impact on their facilities' resources, and particularly about their future abilities to treat all of the veterans who are expected to seek care and treatment of HCV."

The report was requested in June by Rep. Lane Evans (D., Ill.), ranking minority member of the House Veterans Affairs Committee and Rep. Vic Snyder (D., Ark.) to investigate complaints about veterans' access to HCV diagnosis and treatment at several facilities. The inspector general found no evidence of HCV treatment rationing at eight VA medical centers throughout the country, although a situation was discovered at the Tampa, Fla. medical center in which all the veterans who needed Rebetron treatment may not have received it because of fiscal constraints. The report stated that the network director promptly remedied the situation after he became aware of it.

The primary dilemma in the VA's HCV initiative appears to be the expensive cost of detecting and treating the disorder. According to the IG report, an analysis applied to the San Francisco VAMC indicates that screening 1,000 veterans and treating only appropriate cases would cost $737,000 and lead to the virologic cure of just eight patients.

House VA minority staff members said the HCV initiative is a great idea, but there is not enough money in the VA budget for it. The VA is operating on a budget to cover its basic health services, they said. "This is clearly a mandate that requires new dollars if we want to avoid the tragic consequences we've faced in other epidemics, such as AIDS," said Rep. Evans. "Without an adequate appropriation, VA will be robbing Peter to pay Paul."

Although the inspector general found that VA has provided national satellite broadcast forums for ongoing clinical education and guidance on HCV, the report stated that the HCV "mandate is not fully implemented because VAMCs are not uniformly screening" all veterans who seek care. "Some facilities did not have any HCV risk factor screening procedures for new patients," the report stated. "While VA's full implementation of the HCV initiative will take time, uniformity of HCV risk evaluation or screening mechanisms needs to be addressed soon."

Rep. Evans said VA's central leadership has taken steps to try to educate the workforce to ensure that hepatitis C, which disproportionately afflicts Vietnam era veterans, is considered a high priority nationwide. "My concern is that some hospital directors don't seem to want to implement the guidance they have, and headquarters currently has little means of changing their behavior," said Rep. Evans.

The IG report also recommended that VHA conduct a cooperative study at multiple facilities to refine and improve HCV care and treatment, especially for veterans. The current combination treatment with Rebetron is not effective for all veterans and its side effects can be severe in some cases.
The report further recommended the establishment of an HCV national policy or advisory board sponsored by VHA and composed of nationally recognized clinical experts in the field.

Test At Home For Hepatitis C

Nearly 4 Million Americans Have The Disease, And Don't Know It

CLEVELAND, Posted 4:05 p.m. April 29, 1999 – Test yourself for hepatitis C at home.

If you had a blood transfusion or organ transplant before 1992, ever injected drugs or had sex with someone who did – you should be tested for hepatitis C.

NewsChannel5 reports nearly four million Americans have hepatitis C, but many don't know it.

To help raise awareness of the disease, the Food and Drug Administration has approved the first at home test called the Home Access Health's Hepatitis C Check. The test determined whether a person has ever been infected with hepatitis C, but cannot tell if that infection is currently active.

The kit will be available in June and is expected to cost under $70.

For More Information:

- Home Access

Compiled by NewsNet5 Staff

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Herpes Virus Associated with MS

A strain of reactivated herpes virus may be associated with multiple sclerosis (MS). In the study, more than 70 percent of individuals with the relapsing-remitting form of MS showed an increased immune response to human herpes virus-6 (**HHV-6**) and approximately 35 percent of all participants in the study had detectable levels of active HHV-6 in their serum.

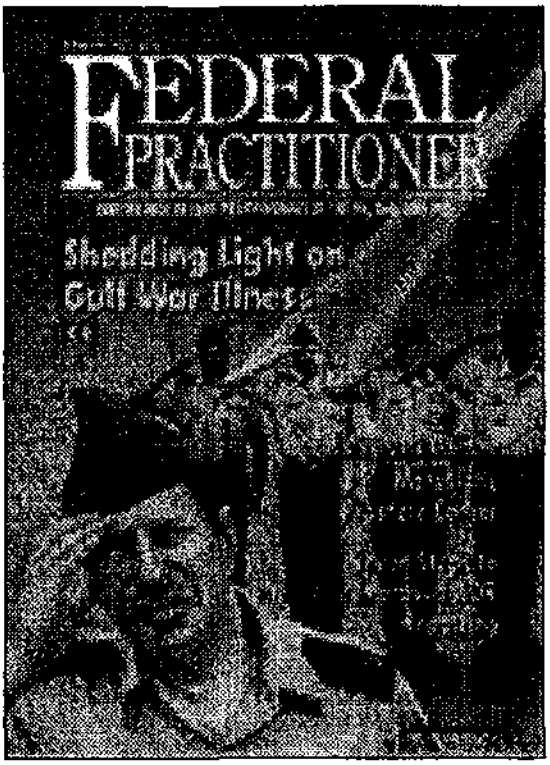
Scientists believe that the reactivation of HHV-6 virus may be associated with the breakdown of the protective covering of nerves, called myelin.

Reactivation is characteristic of herpes viruses. --

Source: National Institute of Neurological Disorders and Stroke,
November 24, 1997

PERSIAN GULF ERA VETERANS
would like to know if the studies of Gulf Veterans who have developed MS reviewed this possible situation ????

Military Anthrax Program Criticized



GAO Finds Serious Problems

October 25, 1999, By The Associated Press

WASHINGTON (AP) -- The Pentagon's program to vaccinate all 2.4 million service members against anthrax remains troubled with delays, supply problems and uncertainties, congressional auditors said Monday.

The General Accounting Office, an investigative arm of Congress, criticized the Defense Department's procedures for keeping track of vaccinations. The Pentagon also is not doing a good job screening ``adverse reactions,'' the report said.

Anthrax is an infectious bacterium that is frequently fatal if it is inhaled by unprotected humans. The Pentagon considers it as perhaps the greatest biological warfare threat to U.S. military forces.

In 1997, Defense Secretary William Cohen ordered all active duty and reserve troops to get shots of the anthrax vaccine, but only 340,000 of the 2.4 million have been immunized so far.

The program is at least five months behind schedule, the GAO report said.

``The most critical component of the program, an adequate supply of vaccine, is threatened by testing delays and possible loss of production capability,'' the GAO said. ``Testing problems have already delayed release of stockpiled vaccine.''

It also cited financial problems facing the only licensed producer of the vaccine, BioPort Corp. of Lansing, Mich.

Last August, the Pentagon agreed to pay more per dose and to make an $18.7 million advance payment to BioPort to enable the financially troubled company to pay off creditors.

Those contract renegotiations ``have somewhat mitigated'' BioPort's problems, the GAO said. Still, it said, ``BioPort's financial problems have reduced the program's vaccine supply in the short term and may threaten future supplies altogether if production does not resume.''

``BioPort must improve its financial health if DOD is to retain this sole source of anthrax vaccine,'' the GAO said.

The Two "Variants" Of HHV-6 Appear To Act Very Differently

There are many strains of HHV-6 -- that is, viruses that are enough alike to be considered HHV- 6, but which differ from each other in small ways. Those strains are further classified as being in a larger grouping, called a "variant." The two variants of HHV-6 appear to have very different disease-causing properties. While this is rather technical information, it may have important implications for understanding both Chronic Fatigue Syndrome and AIDS.

The easiest way to visualize different virus strains is to imagine that a virus is like a string of different-colored beads. If you have three strings of beads that have exactly the same color sequence except for one bead, those strings would be analogous to strains of a virus.

There are many different strains of HHV-6, and more appear to be discovered all the time. Those strains, like the imaginary strings of beads, differ from each other only very slightly. But as more has been learned about HHV-6, it has become clear that the virus strains differ from each other in ways that allow them to be divided into two groups, called "Variant A" and "Variant B" HHV-6.

These two variants appear to be able to cause very different kinds of illness, and may resolve the apparent paradox that HHV-6 infects about 90 percent of the world population as an apparently harmless, asymptomatic infection, yet can also be associated with catastrophic immune system diseases like AIDS, cancer, and Chronic Fatigue Syndrome.

Recent research has shown that Variant B HHV-6 is the type that infects infants and children, usually by age three, and is associated with a mild illness with fever and rash called roseola.

Variant A HHV-6, however, is the type that is found in very sick adults with AIDS and CFS. Variant A HHV-6 appears to be able to attack the immune system, and infect and kill very important cells. Cells that HHV-6 is known to be able to infect include the cell considered to be the primary target of HIV, the T4 cells, and other very important immune system cells, natural killer cells. Because HHV-6 can infect the same cells as HIV -- and both viruses have been found cohabitating in the same cell -- some researchers have suggested that HHV-6 may be a "co- factor" in causing AIDS.

Now, however, it is known that HHV-6 is the only virus capable of infecting and killing natural killer cells, the immune system's front-line defense against viruses and some kinds of cancers.

So, along with HHV-6's ability to infect T4 cells, it is becoming clear that HHV-6 is capable of inflicting a considerable amount of damage on the immune system.
Although some scientists consider HHV-6 to be a "co-factor," along with HIV, in causing AIDS, it might be more prudent to determine how much HHV-6 can damage the immune system all by itself. Is HHV-6 the real AIDS virus?

Eur J Clin Invest 1999 Nov;29(11):960-3

Persistent symptoms in former UNTAC soldiers are not associated with shifted cytokine balance.

Soetekouw PM, De Vries M, Preijers FW, Van Crevel R, Bleijenberg G, Van Der Meer JW St Radboud University Hospital, Nijmegen, the Netherlands.

[Medline record in process]

BACKGROUND:
The pathogenesis of post-combat syndromes, such as Gulf War syndrome, is poorly understood. Recently, it has been postulated that the symptoms of veterans with such syndromes are due to a disturbed cytokine balance shifted towards a T-helper (Th) 2 profile. We investigated this hypothesis in 21 symptomatic former UNTAC soldiers and compared their results with those obtained in 21 healthy former UNTAC soldiers matched for age, sex andmilitary force.
DESIGN:
The numbers of intracellular interleukin 4 (IL-4) and interferon gamma- (IFN-gamma) producing CD4+ and CD8+ T lymphocytes (CD3+) were determined after in vitro stimulation with phorbol myristate acetate and calcium ionophore in the presence of brefeldin to block secretion of induced cytokines. Circulating concentrations and lipopolysaccharide- (LPS) or phytohaemagglutinin- (PHA) stimulated whole-blood production of the proinflammatory cytokines IL-1beta, IL-1ra, tumour necrosis factor alpha (TNF-alpha) and IL-10 and IFN-gamma were measured.
RESULTS:
The numbers of CD4+ and CD8+ T lymphocytes positive for IL-4 or IFN-gamma production were not significantly different in patients and control subjects. After stimulation with LPS or PHA, the in vivo circulating concentration and concentration of IL-10 and IFN-gamma were also similar.
CONCLUSIONS:
The present study demonstrates that there is no shift in cytokine balance towards a Th2 profile in former UNTAC soldiers with symptoms similar to those of the Gulf War syndrome.
PMID: 10583441, UI: 20051286

PERSIAN GULF ERA VETERANS would like to know which Study reviewed this question :

We need to know if these Danish soldiers got the shots??
This might be a key determining factor on the difference with the UJ study done earlier.

Metcalf Report on the Potential Role of Squalene in Gulf War Illnesses

Prepared by the office of
Congressman Jack Metcalf
September 27, 2000

JACK METCALF
2D DISTRICT, WASHINGTON

COMMITTEE ON TRANSPORTATION AND INFRASTRUCTURE
SUBCOMMITTEES:
AVIATION
GROUND TRANSPORTATION

COMMITTEE ON SCIENCE
SUBCOMMITTEE
ENERGY AND ENVIRONMENT

Congress of the United States
House of Representatives
Washington, DC 205131702

COMMITTEE ON BANKING AND FINANCIAL SERVICES
SUBCOMMITTEES
HOUSING
FINANCIAL INSTITUTIONS
DOMESTIC AND INTERNATIONAL MONETARY POLICY

CHAIR, REPUBLICAN HOUSING OPPORTUNITY CAUCUS

REPUBLICAN POLICY COMMITTEE

Statement of Congressman Jack Metcalf
Subcommittee on National Security, Veterans Affairs, and International Relations
September 27, 2000

Mr Chairman, I want to thank you for the opportunity to once again be a small part of your courageous effort to answer questions regarding Gulf War Illnesses and vaccines used by our military personnel. Your determination to move forward and find answers has provided vital leadership for this Congress on this critically important issue.

Indeed, we have an obligation to pursue the truth, wherever it may lead us. To do less would be to act dishonorably toward the dedicated men and women who stand between us and a still dangerous world.

For that reason, I have issued a report culminating a three year investigation into the conduct of the DOD (Department of Defense) with regard to **the possibility that squalene, a substance in vaccine adjuvant formulations not approved by the** FDA, **was used in inoculations given to Gulf War era service personnel.** According to the GAO (General Accounting Office), scientists have expressed safety concerns regarding the use of novel adjuvant formulations in vaccines, including squalene.

The report reveals that **the** FDA **has found trace amounts of squalene in the anthrax vaccine. The amounts recorded are enough to "boost immune response,"** according to immunology professor Dr. Dorothy Lewis of Baylor University. Therefore, my report concludes that, Mr Chairman, you are absolutely correct in demanding an immediate halt to the current AVIP (Anthrax Vaccination Immunization Program).

My report further states that an aggressive investigation must be undertaken to determine the source of the squalene, and the potential health consequences to those who have been vaccinated, both during and after the Gulf War.

The report also documents at length DOD "stonewalling" attempts to resolve the squalene issue, which GAO **investigators characterized as "a pattern of deception."** The GAO stated the DOD denied conducting extensive squalene testing before the Gulf War, then admitted it after being confronted with the public record. The GAO revealed that DOD officials deliberating deployment of the anthrax vaccine expressed a "willingness to jump out and use everything," in discussing experimental vaccines containing adjuvants not approved by the FDA.

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Congress of the United States
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REPUBLICAN POLICY COMMITTEE

GAO also found Peter Collis, DOD **official who headed vaccine efforts, refused to cooperate with them.** The report states that the DOD has refused to act in good faith upon the GAO recommendation to replicate the findings of a test developed by renowned virologist Dr. Robert Garry of Tulane University, although DOD admitted they could easily do so. The work of the Tulane researchers has been peer-reviewed in a scientific publication of high standing.

Finally, my report states that "Congress should take immediate action to review the findings of the GAO and the Armed Services Epidemiological Board, and provide independent oversight for the immediate implementation of their recommendations." **The board called on the** DOD to **engage in close cooperation with the Tulane researchers.**

Congress must get to the bottom of the labyrinth that has become known as "Gulf War Illnesses." Mr Chairman, you have been in the forefront of this effort. As I am about to leave the Congress, I just want to once again commend you for your courage in this leadership role. Please stay the course. Veterans, active service members and their families deployed around the world are counting on you. Thank you so much.

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Executive Summary

Congressman Jack Metcalf has issued a report culminating a three year investigation into the conduct of the DOD (Department of Defense) with regard to **the possibility that squalene, a substance in vaccine adjuvant formulations not approved by the FDA, was used in inoculations given to Gulf War era service personnel.** According to the GAO (General Accounting Office), scientists have expressed safety concerns regarding the use of novel adjuvant formulations in vaccines, including squalene.

The report reveals that **the FDA has found trace amounts of squalene in the anthrax vaccine. The amounts recorded are enough to "boost immune response,"** according to immunology professor Dr. Dorothy 'Lewis of Baylor University. Therefore, the report concludes that immediate action should be taken to halt the current **AVIP** (Anthrax Vaccination Immunization Program). It further states that an aggressive investigation must be undertaken to determine the source of the squalene, and the potential health consequences to those who have been vaccinated, both during and after the Gulf War.

The report also documents at length DOD "stonewalling" attempts to resolve this issue, which **GAO investigators characterized as "a pattern of deception."** The GAO stated the DOD denied conducting extensive squalene testing before the Gulf War, then admitted it **after** being confronted with the public record. The GAO revealed that DOD officials deliberating deployment of the anthrax vaccine expressed a "willingness to jump out and use everything," in discussing experimental vaccines containing adjuvants not approved by the FDA.

GAO also found Peter Collis, DOD official who headed vaccine efforts, refused to cooperate with them. The report states that the DOD has refused to act in good faith upon the GAO recommendation to replicate the findings of a test developed by renowned virologist Dr. Robert Garry of Tulane University; although DOD admitted they could easily do so. The work of the Tulane researchers has been peer-reviewed in a scientific publication of high standing.

Finally, the report states that "Congress should take immediate action to review the findings of the GAO and the Armed Services Epidemiological Board, and provide independent oversight for the immediate implementation of their recommendations." **The board called on the DOD to engage in close cooperation with the Tulane researchers.**

Congressman Metcalf believes it is clearly within the oversight responsibility of the Congress to get to the bottom of the labyrinth that has become known as "Gulf War Illnesses." **We have an obligation to pursue the truth, wherever it may lead us.** To do less would be to act dishonorably toward the dedicated men and women who stand between us and a dangerous world, willing to die if necessary to defend our nation.

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The Request For Investigation

- **August 29, 1997 Congressman Jack Metcalf requested the General Accounting Office (GAO) investigate reports that the presence of antibodies for squalene had been discovered in the blood of some sick Gulf War-era veterans.** The assay (test) being used to detect the antibodies had been developed at Tulane University by Dr. Robert Garry, world renowned virologist.(Appendix 1)

  At the time of Congressman Metcalf s request, the research by Drs. Garry, Asa and Cao had not yet been published in a peer-reviewed scientific journal. Their work, "Antibodies to Squalene in Gulf War Syndrome," was published in the February 2000 issue of *Experimental and Molecular Pathology.* (Appendix 2)

  NOTE: Squalene is a component of adjuvant formulations used in some experimental vaccines but not in any licensed vaccines. Squalene is found in shark liver oil, some vegetable oils, and the human liver and can also be manufactured through chemical engineering. (GAO/NSIAD-99-5).

Section One
The Investigation: A Pattern of Deception

- **September 1997 - March 29, 1999 General Accounting Office (GAO) investigators initiated their study and completed the report "GULF WAR ILLNESSES: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved"** (GAO/NSIAD-99-5). The investigation was significantly slowed by government officials withholding or presenting incomplete information, ***leading GAO investigators to document their concerns questioning a "pattern of deception."*** (1) The following six dated entries are found in the background material for the GAO report. They illustrate the pattern of deception that clouded the investigation.

  November 14, 1997 GAO entrance conference with Department of Defense (DOD) officials, GAO notes state,

  1) "They said DOD had not performed or sponsored any research on synthetic or natural squalene or squalane until after the Gulf War. The sponsorship was through two CRADAs [Cooperative Research and Development Agreement]. However, they could not tell us who the CRADA's were with, what stage they were in, or what tests had been performed.

  2) "Squalene was used in two experimental adjuvants, after the war and involving fewer than 100 subjects. These were for HIV and Malaria vaccines. They said NIH had also used in some of their research protocols. DOD officials also stated that DOD was involved after animal testing stage." (2)

  In background papers, GAO investigators stated, "However, GAO found evidence of several other studies in our searches ofpublication &abases, references and articles. Various DOD officials gradually acknowledged on apiece meal basis that their clinical research had started before the war, that they had conducted 5 clinical studies with squalene and had planned a sixth, that the size of these studies was increasing and now has involved 572 human subjects, and that some of these studies were purely their own investigational New Drug (IND) Studies. Moreover they had conducted numerous animal studies, particularly to develop a modern vaccine for anthrax In fact, in most cases they only admitted to conducting research after we had discovered it in public records. On three occasions people attending a meeting did not report their own research on squalene adjuvants." (3)

  December 10, 1997 GAO entrance conference with Food and Drug Administration (FDA) officials, GAO investigators noted that it was a very productive meeting and recorded:

1) "The purpose of developing new adjuvants, even though alum is safe, is to use fewer inoculations, get a better response, and to check unconquered antigens. Earlier adjuvant ran into problems in animal testing... Most of DOD's work has been with Ribi Detox for malaria. **Their person most interested in developing own adjuvants at WRAIR** [Walter Reed Army Institute of Research] **is Carl Alving.**
2) "Allied had concerns about the quality of our vaccines. Michigan had some manufacturing problems.
3) "Karen is sure DOD used plague vaccine. They pushed it. She confirmed that squalene was used in placebos.
4) "FDA testine of drugs and vaccines: Good Manufacturing Practices inspection every 2 years. Test each lot released. No routine random sample. For bot tox [botulism toxoid] they also checked for safety and sterility, but not the makeup of the compound. DOD should have reserve samples. Required to have them for each lot. **Squalene should not be there."** (4)
NOTE: See Appendix 25 regarding the discovery by FDA in 1999 of trace amounts of squalene found in limited testing of Anthrax Vaccine, Adsorbed in the lots tested.

March 30, 1998 **GAO interview with Donald Burke, Director of AIDS research for DOD durine the Persian Gulf War.** GAO recorded, "Burke said he was involved with AIDS trials at time of war and purposely chose not to get involved in BWD [biological weapons defense] issues at that time... In his AIDS work he experimented with **MF59** [an **adjuvant** containing squalene] because alum was destructive to HIV prqteins. He has had good cooperation with **NIH** [National Institutes of Health]. He recounted various studies, including a large one with 300 subjects getting MF59. He suggested we talk to Carl Alving about DOD adjuvant research." (5))
*GAO investigators noted, "Don Burke the former director of DOD's HIV research and Debbie **Birx**, the current director disagreed on the existence of a large early HIV trial with squalene with over 600 volunteers. She said he was thinking of an NIH trial. However, NIH reported no trials of that magnitude. (6)*

April 6, 1998 **GAO interview with Dr. Carl Alving, DOD's too adiuvant researcher.** GAO stated,
1) **"Alving opened by saying he didn't know anything about Operations Desert Storm and Desert Shield (ODS) and the vaccines that were used. He is a researcher, and an expert, but not in the policy loop.**
2) "GAO pressed why he was not consulted about gulf war inoculations given his world class expertise. He admitted that just prior to gulf war he was asked if he could develop an anthrax vaccine on a crash basis. He stated that **WRAIR** has manufacturing capability, Ft. **Detrick** does not. He could have done it in *3-6* months but never received a follow on phone call to formally authorize the work. If asked, he could have done it but would have recommended MF59 for anthrax because Chiron had the manufacturing capacity and the desire to market it. **Ribi,** Chiron and Hunter

were the adjuvant leaders at the time. He was subsequently asked again (by DOD?) to develop an anthrax vaccine using liposomes, but it and all others. tested failed to protect monkeys with a single shot, which he thought was an absurd criteria. But he thought commercial considerations may have driven the criteria.
3) "He also said that as the world's foremost expert on lipids he knew quite a bit about cholesterol and its precursor, squalene. He doubted that a vaccine with squalene would produce a meaningful antibody response.
4) "Analysis: Overall, the commercial links appear to be crucial to the course of DOD vaccine R&D" (7))
GAO investigators recorded the following observation in a section titled, ***DOD officials were less than forthcoming about their role in Gulf War vaccine decision making:*** *"Carl Alving, DOD's top adjuvant researcher was not included in our meetings at WRAIR where he worked, nor even mentionedas someone we should interview. However, both NIH and FDA had said he was the person at DOD most involved with adjuvants. We subsequently met and while he acknowledged that he was probably the army's best expert on aajuvants, he at first denied having any role in the gulf war vaccine deliberations. After Kwai Chan left, Sushil Sharma pressed him on this, asking how could it be that they would discuss these issues without their principle expert. He then remembered that he had been called by someone from the army's biological warfare defense program at USAMRID [United States Army Medical Research Institute of Infectious Diseases], who asked* if *he could develop a new. more potent anthrax vaccine on a crash basis to use in the Operation Desert Shield. He worked on it and thought he could do it. but no one ever called him back. He wouldn 't say who called from USAMRID or why he just didn 't return the call."* **(8))**

April 19, 1998 **Interview with Dr. Anna Johnson-Winegar, Director Environmental and Life Sciences, key participant in the tri-service committees advising on the science and vaccine production issues.**
1) "Project Badger. [**Tri-Service** Task Force established prior to the Gulf War, (9/90) to investigate ways to increase production of biological warfare vaccines.] Badger was a discussion about the scientific issues involved in improving troop vaccine coverage. Discussions were wide-ranging and interesting, e.g. nonspecific immune 'enhancements, but there was not much data. Carl **Alving** was our in-house adjuvant expert, and a participant in our discussion. [Dr. Alving first told GAO he did not have any role in the gulf war vaccine deliberations, then minimized his involvement.] We discussed using liposomes, but they didn't have enough. You have to go to war with what you have, not novelties that don't have your full confidence.
2) " Adjuvants discussion and recommendations. Discussion of adjuvants was limited. Its one thing to discuss interesting phase 1 research, quite another to apply it to short term shortages. In the long run they can be of potential *use.* But scientific inference doesn't lead to immediate military operations. Some in the group were willing to jump out and use everything. (She refused to say who.) Our group advised

the Surgeon General who in turn worked with the JCS. There was not any data on what happens to people getting the anthrax and botulism vaccines at the same time. But we had to do it.

3) "Safety issues. There was little discussion of long term safety issues. They were thinking short term and immediate. Generally inactive vaccines don't have a problem. They used inactive antigens. But there were a lot of discussions regarding GMP [Good Manufacturing Practice] issues. For instance, they had trouble finding the exact same fermenter. Getting approval for a new one could take FDA 30 months. They went ahead started production with it and got retroactive approval. Anthrax vaccine is stable for up to 20 years if kept at right cool temperature." (DI-9)

NOTE: In a DOD Badger document File 120396_sep96_decis10_0002.txt, Subject: Desert Shield Biological Warfare HOC Working Group, the following statement is found:

"It was reported that the individuals from logist ___ USAMRIID, were expected back from theater today with the ___ anthrax and botulinum vaccines, antitoxin, ribavirin and centoxin. While in theater the items were under refrigeration; however, there was a report that the refrigerator failed to operate for a period of time and possibly these items were damaged. The items will be re ___ to USAMRIID and a determination made with regard to the disposition." (Appendix 3)

GAO notes state, "Anna Johnson- Winnegarplayed a major role in Project Badger, leading the effort seeking the urgent assistance of vaccine manufacturers. She sat in on most of the Project Badger meetings addressing B Wdefenses. Our interview with her revealed several contradictions. At first she said they had limited discussion about adjuvants, but then added that discussions were wide ranging and interesting, e.g. 'nonspecific immune enhancements, but there was not much data to base a decision. Alving, she said, was their in-house adjuvant expert, and a participant in their discussions. Some in the group felt is was one thing to discuss interesting Phase I research, quite another to apply it to short ferm shortages, but others were willing to jump out and use everything. She declined to tell us who advocated pushing forward the use of experimental vaccines." (IO)

April 23, 1998 **GAO meeting with General Ronald Blanck Surgeon General of the Army, a discussion on the deliberations, decision making of DOD on vaccine production and administration for the Persian Gulf War.** GAO summarized Gen Blanck's recollection:

1) "One manufacturer, Michigan for both botulism and anthrax vaccine. We had a fair amount of anthrax vaccine but only a small amount for botulism (BT). However, we found Iraqis might have F and G strains so we contracted with Porton to make them. To best of his knowledge none were administered. We got it but didn't use it. Everything we used was from Michigan. Salk at Swifhvater had the capacity to help produce, but got nothing from them. He got NIH to approve NCI use.

Section *Two*
The Stonewalling and Obfuscation

- **March, 1999** **GAO presented to Metcalf their findings (GAO/NSIAD-99-5).** GAO recommended DOD not wait for the peer-review and publication process, but take immediate action to: **"conduct research designed to replicate or dispute the independent research results** that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans." Surprisingly, DOD's comments regarding the GAO recommendations, contained in the report, **accused GAO of being "scientifically and fiscally irresponsible," even though their own officials had stated there was no reason to wait for publication. (14)** The GAO report stated, "Safety concerns have been cited regarding the use of novel adjuvant formulations in vaccines, including squalene, and the associated adverse reactions. It has also been suggested that the safety of vaccines containing these formulations must be evaluated in conservative ways." (GAO/NSIAD-99-5 Page 3)

- **May 13, 1999** **Congressman Metcalf wrote Secretary of Defense William Cohen challenging DOD's refusal to carry out the GAO recommendations, and encouraging DOD to get to the truth by doing the research necessary to validate or dispute the Tulane test results.** (Appendix 4)

- **May. 24, 1999** **Dr. Carl Alving called Dr. Robert Garry of Tulane, and indicated his "purely scientific" interest in Dr. Garry's work** Dr. Alving also asked to review a draft of the manuscript on anti-squalene antibodies which was subsequently published. Dr. Garry agreed to fax him a copy of the ***in progress*** work for his personal review, requesting that he not circulate the copy. **Dr. Garry was not made aware of Dr. Alving's intent to circulate the paper and publicly subject it to scathing reviews as published on the DOD website prior to publication.** (Appendix 5)

- **May** 25, 1999 **Dr. Russell Wilson of Autoimmune Technologies, Tulane's exclusive licensee for the anti-squalene antibodies technology, sent a letter to Dr. Carl Alving sharing information, and offering to provide information regarding the ASA (anti-squalene antibody) assay and research with DOD.** (Appendix 6)

- **May 28, 1999** **Dr. Sue Bailey, Assistant Secretary of Defense for Health Affairs, provided GAO the DOD's final response to the March, 1999 report.** She stated, "Our position and the concerns expressed in our comments to the draft report have not changed The test methods proposed by the investigators at Tulane University need to be reviewed and validated by other scientists."***DOD would not take action until the peer-reviewed publication process was complete*** (Appendix 7)

- **Summer 1999** **An anonymously written DOD** memo was obtained by **the defense team representing five young Marines at Twenty-Nine Palms who were being court-martialed for their refusal of the anthrax vaccine.**
The six page document entitled, "Issues Relating to Antibodies to Squalene" was a scathing review by Dr. Carl Alving and Dr. Matyas of the unpublished work of Dr. Garry and his colleague Dr. Pamela **Asa**. It discussed the phone calls of May 24 and 25 between Dr. Alving and Drs. Garry and Wilson. With absolutely no proof, it accused Drs. Garry and Asa of an apparent anti-military agenda. It **concluded by stating "There is an obvious need for independent in-house research by the Army to examine the issues and implications, if any, of antibodies to squalene." Attached was a chart detailing a three year study, with a total cost of $1,260,834.00**. (Appendix 8)

- **July** 23, 1999 **Dr. Bailey responded to Metcalf's May 13, 1999 letter to Secretary Cohen.** Once again she commented, " The Department's position and concerns have not changed from those published as Appendix VI of the GAO report" (Appendix 9)

- **September 27, 1999** **Metcalf letter to Secretary Cohen.** Metcalf replied, " because of your department's years of research in this area, I ask that you reconsider and proceed with the GAO recommendations. Your current position of waiting for the completion of the peer review and publication process does not recognize the vast amount of research that the DOD has already accomplished regarding adjuvant formulations containing squalene. **The men and women who served honorably and are suffering from Gulf War illnesses deserve truthful answers and *immediate action.*"**(Apdx. 10)

- **October 25, 1999** **Because of DOD's refusal to cooperate with GAO recommendations, Congressman Metcalf asked for congressional intervention.** With the help of Congressman George Nethercutt, the House Report to H.R. **2561**, the Fiscal Year 2000 Department of Defense Appropriations Bill, included language instructing DOD to develop and/or validate the assay to test for the presence of squalene antibodies. This legislative action was signed into law by the President on October 25. (Appendix 11)

- **November 5, 1999** **Metcalf received a reply to his September 27 letter from Secretary Cohen.** While stating: "The Department's position has been consistent and remains unchanged," he went on to inform Congressman Metcalf that **a DOD investigator** has been funded to "pursue a study to determine the feasibility of developing a test for antibodies to squalene." (Appendix 12)
*Although Secretary Cohen did not **identify** the DOD **investigator**, GAO discovered **that** DOD had awarded the **study** to Dr. Carl Alving. The project was not designed to **replicate** or dispute **the Tulane findings** as had been recommended by GAO, but to develop a **different** means **of testing for** antibodies to squalene. (Appendix 13)*

- January 2000 **DOD provided some members of Congress a report titled, "Development and Validation of an Assay to test for the Presence of Squalene Antibodies."** It stated, "This Report has been prepared in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill." It acknowledged that DOD had funded a DOD researcher to "determine the feasibility of developing a test for antibodies to squalene." It **did not suggest a collaborative effort with Dr. Garry and his colleagues at Tulane to save valuable time for those who are suffering from Gulf War Illnesses, even though the researchers at Tulane had expressed their willingness to assist.** (Appendix 14)

- **January 31, 2000 Congressman Metcalf was joined by nine colleagues requesting DOD** do **an objective analysis** of "Antibodies to Squalene in Gulf War Syndrome" - the peer-reviewed article published in the February 2000 issue of *Experimental and Molecular Pathology* by Drs. Asa, Cao and Garry. **The question from Congress was clear, "Given the published article, it seems prudent to use the assay if it could help sick Gulf War era veterans.** Do you **agree?"** (Appendix 15)

- **February 25, 2000 Congressman Metcalf sent a strong letter to Secretary Cohen asking for immediate action to remove misleading information from the DOD's official Anthrax Vaccination Inoculation Program (AVIP) website regarding the peer-reviewed, published article on squalene antibodies.** Earlier in the week, the information had been discovered, prior to receipt of the DOD's official reply to the January 3 1 letter. (Appendix 16)

- **February 28, 2000 The official DOD response to the January 31 letter was delivered to Congressman Metcalf's office.** ***Most*** **of** ***the information provided*** *was based on a review of the early* ***draft,*** not the published study which included significant changes. The half-page critical analysis of the peer-reviewed article was anonymously written, with no indication of the author's professional credentials to conduct and provide the review. DOD **did not address the congressional question regarding the potential use of the assay to help sick Gulf War era veterans.** (Appendix 17)

- **March 3, 2000 Congressman Metcalf challenged Secretary Cohen to halt the obfuscation campaign that DOD was waging concerning the issues surrounding antibodies to squalene research. Metcalf provided ample evidence to demonstrate his conclusion..** (Appendix **18)**

- **March 27, 2000 On behalf of Secretary Cohen, Dr. Sue Bailey responded to Congressman Metcalf s February 25 and March 3 letters.** She acknowledged needed modifications on the DOD **AVIP website** to more objectively reflect the Tulane research. She also informed Metcalf that the Armed Forces

Epidemiological Board (AFEB) would convene a subcommittee of experts to review and critique the published article in response to Congressman Metcalf s March 3 letter. (Appendix 19)

June 2000 **An exchange of letters in Experimental and Molecular Pathology. Dr. Carl Alving and Dr. John Grabenstein submitted a critique of the Tulane research, and Drs. Asa, Cao and Garry co-authored the response.** The journal Editorial Note made the following statement: "New findings require confirmation within the bounds of comparability. This is as true for methodology as it is for the data produced from a particular study. This exchange of letters . ..relates to methodology **Drs. Alving and Grabenstein offer no data against the conclusions of Asa et al.** (Appendix 20)

August 10, 2000 Congressman Metcalf was presented the DOD 'objective analysis' of the article "Antibodies to Squalene in Gulf War Syndrome" by an Armed Forces Epidemiological Board subcommittee of experts. They concluded unanimously that the research reported in the paper does not support its claim that the laboratory test created by Dr. Garry at Tulane may identify persons ill with Gulf War Syndrome. **However, on the last page of the report, they state, " Whatever the paper's flaws and since the AFEB cannot exclude the remote possibility that the authors have identified a laboratory means of distinguishing persons with possible Gulf War Syndrome (GWS) from all others, reolicability becomes the major unresolved issue...Therefore we recommended that a suitable test of replicability be done in cooperation with the authors..."** They go on to state, **" . . . we are trying to . . . get quickly and inexpensively to a more meaningful bottom line: does the ASA assay clearly, reliably and unequivocally distinguish people with GWS from all others, and, if so, with what specificity and sensitivity?"** (Appendix 21)

Section Three
FDA Testing Reveals Squalene in Anthrax Vaccine

For over a year, the DOD has been contracting with SRI International to test for squalene in vials of the anthrax vaccine preparations which have been and are being given to military personnel, For some time, DOD documents have made two claims regarding squalene:
I) The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant; and
2) they have found NO squalene in their testing of anthrax vaccine lots. *(Appendix 13 and* 22)
Documents on the DOD AVIP website from SIR International confirm their tests revealed no squalene in the anthrax vaccine sent to them for analysis. (Example: Appendix 23)

- **January 31, 2000** **Congressman Metcalf wrote the FDA asking them to confirm the following DOD statement made to Congress. "The FDA verified that none of the vaccines used during the Gulf War contained Squalene as an adjuvant."** (Appendix 24)

- **March 20, 2000** **The FDA responded to Congressman Metcalf and provided their official position.** "In fact FDA did verify to the Senate Special Investigations Unit on July 23, 1997, in a telephone conversation with Committee staff of the SIU, not with DOD, **that neither the licensed vaccines known to he used in the Gulf War, nor the one investigational product known to have been used,** contained squalene as an adjuvant in the formulations on file with FDA."

Most importantly, the FDA closed their letter with the following statement: "Very limited testing of Anthrax Vaccine, Adsorbed, conducted by CDER in 1999 determined that there were only trace amounts of squalene in the lots tested ... (Appendix 25)

- **Dr. Dorothy Lewis of Baylor College of Medicine sent a letter to Congressman Metcalf explaining that the test used by FDA which found low levels of squalene in Anthrax vaccine samples is a "much more sensitive technique" than the one used by DOD.** ***(Why would DOD use a less sensitive test procedure?)***

  Dr. Lewis determined, ***"The real issue is whether squalene in parts per billion was added to the vaccine preparations given to the military, as well as whether this concentration of squalene could alter the immune response "***

  While acknowledging the need for research to respond to the findings, she stated, "it is possible that very small amounts of a biologically active product could induce an immune response, either to the molecule itself or it could boost immune responses to other agents in the mixture " (Appendix 26)

CONCLUSION

1. Despite numerous denials by the Department of Defense, FDA has found squalene in the Anthrax Vaccine in limited testing. This vaccine is still being forced upon our active military duty personnel. Immediate action must be taken to halt the current AVIP (Anthrax Vaccination Immunization Program) until this matter is resolved. Aggressive research must be undertaken to determine the source of the squalene, if it could alter the immune response, and the potential health consequences to those who have been vaccinated, both during the Gulf War, and as a result of the mandatory, force-wide AVIP.

2. The recommendation of the Armed Forces Epidemiological Board subcommittee that, "...a suitable test of replicability be done in cooperation with the authors..." mirrors the findings of the GAO over eighteen months ago— "DOD should conduct research designed to replicate or dispute the independent research results that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans."

3. Congress should take immediate action to review the findings of the GAO and the Armed Services Epidemiological Board, and provide independent oversight for the immediate implementation of their recommendations. The Department of Defense has wasted years in their determined effort to stonewall this issue. The researchers at Tulane are willing to work with DOD to pursue answers for those suffering from Gulf War Illnesses. Within a few months, and for a small investment of money, important knowledge will be acquired that may offer real hope. For the men and women who honorably serve this nation, there is no valid reason for further delay.

All foomotes are references to General Accounting Office (GAO) background working documents for GAO final report "Gulf War Illness: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved, (GAO-NSIAD-99-5)March 1999.

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14. DI-13

Bolding and italics added for emphasis.

Appendices can be requested from the office of:

Congressman Jack Metcalf
1510 Longworth House Office Building.
Washington, D.C. 20515

Phone: 202.225.2605

JACK METCALF
2ND DISTRICT, WASHINGTON
COMMITTEE ON
TRANSPORTATION
AND INFRASTRUCTURE

Congress of the United States
House of Representatives
Washington, DC 20515–4702

[illegible] ON BANK...
AND FINANCIAL SERVICE;

CHAIR, REPUBLICAN HOUSING
OPPORTUNITY CAUCUS

August 29, 1997

Mr. James F. Hinchman
Acting Comptroller General
U.S. General Accounting Office
441 G. Street NW
Washington DC 20548

Dear Mr. Hinchman:

My office has been contacted by several veterans and other constituents concerned about recent reports that the presence of antibodies for synthetic squalene has been discovered in blood samples of some Gulf War veterans.

I would like to request that you do a preliminary investigation into these reports. It is important that Members of Congress be fully informed of the facts surrounding this issue. If I can be of further assistance, please feel free to c&tact either myself. or Norma Smith in my Everett office.

Thank you for your attention to this matter.

Sincerely,

Jack Metcalf

WASHINGTON OFFICE:
1510 LONGWORTH HOB
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2930 WETMORE AVENUE, #901
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GAO

United States
General Accounting Office
Washington, D.C. 20548

National Security and
International Affairs Division

November 14, 1997

The Honorable Jack Metcalf
House of Representatives

Dear Representative Metcalf:

This letter confirms our intent to provide you with information pursuant to your August 19, 1997 request that we conduct a preliminary investigation in reports that antibodies for synthetic squalene have been discovered in blood samples of some Gulf War veterans. Norma Smith of your Everett, Washington office provided us with background regarding your request in conversations on August 29 and September 9, 1997.

Due to the complexity of issues addressed in you August 29 letter, we need to proceed with a separate design phase to examine what preliminary evidence exists for these allegations. The objectives of the study will address the following issues:

- Has DOD ever performed or sponsored any research on synthetic or natural squalene or squalane;
- was synthetic squalene used as an adjuvant in any developmental drugs and/or vaccines;
- are there any pharmaceutical firms involved in the development and production of drugs using squalene in any form;
- what tests have been done regarding its safety, efficacy and effectiveness;
- have our troops or DOD civilian personnel ever been given squalene in any form. If yes, for what purpose and under what circumstances?

The design phase will be completed by January 15, 1998. We will remain in contact with your staff, and by the end of January, we will provide you with a projected completion date for the total study. If you have any questions regarding this work, please contact me at (202) 512-3092, or my Assistant Director, Sushil Shanna, at (202) 612-3460.

Sincerely yours,

Kwai-Cheung Chan
Director
Special Studies and Evaluation

Experimental and Molecular Pathology 68, 55–64 (2000)
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Antibodies to Squalene in Gulf War Syndrome

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Received September 23, 1999

Gulf War Syndrome (GWS) is a multisystemic illness afflicting many Gulf War-era veterans. The molecular pathological basis for GWS has not been established. We sought to determine whether the presence of antibodies to squalene correlates with the presence of signs and symptoms of GWS. Participants in this blinded cohort study were individuals immunized for service in Desert Shield/Desert Storm during 1990–1991. They included 144 Gulf War-era veterans or military employees (58 in the blinded study), 48 blood donors, 40 systemic lupus erythematosus patients, 34 silicone breast implant recipients, and 30 chronic fatigue syndrome patients. Serum antibodies to squalene were measured. In our small cohort, the substantial majority (95%) of overtly ill deployed GWS patients had antibodies to squalene. All (100%) GWS patients immunized for service in Desert Shield/Desert Storm who did not deploy, but had the same signs and symptoms as those who did deploy, had antibodies to squalene. In contrast, none (0%) of the deployed Persian Gulf veterans not showing signs and symptoms of GWS have antibodies to squalene. Neither patients with idiopathic autoimmune disease nor healthy controls had detectable serum antibodies to squalene. The majority of symptomatic GWS patients had serum antibodies to squalene. © 2000 Academic Press

INTRODUCTION

The illnesses afflicting men and women who served in the military conflict in the Persian Gulf during 1990–1991 remain ill-defined. A constellation of symptoms including fatigue, rashes, headaches, arthralgias, myalgias, lymphadenopathy, diarrhea, memory loss, autoimmune thyroid disease, increased allergies and sensitivities to environmental elements, and neurological abnormalities collectively referred to as Gulf War Syndrome (GWS) have been described in veterans from this conflict (Persian Gulf Veterans Coordinating Board, 1995; Grady *et al.*, 1998; Fukuda *et al.*, 1998; Unwin *et al.*, 1999; Coker *et al.*, 1999). A symptom-based case definition of GWS has recently been described (Fukuda *et al.*, 1998). While GWS patients in general do not suffer from classic rheumatic diseases, the signs and symptoms are reminiscent of entities, such as arthralgias, fibromyalgia, lymphadenopathy, autoimmune thyroid disease, chronic fatigue syndrome, malar rashes, and musculoskeletal signs and symptoms associated with various autoimmune conditions and exposure to silicone, an organic material developed, in part, to be used as an immunological adjuvant for vaccines (Ismail *et al.*, 1999; Straus, 1999; Hyams *et al.*, 1996). Many, if not most, of these signs and symptoms are caused, promoted, or modulated by cytokines (Dinarello, 1988; Akiro *et al.*, 1990), further details of which are beyond the scope of this paper. Serological abnormalities including hypergammaglobulinemia and abnormal serum proteins have been reported in 45% of GWS patients (Grady *et al.*, 1998). A variety of possible explanations for GWS have been proposed. The Persian Gulf Veterans Coordinating Board addressed the issues of possible chemical and biological

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0014-4800/00 $35.00

weapons to account for these illnesses (Persian Gulf Veterans Coordinating Board. 1995). Haley *et al.* (1997) grouped various reported symptoms into six different syndromes based upon self-reported possible exposure to chemicals in the Persian Golf. It has been suggested that a combination of chemical and biological weapons exposure may account for GWS illnesses. Abou-Donia *et al.* (1996) examined the acute effects of pyridostigmine bromide and organophosphate exposure in chickens and suggested that the toxicity observed may be similar to that suffered by Gulf War veterans. Another explanation for GWS is that it is posttraumatic stress syndrome (Hyams *et al.*, 1996).

It has also been suggested that GWS may be due to exposure to biological weapons, dysregulation of the immune system (Rook *et al.*, 1998), or imbalance in *t/c* TH1/TH2 ratio, either as an adverse reaction to the intense vaccination schedule or as a result of exposure to biological agents in the Persian Gulf (Rook *et al.*, 1998).

Gulf War veterans and attendant civilian personnel received a variety of immunizations in preparation for possible deployment to the Persian Gulf theater. A similar intensive vaccination regimen was also used in British troops (David *et al.*, 1997). Epidemiological studies indicate that multiple vaccinations or vaccination against biological warfare agents are the factors with the highest correlation with GWS symptomatology (Unwin *et al.*, 1999).

We have identified a group of GWS patients who served in American and British military forces or worked as civilian employees to the U.S. military or their contractors during Desert Shield/Desert Storm in the Persian Gulf, 1990–1991. These patients served in all branches of the military and received the required immunizations. They served throughout the Persian Gulf, including 0" ships of the U.S. Navy nor in combat or exposed to environmental toxins at ground level. We have found antibodies to squalene, a" experimental immunological adjuvant, in a high percentage of these GWS cases.

MATERIALS AND METHODS

Patients were admitted to the study based upon service in the United States or the United Kingdom military or as civilian employees of the U.S. military or their contractors in the Persian Gulf during 1990–1991. Patients became aware of the study via the Internet and word of mouth with other veterans and were enrolled consecutively on a voluntary basis. No fees were paid by the subjects or to the subjects who participated in this study. Included were individuals who fit the recently proposed case definition for GWS (Fukuda *et al.*, 1998) and others without GWS symptoms. Service occurred in Desert Shield/Desert Storm, Operation Provide Comfort (in northern Iraq after there were no chemical weapons), CENTCOM in Saudi Arabia, Kuwait, Camp 4 (front lines), and medical units in various locations in Saudi Arabia. Some were in theater for months. Others were evacuated due to illness after as little as 48 h after arrival and before the war commenced. We tested deployed personnel who served in various parts of theater during the war, but were and are not sick. We tested patients referred to as nondeployed veterans, those immunized for duty in the Persian Gulf, but who did not leave the United States or were deployed elsewhere. None participated in NIH experimental vaccination trials, although our positive control subjects had participated in such trials and were known to have received squalene-containing adjuvant injections. Further controls had idiopathic autoimmune disease or silicone breast implants or were healthy subjects with no stigmata of autoimmune disease.

Patient records and histories were obtained from the Gulf War-era participants. Board-certified rheumatologists, neurologists, and endocrinologists made all diagnoses. Compilation of data, including commercial lab results, was done by chart review by one investigator (P.B.A.) and was reviewed by board-certified rheumatologists.[2] Serum samples from study participants were collected by laboratory personnel via standard phlebotomy procedures using vacutainer tubes and butterfly needles and were stored at −20°C until they were shipped to Tulane University School of Medicine in New Orleans. Samples from Gulf War-era veterans were blinded. The identities or exact number of samples from each category was not made available to the Tulane laboratory until after completion of the diagnostic testing. All samples were tested twice under the same conditions. Results from all samples in both tests were consistent. At the end of the study, patient data were matched with the outcome of the anti-squalene antibody (ASA) assay and results were tabulated.

Anti-squalene Antibody Assay

The ASA assay measures the binding of serum immunoglobulin (IgG) to squalene immobilized on nitrocellulose. It is similar in format to the antipolymer antibody (APA) assay

[2]Dr. D. Kevin Asa, M.D., Memphis, Tennessee. Dr. Michelle Fern, Johns Hopkins University, Baltimore, Maryland.

for partially polymerized acrylamide (Tenenbaum *et al.*, 1997). Seropositivity on the #A assay has been shown to correlate with severe musculoskeletal signs and symptoms present in a subset of silicone breast implant recipients (Tenenbaum *et al.*, 1997). For the blinded study, squalene (>99% purity) was diluted 10-, 100-, 1000-, and 10,000-fold in distilled water, applied to nitrocellulose membranes, and allowed to air-dry. The nitrocellulose membranes were then cut into 4-mm-wide strips, placed in 20-well trays, and rinsed in wash buffer (Tris-buffered saline containing 0.3% polyoxyethylene sorbitan monolaurate and 0.005% thimerosal, pH 7.4). The strips were incubated in 2 ml blocking buffer (Tris-buffered saline containing 5% powdered instant milk, 4% goat serum, and 0.006% thimerosal, pH 7.4) for 45 min prior to the addition of 5 μl of patient sera (1:400 dilution) followed by a further 90-min incubation. This dilution factor was chosen based upon the very strong antibody responses found in GWS patients. All incubations and washes were carried out at room temperature on a rocking platform. The blocking buffer was then removed and the strips were washed with washing buffer (three times for 5 min each). After the strips were washed, 2 ml of blocking buffer containing biotin conjugated to goat anti-human IgG (Kirkegaard & Perry Laboratories, Gaithersburg, MD), diluted 1:1000, was added. After a 60-min incubation, the strips were again washed as above, and 2 μl of blocking buffer containing avidin-conjugated horseradish peroxidase (Jackson ImmunoResearch, West Grove, PA), diluted 1:500, was added. Following another 60-min incubation, the strips were washed, as above, and 2 ml of detection-buffered saline containing 30% methanol, 0.6 mg/ml 4-chloro-1-napthol, 0.03% hydrogen peroxide; pH 7.4) was added. The reaction was allowed to proceed for 15 min and was stopped by rinsing the strips in distilled water. The strips were allowed to air-dry for visual scoring on a scale of 0 to +4.

Statistical Analysis

The strength of binary relationships was tested using χ^2 tests of independence. This protocol was a feasibility study. Accordingly, no power studies were performed.

RESULTS

Primary Studies

To ascertain that our assay could detect antibodies to squalene, we had positive controls who were two subjects who had volunteered to participate in a vaccine trial at the NIH involving the use of a squalene-containing adjuvant (Table 1). Subsequent to vaccination, they developed a multisystem disorder similar to that of Persian Gulf veterans. Their symptoms are listed in Table 2.

TABLE 1
Squalene Reactivity of NIH Vaccine Trial Participants

Patient	Doses of squalene	
A	1	
B		

Patient A received a single injection and became ill within 3 weeks, with signs and symptoms including arthritis, fibromyalgia, lymphadenopathy, photosensitive rashes, fatigue, headaches, and fasciculations. This patient had lower than normal acetylcholinesterase and histological evidence of IgG-mediated demyelinization. The NIH vaccine study code was broken; only adjuvant containing squalene had been administered as a placebo. This patient was weakly positive for ASA. Patient B went through the complete experimental vaccination protocol before manifesting a similar set of signs and symptoms and was +3 for ASA.

Fukuda and co-workers (1998) have reported that individuals deployed to the Persian Gulf who became sick have a chronic multisystem disease. The cohort of GWS patients in our study have many signs and symptoms of autoimmune connective tissue and neurological disease with arthritis (94%), fibromyalgia (94%), lymphadenopathy (94%), rashes (94%), weakness (86%), fatigue (81%), chronic headaches (78%), and memory loss (72%) as the most frequent symptoms (Table 3).

It should be noted, however, that most patients did not have

TABLE 2
Symptoms Which Appeared after a Single Adjuvant Injection

Arthritis
Fibromyalgia
Lymphadenopathy
Rashes
Photosensitive rashes
Malar rashes
Chronic fatigue
Chronic headaches
Fasciculations
Lymphocytic infiltrates around vascular tissue
IgG-mediated demyelinization
Lower than normal levels of acetylcholinesterase

TABLE 3

Symptoms and Diagnostic Lab in GWS Patient Groups

	D-S (%)	D-W (%)	ND-S (%)	UK-D (%)
Arthritis	94	8	100	100
Fibromyalgia	94	8	100	100
Lymphadenopathy	94	0	100	100
Rashes	94	0	100	100
Photosensitive rashes	25	0	75	100
Malar rashes	17	0	63	100
Chronic fatigue	81	33	100	100
Chronic headaches	76	0	100	100
Abnormal body hair loss	19	0	38	33
Nonhealing skin lesions	42	0	63	66
Aphthous ulcers	36	0	63	66
Dizziness	47	8	100	66
Weakness	86	17	100	66
Memory loss	72	25	100	66
Seizures	14	0	50	66
Mood changes	72	0	63	100
Neuropsychiatric problems	44	0	88	66
+FANA	20	0	50	Unknown
Anti-dsDNA	14	0	Unknown	Unknown
Low C3 and C4	14	0	Unknown	Unknown
Anti-thyroid	14	0	Unknown	Unknown
Anemia	14	0	50	Unknown
Elevated ESR &/or CRP	25	0	75	Unknown
SLE	17	0	50	Unknown
MS	3	0	Unknown	Unknown
ALS	8	0	0	0
Raynaud's phenomenon	42	0	75	66
Sjogren's syndrome	8	0	Unknown	33
Chronic diarrhea	36	0	63	66
Night sweats	36	0	88	66
Low grade fevers	39	0	88	66

Note. D-S, deployed, sick ($N = 38$); D-W, deployed, well ($N = 12$); ND-S, nondeployed, sick ($N = 8$); UK-D, deployed, sick, UK ($N = 3$).

an optimal workup for connective tissue and neurological autoimmune diseases because of the limited resources in the Veterans' Administration hospitals or military hospitals. Nevertheless, all patients reported here meet the case definition recently established (Fukuda *et al.*, 1998). In agreement with a prior study (Grady *et al.*, 1998), some of these GWS patients also had abnormal laboratory values, including positive antinuclear antibodies (ANA;17%), anti-dsDNA (14%), low C3 and C4 (14%), anemia (14%), anti-thyroid microsomal antibodies (14%), and elevated ESR and/or CRP (22%). A minority of symptomatic patients met diagnostic criteria for classical autoimmune diseases, including Sjogren's syndrome (8%), multiple sclerosis (3%), ALS (8%), and systemic lupus erythematosus (17%).

Likewise, military personnel from the United Kingdom have shown the same array of signs and symptoms as those from the United States. Their signs and symptoms included arthritis (100%), fibromyalgia (100%), lymphadenopathy (100%), rashes (100%), chronic fatigue (100%), chronic headaches (100%), and memory loss (66%). Laboratory data are not unavailable for this group. They also had malar rashes, Raynaud phenomenon, and sicca syndromes. Thus, our cohort represents a subset of veterans that displays manifestations of GWS. The severity of symptoms in our cohort can be explained by a self-selection bias in that the patients volunteered for our study.

Persons activated to deploy who were vaccinated, but did not deploy for a variety of reasons, had an array of signs and symptoms with even higher frequencies of arthritis (100%), fibromyalgia (100%), lymphadenopathy (100%), rashes (100%), weakness (100%), fatigue (100%), chronic headaches (100%), and memory loss (100%) (Table 3). The nondeployed individuals had higher rates of dizziness (100%), seizures (50%), and neuropsychiatric abnormalities (88%). The number in this group was small, and these differences were not statistically significant. Laboratory values for the nondeployed individuals with GWS were abnormal with positive ANA (50%), anemia (50%), and elevated ESR and/or CRP (75%).

In contrast, abnormal signs, symptoms, and laboratory values were rare in the cohort of Gulf War-era veterans who considered themselves well and upon examination did not have debilitating health problems. They reported some signs and symptoms, but their illnesses were not multisystemic (Table 3). The signs and symptoms reported included fibromyalgia (8%), chronic fatigue (33%), weakness (17%), memory loss (25%), and thyroid disease (8%). None reported positive laboratory values for autoimmune processes or were so diagnosed.

Musculoskeletal signs and symptoms are more common in females than males, and autoimmune diseases are predominantly found in females in ratios ranging from 8:1 to 14:1 (Michet *et al.*, 1985; Geirsson *et al.*, 1994). We wished to determine why predominantly male military personnel, both deployed and nondeployed, initially found fit for duty during the war, would develop signs and symptoms common to autoimmune diseases. Many studies have shown that adjuvants used to enhance vaccine efficacy can induce autoimmune disease (Zamnia, 1983; Lorentzen *et al.*, 1995; Hadzhidov *et al.*, 1986; Kleinau *et al.*, 1995). Thus, we sought whether GWS patients who received immunizations had antibodies to an immunological adjuvant. Squalene was chosen as it has been used in many experimental vaccine adjuvant formulations since 1987. A variation of a previously

described assay, one which measures the binding of serum antibodies to low-molecular-weight polymers (Tenenbaum *et al.*, 1997), was used in the current study. This immunological assay, similar in format to Western immunoblotting, quantitates the biding of antibodies to squalene immobilized on nitrocellulose (fig 1). Serum samples were tested blindly. We found that GWS patients who deployed had ASA responses ranging in intensity from +1 to +4. Most of the sick Gulf War veterans had +2 and +3 reactivity to squalene at a serum dilution of 1:400. One individual had an especially strong reaction rated as +4. A high majority (95%) of symptomatic deployed individuals with GWS were positive on the ASA assay (Fig. 2A).

Interestingly, all sick veterans who did not deploy but had received immunizations as preparation for deployment also had antibody reactivity to squalene. In contrast, none of the persons deployed to the Gulf who thought of themselves as well were ASA positive.

Other Studies

Squalene is an organic polymer, with some antigenic epitopes which might be shared with other organic polymers, acting as immunostimulants. Antibodies to silicone and partially polymerized acrylamide (the antigen in the antipolymer assay) were weakly positive in fewer than 10% of the symptomatic Gulf War-era veterans. Four patients with musculoskeletal signs and symptoms and exposure to silicone breast devices were tested to see if antibodies to squalene were present; none were reactive (see below). To determine if antibodies to squalene occurred in idiopathic autoimmune diseases, samples were taken from patients who had defined autoimmune diseases, both rheumatic and neurologic, but none were reactive. To determine if healthy individuals from the general public might have antibodies to squalene we tested members of the general public. Again, none showed antibody reactivity (Table 4).

In a broader unblinded antibody-screening study, antibodies to squalene were studied in larger groups of individuals (Fig. 2B). Blood samples of Gulf War veterans from different medical centers were tested for ASA. This group contained a high percentage of ASA-positive individuals (69%). The samples included were not segregated according to their clinical status and included healthy controls. Squalene is in some cosmetic products, so we tested to determine if antibodies were present in the general population. Samples of blood from blood banks indicated only 5% antibody reactivity to squalene and the reactions were much less intense (Fig. 1). To determine if antibody to squalene was a marker for autoimmune disease processes, tests were conducted on blood samples from patients with systemic lupus erythematosus. This group had 10% ASA weakly positive reactivity (Fig. 2B). Patients suffering from chronic fatigue syndrome have some of the signs and symptoms of GWS patients, but showed only 15% weak reactivity. Prior studies have shown that most individuals exposed to silicone breast devices with

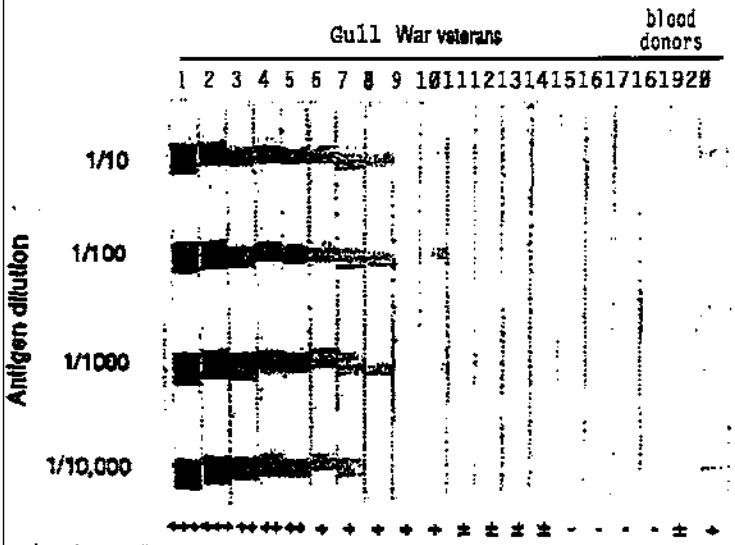

FIG. 1. Antisqualene antibody responses in representative Gulf War Syndrome patients and blood donors.

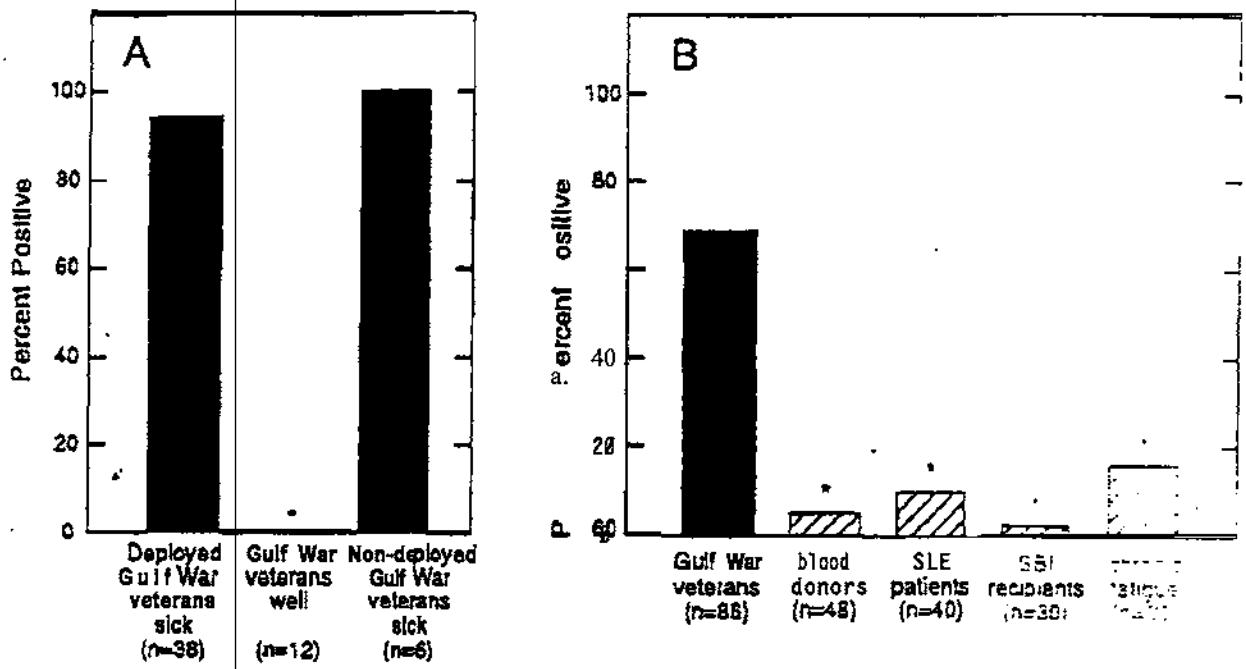

FIG. 2. Antisqualene antibody responses in Gulf War Syndrome patients, blood donors, systemic lupus erythematosus (SLE) patients, chronic fatigue syndrome patients, and symptomatic silicone breast implant (SBI) recipients. (A) Blinded samples. *, $P < 0.001$ compared to percentage positive in well Gulf War veterans by χ^2 test. (B) Unblinded samples. *, $P < 0.001$ compared to percentage positive in Gulf War Syndrome patients.

severe musculoskeletal signs and symptoms have serum antibodies reactive to a synthetic polymer (polyacrylamide) (Tenenbaum *et al.*, 1997). Both silicone and acrylamide, like squalene, are potent immunological adjuvants (Naim *et al.*, 1997; Nicholson *et al.*, 1996; Yoshida *et al.*, 1994; Sergon *et al.*, 1986). Therefore, we tested for cross-reactive antibodies to squalene in serum from patients exposed to SBL Only 10% of this group were weakly positive for antibodies to squalene (Fig. 2B), confirming the results with the smaller sample in the blinded portion of the study.

TABLE 4

Squalene Antibodies—Blinded Study Patient Groups

Patient group	ASA reactivity (%)
D-S	95
D-W	0
ND-S	100
UK-D	100
Breast implants	0
NIH vaccine participants	100
Idiopathic autoimmune disease	0
Healthy general public	0

Note. D-S, deployed, sick ($N = 38$); D-W, deployed, well ($N = 12$); ND-S, nondeployed, sick ($N = 8$); UK-D, UK deployed, sick ($N = 3$); NIH vaccine trial patients ($N = 2$).

DISCUSSION

The illnesses afflicting military veterans and civilians who served in the Persian Gulf in 1990–1991 have remained clouded in confusion and controversy. Several recent studies have indicated that the Gulf War-era patients are suffering from a chronic multisystemic illness, but with a continuum of signs and symptoms not within the definitions of "classic" rheumatic diseases or other specific disorders (Fukuda *et al.*, 1998; Ismail *et al.*, 1999; Straus, 1999). In some, onset of illness occurred within a few weeks after receiving immunizations. This includes personnel never deployed due to illness. It also included some who did deploy, but were in theater for as little as 48 h before being sent home before the war began because of severe joint and muscle pain and neurological problems. Other Gulf War veterans became ill

years after the war, but showed illnesses similar to those who became ill soon after vaccination. The variability of expression of symptoms and severity may be due to individual immune responses genetically regulated by the histocompatibility complex (Lorentzen *et al.*, 1995; Madzhidov *et al.*, 1986).

Our results suggest that ASA reactivity is a marker for the signs and symptoms of GWS. Finding serum antibodies to squalene in Gulf War patients is unexpected, and the basis for the presense of these antibodies remains unclear. ASA are not a general marker for autoimmune disease due to their absence in idiopathic autoimmune patients and rarity in patients with other, presumed environmentally induced, autoimmune diseases. The signs and symptoms of our Gulf War patients are similar to those of a subset of female patients following exposure to silicone. Some individuals with silicone exposure suffer from many of the multisystem symptoms, viz, arthralgias, myalgias, lymphadenopathy, and neurological disorders prevalent in GWS patients in the current study (Bridges *et al.*, 1993; Brautbar *et al.*, 1995; Wolford, 1997). Symptomatic silicone breast implant recipients also have high levels of antibodies to synthetic polymers (Teneubaum *et al.*, 1997) and to silicone,[3] but did not have high prevalence of ASA.

It has been suggested that abnormal immune responses may be involved in GWS (Rook *et al.*, 1997). Immunological adjuvants have the generally desirable property of eliciting cell-mediated immunity and antibodies when administered with an antigen. They may also cause a more generalized and indiscriminate stimulation of the immune system and disrupt the balance of immune self-regulatory mechanisms, which may lead to autoimmune disease (Zamma, 1983; Lorentzen *et al.*, 1995; Madzhidov *et al.*, 1986; Kleinau *et al.*, 1995). Squalene has been used extensively as an adjuvant in animal models to induce autoimmune diseases (Lorentzen, 1999; Beck *et al.*, 1976; Kohashi *et al.*, 1977; Garren *et al.*, 1985; Whitehouse *et al.*, 1974; Yoshino *et al.*, 1994). Cytokines are mediators of immunological regulation and inflammatory responses (Van der Meide *et al.*, 1996), and increased cytokine levels are associated with the development of autoimmune disease in established rodent models of autoimmunity (Fitzpatrick *et al.*, 1996). Squalene has been shown to induce increased levels of interleukin-5 (IL-5), IL-6, and interferon-γ (Valensi *et al.*, 1994). Several different adjuvants have been demonstrated to produce or exacerbate autoimmune diseases in experimental models. Adjuvant-induced arthritis is a well-characterized autoimmune disease induced in rats and other species (Zamma, 1983; Lorentzen *et al.*, 1995; Madzhidov *et al.*, 1986; Kleinau *et al.*, 1995). The disease process in adjuvant-induced arthritis is complex, affecting multiple organ systems. For example, a cachetic syndrome (Rolfe *et al.*, 1996) and testicular dysfunction (Clemons *et al.*, 1998) have been associated with adjuvant-induced arthritis. Uveitis, a T-cell mediated intraocular inflammatory disease, can also be induced by adjuvants (Petty *et al.*, 1996). Neurological disease can be the result of immunological mechanisms including autoimmunity (Rogers *et al.*, 1996; Tebin *et al.*, 1995; Hemmer *et al.*, 1995; Wucherpfennig *et al.*, 1990; Cross *et al.*, 1991; Bansal *et al.*, 1994), and neurological symptoms are commonly seen in autoimmune diseases (McNicholl *et al.*, 1994; Zapone *et al.*, 1993; Moll *et al.*, 1993).

All pharmacology is controlled toxicology. Although not approved by the Food and Drug Administration for human use, squalene has been used as an adjuvant in experimental vaccines against a variety of pathogens, including *Bacillus anthracis* (Ivins *et al.*, 1994), *Plasmodium falciparum* (Hoffman *et al.*, 1994), and herpes simplex virus (Burke *et al.*, 1994). Effectiveness of adjuvants has been shown to parallel toxicity defined as the initiation of autoimmune disease processes (Zamma, 1983; Koga *et al.*, 1986). Adjuvants should not produce reactions at injection sites, be pyrogenic, or induce anterior uveitis, arthritis, or other protean autoimmune processes (Allison *et al.*, 1991). A study using squalene as an adjuvant in influenza vaccine reported moderate to severe local and systemic reactions in humans (Keitel *et al.*, 1993). The participants suffered induration, erythema, lymphadenopathy, fever, chills, nausea, and dizziness as symptoms which lasted for several days. Another squalene-containing adjuvant was used with gp120 in a human immunodeficiency virus vaccine, where it induced severe systemic and local reactions in 15 of 30 vaccinees (Keefer *et al.*, 1996). Similarly, in a study of simian immunodeficiency vaccine in macaques, squalene was used as an adjuvant and the animals developed anti-human-cell antibodies and autoimmune-like symptoms (Vaslin *et al.*, 1992). Future studies should determine whether or not ASA have a role in these pathological processes.

Squalene is a naturally occurring molecule absorbed from food and synthesized as a precursor for cholesterol, myelin, and hormones. This synthesis occurs within the hepatocytes and is further processed into cholesterol in the endoplasmic reticulum (Stamellos *et al.*, 1993). Fecal analysis indicates that about 60% of dietary squalene is absorbed (Grundberg *et al.*, 1990). Dietary squalene is absorbed through lymphatic vessels after being cyclized to sterols during transit through

[3]Cao, Yan *et al.*, unpublished observations.

the intestinal wall (Tilvis *et al.*, 1983). It is processed into chylomicrons by the epithelial cells of the small intestines. It becomes a lipid droplet covered by β-lipoprotein containing triglyceride and cholesterol ester. This increases serum levels of free and esterified methyl sterol contents. About 90% of absorbed squalene is in lipoproteins, appearing in chylomicrons and VLDL, suggesting that removal of dietary squalene may indicate metabolism of intestinal lipoproteins (Gylling *et al.*, 1994).

Squalene is a nonsteroid precursor of cholesterol. Reports have indicated that high titers of autoantibodies to cholesterol, once considered to be a poorly immunogenic molecule, could be generated by immunization with liposomes containing cholesterol and lipid A as adjuvant (Swartz *et al.*, 1988; Alving *et al.*, 1991; Dijkstra *et al.*, *1996).* Injection of either silicone *gel or silicone oil* intraperitoneally also resulted in high titers of autoantibodies to cholesterol (Alving *et al.*, 1996). The silicone component serves as an adjuvant as well as initiating the autoimmune process. The high titers were IgM with relatively low titers of IgG to cholesterol (Dijkstra *et al.*, 1996; Alving *et al.*, 1996). The specificity of these antibodies was to cholesterol and structurally similar sterols containing a 3β-hydroxyl group. Anticholesterol binding activity was significantly diminished if the 3β-hydroxyl domain was altered by oxidation, substitution, epimerization, or esterification (Dijkstra *et al.*, 1996). It has been reported that naturally occurring autoantibodies have been detected in humans (Alving *et al.*, 1989), but these were much lowa in tier than those produced with either lipid A or silicone.

Several facts argue against our assay detecting cross-reactive antibodies to cholesterol instead of antibodies specific for squalene. First, squalene is neither a sterol nor does ir have a 3β-hydroxyl group. I-he respective molecular structures, internal molecular bonding, charge distribution, and antigenic epitopes are different. Second, if high-titer autoantibodies to cholesterol that are cross-reactive with squalene are normal, We should see no difference between our various patient groups. The GWS patients and NIH positive control patients are very distinct in their strong IgG antibody reactivity to squalene. Third, if silicone alone can generate antibodies to cholesterol and these are cross-reactive to squalene, we should see high antibody reactivity to squalene in patients exposed to silicone in addition to the GWS and NIH patients. This did not occur.

In the course of these smdii. we examined two volunteers for a vaccine trial at the NIH involving squalene as adjuvant. They developed a multisystem disease similar to that seen in Persian Gulf veterans subsequent to their participation in the trial. One received a single injection and became ill within a few weeks with signs and symptoms including arthritis, fibromyalgia, lymphadenopathy, pruritic macular rashes, fatigue, headaches, and fasciculations. The individual had lower than normal acetylcholinesterase. Autoptical evidence of lymphocytic infiltrates around vascular tissue, and IgG-mediated demyelinization. After this NIH vaccine study code was broken, it was found that only adjuvant squalene had been administered as placebo. This patient was weakly positive for ASA. Another patient who went through the whole experimental protocol before manifesting a similar set of signs and symptoms was 3+ positive for ASA.

Multiple vaccinations and vaccination against biological warfare agents are the factors with the highest correlation with GWS symptomatology (Unwin *et al.*, 1994). It is important to note that our laboratory-based investigations do not establish that squalene was added as adjuvant to any vaccine used in military or other personnel who served in the Persian Gulf War era. Several investigators have speculated that GWS is the result of either exposure to chemicals, chemical weapons, or to biological agents encountered in the Persian Gulf (Persian Gulf Veterans Coordinating Board, 1995; Abou-Donia *et al.*, 1996; David *et al.*, 1997; Haley,1997). However, such exposure would likely have immediate effects and many Gulf War veterans were ill until months or years after the military conflict. Many of these GWS patients have improved on treatment regimens prescribed by their personal physicians, rheumatologists, and neurologists, namely the immunosuppressives used for classical rheumatological conditions.[4] These treatments have included steroids, methotrexate, hydroxychloroquine, and cytoxan. Such treatments would have no effect on subjects exposed to chemical weapons. If GWS was due to an exogenous infectious agent, the immunosuppressive regimens used would likely result in an exacerbation of the symptoms. This did not occur. The molecular pathology of GWS must be defined before its etiology can be assigned. We present here evidence of an immune factor based upon the adjuvancy of squalene. Further studies are required to define the role of ASA, if any, in the pathogenesis of GWS.

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[4]Asa, P.B. *et al.*, unpublished observations.

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protective. A second challenge of these animals, withoi additional antibiotic prophylaxis, found them to be susci e to anthrax exposure. The animals who had previously reci

6. (U) BW Vaccines, Botulinum Antitoxin and IND Drugs Theater.

a. COL Tomlinson reported on an outbreak of foodbor: botulinum in Cairo, Egypt, and that a quantity of the bo@ LM antitoxin from theater was shipped to Egypt. LTC McKee there were approximately 80 cases; with 15 of these resu in death. The outbreak was believed to be associated wi@ under cooked fish. He also reported individuals from CD, to Egypt to investigate the outbreak and took antitoxin i them. LTC McKee stated that in addition to the Army's a: CDC's antitoxin, antitoxin was also supplied by a Europe, manufacturer. Since several sources of antitoxin were u Ld some individuals may have received several doses of diff, antitoxin, evaluation of the efficacy of the Army produc be difficult at best.

b. It was reported that the individuals from logist USAMRIID, were expected back from theater today with the anthrax and botulinum vaccines, antitoxin, ribavirin and centoxin While in theater the items were under refrigeration: however, there was a report that the refrigerator failed to operate for a period of time and possibly these items were damaged. The items will be re I to USAMRIID and a determination made with regard to the disposition

7. (U) Documentation of Vaccine Usage in Theater.

2D DISTRICT, WASHINGTON

COMMITTEE ON TRANSPORTATION AND INFRASTRUCTURE
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CHAIR, REPUBLICAN HOUSING OPPORTUNITY CAUCUS

REPUBLICAN POLICY COMMITTEE

May 13. 1999

The Honorable William S. Cohen
Secretary of Defense
The Pentagon
Washington, DC 20301-1010

Reference: "Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolve& GAO, March 1999

Dear Secretary Cohen:

On March 29, 1999, the General Accounting Office released the report I had requested regarding squalene antibodies in veterans suffering from Gulf War Illnesses. As DOD prepares its response to the final report issued by the GAO, I am requesting answers to a number of questions that remain outstanding.

In the repon DOD commented, "There is no basis for believing that Gulf War-era veterans were exposed to squaknc-containing vaccines. The 'DOD has indicated that no experimental vaccines with squalenc containing adjuvants had been used in U.S. troops during the Gulf War." (Page 23)

Contrary to the above assertion, the GAO report did not implicate the Department of *Defense.* Rather, the report concluded it would be prudent for DOD to "review the independent research that researchers report has revealed the presence of squalene antibodies in the blood of ill gulf War-era veterans, and conduct its (DOD) own research. designed to replicate or dispute these results." (Pg 8.9)

1. DOD officials told the GAO, that DOD could develop an assay for detecting antibodies to squalene, and a sample testing could be done for a small investment, Will the DOD reassess their former position, and aggressively pursue this first step? Determining if the antibodies are present is vitally important. If they are present, then the process to ascertain the significance of that finding can begin,

2. If the DOD is concerned that it does not have the resources, or that it would require a lengthy period of time (over six months) to conduct an initial investigation, is there a reason why you cannot send a team of experts to Tulane University where the research has been done to validate or dispute its integrity?

3. In tight of the missing shot records of so many of our Gulf War-era veterans, is it possible to determine absolutely that they did not receive any vaccine formulations containing squalenc during or prior to the Gulf War? Is this conclusion based solely on the statement of the vaccine manufacturer?

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The DOD stated in its response, "The assay for anti-squalene antibodies developed by the independent researchers has not been validated through peer review or publication in the scientific literature Data obtained from a methodology that has not been validated have significant potential to harm or mislead Gulf War veterans through the medical misinformation the data may support." (Page 23)

The researchers at Tulane have made clear their willingness to work with DOD. Time is critical for thousands of sick Gulf War-era veterans who continue to suffer and have been waiting the last seven years for help. The truth cannot harm or mislead Gulf War veterans. You have the capability to validate or dispute the methodology.

However, not getting ta the bottom of this perplexing problem will no doubt continue to have serious ramifications. 1 am sure you are aware of the growing concern among active military members regarding the current anthrax vaccination program. Reports of serious adverse reactions are increasing. The oversight hearing of the Subcommittee on National Security, Veterans Affairs, and International Relations on April 29. 1999, revealed troubling testimony. Members of the Michigan Air National Guard are suffering significant health consequences following their anthrax vaccinations. During the hearing, the GAO raised a number of critical questions regarding the safety and efficacy of the anthrax vaccine. Combined with the squalene issue, these factors are escalating a climate of distrust. Inaction, while waiting for the lengthy peer review process, will only exacerbate this disturbing situation.

4. Confirmation exists that several active duty personnel recently inoculated have tested positive for antibodies to squalene. Several publications have alleged a potential connection between anthrax vaccinations and squalene. Therefore, is it not in the best interest of the United States active duty forces to immediately take action to determine the facts and potential health consequences?

This situation provides the DOD an extraordinary opportunity to demonstrate our nation's commitment to the honorable men and women who serve our country. Thank you for your assistance. I look forward to your personal reply.

Sincerely,

Jack Metcalf

Jack Metcalf

Tulane University Medical Center

SCHOOL OF MEDICINE
Department of Microbiology & Immunology SL36
1430 Tulane Avenue
New Orleans, Louisiana 70112-2699
(504) 587-2027 Fax: (504) 584-1994
E-mail: rgarry@tmcpop.tmc.tulane.edu

Robert F. Garry, Ph.D.
Professor

8/14/00

RE: Note to file regarding conversation with COL Carl R. Alving, M.D.

To whom it may concern:

On or about May 24. 1999 I received an unsolicited telephone call at my office from COL Carl R. Alving, M.D. Dr. Alving, whose work on lipids and adjuvants I was somewhat familiar with, indicated that he had a scientific interest in the work on squalene antibodies conducted by Drs. Pamela Asa and Yan Cao and myself.

Dr. Alving indicated that his interest in my studies was "purely scientific" and that he wished to get more information because of his interest in the general area of lipids, antibodies and adjuvants. This was plausible because of Dr. Alving's prior work in this general area. The conversion, which lasted from about 45 minutes, was almost entirely scientific and covered a broad range of topics related to anti-lipid antibodies.

During the course of our conversation, Dr. Alving shared some of his recent studies on anti-cholesterol antibody with me. At that time, I was only vaguely familiar with those studies. Dr. Alving offered the opinion that the anti-squalene antibodies might be a subclass of the anti-cholesterol antibodies. I replied that this might be worth looking into.

Dr. Alving also asked to review a draft of the manuscript on anti-squalene antibodies which was subsequently published in ***Experimental and Molecular Pathology.*** I agreed to fax him a copy of the in ***progress*** work for his personal review. Because the work had not yet been accepted for publication, I asked that he not circulate the copy.

At no time was I made aware that Dr. Alving's intent was to circulate our paper and subject it to the scathing reviews subsequently published on the DoD website prior to publication and in abbreviated form as a letter to the editor of ***Experimental and Molecular Pathology.***

Robert F. Garry

Robert F. Garry, Ph.D.
Professor

Autoimmune Technologies, LLC
144 Elks Place, Suite 1402
New Orleans, Louisiana 70112
Telephone: (504) 529-9944 Facsimile: (504) 568-0634
E-mail: rwilson@communique.net

May 25, 1999

Col. Carl Alving, M.D.
Department of Membrane Biochemistry
Walter Reed Army Institute of Research
Building 40, Room 1022
Washington, DC 20307-5100

Dear Dr. Alving:

It was a pleasure talking with you today. As we discussed, I am enclosing two reprints and a copy of a manuscript that deal with our work on anti-polymer antibodies. I would appreciate any comments or questions that you might have concerning our work.

In regards to the anti-squalene antibody assay, I mentioned to you that Tulane University Medical Center has filed for patent protection concerning the use of anti-squalene antibodies in evaluating Gulf War Syndrome. As Tulane's exclusive licensee for this technology, we would be happy to discuss information regarding the assay and our research with you. If you need additional information or have any questions, please contact me.

By the way, I wanted to mention to you that I have read many of your papers concerning liposomes and toxins. My dissertation project. many years ago, concerned the cloning of exotoxin A from *Ps. aeruginosa,* and after our phone conversation, I remembered reading your paper on the interaction of diphtheria toxin and phospholipids. Again, it was a pleasure talking with you today, and I look forward to talking with you soon.

Sincerely,

Russell B. Wilson

Russell B. Wilson, Ph.D.
President

enclosures

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 2030 I-1 200

HEALTH AFFAIRS

28 MAY [illegible]

Mr. Kwai-Cheung Chan
Director, Special Studies and Evaluations
National Security and International Affairs Division
U.S. General Accounting Office
Washington, DC 20548

Dear Mr. Chan:

This is the Department of Defense (DoD) response to the General Accounting Office (GAO) final report, GAO/NSIAD-99-5, "GULF WAR ILLNESSES: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved," dated March 29, 1999 (GAO Code 713014/OSD Case 1711).

The Department acknowledges receipt of the final report and inclusion of the DoD response to the draft report as Appendix VI. We acknowledge the extensive changes that GAO made to the report based on the published DoD response and the other comments and annotations to the draft report, which we had provided to GAO separately.

Our position and the concerns expressed in our comments to the draft report have not changed. The clinical significance and origin of antibodies to squalene, if their existence is corroborated, remain unknown. The test methods proposed by the investigators at Tulane University need to be reviewed and validated by other scientists. Finally, no vaccines with squalene-containing adjuvants were used in U.S. troops during the Gulf War.

The Department continues to solicit and fund research designed to better understand and treat the health problems of Gulf War veterans. Requests for research proposals are published as Broad Agency Announcements in the Commerce Business Daily and are readily available to interested civilian and Federal investigators. We encourage investigators, including those at Tulane University, to submit research proposals that further our understanding of illnesses among Gulf War veterans. Our commitment to civilian and Federal researchers and to Gulf War veterans is to the support and funding of high quality research, which is best assured when all decisions on research funding are based on a process of rigorous, competitive, and independent peer review of all research proposals.

Sincerely,

Dr. Sue Bailey

ISSUES RELATING TO ANTIBODIES TO SQUALENE

Background

Recently, Pamela H. Asa, Ph.D. (of Memphis, TN) and Robert F. Garry (of Tulane University, New Orleans, LA) have been quoted in the popular press as claiming that a higher percentage of sick Gulf War veterans than healthy Gulf War veterans, or than normal blood donors, have antibodies to squalene in their blood. Squalene is a naturally-occurring, oil (a molecule that is in the category of fats and lipids) that is widely distributed in large quantities in the human body. and that has been proposed for use as a commercial adjuvant for increasing the potency of vaccines. Based on the claims by Drs. Asa and Gory, numerous accusations have been leveled at DoD. These include (among others) the allegation that the U.S. Army spiked the anthrax vaccine with squalene as an adjuvant during the Gulf War, and the claim Ural antibodies to squalene are responsible for the symptoms observed in sick Gulf War veterans.

A detailed investigation of numerous issues relating to squalene and squalene antibodies has been made by the U. S. Army Medical Research and Material Command (USAMRMC) and the Walter Xoed Army Institute of Research (WRAIR). The commanding general of USAMRMC, MG John Parker, personally telephoned Dr. Garry, and also assigned COL Carl R. Alving, M.D. (Colonel, U. S. Medical Corps) to call Dr. Garry end to investigate the technical aspects of squalene and antibodies to squalene. COL Alving, who is Chief of the Department of Membrane Biochemistry at WRAJR, has had mom than 30 years of research and clinical experience in studying the biochemistry and immunology of lipids, fats, and oils. and is internationally recognized for his research and clinical experience with lipids and oils as adjuvants for vaccines. He is also one of the world's foremost experts in the study of antibodies to lipids. The comments that follow result from this investigation.

Conversation with Dr. Garry

On Monday 24 May 1999 COL Alving and one of his staff members, Gary R. Matyas, Ph.D. (another expert in biochemistry, lipids, antibodies to lipids, immunology, and oil-based adjuvants), called Dr. Garry to discuss Garry's method of measuring antibodies to squalene. Based on the telephone conversation, at the present time the results claimed by Drs. Asa and Garry that have been made in the popular press have not even been minimally validated by scientific pear review. According to Dr. Garry, an attempt has been made Dr. Asa and him (together with Yan Cao, M.D. of Tulane) to achieve at least some measure of scientific peer acceptance by submitting a paper for publication in the Journal of the American Medical Association. However, to date, this effort has not been successful. Dr. Garry faxed a copy of the manuscript (that was marked as being a "revised" version) to COI. Alving. Dr. Garry stated that the manuscript had somehow been published without his permission on the internet and that because of lhc publicity he doubted that it would he published us a sciemifio peer-reviewed paper.

Analysis of the purported assay for antibodies to squalene

When Garry was asked to provide a detailed standard operating procedure for detecting antibodies to squalene, he said that the complete details were given in the manuscript that he faxed. However, COL Alving and Dr. Matyas found literally dozens of important technical and theoretical flaws in the assay that was faxed by Dr. Garry. Many of these were fatal flaws. Although many of the flaws that were detected by Alving and Matyas require a detailed technical knowledge of such assays, some can be explained rather simply, as shown below.

First, the conclusions are entirely based on faulty, nonscientific, circular reasoning. Positive results in an unproven assay that has not been previously validated to detect antibodies against an antigen cannot then be used be used as scientific proof that antibodies to the antigen exist in an unknown sample. The assay must first be validated by independent means. In scientific terms, it would be said that there were ***no validated positive controls***.

Second, the assay is notable for its lack of negative controls. There is no control in which the human serum containing the presumed antibodies is omitted. There is no control in which the avidin-conjugated horse radish peroxidase is omitted. Finally in a new unproven assay it is essential to prove specificity of the assay. There is no evidence that the assay is not simply measuring nonspecific IgG molecules that are not antibodies to squalene but nonspecifically stick to squalene. Although IgG molecules were detected in the assay with second antibodies to human IgG, there were no controls to show that Second antibodies to other normal serum proteins (e.g., albumin, fibrinogen, alpha 2 macroglobulin, complement, etc.) could not also have have been detected. The entire assay may be completely due to nonspecific binding of squalene to IgG molecules that are not actually antibodies.

Third, the ***unknown*** human serum samples were tested only at a single very high dilution (a dilution of 1/400). Most assays for naturally-occurring antibodies, particularly antibodies to lipids, start at a much higher concentration of serum, typically a dilution of 1/50. Thus, the Garry method would be expected to miss the presence of all of the antibodies that would be detected at a higher concentration of serum. In fact, it is possible that at a higher concentration of serum 100% of normal blood donors might give positive results. [When Ibis was pointed out to Dr. Garry, he admitted that a much higher percentage of positives in normal serum might have been detected with more concentrated serum.] *A* further drawback of the use of only a single dilution of serum rather than a series of dilutions, is that there is a no way to obtain a titer, i.e., a quantitative measure *of* the degree of activity in the sample. Titers are routinely obtained in measurement of antibody levels, and the absence of quantitation in the Garry assay prevents any meaningful comparison between unknown serum samples.

Fourth, *no* specificity controls were run to determine if the antibody binds to other structurally related compounds, such as cholesterol. Although Dr. Garry verbally stated that the antibodies did not bind to squalane (the fully hydrogenated analog that lacks double bonds), there was no evidence of any specificity whatsoever in the manuscript that was sent for peer review. One can only wonder why such important information would

be left out of the first description of an unproven assay that purports to measure specific antibodies.

As stated earlier, numerous other important and fundamental flaws were detected in the assay. This can only lead to the conclusion that even if the paper is ultimately published in its present form, there will continue to be, at the least, considerable controversy over the scientific validity of the assay and the conclusions derived from the assay.

Commercialization of Dr. Garry's assay

On Tuesday, 25 May 1999 COL Alving and Dr. Matyas had a detailed telephone conversation with Dr. Russell Wilson, President of Autoimmune Technologies, L.L.C. (New Orleans, LA). This was done because Dr. Garry had indicated that, even in the absence of peer-reviewed scientific validation, the patent rights to the technology for measuring antibodies to squalene had been exclusively licensed by Tulane University for commercial development by this company. Jk. Wilson confirmed that Drs. Garry and Am are listed as coinventors on the patent for the assay that has been exclusively licensed by Autoimmune Technologies. This was further confirmed in a letter dated 25 May that was shipped Lo COL Alving by Dr. Wilson. According to Dr. Wilson, the company doer not currently have any type of kit or other product that can be purchased for detecting antibodies, but is in the process of developing a product. Dr. Wilson stated that the company is working on an "ELISA-based version" of the assay. If this is true, then it might represent still another assay that has not been validated in a normal scientific manner.

Financial conflict of interest of Drs. Asa and Garry

The exclusive licensing of the above patent application. on which Asa and Garry are coinventors, to Autoimmune Technologies establishes an obvious, and highly disturbing, economic motive Io achieve widespread testing for profit. In the absence of such testing for antibodies to squalene, the exclusive license to Autoimmune Technologies would be worthless. Furthermore, Dr. Wilson stated, and the faxed manuscript confirmed, that Autoimmune Technologies also provides professional financial support for Dr. Garry at Tulane in the form of a grant. Although tho issue was not investigated in depth with Dr. Garry or Wilson. it ix likely that Drs. Asa and Garry also stand to benefit personally from commercialization of the patent. The financial benefits that would accrue to Drs. Asa and Garry, both professionally and personally, therefore create an obvious conflict of interest that, at a minimum, could be expected to color their scientific objectivity.

Anti-military agenda of Drs. Asa and Curry

It is disturbing to note that the strongest thrust of the above manuscript by Asa, Cao, and Garry, that is based on an unvalidated and unproven assay, is apparently directed to trying to convince sick Gulf War veterans that their illnesses are due to the presence of antibodies Lo squalene. There is an apparent agenda Lo convince veterans who put their lives on line in the Gulf War, that such antibodies were actually caused by their Gulf War experience. From the quotations in the popular press it is clear that there is also an agenda by some to claim that the antibodies were

induced by the alleged secret use of squalene as an adjuvant in the anthrax vaccine. To his credit, when asked about this, Dr. Garry stated that he did not believe that the antibodies were caused by any conspiracy to spike the anthrax vaccine with squalene. Instead, he apparently adhers to an alternative, but also unproven, theory that some constituent of the anthrax vaccine exhibits structural homology with squalene, a phenomenon sometimes referred to as molecular mimicry, and that the antibodies were induced by the anthrax vaccine in this manner. None of this is proven. No such structural homolog has ever been identified. This is an untested theory that has no basis whatsoever in fact. The only evidence, if it were viewed as such, is the unvalidated and unproven assay of Garry that purports to detect higher levels of antibodies to squalene in sick Gulf War veterans than in the normal population. The apparent anti-military agenda of Drs. Asa and Garry is a clear factor that could color their scientific results. Because of this, the Army could be made vulnerable by exclusive reliance on collaboration with Dr. Garry or Autoimmune Technologies. There is an obvious need for independent in-house research by the Army to examine the issues and implications, if any, of antibodies to squalene.

Antibodies to lipids are not new or unique: Antibodies to cholesterol in normal human sera

The concept of the presence of antibodies to lipids in human serum is not a new idea. COL Alving is particularly well-known for having discovered that 100% of normal human sera contain naturally-occurring antibodies to cholesterol. This observation was first made in 1988 and has been independently confirmed in the peer-reviewed literature. COL Alving has even created and patented a monoclonal antibody to cholesterol, and the clone is on deposit in the American Type Culture Collection. It has been proposed that naturally-occurring antibodies to cholesterol in humans actually serve a useful and beneficial function in helping to remove low density lipoprotein cholesterol (so-called "bad" cholesterol) from the blood. Because squalene is a precursor and building block for cholesterol in the human body, and is structurally very similar to cholesterol, it is the opinion of COL Alving that so-called antibodies to squalene might actually be antibodies to cholesterol that are cross-reacting with squalene. Thus it is possible that the apparent antibodies to squalene, per se, do not exist but rather are antibodies to cholesterol that have beneficial effects. When this was raised as an issue by COL hiving in his conversation with Dr. Garry, it was obvious that Dr. Garry was completely unaware of the scientific literature that exists on antibodies to cholesterol. When informed of the antibodies to cholesterol, Dr. Garry agreed that the purported antibodies that he observed might very well represent antibodies that react with cholesterol.

Port Chart for Completion of Studies on Antibodies to Squalene

	FY99		FY00				FY01				FY02				FY03			
	$154,792		$509,256				$596,786				$493,606				$230,298			
Milestones	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	
Development and Testing of ELISA Assay for Antibodies to Squalene																		
Evaluation and Development of Other Assays for Antibodies to Squalene																		
Development of a Positive Control Antibody to Squalene																		
Large Scale Production of a Positive Control Antibody to Squalene for Use in Assays																		
Testing of Normal Human Serum for Antibodies to Squalene by ELISA																		
Testing of Normal Human Serum for Antibodies to Squalene by Other Methods																		
Development of a High Volume Throughput ELISA for the Measurement of Antibodies to Squalene in Serum																		
Development of a High Volume Throughput Assay Using an Alternative Method for the Measurement of Antibodies to Squalene in Serum																		
Testing of Gulf War Veterans for Antibodies to Squalene																		
Determination of Specificity of Antibodies to Squalene																		
Biological Significance of Antibodies to Squalene																		

SUMMARY BUDGET SQUALENE ANTIBODY TASK

Milestones	FY 99				FY 00				FY 01			
	Materials	Personnel	Overhead	Total	Materials	Personnel	Overhead	Total	Materials	Personnel	Overhead	Total
Development and Testing of ELISA Assay for Antibodies to Squalene	10,000	41,880	3,125	56,005	0	41,880	4,720	46,600	N/A	N/A	N/A	N/A
Evaluation and Development of Other Assays for Antibodies to Squalene	10,000	32,500	4,256	47,256	10,000	84,000	10,000	104,000	N/A	N/A	N/A	N/A
Development of a Positive Control Antibody to Squalene	13,320	52,000	4,440	71,120	45,000	90,000	14,256	150,256	N/A	N/A	N/A	N/A
Large Scale Production of Positive Control Antibody to Squalene for Use in Assays	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	15,000	0	1,500	16,500
Testing of Diseased Human Serum for Antibodies to Squalene by ELISA and Other Methods	N/A	N/A	N/A	N/A	20,000	37,440	4,560	62,000	10,000	32,500	3,200	45,700
Development of a High Volume Throughput ELISA for the Measurement of Antibodies to Squalene in Serum	N/A	N/A	N/A	N/A	15,000	57,000	5,280	78,000	N/A	N/A	N/A	N/A
Development of a High Volume Assay Using an Alternative Method for the Measurement of Antibodies to Squalene in Serum	N/A	N/A	N/A	N/A	10,000	28,000	3,000	42,000	10,000	20,000	3,000	43,000
Testing of Gulf War Veterans Sera for Antibodies to Squalene	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	50,000	37,440	10,560	111,000
Determination of Specificity of Antibodies to Squalene	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	40,000	131,000	17,104	188,104
Preparation/Submittance of Antibodies to Squalene	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	45,135	131,000	11,681	187,816
Total	33,320	107,380	14,072	154,772	100,000	383,880	44,256	588,136	200,135	340,000	64,920	906,106

Total Cost for First Three Years $1,360,134

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, D.C. 20301-1200

HEALTH AFFAIRS

Honorable Jack Metcalf
United States House of Representatives
Washington, DC 205154702

Dear Representative Metcalf:

This is in reply to your letter to Secretary Cohen regarding the United States General Accounting Office (GAO) report, GAO/NSIAD-99-5, "GULF WAR ILLNESSES: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved." Thank you for your letter and for your concern for the health and welfare of military members and veterans.

The Department's position and concerns have not changed from those published as Appendix VI of the GAO report. The clinical significance and origin of antibodies to squalene, if their existence is corroborated, remain unknown. The test methods proposed by the investigators at Tulane University need to be reviewed and validated by other scientists. Finally, no vaccines with squalene-containing adjuvants were used in U.S. troops during the Gulf War.

Learning the clinical significance and origin of antibodies to squalene is a more important first step than knowing if such antibodies exist in a given person or group of persons. Well-designed laboratory and animal studies must precede studies in humans to answer these questions.

The forum for validating or disputing the integrity of medical research findings or clinical hypotheses is through subjecting one's work to peer review by scientists through presentation at scientific meetings and publication in peer-reviewed scientific publications. The assay for anti-squalene antibodies, which independent researchers at Tulane University developed, has not been validated at other laboratories nor have their methods and findings been subjected to broad peer review. A draft manuscript reporting the Tulane scientists' methods and findings was provided to the Research Working Group of me Persian Gulf Veterans' Coordinating Board. The Research Working Group is currently evaluating the work, will review other available literature, and will produce a White Paper on the significance of the unpublished findings.

No vaccines with squalene-containing adjuvants were used in U.S. troops during the Gulf War. There was no mention in Gulf War era documents that the DoD ever considered producing or using a vaccine that would not comply with the Food and Drug Administration's requirements for a licensed product or a product in an investigational new drug status. For several years, however, one of the scientists on the Tulane report has speculated that an autoimmune response to a vaccine adjuvant may be the cause of illnesses among Gulf War veterans. The initial speculation was that vaccines given to service members during the Gulf War contained squalene

as an adjuvant. Subsequently, the speculation was that Gulf War era service members received an experimental anti-HIV vaccine containing squalene without their knowledge.

Only recently has the speculation, as presented in the lay press, shifted to theories of adjuvants containing squalene in the anthrax vaccine. The anthrax vaccine did not and does not contain squalene. We are extremely confident of that statement; however, to reassure our service members and the public we have begun testing existing anthrax vaccine lots for the presence of squalene. The independent civilian laboratory conducting the test reports that no squalene was detectable in any vials from the six anthrax vaccine lots that have been tested to date.

The Tulane scientists have been encouraged to submit a research proposal in response to existing DoD broad agency announcements requesting proposals for Gulf War illnesses-related research. If and when the independent researcher or any other scientist submits for funding a research proposal for further studies of the alleged finding of antibodies to squalene, the DoD will ensure that the proposal receives a fair evaluation by the independent scientific review panel, which assesses all such proposals. The Department of Veterans Affairs (VA), Office of Research and Development, also has encouraged the Tulane investigators to identify a VA researcher as a collaborator and submit a proposal for funding. Since VA has an intramural research program and does not award funds to non-VA scientists, such collaboration could allow for the submission of a research proposal to VA's investigator-initiated Merit Review Program in the Medical Research Service for possible merit-based funding. The Tulane investigators have indicated to VA officials that they intend to do this.

Our commitment to civilian and Federal researchers and to Gulf War veterans is to the support and funding of high quality research, which is best assured when all decisions on research funding are based on a process of rigorous, competitive, and independent peer review of all research proposals.

Sincerely,

Dr. Sue Bailey

JACK METCALF
2D DISTRICT, WASHINGTON

COMMITTEE ON TRANSPORTATION AND INFRASTRUCTURE
SUBCOMMITTEES
AVIATION
GROUND TRANSPORTATION

COMMITTEE ON SCIENCE
SUBCOMMITTEE
ENERGY AND ENVIRONMENT

Congress of the United States
House of Representatives
Washington, DC 20515–4702

COMMITTEE ON BANKING AND FINANCIAL SERVICES
SUBCOMMITTEES
HOUSING
FINANCIAL INSTITUTIONS
DOMESTIC AND INTERNATIONAL MONETARY POLICY

CHAIR, REPUBLICAN HOUSING OPPORTUNITY CAUCUS

REPUBLICAN POLICY COMMITTEE

September 27, 1999

The Honorable William S. Cohen
Secretary of Defense
The Pentagon
Washington, DC 20301-1010

Dear Secretary Cohen:'

I was deeply disturbed by the response I received from Dr. Sue Baily regarding my letter to you dated May 13, 1999. I had requested that the Department of Defense (DOD) reconsider its answer to the General Accounting Office (GAO) in regards to their investigative report (GAO/NSIAD-99-5, "GULF WAR ILLNESSES: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved," dated March 29, 1999) on the presence of squalene antibodies in some sick Gulf War-era veterans. Unfortunately, her letter of refusal only raised additional concerns about DOD's unwillingness to aggressively pursue answers for those suffering from Gulf War Illnesses.

One of the things most troubling to me over the past months, is the misinformation that DOD continues to provide publicly regarding this issue. The Tulane study demonstrates that ill Gulf War-era veterans have statistically distinct antibody levels to squalene when compared to other population groups. Various sources within DOD continue to assure the public and military members that squalene is naturally occurring in the human body and is found in over-the-counter items. Are you alleging that those who use these over-the-counter products containing squalene have similar antibody levels to sick Gulf War-era veterans being tested? If so, on what evidence are you basing your conclusion? How can we know unless we have an assay that is reliable? Is it not disingenuous for DOD to make such statements while avoiding the significant research it has done and continues to pursue in the area of adjuvant and vaccine development, and the potential use of squalene as an adjuvant component?

The recommendations of GAO are based on the sound belief that the first step in determining the significance of the Tulane results is to review the assay being used to produce the finding. The assay being used at Tulane is a variant of the common Western blot assay used routinely by the scientific community. If it is validated, then the work can begin to discover the clinical significance for those who are suffering. DOD has the scientists and resources to conduct a timely review that is inexpensive, expands on the research already conducted, and responds to the veterans who have waited over seven years for answers.

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WASHINGTON, DC 20515
(202) 225-2605

EVERETT OFFICE:
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EVERETT, WA 98201
(425) 252-3188
(800) 562-1385

BELLINGHAM OFFICE:
322 NO. COMMERCIAL, #303
BELLINGHAM, WA 98225
(360) 733-4500

While expressing assurance that DOD did not use adjuvants containing squalene during the Gulf War, Dr. Bailey closes her letter by encouraging the Tulane scientists to submit a research proposal. Why on the one hand has DOD been absolutely unyielding in their refusal to cooperate with GAO recommendations (for the DOD to conduct its own research designed to replicate or dispute the findings), while on the other, encouraging a formal research proposal on the very study we have repeatedly asked DOD to review?

In light of these events, I am requesting a complete review of DOD's work on squalene to date. Surely the DOD's research on experimental vaccines using adjuvant formulations containing squalene has provided data and meaningful insight regarding the consequences of their use. What research has been done by your department to assess the adverse health effects of these adjuvants? Did the trials include an 'adjuvant-only' test group to provide data regarding its safety? I am asking that you provide a clear picture for Congress and the public, of your work regarding adjuvant formulations so that rumor can be dispelled and replaced with fact.

Once again, because of your department's years of research in this area, I ask that you reconsider and proceed with the GAO recommendations. Your current position of waiting for the completion of the peer review and publication process does not recognize the vast amount of research that the DOD has already accomplished regarding adjuvant formulations containing squalene. The men and women who served honorably and are suffering from Gulf War Illnesses deserve truthful answers and immediate action.

I look forward to your personal reply

Sincerely,

Jack Metcalf

Jack Metcalf

H.R. 2561

Title VI

Dept of Defense Appropriations Bill 2000

Report of the Comm on Appropriations 280

mittees by no later than January 31, 2000 on actions taken in the military health system to establish a systematic program for early detection and prevention of cervical cancer using the most modern and up to date screening methods.

GULF WAR ILLNESS

The Committee concurs with the findings of a recent GAO report on squalene antibodies and is concerned by the Department's reluctance to test for squalene antibodies since squalene is a potential contributing factor in illnesses of veterans of the Persian Gulf War. The Secretary of Defense is directed to develop and/or validate the assay to test for the presence of squalene antibodies. A report detailing the proposals to carry out this requirement shall be submitted to the Committee by January 1, 2000.

COMPUTER BASED MODELING IN HEALTH CARE

The Committee believes that computer based modeling and simulation capabilities may assist military health planners to assess the cost, access and quality impacts of reengineering delivery processes, delivery of protocols, and insertion of technology before committing vital resources. The Committee urges the Department to consider these management tools.

CHEMICAL AGENTS AND MUNITIONS DESTRUCTION, ARMY

Fiscal year 1999 appropriation	$780,150,000
Fiscal year 2000 budget request	1,169,000,000
Committee recommendation	781,000,000
Change from budget request	-388,000,000

COMMITTEE RECOMMENDATIONS

PROGRAM REDUCTIONS

The Army requested $1,169,000,000 for Chemical Agents and Munitions Destruction, Army. The Committee recommends $781,000,000, a decrease of $388,000,000. Of the decrease, $4,500,000 is taken with prejudice against program management consultants. Of the funds available, $75,503,000 shall be transferred to the Federal Emergency Preparedness Program to provide off-post emergency response and preparedness assistance to the communities surrounding the eight continental United States chemical storage and disposal sites.

The Chemical Agents and Munitions Destruction Program, Army mission is to safely destroy all U.S. chemical warfare munitions and related material while ensuring maximum protection of the public, personnel involved in the destruction effort, and the environment. The Committee commends the Army for its efforts in destroying chemical munitions in a safe manner. As of March 17, 1999, over 13.5 percent, or 4,259 tons, of the stockpile has been destroyed. Currently there are two sites operational and five sites in the design phase. Despite the fact that two additional sites are on hold until completion of the Assembled Chemical Weapons Assessment Demonstration, the Committee is hopeful that the U.S. will meet the deadline of April 2007 for the destruction of chemical munitions as called for by the Chemical Weapons Convention.

signed into law

10/25/99

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Honorable Jack Metcalf
House of Representatives
Washington, DC 205 15-4702

Dear Jack:

Thank you for your letter on the Department's position regarding the U.S. General Accounting Office report "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" (GAO/NSIAD-99-5).

We share your concern about troubling misinformation on this issue The Department's position has been consistent and remains unchanged. Squalene was not used as an adjuvant in the anthrax vaccine. DoD gave no vaccines with squalene-containing adjuvants to U.S. troops deploying to the Gulf War. The Food and Drug Administration has verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant. DoD contracted with an independent laboratory that verified that the anthrax vaccine does not contain squalene.

We asked the Tulane investigators to submit an application for research funding to validate their testing, but they did not. Our commitment to non-Government and Federal researchers and to Gulf War veterans is to support and fund research on potential causes of illnesses in Gulf War veterans. DoD is interested in looking at whether illnesses in service members are associated with antibodies to squalene. To do this, we need a scientifically proven test for squalene antibodies to assess whether Gulf War veterans have antibodies to squalene, hence our *reason* for pursuing additional research. In response to a DoD solicitation for research on illnesses among Gulf War veterans, a DoD investigator who is a nationally recognized expert in antibodies to cholesterol and other lipids, has been funded to pursue a study to determine the feasibility of developing a test for antibodies to squalene.

To date, the Tulane investigators have not succeeded in publishing their work in the medical literature. A draft of the Tulane paper was provided to the Research Working Group (RWG) of the interagency Persian Gulf Veterans' Coordinating Board. I have asked the RWG to provide you with a copy of its review of the draft Tulane paper. The review will contain the additional information on squalene that you requested.

Sincerely.

TOTAL P.02

Title: Antibodies to Squalene
Project #: DoD-100
Agency: DoD
Study Location: Walter Reed Army Institute of Research (WRAIR), Forest Glen, MD
Project Status: Ongoing
Principal Investigator: Colonel Carl Alving, MD
Start Date: 1999
Completion Date: 2001
Phone: 301-319-9611

OVERALL PROJECT OBJECTIVE: Establish an effective means of testing for antibodies to squalene and determination of whether such antibodies are present in the blood of sick Gulf War veterans.

SPECIFIC AIMS: See objective.

METHODOLOGY: Clinical (immunologic) research.

EXPECTED PRODUCTS (MILESTONES): Establishment of appropriate testing method(s) for squalene antibodies and determination of whether such antibodies are present in a sample of ill Gulf War veterans.

STATUS/RESULTS TO DATE: The ELISA assay development is complete and control monoclonal antibodies have been successfully developed.

PUBLICATIONS: none to date

NOTES:

1. Colonel Alving submitted this proposal to the U.S. Army Medical Research and Materiel Command (USAMRMC) in FY99 under the Broad Agency Announcement (BAA) for Gulf War Illnesses Research projects.

2. An independent scientific peer review of Colonel Alving's proposal recommended that initial studies be limited to that part of the proposal directed toward induction of squalene antibodies. The peer review panel stated, "If antibodies to squalene cannot be induced, the subsequent studies proposed should not be initiated." The panel's final recommendation was, "...that only the first year of the proposal be funded until more information is provided on the experimental design and more importantly on whether or not antibodies to squalene exist."

3. The USAMRMC's Military Operational Medicine Research Program provided adequate funding to WRAIR to accomplish this objective. The funded project comprises five specific tasks to be completed by the end of FY00:

a. Develop and test ELISA assay for antibodies to squalene.

b. Evaluate and develop other assays for antibodies to squalene.

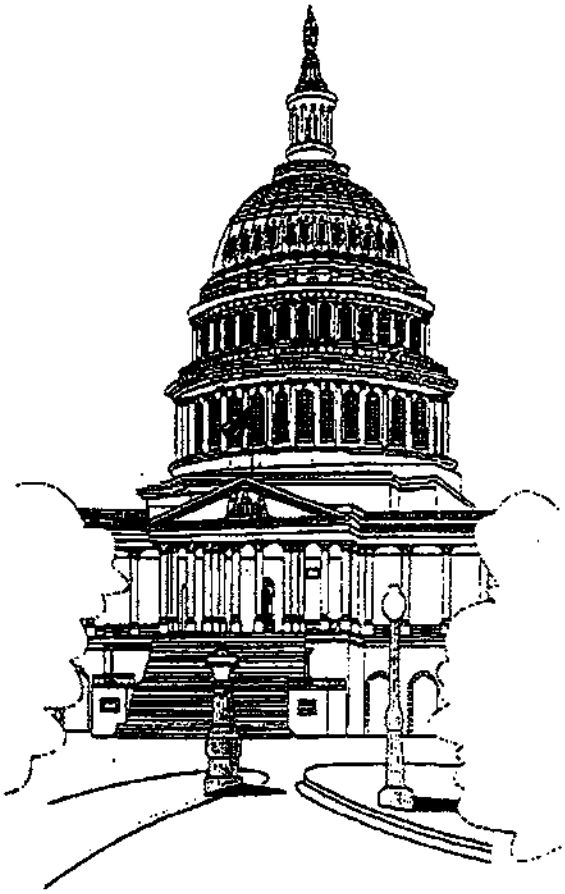
c. Develop a positive control antibody to squalene.

d. Large scale production of positive control antibody to squalene for use in assays.

e. Test normal human serum for antibodies to squalene by ELISA and other methods.

REPORT TO CONGRESS

GULF WAR ILLNESS



Development and Validation of an Assay to Test for the Presence of Squalene Antibodies

Executive Summary

This Report has been prepared in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill:

> The Committee concurs with the findings of a recent GAO report on squalene antibodies and is concerned by the Department's reluctance to test for squalene antibodies since squalene is a potential contributing factor in illnesses of veterans of the Persian Gulf War. The Secretary of Defense is directed to develop and/or validate the assay to test for the presence of squalene antibodies. A report detailing the proposals to carry out this requirement shall be submitted to the Committee by January 1, 2000.

A May 1999 *Vanity Fair* article, "The Pentagon's Toxic Secret," alleged that the Department of Defense possibly used "an illicit and secret anthrax vaccine" on its own soldiers.[31] According to a Vanity Fair news release, "the licensed formula for...anthrax vaccine may have been altered, without formal FDA approval, to contain an experimental, and potentially dangerous, additive," squalene, that reportedly "causes incurable diseases in lab animals and may be the cause of some cases of Gulf War syndrome." The *Vanity Fair* article went on to suggest that the modified anthrax vaccine "may be part of the stockpile now being administered in the wake of the DoD's December 1997 decision to immunize 2.4 million people in the armed services against anthrax." A NewsWatch Associate editor presented an opposing review of the allegations entitled "Vanity Scare" in May 1999.[32]

On March 29, 1999, Congressman Jack Metcalf announced the release of a General Accounting Office (GAO) report, which he had requested, regarding squalene antibodies in veterans suffering from Gulf War illnesses. The GAO Report, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" (GAO/NSIAD-99-5) recommended that DoD "conduct research designed to replicate or dispute the unpublished independent research results that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans."[33]

In its investigations of illnesses among Gulf War veterans, the Senate Special Investigations Unit (SIU) found no credible information indicating that vaccines used during the Gulf War contained squalene.[38] In its report, the SIU stated that according to the Food and Drug Administration (FDA), squalene can be contained in a vaccine due to two different processes: 1) as an adjuvant, which is an agent to enhance the immune response; or 2) in minute quantities in vaccines manufactured using eggs, since eggs are rich in squalene and cholesterol. The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant.

To investigate the squalene hypothesis, a scientifically proven test for squalene antibodies is needed to assess whether Gulf War veterans have antibodies to squalene. In response to a DoD solicitation for research on illnesses among Gulf War veterans, a DoD investigator and nationally recognized expert on antibodies to cholesterol and other lipids submitted a research proposal to determine the feasibility of developing a test for antibodies to squalene.

The funded research project to determine whether antibodies to squalene exist has five main objectives:

1) Development and validation of an ELISA assay for antibodies to squalene.
2) Evaluation and potential development of other assays for antibodies to squalene.

3) Development of a positive control antibody to squalene.
4) Production of the positive control antibody to squalene for use in the assays.
5) Testing of normal human serum for antibodies to squalene by ELISA and other methods.

The DoD funded study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and can be detected in human serum.

Background

Squalene is a relatively simple, linear hydrocarbon. It is a naturally occurring molecule in the human metabolic process that synthesizes cholesterol.[1] Squalene is present in human sebum and cell wall structures. Squalene is also a component of shark liver oil, some vegetable oils, and plant and animal cell membranes.[2] It is licensed by the FDA as a dietary supplement in the United States and is listed in the *Physicians' Desk Reference*. Squalene is used commercially in the cosmetic industry and in sunscreen products.[3]

Epidemiological studies of breast and pancreatic cancer in several Mediterranean populations have demonstrated that increased dietary intake of olive oil is associated with a small decreased risk or no increased risk of cancer, despite a higher proportion of overall lipid intake. Experimental animal model studies of high dietary fat and cancer also indicate that olive oil has either no effect or a protective effect on the prevention of a variety of chemically induced tumors. As a working hypothesis, it is proposed that the high squalene content of olive oil, as compared to other human foods, is a major factor in the cancer risk-reducing effect of olive oil. Experiments in vitro and in animal models suggest a tumor-inhibiting role for squalene.[4] In addition, studies using squalene in combination with low-dose pravastatin have demonstrated combination therapy significantly reduces total cholesterol and LDL cholesterol and increases HDL cholesterol to a greater extent than either drug alone.[5]

Squalene is one of several components of adjuvant formulations in a variety of vaccines.[6] One common formulation is MF59. MF59 is a safe, practical, and potent adjuvant for use with human vaccines.[7] Toxicology studies in animal models and Phase I-III studies in humans have demonstrated the safety of MF59 with HSV, HIV, and influenza vaccines.[7-17] Hilhers, et al, concluded that reactogenicity and stability but not adjuvanticity of synthetic sulfolipo-polysaccharide/squalane/water formulations depended on the molecular weight of synthetic sulfolipo-polysaccharide and that synthetic sulfolipo-cyclodextrin/squalane/water is a promising non-mineral oil adjuvant as it combines strong adjuvanticity (i.e. better than the mineral oil-based adjuvant presently applied) with low reactogenicity and good stability.[18]

However, Lorentzen has reported that the cholesterol precursor squalene (C30H50), through nonspecific activation of the immune system, can precipitate arthritis in rats. Using arthritis-prone rat strains to search for disease-triggering factors among molecules which initially induce innate defense reactions rather than specific immune responses, Lorentzen reported on the potential for endogenous lipids to precipitate arthritis.[19] In addition, there is evidence that in some instances squalene has a negative effect on the nervous system.[20-21]

Pamela B. Asa, Ph.D., an unaffiliated molecular biologist from Memphis, Tennessee and Yan Cao, M.D. and Robert F. Garry, Ph.D., from Tulane University, New Orleans, Louisiana have theorized that illnesses afflicting veterans of the Gulf War are an atypical connective tissue disease (an autoimmune disease) resulting from use of the vaccine adjuvant, squalene.[22-23] These investigators have reportedly developed an immunoassay for detecting anti-squalene antibodies and used the assay to test blood serum samples from various patient and control groups.

To investigate this hypothesis, DoD has funded a scientific program which will answer several major questions. Initially, the research staff will determine if antibodies to squalene exist and if an assay can be developed to detect and quantify these antibodies. In addition, an animal model will be used to induce anti-squalene antibodies to use as positive controls to characterize anti-squalene antibodies in

humans. If a positive antibody response to squalene can be induced in mice, then normal human serum can be tested for possible antibodies to squalene. Next, the research program will focus on qualitative detection of squalene and development of a chemical assay. Finally, the research program will examine the biological implications of antibodies to squalene.

Discussion

Pamela B. Asa, who has worked in the area of rheumatology and silicone-gel breast implants, presented a theory in 1995 of "human adjuvant disease" and its possible link to Persian Gulf War (PGW) Veterans' Illnesses. She theorized that silicone adjuvant (an agent added to a vaccine to increase antigenic response) was responsible for PGW veterans developing "human adjuvant disease."[24] A scientific review prepared by an independent non-governmental medical expert on September 13, 1995 of Dr. Asa's "Report on Gulf War Syndrome" found the basic hypothesis and supporting evidence presented was based on a series of erroneous assumptions and unsupported conjectures.[25] A similar review by the Medical, Chemical and Biological Defense Research Program found the basic hypothesis and supporting evidence presented by Dr. Asa were flawed or inaccurate.[26] Available information also strongly argues against Dr. Asa's hypothesis:

All vaccines used during the Gulf War have a long history of safety and all, except BotTox that was used under an Investigational New Drug (IND), were licensed by the FDA at the time of the Gulf War.

Since the standard immunization series is given to individuals in basic and advanced training, only a relatively small number of additional vaccines were given during deployment to the Persian Gulf, and the previous use of these vaccines has not resulted in problems similar to those reported by GW veterans.

All vaccine lots are individually licensed for safety and efficacy. The vaccines used, therefore, are unlikely to be contaminated or of low quality.

The only adjuvant used in the vaccines given to Gulf War personnel was alum. Alum is an FDA-approved adjuvant with a long history of safety. It has been given to millions of people worldwide without significant problems. No experimental adjuvants were used by the military.

There are no reports of alum causing human adjuvant disease or any other chronic disease.

There are no reports of chronic inflammatory responses at the sites of immunization with vaccines containing alum as would be expected if human adjuvant disease were to occur.

Several recent studies have failed to show any association between silicone-gel implants and increased incidence of connective tissue disease. There is little supporting evidence, other than anecdotal reports, that silicone-gel implants cause an increase in connective tissue diseases or human adjuvant disease.

Dr. Asa's current work focuses on the presence of antibodies to squalene in a cohort of 142 Gulf War-era veterans or military employees. She theorizes that "Gulf War Syndrome" manifests a spectrum of signs and symptoms similar to that of other atypical connective tissue diseases and that most "Gulf War Syndrome" patients have serum antibodies to squalene, an immunological adjuvant. The study protocol attributes the hypotheses to findings in one (1) patient from a NIH-sponsored trial using squalene as an adjuvant.[22] The findings of the current unpublished work apparently originate from samples collected under this protocol. It is unknown if informed consent was obtained from individuals submitting samples for testing or if an Institutional Review Board (IRB) reviewed and approved the research protocol. Review of the draft manuscript indicates the basic hypothesis and supporting evidence presented as flawed or inaccurate. The findings from the study must be interpreted with caution as flawed methodology including biased sample selection and potential cofounders weaken any potential association. The following information also strongly argues against the current hypothesis:

If in fact antibodies to squalene are present in Gulf War veterans, the clinical significance of finding these antibodies in humans is unknown. Squalene is normally present in humans as part of the body's production of

cholesterol. In addition, it is found in human sebum (skin oils) and plant and animal cell membranes. Antibodies to cholesterol in humans are common.

There may be alternative explanations for the reported laboratory findings, including: detection of naturally occurring squalene; cross-reaction with compounds similar to squalene; elevated levels of squalene due to a known or unknown disease process causing human illnesses, or; laboratory error or contaminant.

If in fact anti-squalene antibodies are present in the blood of Gulf War-era veterans, this is not sufficient to establish an association of squalene or squalene antibodies with any illness(es) among Gulf War veterans.

The assay for anti-squalene antibodies, which independent researchers at Tulane University developed, has not been validated at other laboratories nor have their findings been subjected to minimal peer review through publication in the scientific literature.

The only adjuvant used in the vaccines given to Gulf War personnel was alum. Alum is an FDA-approved adjuvant with a long history of safety. It has been given to millions of people worldwide without significant problems. No experimental adjuvants were used by the military.

The anthrax vaccine given to service members during the Gulf War and subsequently did not and does not contain squalene.

The Army Surgeon General has verified that the anthrax vaccine was never produced at any alternate production facilities in the U.S. during the Gulf War, and anthrax vaccine production at the Michigan Biologic Products Institute (MBPI, now BioPort) never contained squalene. Stanford Research Institute, International has recently completed verification testing for squalene on 6 lots of anthrax vaccine and verified that no squalene was detectable in any of the vials.

There are no data demonstrating increased rates of autoantibodies in ill Gulf War veterans.

Unfortunately, we cannot be sure that the theorists actually detected antibodies to a synthetic squalene adjuvant in the veterans they tested. They reportedly used a variation of a previously described assay.[27] This technique was used to claim findings of the first evidence from a blinded study of the existence of a laboratory marker that correlates with the severity of local and systemic complications in silicone breast implant recipients. The assay in question detects antibodies, not to silicone, but to a synthetic polymer whose characteristics have not been fully described. In subsequent letters to the editor, many noted the methodological flaws in the study, argued that since the antibody is not against silicone, there was no reason to suppose the implants had anything to do with the symptoms or antipolymer antibody assay test results, and noted that the investigators had reported similar high seroactivity in fibromyalgia patients.[28] A Committee named by the Institute of Medicine (IOM) recently reported that a careful study of all the evidence indicates that women with silicone breast implants are no more likely to develop chronic disease than women without the implants. The IOM Committee did not address antipolymer antibodies; however, they stated that "The clinical significance of a recently described antipolymer antibody test is unclear, although the polymer in question is not silicone or silicon containing, and it is extremely unlikely that it measures an antisilicone antibody."[29]

Dr. Garry and Tulane University reportedly received a U.S. patent in 1997 for an assay that could detect antibodies to polymers, of which squalene is one. In a letter from Dr. Garry to DoD, Re: Anti-Squalene Antibodies, dated May 7, 1999, Dr. Garry informed DoD that Tulane University Medical Center had applied for a patent on the use of anti-squalene antibodies in assessing Gulf War Syndrome. Dr. Garry also informed DoD that Tulane was the sole owner of the intellectual property provided in the letter of May 7, and that DoD should share the data only with those who have a specific need to know. In this letter, Dr. Garry reviewed the specifics of the anti-squalene antibody assay, or ASA Assay, that measures the binding of serum immunoglobulins to squalene.

The Office of the Army Surgeon General (OTSG) requested an update in early May 1999 on investigations, tests, and projects to investigate allegations regarding squalene in the anthrax vaccine and plans for developing an assay for squalene antibodies.[30] In the update, the Army stated that all lots of the anthrax vaccine released by DoD would be tested and that current testing to date by Stanford Research Institute, International confirmed that no squalene was detectable in any of the vials. The FDA is doing additional testing. Dr. Garry provided the manuscript outlining the details of his proposed assay to OTSG for review. It was the opinion of COL Alving and Dr. Matyas that there were "dozens of important technical and theoretical flaws" in the assay-many described by COL Alving as "fatal flaws." Dr. Garry had informed COL Alving and Dr. Matyas that, "even in the absence of peer-reviewed scientific validation, the patent rights to the technology for measuring antibodies to squalene had been exclusively licensed by Tulane University for commercial development by a company called, Autoimmune Technologies, L.L.C." Dr. Garry was unaware of the scientific literature that exists on antibodies to cholesterol. When informed of the antibodies to cholesterol by COL Alving, Dr. Garry "agreed that the purported antibodies that he observed might well represent antibodies that react with cholesterol."

Excerpts of the GAO report entitled, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" stated that independent researchers had developed a test based on a Western blot assay and had detected antibodies to squalene in the blood of sick Gulf War veterans. If the description of the test described in the GAO report is accurate, there are some technical points that would seem to invalidate such a test:

> Squalene is a non-charged long chain hydrocarbon that would not be expected to migrate on a gel such as required in a Western blot assay.
>
> Because squalene lacks charge, it would not be expected to transfer to nitrocellulose as is done in a Western blot assay.

On March 29, 1999, Congressman Jack Metcalf (Washington) announced the release of a GAO report, which he had requested, regarding squalene antibodies in veterans suffering from Gulf War illnesses. The GAO Report, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" (GAO/NSIAD-99-5) recommended that DoD "conduct research designed to replicate or dispute the independent research results that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans."[33] The GAO did not comment on the ethical conduct of the research including a requirement for informed consent and IRB review of the protocol. The GAO did note that Chiron and Ribi ImmunoChem reported that their squalene adjuvant formulation had been tested on over 9,000 and 1,000 human subjects, respectively.

The clinical significance of finding antibodies to squalene is unknown. Squalene is normally present in humans as part of the body's production of cholesterol. It is found in human sebum (skin oils) and plant and animal cell membranes. The scientific work that has been done on squalene's role in human health and disease notes the positive effects of dietary squalene on cancer prevention and cholesterol regulation and the safety and efficacy of squalene as a vaccine adjuvant. There may be alternative explanations for the reported laboratory findings, including: detection of antibodies to cholesterol;[34-37] detection of antibodies to naturally occurring squalene; cross-reaction with compounds similar to squalene; elevated levels of squalene due to a known or unknown disease process causing human illnesses, or; laboratory error or contaminant.

The assay for anti-squalene antibodies developed by independent researchers at Tulane University has not been minimally validated through publication in the scientific literature. The investigators have

reportedly submitted a manuscript to a peer-reviewed medical journal; to date, however, this effort apparently has not been successful.

Since the Gulf War, squalene has been a component of vaccines undergoing testing by the Walter Reed Army Institute of Research (WRAIR). Volunteers received the vaccines in well-controlled studies that followed FDA regulations. Squalene is one of several components of the adjuvants found in each of two vaccine products undergoing testing by WRAIR. Pharmaceutical grade squalene is used to produce the oil emulsion used in these vaccine products. The exact compositions of the adjuvant in these vaccines are proprietary and belong to DoD Cooperative Research and Development Agreement (CRDA) partners. Development, evaluation, and FDA approval for the use of these adjuvant systems has been conducted by DoD CRDA partners and WRAIR. The two vaccines are investigational products for the prevention of malaria and human immunodeficiency virus (HIV) infection. Information on the study on the HIV vaccine has not yet been published and is considered proprietary information. Information on the study involving the malaria vaccine has been published in the scientific literature.[39]

Prior to its use in humans, the vaccines containing the emulsion underwent extensive FDA-mandated Good Laboratory Practices repeat dose toxicology studies involving rodents, rabbits, guinea pigs and nonhuman primates. The details of these studies (four volumes) were filed with the FDA as part of the IND application. The studies revealed anticipated inflammatory responses surrounding the site of injection. No gross changes were observed. No laboratory abnormalities were found.

Conclusion

Allegations of an ongoing conspiracy by the media and others is troubling. Squalene is not a foreign substance. It is normally present in the human body in large quantities because it is a precursor to the biosynthesis of cholesterol in the liver. The DoD funded study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and if they can be detected in human serum. Since squalene is being used as an adjuvant in some newer generation vaccines, this question becomes of interest not only to the military but also to the general public. Previously, these investigators were able to demonstrate antibodies to cholesterol. Squalene may not be immunogenic by itself, but under certain circumstances antibodies to the compound may arise. Although antibodies to cholesterol and possibly squalene occur naturally, this does not necessarily mean they have an adverse effect.

This research proposal was submitted in response to a competitive solicitation for proposals. The proposal was peer reviewed independent of the Department, by the American Institute of Biological Sciences, and received a high scientific merit score. Programmatic review was accomplished by the Department and the Research Working Group of the Persian Gulf Veterans Coordinating Board. Based on the results of this research, further studies can be pursued, if appropriate, to look at the existence of these antibodies in Gulf War veterans and their correlation to disease.

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COMMITTEE ON SCIENCE
SUBCOMMITTEE
ENERGY AND ENVIRONMENT

Congress of the United States
House of Representatives
Washington, DC 20515–4702

HOUSING
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DOMESTIC AND INTERNATIONAL
MONETARY POLICY

CHAIR, REPUBLICAN HOUSING
OPPORTUNITY CAUCUS

REPUBLICAN POLICY COMMITTEE

January 31, 2000

The Honorable William S. Cohen
Secretary of Defense
The Pentagon
Washington, DC 20301-1010

Dear Secretary Cohen:

We are writing to ask for an objective analysis of "Antibodies to Squalene in Gulf War Syndrome" - an article that has just been published in the February 2000 issue of *Experimental and Molecular Pathology*.

This peer-reviewed article found anti-squalene antibodies in a very high percentage of sick Gulf War-era veterans. As a bio-marker for the disease process involved in Gulf War Illnesses, the assay/blood test cited in the study could provide a vital diagnostic tool. We hope this will quickly lead to improved medical treatments for many who are suffering.

Many who have heard about this issue are anxious to understand the ramifications, especially those veterans and their families whose lives sadly have been directly affected. We certainly acknowledge the need for further research. However, that should not preclude a vigorous examination of the immediate benefits this study may provide medical practitioners treating those who suffer from Gulf War Illnesses.

The House passed version of the Fiscal Year 2000 Defense Appropriations Bill included report language instructing the Department of Defense to develop and/or validate the assay to test for the presence of squalene antibodies. This action was taken in response to DOD unwillingness to cooperate with the March 1999, General Accounting Office recommendation [NSIAD-99-5].
It reflected our firm belief that the integrity of the assay was the first step in finding answers.

Now that this study has been peer-reviewed and published, we need to take the next step and build on established science. An internal review by the same individuals within the DOD who were unwilling to cooperate for months does not constitute the kind of science that those who sacrificed for this nation deserve. Given the published article, it seems prudent to use the assay if it could help sick Gulf War era veterans. Do you agree?

We look forward to hearing from you by March 1, 2000. We thank you for your commitment and efforts on behalf of our Gulf War-era veterans.

Sincerely,

Jack Metcalf

Norm Dicks

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Norm Dicks

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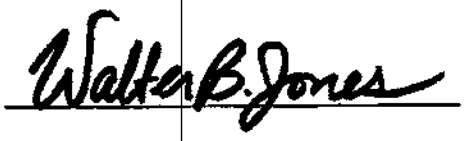
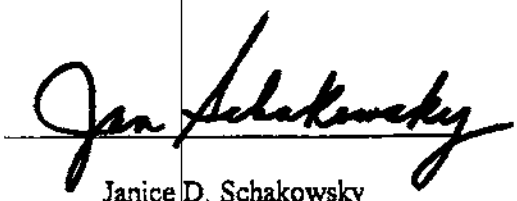
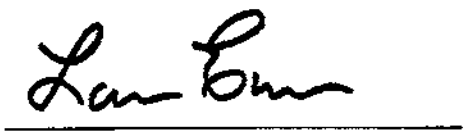


Walter B. Jones

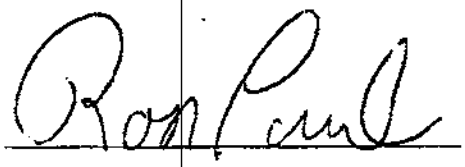
Bob Filner



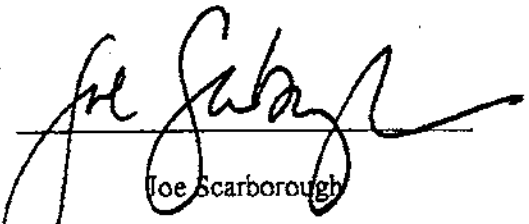
Janice D. Schakowsky



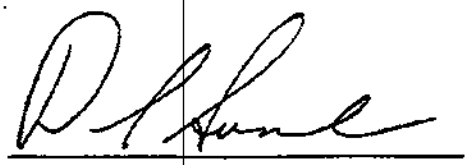
Lane Evans



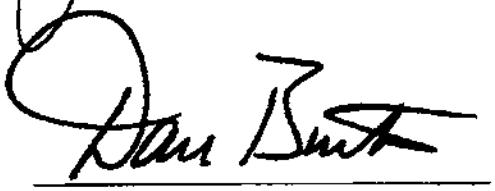
Ron Paul



Joe Scarborough



Bernard Sanders



Dan Burton

JACK METCALF
2D DISTRICT, WASHINGTON

COMMITTEE ON TRANSPORTATION AND INFRASTRUCTURE
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via facsimile 703-697-9080 - FINAL COPY

February 25, 2000

The Honorable William S. Cohen
Secretary of Defense
The Pentagon
Washington, DC 20301-1010

Dear Secretary Cohen:

I am exasperated and deeply disturbed by the Department of Defense's addition to its Anthrax Vaccination Inoculation Program (AVIP) website in the "Q & A" section under the heading "Production Issues" and the title "Accusations - Squalene."

On January 31, 2000, nine of my colleagues and I sent you a letter requesting an objective analysis of "Antibodies to Squalene in Gulf War Syndrome" - an article that had just been published in the February 2000 issue of *Experimental and Molecular Pathology* - a respected scientific peer-review journal. The letter represented our hope that DOD would seize the opportunity to do the kind of serious, scientific review that those who serve and sacrifice for our nation deserve.

Instead, a review of the AVIP website shows that DOD has chosen to do a hit-piece, dismissing "Antibodies to Squalene in Gulf War Syndrome" with the wildly expansive claim that "conclusions derived from the test results have NO scientific basis" (emphasis added). The marines, airmen, sailors and soldiers who access this site are not provided the courtesy of a rebuttal from the internationally respected scientist who developed the assay used in the research.

I am dismayed you would allow this posting to the website before you fully respond to the letter sent on January 31. DOD's action certainly reinforces the letter's concern regarding the inappropriateness of an internal review by the same individuals within DOD who have been unwilling to cooperate for nearly a year.

Additional information in this section is also troubling in its incompleteness. One section outlines "What does the U.S. Senate say about squalene?". Unfortunately, the site neglects to state that the 1998 conclusions made by the Senate Special Investigations Unit were made prior the GAO investigation, prior to the gathering of additional scientific data and more recently, findings in the House of Representatives.

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Page two--The Honorable William S. Cohen--February 25, 2000:

How can the DOD expect to regain the seriously eroded trust of its military personnel if misrepresentations posted on your official website are allowed to go unchallenged? Please take immediate action to remove the inappropriate and misleading response from DOD's information page, and do what is right - an objective analysis of the merits of this study.

Sincerely,

Jack Metcalf

Jack Metcalf
House of Representatives

cc: Representative Norm Dicks
Representative Walter Jones
Representative Bob Filner
Representative Janice Schakowsky
Representative Lane Evans
Representative Ron Paul
Representative Joe Scarborough
Representative Bernard Sanders
Representative Dan Burton

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

FEB 28 REC'D

FEB 24 2000

Honorable Jack Metcalf
House of Representatives
Washington, DC 20515

Dear Representative Metcalf:

Thank you for your letter asking for an objective analysis of Antibodies to Squalene in Gulf War Syndrome – an article published in the February 2000 issue of *Experimental and Molecular Pathology*. Prior to publication of the article, the Research Working Group (RWG) of the interagency Persian Gulf Veterans' Coordinating Board had objectively reviewed the work of Dr. Asa and her colleagues. We look forward to the scientific dialog and additional research that will now go forward as a result of long awaited publication of this data. I have enclosed the RWG review, our Report to Congress in response to the Fiscal Year 2000 Defense Appropriations Bill report language, and a review of the published article.

As you know, we have encouraged and awaited publication by these scientists ever since Dr. Asa first presented her theory on "human adjuvant disease" and its possible link to Persian Gulf War (PGW) veterans' illnesses. Prior to speculation about squalene, Dr. Asa theorized that silicone adjuvant (an agent added to a vaccine to increase antigenic response) was responsible for PGW veteran's developing "human adjuvant disease."

The Department published in the February 10, 1999 Commerce Business Daily a specific request for research proposals on "Interactions Of Drugs, Biologics And Chemicals In Service Members In Deployment Environments," supporting our research on illnesses among Gulf War veterans. This preceded the recommendation of the General Accounting Office to pursue research in this area. In response to this solicitation, a research proposal was submitted to develop and validate an assay to test for the presence of squalene antibodies. This proposal received a high independent scientific review merit score, was funded, and the research is ongoing.

We wholeheartedly agree that the integrity of the assay is the first step in finding answers. Our commitment to Gulf War veterans is to support and fund quality research. This is best assured when all decisions on research funding are based on a process of rigorous, competitive, and independent peer review of all research proposals. We are committed to responsible and aggressive pursuit of research that will further our understanding of illnesses among Gulf War veterans and prevent similar illnesses following future deployments.

Sincerely,

Dr. Sue Bailey

Enclosures:
As stated

Scientific Manuscript: "Antibodies to Squalene in Gulf War Syndrome"

The study, by Drs. P. B. Asa, Y. Cao and R. F. Garry, appeared in the February 2000 issue of Experimental and Molecular Pathology. The paper by Asa and colleagues presents data obtained by using an immunological assay that reportedly can detect previously unknown antibodies against squalene, a relatively simple, linear hydrocarbon that is a naturally occurring molecule in humans, animals and plants. Squalene is normally found in cell membranes in humans and is one of the building blocks for producing cholesterol.

Summary: Using this novel assay, the authors' report finding anti-squalene antibodies in a high percentage of "Gulf War Syndrome" patients. The antibody test developed at Tulane University Medical Center is called the Anti-Squalene Antibody Assay, or ASA Assay. Tulane has a patent pending on the ASA Assay, and Autoimmune Technologies LLC, a New Orleans biomedical company, has licensed the rights to the ASA Assay from Tulane.

The published research reportedly included both blinded and unblinded studies. In the blinded study, the ASA Assay was reportedly used to test blood samples from 56 individuals who were in active military service or who were civilian employees of the U.S. armed forces or their contractors during 1990-1991. Most, but not all, of the members of this group were reportedly deployed to the Persian Gulf theater of operations. The group comprised 38 deployed individuals who were ill, 12 deployed individuals who were healthy, and 6 non-deployed individuals who were ill. The results of the blinded study showed that 95% of the deployed sick individuals tested positive, none of the deployed healthy individuals tested positive, and 100% of the non-deployed sick individuals tested positive for anti-squalene antibodies.

In the unblinded study, the ASA Assay was used as a screening tool to gather further data. Blood samples from 86 additional individuals who were in active military service or who were civilian employees of the U.S. armed forces or their contractors during 1990-1991, including healthy individuals, were tested, and 69% of them tested positive. Because squalene is used as an ingredient in some cosmetics, 48 samples from blood banks were tested to see if the antibodies were present in a larger segment of the general population. Of these, 5% tested positive. To see if the antibodies were a marker for other autoimmune disease processes, 40 samples from patients with systemic lupus erythematosus were tested. Of these, 10% tested positive. Because patients with chronic fatigue syndrome have many symptoms similar to those of "Gulf War Syndrome" patients, 30 chronic fatigue patients were tested. Of these, 15% were positive.

The research also included a small adjunct study in which two individuals who had previously volunteered to participate in a vaccine trial in which squalene was an adjuvant in the vaccine were tested for the presence of anti-squalene antibodies. Both subjects tested positive. These two were the only patients in the research group who had a known exposure to squalene from vaccines.
The conclusion reached as a result of this research study is that most patients in the study groups who are ill with "Gulf War Syndrome" have serum antibodies to squalene while most other people do not. The clinical significance of the presence of the antibodies, however, is still not known, and while it is possible that the antibodies play a role in the disease process itself, the study does not explore the mechanisms involved in developing the antibodies.

Critical analysis: It is unknown if informed consent was obtained from individuals submitting samples for testing or if an Institutional Review Board (IRB) reviewed and approved the research protocol.

The authors claim to create a novel assay that detects antibodies to squalene. The authors however, do not use valid positive or negative controls. There are no positive controls (i.e., sera previously proven to contain antibodies to squalene) to validate the argument that the assay can detect antibodies to squalene. For positive controls, the authors cite only results obtained using this novel assay on two individuals reportedly vaccinated once and thrice with a squalene-containing adjuvant in a clinical trial sponsored by the National Institutes of Health. The authors provide no preimmunization results to demonstrate that the presumptive anti-squalene activity in the so-called positive controls was not present before immunization with the squalene adjuvant.

Fundamental to interpretation of novel assay data are negative controls. Such negative controls are critical to prove that the assay is not detecting artifacts (extraneous, cross-reacting substances). The authors have no negative control in which the human serum containing the presumed antibodies is omitted; there is no negative control in which the avidin-conjugated horse radish peroxidase is omitted; there is no negative specificity control for nonspecific binding of IgG, i.e., for normal IgG molecules sticking nonspecifically to squalene.

A further criticism of the paper is the authors use of only a single dilution of serum, rather than a series of dilutions. Without using this technique, there is a no way to obtain a titer, i.e., a quantitative measure of the degree of activity in the sample. The test results were scored at +++, ++, +, +/-, and -, raising the possibility that at high concentrations most normal sera might give a positive result; and the total absence of antibodies in a "normal" population must be regarded with some suspicion. If "squalene antibodies" or derivatives are associated with "Gulf War syndrome," one may expect titers to parallel severity of symptoms. The paper gives no evidence of this.

The assay by Asa and colleagues remains an unvalidated and unproven assay.

JACK METCALF
2d District, Washington

COMMITTEE ON TRANSPORTATION AND INFRASTRUCTURE
Subcommittees:
Aviation
Ground Transportation

COMMITTEE ON SCIENCE
Subcommittee:
Energy and Environment

Congress of the United States
House of Representatives
Washington, DC 20515–4702

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CHAIR, REPUBLICAN HOUSING OPPORTUNITY CAUCUS

REPUBLICAN POLICY COMMITTEE

via facsimile 703-697-9080

March 3, 2000

The Honorable William S. Cohen
Secretary of Defense
The Pentagon
Washington, DC 20301-1010

Dear Secretary Cohen:

Please intervene to halt the obfuscation campaign Department of Defense officials seem intent on conducting concerning the issues surrounding antibodies to squalene research. Monday, February 28, 2000, I received a response to the letter I had sent to you. Nine of my colleagues in the House of Representatives joined me to request that DOD do an objective analysis of "Antibodies to Squalene in Gulf War Syndrome" -- an article recently published in the February 2000 issue of *Experimental and Molecular Pathology*.

DOD's letter, authored by Dr. Sue Bailey, avoids providing Congress a clear and direct answer to our request. The following excerpts illustrate my concerns with DOD's official reply.

1. In paragraph one, Dr. Bailey states that she has enclosed the Research Working Group (RWG) review. She does not mention that the RWG reviewed an early draft of the study, provided to them as a professional courtesy. The text of the final peer-reviewed article contains some significant changes. Members of Congress asked for an objective analysis of the peer-reviewed article. It is difficult to understand why Dr. Bailey chose to include a review not based on the published scientific article, unless her goal was confusion rather than clarity.

2. Also provided as an attachment, and referenced in paragraph one, is a review of the published article. I was dismayed that Dr. Bailey would provide this brief summary with no indication of the author's name or professional credentials to conduct and provide such a review. My colleagues and I stated clearly, "An internal review by the same individuals within the DOD who were unwilling to cooperate for months does not constitute the kind of science that those who sacrificed for this nation deserve." A half-page critical analysis, anonymously written, is not an appropriate response to the congressional request.

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3. Dr. Bailey continues in paragraph two by making a reference to an early theory that is completely irrelevant to our request. Dr. Asa's early and *confidential* correspondence with DOD regarding potential cause was motivated by concern for those suffering from Gulf War Illnesses. DOD must encourage researchers to explore hypotheses rather than setting them up for public criticism, if we are going to solve the mystery of Gulf War Illnesses. The congressional inquiry's focus is the peer-reviewed study and the assay used to detect the antibodies. Dr. Bailey's reference is an unnecessary distraction from the facts.

4. Dr. Bailey's third paragraph attempts to portray DOD as proactive in developing and validating an assay to test for the presence of squalene antibodies prior to the GAO recommendations. Nothing could be further from the truth:

A. DOD's response to the GAO accused them of being "scientifically and fiscally irresponsible" for suggesting that DOD conduct research to dispute or validate the independent research findings. DOD's position was clear: until the peer-review and publication process by the private scientists was completed, it would not consider action that could provide answers to those suffering from Gulf War Illnesses. (GAO/NSIAD-99-5)

B. When DOD was interviewed by GAO during the investigation, its spokespersons acknowledged DOD had the know-how to develop such an assay and could have tested for squalene antibodies but did not.

C. When Dr. Bailey provided DOD's final comments to the GAO report, she stated, "Our position and the concerns expressed in our comments to the draft report have not changed." (DOD letter to the GAO dated May 28, 1999)

D. It was only after the U.S. House of Representatives took action and instructed DOD to cooperate with the GAO recommendations that Congress received notice from DOD of its funding of related research. This confirmatory research is being conducted by a DOD researcher. *(House of Representatives Report 106-244, Department of Defense Appropriations Bill, 2000)*

In light of these facts, it is disturbing that Dr. Bailey would construct paragraph four in such a way as to revise the sequence of events, and in doing so, misrepresent DOD's consistent position prior to legislative action.

In closing, Dr. Bailey states, "We are committed to responsible and aggressive pursuit of research that will further our understanding of illnesses among Gulf War veterans and prevent similar illnesses following future deployments." Unfortunately, something vital is missing from her statement: treatment and answers for those who are suffering. It is not acceptable to ask sick Gulf War-era veterans and their families to wait decades for endless research projects which do not generate help and treatment for those suffering. The consequences of this failed policy approach are all too clear to Congress, the American public, and especially the veterans exposed to and sickened by Agent Orange during the Vietnam War.

Our request to you on January 31, 2000 was straightforward and simple: determine if the assay used in the peer-reviewed, published study could be utilized as a diagnostic tool to help sick Gulf War era veterans. I would greatly appreciate your personal assistance to insure that DOD provide the objective analysis initially requested, including identification of those who are providing the analysis and their

professional credentials.

Thank you.

Jack Metcalf

Jack Metcalf
House of Representatives

cc: Representative Norm Dicks
Representative Walter Jones
Representative Bob Filner
Representative Janice Schakowsky
Representative Lane Evans
Representative Ron Paul
Representative Joe Scarborough
Representative Bernard Sanders
Representative Dan Burton

THE ASSISTANT SECRETARY OF DEFENSE

1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

MAR 27 REC'D

Honorable Jack Metcalf
United States House of Representatives
Washington, DC 20515-4702

Dear Congressman Metcalf:

Thank you for your recent letters on the Anthrax Vaccine Immunization Program's website and on the information I provided to you as requested in your inquiry of January 31, 2000. To address your request for additional objective analysis of this article, I have asked the Armed Forces Epidemiological Board to convene a subcommittee of experts to review and critique this work. I will provide you with this critique and, as requested, the curricula vitae of the reviewers. In addition, the National Academy of Sciences, Institute of Medicine (IOM), is assessing the role squalene may play as a cause of illnesses among Gulf War veterans and reviewing the work of Dr. Asa and her colleagues. The IOM expects to publish a report in August of this year.

The Department has considered your comments and suggestions regarding the Anthrax Vaccine Immunization Program's website. On March 10, 2000, the portion of the website describing the antibody test developed by Dr. Asa and colleagues was modified to read as follows: "Whether or not this test has any clinical meaning will be settled by medical experts over time. For now, it is sufficient to recognize the conclusions of the authors: "It is important to note that our laboratory-based investigations do not establish that squalene was added as adjuvant to any vaccine used in military or other personnel who served in the Persian Gulf War era.""

Our commitment to Gulf War veterans is unwavering. All known, testable hypotheses concerning illnesses among Gulf War veterans have been or are being pursued through our program of basic science research. All decisions on research funding are based on a process of rigorous, competitive, and independent peer review. We are committed to responsible and aggressive pursuit of research that will further our understanding of illnesses among Gulf War veterans and prevent similar illnesses following future deployments.

Sincerely,

Dr. Sue Bailey

Dr. Sue Bailey

Experimental and Molecular Pathology 68, 196–198 (2000)
Available online at http://www.idealibrary.com on IDEAL®

LETTERS TO THE EDITOR

To the Editor:

A recent article in this journal by Asa *et al.* (2000) purports to measure serum antibodies to squalene. The paper fails to establish the validity of the test. The essential flaws involve selection of proper positive controls and proper negative controls, quantitative methods, and selection of study populations.

The authors hypothesize that antibodies are induced by "the adjuvancy of squalene," such that injection of squalene could elicit antibodies to squalene. One approach might be to inject squalene into an experimental animal to determine *first* whether the injection can induce the purported antibodies and *second* whether the assay can detect the induced antibodies. Antibodies induced by injection, if they exist, could then serve as a positive control for the unvalidated assay.

The assay describes no positive controls that actually validate the assertion of detecting antibodies to squalene. Such positive controls would consist of comparable serum samples demonstrated to contain anti-squalene antibodies after injection with squalene.

The authors assert that they have positive controls, in the form of two human subjects previously injected with a squalene-containing placebo during a clinical trial at the National Institutes of Health. However, the authors provide no preinjection results to establish that intentional injection of squalene led to antibodies to a substance already present in the body.

The assay also lacks elementary negative controls routinely run in enzyme-linked immunoassays. Such negative controls are required to prove that the assay is not detecting cross-reacting substances. In a new, unproven assay that claims to detect a novel antibody, one must prove specificity. There were no negative controls in which the human serum containing the presumed antibodies was omitted or in which the avidin-conjugated horseradish peroxidase was omitted. There is no evidence that the assay was not simply measuring other IgG molecules with nonspecific binding to squalene. This could be easily accomplished by substituting an oil molecule similar to squalene. An excellent negative control would be squalane, the fully hydrogenated form of squalene.

The unknown human serum samples were tested only at a single dilution (1:400). Most assays for naturally occurring antibodies, particularly antibodies to lipids, start at a higher concentration of serum, typically a dilution of 1:50. Thus, the method of Asa *et al.* could miss the presence of antibodies detectable at a higher concentration of serum. It is possible that normal blood donors could give positive results at a higher concentration of serum.

A further drawback of using only a single dilution of serum, rather than a series of dilutions, is that there is no way to obtain a quantitative measure of the degree of activity in the sample. Titers are routinely obtained when antibody levels are measured. The absence of quantitation in this assay weakens meaningful comparisons between unknown serum samples from subjects accrued in a nonrandom manner.

Figure 1, said to show "antisqualene antibody responses," is particularly flawed. In this figure, unspecified quantities of squalene were added as aqueous dilutions of 1:10, 1:100, 1:1000 and 1:10,000 for impregnation of nitrocellulose. No explanation is provided for how an oil such as squalene, not soluble in water, could be diluted in water by the published methods. Further, a washing solution containing polyoxyethylene sorbitan monolaurate could have detergent-like qualities that could remove squalene. Despite the extensive dilutions of the squalene, there is no evidence of a dilution curve (assessing each strip vertically), regardless of whether the antibody reactions were rated as 3+, 2+, or 1+. This suggests that nonspecific binding of serum immunoglobulin may have occurred.

The conclusions of Asa and colleagues, purporting to correlate anti-squalene with Gulf War illnesses, in our opinion, rely on circular logic. Positive results with an assay not previously validated to detect antibodies cannot be used as scientific proof that antibodies to the antigen exist in samples of unknowns. It is premature to proceed directly to testing

serum samples from healthy people and sick people before conducting the fundamental validation steps.

The critique offered here is not meant to imply that antibodies to squalene do not or cannot exist. As pointed out by the authors, extensive work demonstrates that antibodies to cholesterol, a molecule for which squalene serves as a precursor, are found in virtually all normal human sera. A recent report proposes that naturally occurring antibodies to cholesterol may serve a vital physiologic function in helping regulate low-density lipoprotein metabolism in humans (Alving and Wassef, 1999).

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Asa, P. B., Cao, Y., and Garry, R. F. (2000). Antibodies to squalene in Gulf War Syndrome. *Exp. Mol. Pathol.* **68**, 55–64. doi:10.1006/exmp.1999.2295.

Carl R. Alving

Walter Reed Army Institute of Research
Silver Spring, Maryland 20910

John D. Grabenstein

U.S. Army Medical Command
Falls Church, Virginia 22041

This letter is doi:10.1006/exmp.2000.2314

Reply

To the Editor:

Alving and Grabenstein declare that our methods "do not establish the validity of the test." They are mistaken and have made a number of false assumptions about our methods and about which experiments were and were not performed to validate the anti-squalene antibody (ASA) assay. We also strongly disagree that animal work must precede human studies.

Our study (1) is the first description of anti-squalene antibodies in humans. Replicating our results in an animal model may well be useful for studying the possible role of ASA in Gulf War Syndrome (GWS), but is not a prerequisite by any standards we (or the peer reviewers of our manuscript) are aware of for establishing the validity of an immunoassay. For example, it was not essential to demonstrate antinuclear antibodies (ANA) in animals to develop a useful ANA assay for human autoimmune disease. Moreover, there is no assurance that small animals or even primates would respond immunologically to a squalene challenge. Production of ASA may require coinjection with or coexposure to additional substances or an autoimmune process not readily reproduced in an animal model.

It would also be unethical to inject squalene, a substance that has a 25-year history of causing both autoimmune rheumatological disease and neurological disease (Lorentzen, 1999; Grajkowska *et al.*, 1999), into humans to see if we could raise antibodies to it.

The ASA assay, a variation on the well-characterized Western blot assay, was validated by standard approaches used in immunoassay development. Alving and Grabenstein assert that "the assay lacks negative controls." However, each of the "elementary" negative controls they suggested, as well as many other controls, was in fact performed. The descriptions of these simple tests were not included in our paper for brevity. Assays in which either human serum or avidin-conjugated horseradish peroxidase was omitted gave no reaction. It should be noted that the reagents we used are precisely the same stringently validated reagents used to detect human antibodies to human immunodeficiency virus in commercially available Western blot assays. Squalane, a molecule similar to squalene, also gave no reaction in this assay. Furthermore, preincubation of positive human sera with squalene (but not squalane or other oils) blocked the assay in a dose-dependent manner. Squalene did not block another immunoassay, the HIV Western blot, further confirming the validity of the ASA assay.

Alving and Grabenstein are incorrect in their assumption that "the samples were tested at *only* a single dilution." In the process of optimizing the ASA assay, samples were tested at varying dilutions between 1:25 and 1:4000. 1:400 was determined to be the optimal dilution.

We did not indicate that squalene was soluble in water. Squalene, like many oils, can be finely dispersed in water and diluted as indicated. Western blot-style immunoassays differ from other types of immunoassays. Titers are not routinely obtained in Western blot-style immunoassays. At lower serum dilutions, some normal donors do react on the

ASA assay. This is to be expected and does not change the conclusions stated in our paper in any way.

Alving and Grabenstein assert that "a washing solution containing polyoxyethylene sorbitan monolaurate could have detergent-like properties that could remove squalene." This speculation is directly refuted by the results we presented. The ASA assay is similar in format to Western immunoblotting, in which proteins are tightly bound to nitrocellulose strips simply by drying. A similar method was used to apply squalene to the nitrocellulose strips used in the ASA assay. For this molecule, as with proteins in Western blots and nucleic acids in Southern and Northern blots, hydrostatic and other interactions with nitrocellulose are strong enough to resist removal by a weak detergent.

It is extremely unlikely that our results can be explained by "nonspecific binding of serum immunoglobulin." If this were the case, then similar or higher percentages of healthy donors or autoimmune patients (many of whom were hypergammaglobulinemic) would have detectable binding of serum antibodies in the ASA assay compared with GWS patients (ASA *et al.*, 2000). As this was not observed, the use of sera from these appropriate control populations further validates the ASA assay.

The ASA assay was rigorously validated by standard immunological methods prior to testing of serum samples from healthy and sick individuals. Circular logic was not used, and we stand firmly by the conclusions of our manuscript.

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This letter is doi:10.1006/exmp.2000.2315

Editorial Note

New findings require confirmation, within the bounds of comparability. This is as true for methodology as it is for the data produced from a particular study. This exchange of letters from the Office of the Surgeon General, United States Army, and the authors of "Antibodies to squalene in Gulf War Syndrome," *Exp. Mol. Pathol.* 68, 55–64 (2000), relates to methodology. Drs. Alving and Grabenstein offer no data against the conclusions of Asa *et al.*

The exchange will be judged by the scientific community on its merits, as all such matters should be. We point out only that Asa *et al.* are correct in their reply when they note that Western blot methods do not routinely measure relative titers, although some laboratories may report an intensity grade from the bands produced (e.g., 1+ to 4+).

The Editors

This note is doi:10.1006/exmp.2000.2316

SEARCH

1 document matched your query: (Anywhere: Carl Alving)

Results 1 to 1

Letter
Carl R. Alving, John D. Grabenstein
Experimental and Molecular Pathology, Vol. 68, No. 3, Jun 2000, pp. 196-197 (doi:10.1006/exmp.2000.2314)

Abstract | Article (PDF 17K)
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THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

AUG 10 REC'D

AUG 2 2000

Honorable Jack Metcalf
House of Representatives
Washington, DC 20515-4702

Dear Representative Metcalf:

I am pleased to provide you with the objective analysis that you requested for the article "Antibodies to Sqaualene in Gulf War Syndrome," published in the February 2000 issue of *Experimental and Molecular Pathology*. The Armed Forces Epidemiological Board convened a subcommittee of experts to review and critique this article and the attached response was unanimously endorsed and approved by the Board.

I hope we have answered the questions raised in your letter. Thank you for your interest in the health of Gulf War veterans.

Sincerely,

J. Jarrett Clinton, MD, MPH
Acting Assistant Secretary

Attachment:
As stated

cc:
Special Assistant for Gulf War Illnesses

AFEB (15-1a) 00-6 11 July 2000

SUBJECT: Armed Forces Epidemiology Board (AFEB) Recommendations Regarding Review of the Paper, "Antibodies to Squalene in Gulf War Syndrome by P. B. Asa, Y. Cao and R. F. Garry."

4. The Board unanimously endorses and approves the above findings and the enclosed report. Details of their findings can be found in the enclosed report.

FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD:

F. MARC LAFORCE, M.D.
AFEB President

BENEDICT M. DINIEGA
Colonel, USA, MC
AFEB Executive Secretary

3 Encls
1. Report
2. Tasking Letter
3. CVs

Copies Furnished:
Board Members
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COL Andrew S. Warde,
BvetMed Msc MRCVA
LCol Maureen Fensom, CFMS

REVIEW OF THE PAPER

ANTIBODIES TO SQUALENE IN GULF WAR SYNDROME
by PB Asa, YCao and RF Garry

published in
***Experimental and Molecular Pathology*, Volume 68, pp 55-64 (2000)**

A REPORT FROM
THE ARMED FORCES EPIDEMIOLOGICAL BOARD
JUNE 22, 2000

SUMMARY OF FINDINGS

The Armed Forces Epidemiological Board has thoroughly reviewed the paper by Dr. Asa and colleagues who describe a laboratory test they feel may identify persons ill with "Gulf War Syndrome." The AFEB has concluded unanimously that the research reported in this paper does not support this claim. The paper contains numerous shortcomings, several of them serious, that combine to invalidate the authors' conclusions. It remains unclear if the assay actually measures antibodies to squalene, as the authors assert; the assay may measure something else, or their findings may be a non-specific chemical reaction.

BACKGROUND

The Armed Forces Epidemiological Board (AFEB) was tasked by the Department of Defense (Health Affairs) to conduct an objective analysis of the above captioned paper by Asa *et al.* The tasking letter is enclosed.

A special subcommittee[1] of the AFEB was formed to initiate the task. The Special Subcommittee read the above captioned paper by Asa *et al.* The subcommittee fully discussed its impressions, questions and concerns, and developed a consensus document. The chair of the subcommittee then formally presented the subcommittee's findings to the entire AFEB[2] which had been supplied with the paper and the consensus document in advance of the meeting. After input from the entire AFEB, this final report is offered to the requester by the AFEB president.

FINDINGS

The AFEB reviewed the paper with great interest. However, the AFEB found the paper to contain a large number of scientific flaws, some of which are extremely grave. These flaws invalidate to an almost complete degree the conclusions regarding squalene and the implications that proceed from them. The major flaws include the following:

Controls: Despite assertions and disclaimers in the paper, there are no valid controls.

- For a valid positive control, one needs serum previously proven to contain antibodies to squalene; only this can validate that the assay can detect antibodies to squalene. What the authors use as and assert is a positive control are two sera from individuals reportedly vaccinated (either once or three times) with an NIH trial vaccine containing squalene. The authors provide no pre-vaccination data to demonstrate that the activity detected in their assay was not present before vaccination with a squalene adjuvant.
- Negative controls are essential to prove that the assay is not detecting something other than anti-squalene antibodies. Missing are controls which omit serum containing the presumed antibodies or which omit the avidin-conjugated horse radish peroxidase. Also missing is a negative specificity control to rule out non-specific binding of normal IgG molecules to squalene.

Blinding: It is unclear if the researchers were blind as to illness/wellness status of study participants.

- The paper asserts at several points that this is a blinded study, but it remains possible that the critical element of knowing the illness/wellness status or category may have been known, even if, as the paper states, "...The identities or exact number of samples from each category were not made available..."

[1] S Music, Chair; E Barrett-Connor, P Landrigan, Members; *curricula vitae* attached per written request of Congressman Metcalf to Defense Secretary Cohen, as "...objective analysis...including identification of those who are providing the analysis and their professional credentials."

[2] During the 30-31 May 2000 meeting of the AFEB at Ft. Detrick, MD.

- Thus, the authors' assertions, that they did not know which subjects had "Gulf War Syndrome" and which did not, are not convincing. If the authors knew which blood samples came from Gulf War veterans, this could have biased their interpretation of their test findings.

Specificity: Does the ASA Assay actually measure antibodies to squalene?

- In this type of blotting experiment, one normally demonstrates specificity of the reaction by blocking (or adsorbing) the antibody with the antigen (in solution). This is not demonstrated.
- Hence, it is not possible to know what the ASA assay detects. It is a Western-blot type assay, and is either positive (+) or negative (–). Since the paper describes it being used in only one dilution of patient serum (1:400), it seems the assay can determine only whether "something" was detectable or not, and this "something" is not presently definable.
- Antibodies to squalene, or to any other substance for that matter, should be detectable across a range of concentrations, so antibody assays are normally constructed to demonstrate this, the most common form today being an enzyme-linked immunoassay (ELISA). The actual level or concentration of antibody, ranging from undetectable to just detectable through high concentration, should have medical/biological correlations and implications, with some threshold point that correlates with the development of symptoms or disease.
- Nitrocellulose is a highly reactive substance that binds many materials. The paper does not show that the squalene deposited on the membrane is actually still there at the end of the assay. For example, one could imagine that squalene could "block" the nitrocellulose membrane long enough to protect the "dot" from the milk treatment and then be washed out, as polyoxyethylene sorbitan laurate is a detergent that could remove a lipid like squalene. This could leave a naked spot of nitrocellulose to react with some other protein.
- If this were a valid assay it should work with another substrate (other nylon membranes, like Immobilon).
- Given the relationship between squalene and cholesterol, do these sera react with cholesterol? The authors raise the question but don't answer it.
- Can one actually raise antibodies, deliberately, to squalene? It is a common component of cells and should be present in amounts that would swamp out any squalene-specific antibodies.

Dose response: None is apparent.

- In the figures of the Asa *et al* paper, there is no obvious dose response in relation to the amount of antigen (squalene) deposited on the nitrocellulose membrane.
- A dose-response should be seen with respect to antigen and antibody concentration; neither is shown.

CONCLUSIONS

In summary, the clear failure to provide positive controls and negative controls as well as unambiguous blinding, invalidates the authors' ability to argue for the meaningfulness of their test and any conclusions they might draw from these results. This is true even before one gets to the more technical issue of the specificity of the ASA assay.

Therefore, the AFEB has little confidence that the patent-pending ASA assay actually measures antibodies to squalene, though we cannot entirely eliminate this possibility.

Whatever the paper's flaws and since the AFEB cannot exclude the remote possibility that the authors have identified a laboratory means of distinguishing persons with possible Gulf War Syndrome (GWS) from all others, replicability becomes the major unresolved issue. The AFEB recognizes the difficulties inherent in defining a possible case of GWS since there is no standardized case definition. However, the AFEB feels that the symptom list in the Asa *et al* paper is a good potential starting point, and that, for example, cases might be selected from tertiary referral centers for GWS such as the one at Walter Reed, with controls from a civilian, non-exposed workforce. Therefore we recommend that a suitable test of replicability be done in cooperation with the authors and with attention to the following design elements:

- selection of participants - cases and control subjects - by an independent *ad hoc* body or committee, chaired by a tenured academic from a well-known medical research institution
- establishing clear *a priori* selection and exclusion criteria for cases and for controls
- serological testing done in a secure and absolutely blind manner with strict chain of custody rules and documentation in place
- a sufficient number of subjects to have statistical power to detect a true difference, if one exists, with 80% likelihood and with a 5% chance or less of finding a difference due to random chance alone.
- a study design with at least two arms – testing done as in the paper by the people who have licensed this patent-pending technique, versus testing done by one or more lipid laboratories using more standard antibody techniques such as enzyme-linked immunoassay to detect antilipid antigens

We wish to be clear that we are not discussing a study to validate whether the ASA assay can detect antibodies to squalene. Rather, we are trying to leap over this intermediate obstacle and get quickly and inexpensively to a more meaningful bottom line: does the ASA assay clearly, reliably and unequivocally distinguish people with GWS from all others, and, if so, with what specificity and sensitivity? Many caveats and qualifiers would have to be in place to assure meaningfulness, and the preceding bulleted list can (and probably should) be usefully expanded and further refined to help assure that any ensuing serological study be definitive.

The AFEB is extremely doubtful that the assay reported by Asa *et al* is a valid or accurate test for illness among Gulf War veterans. However in an effort to leave no stone unturned in evaluating veterans' complaints, the AFEB feels it may be worthwhile to repeat the study, using appropriate scientific methods as outlined above. This recommendation should definitely not be considered an endorsement of the paper by Asa *et al* that we have herewith reviewed.

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

09 MAR

HEALTH AFFAIRS

MEMORANDUM FOR EXECUTIVE SECRETARY, ARMED FORCES EPIDEMIOLOGICAL BOARD

SUBJECT: Objective Analysis of Article "Antibodies to Squalene in Gulf War Syndrome"

I request that the Armed Forces Epidemiological Board (AFEB) convene a subcommittee and review and provide OASD(HA) with an objective analysis of the attached article, "Antibodies to Squalene in Gulf War Syndrome" published in the February 2000 issue of *Experimental and Molecular Pathology*. Congressman Jack Metcalf requested this objective analysis. Congressman Metcalf would also like the curriculum vitas of the reviewers.

OASD(HA) will provide Congressman Metcalf with this critique and the curriculum vitas of the reviewers when complete. Please provide this review NLT 15 May 2000. To assist in this review, I have attached an extensive review of the work on squalene as a cause of illnesses among Gulf War veterans by the interagency Research Working Group of the Persian Gulf Veterans Coordinating Board prior to publication of the article and previous correspondence with Congressman Metcalf's office on this topic.

My point of contact is James R. Riddle, LtCol, USAF, BSC, (703) 681-1703, fax (703) 681-3655, or email james.riddle@ha.osd.mil.

John F. Mazzuchi

John F. Mazzuchi, Ph.D.
Deputy Assistant Secretary of Defense
Clinical and Program Policy

Attachments:
As Stated

CURRICULUM VITAE

I. PERSONAL DATA

A. Name: Stanley I. Music, M.D., DTPH (Lond.)

B. Home Address: 9 Deaver Place, Wyncote, PA 19095-1726

C. Home Telephone: 215-376-0223

II. EDUCATION

Institution	Date	Major/Minor Courses	Degree
University of London; London School of Hygiene and Tropical Medicine	1975-1976	Tropical Public Health	Diploma
Centers for Disease Control and Prevention – Atlanta, GA	1972-1973	Preventive Medicine	Resident
University of Maryland School of Medicine; Baltimore, MD	1966-1970	Fellow in Infectious Disease; Assistant Resident in Internal Medicine; Junior Assistant Res in Internal Medicine; Intern in Internal Medicine	Fellow, Resident, Intern
University of Maryland School of Medicine; Baltimore, MD	1962-1966	Doctor of Medicine	MD
George Washington University Washington, DC	1962	Invertebrate zoology and entomology	BS
George Washington University Washington, DC	1961	Liberal arts	AA

III. MERCK/MRL EMPLOYMENT HISTORY

Title	From – To
Director, Report Evaluation and Safety Surveillance Worldwide Product Safety and Epidemiology Department Merck Research Laboratories, Blue Bell, PA	May 1999 to present

IV. NON-MERCK EMPLOYMENT HISTORY

Title	From - To
Medical Epidemiologist Division of Women's and Children's Health, Department of Health and Human Services; State of North Carolina; Raleigh, NC	June 1998 to May 1999
Chief, Occupational and Environmental Epidemiology Division of Epidemiology, Department of Health and Human Services; State of North Carolina; Raleigh, NC	November 1996 – May 1998
Senior Regional Advisor for the Caucasus and Embassy Physician; United States Agency for International Development and American Embassy; Tbilisi, Republic of Georgia	1995 - 1996
Administrator, Division of Preventive Medicine and State Epidemiologist; then State Health Officer (last 6 months) Department of Health, State of Wyoming; Cheyenne, WY	1991 - 1994

Director, Global EIS Program; CDC, USPHS; Atlanta, GA	1986 - 1990
Deputy Director, Global EIS Program; CDC, USPHS; Atlanta, GA	1983 - 1986
Staff Epidemiologist, Policy Unit Population, Health and Nutrition Department, World Bank; Washington, DC	1982 – 1983
Deputy Director; Field Services Division, Atlanta, GA	1977-1982
Assistant Director; Field Services Division, Atlanta, GA	1976-1977
Full Time Internal Student, CDC Career Development; University of London, School of Hygiene and Tropical Medicine	1975 – 1976
Smallpox Eradication Advisor; Dacca, Bangladesh	1973 – 1975
Epidemic Intelligence Service Officer; Florida Department of Health and Rehabilitative Services; Jacksonville, FL	1971 – 1973

V. ACADEMIC EXPERIENCE

Instructor, Division of Infectious Diseases; University of Maryland School of Medicine; Baltimore, MD	1970 – 1971

VI. ADDITIONAL TRAINING

Source	Date	Type	Certification
American Management Association	1980	3 week course	Yes
Oak Ridge Nuclear Facility: Response to Nuclear Disaster	1992	1 week course	Yes

VII. SOCIETY MEMBERSHIPS and OTHER PFOFESSIONAL EXPERIENCES

Member, Armed Forces Epidemiology Board, US Department of Defense; 1998 to present
Georgian Academy of Sciences of Preventive Medicine and Human Ecology; 1996
Fellow, American College of Preventive Medicine; 1979
Diplomate, American Board of Preventive Medicine; 1978
Fellow, Royal Society of Hygiene and Tropical Medicine; 1975
Chairman, Scientific Advisory Committee; 1989-1991
Member, Scientific Advisory Committee, Caribbean Epidemiology Center (PAHO),
Port of Spain, Trinidad and Tobago; 1988-1991
Consultant, Assessment of Health Needs, USAID Assessment Team, Sultanate of Oman, 1980
WHO Epidemiological Services Consultancies:
Indonesia, 1979; Indonesia, Burma, Bangladesh, 1978; Republic of Korea, 1977
Post-liberation Nutrition Survey, CDC Assessment Team, Bangladesh; 1972
Research Physician, Infectious Diseases Hospital, University of Chile, Santiago, Chile; 1970
Attending Physician, Cholera Hospital, Pakistan-SEATO Cholera Research Laboratory; Dacca, East Pakistan; 1967-1968

VIII. HONORS

US Public Health Service Meritorious Service Medal - 1997
US Public Health Service Outstanding Service Medal - 1985
US Public Health Service Commendation Medal - 1979

IX. PUBLICATIONS

1. Music, S. I., Wenzel, R. P., Libonati, J. P., Snyder, M. J., Hornick, R. B., Woodward, T. E; Induced Human Cholera (abstract), Journal of Clinical Investigation, 49:69-70a, June 1970
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21. Music, S. I., Khetsuriani, N.: Epidemiology Bulletin, Ministry of Health, Republic of Georgia. Vol 1, Nos. 1-6:1-120, January – June 1996. (Though listed officially as *CDC Advisor* my actual role was to first do and then train others in how to do every step from conception and writing through publication and distribution of the first six monthly issues of this official publication of the Georgian government. These are available in English via Internet and the CDC homepage on SANet: http://www.sanet.ge/cdc/index.html.

22. Music, S. I., Georgia's public-health problems. Ltr to the Editor in Lancet, 348 (9043), Dec 21, 1996.
23. Smith, C. G., Music, S. I.: Pfiesteria in North Carolina: The Medical Inquiry Continues. NC Medical Journal, 59(4), Jul-Aug 1998.
24. Furney, W., Music, S. I., Wiley, J.: North Carolina Childhood Asthma Management Initiative: A Summary of the Summary Report. NC Medical Journal, 60(4), Jul-Aug 1999.
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CURRICULUM VITAE

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COLLEGE:	Mount Holyoke College, South Hadley, Massachusetts, 1952-1956 - Zoology
MEDICAL SCHOOL:	Cornell University Medical College, New York City, 1956-1960 - Medicine
INTERNSHIP:	University of Texas, Southwestern Medical School, Dallas, Parkland Memorial Hospital, 1960-1961
RESIDENCY:	University of Texas, Southwestern Medical School, Dallas, Parkland Memorial Hospital, 1961-1963 University of Miami, School of Medicine, Jackson Memorial Hospital, Infectious Diseases, 1963-1964
POST-DOCTORAL:	London School of Hygiene & Tropical Medicine 1964-1965 – D.C.M.T., Diploma in Clinical Medicine of the Tropics University of Minnesota, Minneapolis, 1967 (3-week course) Advanced Epidemiology - Certificate Johns Hopkins University, Bar Harbor, Maine, 1968 (2-week course) Genetics - Certificate

FELLOWSHIPS:

Medical Student Fellowship in Public Health and Preventive Medicine, Cornell University Medical College, 1958
Louisiana State University Interamerican Program in Central America, Summer 1962
National Institutes of Health Post-Doctoral Fellowship, London School of Hygiene and Tropical Medicine, 1964-5
Fulbright Award (declined), 1964

DEGREES:

B.A., Mount Holyoke College, 1956
M.D., Cornell University, 1960
D.C.M.T., London School of Hygiene and Tropical Medicine, 1965

FACULTY APPOINTMENTS:

University of Miami, School of Medicine
Instructor of Medicine, 1965-1968
Assistant Professor of Medicine, 1968-1970

University of California, San Diego School of Medicine
Assistant Professor of Community Medicine and Medicine, 1970-1974
Associate Professor of Community and Family Medicine and Medicine, 1974-1981
Chief, Division of Epidemiology 1974-present
Professor of Family and Preventive Medicine and Medicine, 1981-present
Acting Chair, Department of Community and Family Medicine, 1981-1982
Chair, Department of Family and Preventive Medicine, 1982-1997

HONORS, NAMED LECTURESHIPS, AND VISITING PROFESSORSHIPS:

Frederick Murgatroyd Prize, London, 1965
Invited Participant, Bicentennial Colloquium of the New York Hospital, 1971
Invited Participant, Meeting Commemorating the 25th Anniversary of Dr. Donald W. Seldin's Chairmanship of the Department of Internal Medicine, The University of Texas, Dallas, 1977
Invited Participant, Symposium on the Advances in Diabetes Epidemiology, Colloquium Inserm, NIH, OMS. Abbaye de Fontevraud, France, May 3-7, 1982
Kaiser Award for Excellence in Teaching, University of California San Diego, School of Medicine, 1982

Living Legacy Award, Women's International Center, San Diego, California, March 6, 1984
Alexander D. Langmuir Lecture, Centers for Disease Control, Atlanta, April , 1985
Honorary Doctor of Science Degree, Mount Holyoke College, South Hadley, Massachusetts, May 26, 1985
Doctor of the Year Award, San Diego Health Care Association, San Diego, November 18, 1985
Katharine Boucot Sturgis Lecture, American College of Preventive Medicine, Atlanta, April 5, 1986
Kelly West Memorial Lecture/Award, American Diabetes Association, Indianapolis, June 6, 1987
Merit Award, National Institute of Aging, July, 1987 –1996
Visiting Professor, Royal Society of Medicine, London, May 1989.
John Rankin Lecture, Madison, Wisconsin, October 20, 1989
Don McLeod Memorial Lecture, Halifax Nova Scotia, February 9, 1990.
Member, Institute of Medicine, 1991
Elizabeth Blackwell Lecture, Rochester, Minnesota, September 18, 1991
The Lila Wallace Visiting Professorship, The New York Hospital/Cornell Medical Center, March 4-5, 1992
The Donald P. Shiley Visiting Lectureship, Scripps Clinic and Research Foundation, San Diego, March 13, 1992
Outstanding Educator Award, Association of Teachers of Preventive Medicine, March 22, 1992
Leonard M. Schuman Lecture, University of Michigan, Ann Arbor, July 28, 1993
Wade Hampton Frost Lecture, American Public Health Association, San Francisco, October 25, 1993
Joe Stokes Lecture Research Seminar, Grand Rounds, Boston, November 11, 1993
University of California, San Diego, Faculty Research Lecturer Award, March 10, 1994
James D. Bruce Memorial Award, American College of Physicians, April 21, 1994
Soroptimist International of La Jolla Award, Making a Difference for Women, Health, June 7, 1995
Ancel Keys Lectureship, American Heart Association Scientific Sessions, November 13, 1995
American Heart Association, Elizabeth Barrett-Connor Research Award in Epidemiology and Prevention for Investigators In Training, November 14, 1995
UCSD Chancellor's Associates Faculty Excellence Award in Research, January 31, 1996
Honorary Doctor of Medicine Degree, University of Utrecht, The Netherlands, March 26, 1996
Honorary Doctor of Medicine Degree, University of Bergen (Norway), August 3, 1996
The Florence Mahoney Lecture on Aging, National Institures of Health, September 25, 1996
Arthur Gordon Visiting Professor, University of California, Los Angeles, October, 1996
American Heart Association Council on Epidemiology and Prevention, Distinguished Service Award, November 12, 1996

The Donald P. Shiley Visiting Lectureship, Scripps Clinic and Research Foundation, March, 1997
The Cleveland Clinic Foundation Department of Cardiology Visiting Professor, June, 1997
John Cassell Memorial Lecture, Society for Epidemiologic Research, 30th Annual Meeting, June 12, 1997
Clinical Service Award, Society for the Advancement of Women's Health Research, June 24, 1997.
Raine Distinguished Visitor's Award, The University of Western Australia, October 26 - November 5, 1997
Distinguished Lecturer in Geriatrics, Duke University Medical Center, J January 29-30, 1998
13th Annual Harry S. Feldman Lecture, American Epidemiologic Society (AES) Meeting, Harvard Medical School, March 26, 1998
Award of Meritorious Achievement of the American Heart Association, Dallas, Texas, June 26, 1998
Women's Health Hero Award – American Health for Women, New York, September, 1998
Woman in Science Award – American Medical Women's Association, New Orleans, November, 1998
Nathan J. Kiven Oration and Brownwide Grand Rounds, The Miriam Hospital and Brown University,Rhode Island, April 9, 1998
Alvin L. Schultz Visiting Professor of Internal Medicine, Minneapolis, October 20, 1998
Visiting Professor, Brigham and Women's Hospital, Boston, Massachusetts, November, 1998
National Institutes of Health Award for Outstanding Work in Gender Differences in Osteoporosis, March, 1999
Heath Clark Lectureship, London School of Hygiene and Tropical Medicine, London, England, March, 1999
Invited Participant, Controversies and Dilemmas in Endocrinology, Royal College of Physicians of Edinburgh, Scotland, March, 1999

GRANTS:

National Institutes of Health, Lipid Research Clinic, Veterans Administration Hospital, La Jolla, California, 1970-1989 .
Janssen Drug Study Fund, 1976-1978.
National Institutes of Health, Peripheral Arterial Disease Grant #HL22255-01, April 1, 1978, - November 30, 1980.
American Heart Association, California Affiliate, Grant-in-Aid, #80-S114, July 1, 1980 - June 30, 1981.
National Institute of Arthritis, Diabetes, Digestive & Kidney Diseases, Epidemiology of Diabetes in an Adult Community #1 RO1 AM31801, July 1, 1983 - June 30, 1988.

UCSD/SDSU Teaching Nursing Home Project. #NIA AG03990-01A1, May 1, 1984 - April 30, 1989.

National Institutes of Health, National Heart, Lung and Blood Institute, PHS HL34591, Endogenous Sex Hormones & Cardiovascular Disease Risk in Men, April 1, 1986 - March 31, 1987.

American Heart Association California Affiliate, Orange County Chapter Grant-in-aid-Dietary Factors, Blood Pressure and Cardiovascular Disease, #85-S116, July 1, 1986 - December 31, 1988.

Weight Watchers - Analyzing in Detail Extensive Database with Regard to Obesity and Heart Disease, January 1,1987 - December 31, 1989.

National Institute of Health - National Institute of Aging- Study of Risk Factors for Osteoporosis in the Elderly. #NIH/NIA 1 R37 AG07181-01, UCSD #90-6518, August 1, 1987 - July 31, 1992 (Merit Award).

National Institute of Health - Postmenopausal Estrogen/ Progestin Interventions (PEPI). #NIH 1001- HL40207-01, UCSD #90-6500. September 3, 1987 - August 31, 1992.

University of California Academic Geriatric Resource Program-Interdisciplinary Geriatrics Fellowship Program. #87SD-C2D-2-01, July 1, 1987 - June 30, 1988.

National Institute of Diabetes and Digestive and Kidney Diseases - Epidemiology of NIDDM and IGT in an Adult Community. UCSD #88-5256, July 15, 1988 - June 30, 1990.

American Association of Retired Persons.- The Effects of Husbands' Retirement on Their Wives. UCSD #87-6259, January 1, 1988 - December 31, 1988.

National Institute of Health, NHLBI - LRC Follow-up Study--CPPT and Prevalence. UCSD #6947, June 29, 1971 - September 30, 1991.

National Institute of Health, NIA - Alzheimers Disease Research Center Competitive Supplement. UCSD #89-6638, August 17, 1990 - March 31, 1994.

National Institute of Health - Predictors of Cardiovascular Disease in the Elderly. UCSD #90-6070, January 1, 1991 - December 31, 1991.

National Institute of Health, NIDDK - Epidemiology of NIDDM and IGT in an Adult Community. UCSD #91-6083, December 1, 1991 - November 30, 1996.

National Institute of Health - Epidemiology of NIDDM and IGT Supplement. UCSD #92-6591, June 1, 1992 - February 28, 1993.

National Institute of Health, NIA - Study of Risk Factors for Osteoporosis

in the Elderly (Osteo II). UCSD #91-6122. August 1, 1992 - July 31, 1997. (Merit Award)

Merck, Sharp and Dohme, Fracture Intervention Trial (FIT). UCSD #92-5548, October 1, 1991 - March 31, 1997.

National Coffee Association, "Coffee/Caffeine/Bone Mineral Density". UCSD #92-6164, February 1, 1992 - January 31, 1993 (no cost extension August 31, 1993).

Solvay Pharmaceuticals - A Double-Blind, Parallel Group Study of the Effects of Estratest H.S. vs. Premarin in Surgically Menopausal Women. UCSD #92-6838. June 1, 1992 - May 31, 1995.

Wyeth-Ayerst, Heart & Estrogen/Progestin Replacement Study (HERS). UCSD #91-5180. October 8, 1992 - December 31, 1998.

National Institute of Health, NHLBI - Postmenopausal Estrogen/Progestin Interventions (PEPI). UCSD #92-5242. August 1, 1992 – July 31, 1994.

Weight Watchers. Sex hormones, obesity and diabetes in older women. UCSD #93-7168. November 1, 1993 - October 31, 1994.

National Institutes of Health, NIDDK. NIDDM Primary Prevention Trial. UCSD #94-5368, July 1, 1994 to June 30, 2001. (Co-PI)

National Institute of Health, NHLBI, Postmenopausal Estrogen-Progestin Intervention (PEPI) Safety Followup Study, N01-HV-48136, June 15, 1994 to December 14, 1997.

National Institute of Health, NHLBI, Postmenopausal Estrogen-Progestin Intervention (PEPI) Safety Followup Analysis Study, N01-HV-48136, August 1, 1994 to July 31, 1997.

Lilly Research Laboratory. Comparison of Raloxifene HCL and Placebo in the Treatment of Postmenopausal Women with Osteoporosis. UCSD #95-5368, November 1, 1994 to October 31, 1999.

Wyeth-Ayerst Laboratories. A Randomized, Double-Blind Placebo & Active Controlled, Parallel, Multicenter Study to Assess the Safety & Efficacy of 3 1/2 Day Combinations of 17B-Estradiol Norethindrone Acetate Transderma Delivery Systems for Relief of Menopausal Vasomotor Symptoms & Reduction of Endometrial Hyperplasia. UCSD#97-9150. May 27, 1997 to April 30, 1999.

Osteometer Meditech A/S. Bone Mineral Content & Density in the Forearm, Speed of Sound, & Boradband Ultrasound Attenuation in the Calcancus: Normal Range in US Caucasian Females & Males, 20-80 years of age. UCSD #98-9010. June 15, 1997 to December 31, 1997.

Osteometer Meditech A/S. Forearm Mineral Density in the Normal Caucasian Female Population in the Calcancus: Normal Range in US Caucasian Females & Males, 20-80 Years of Age. UCSD 97-9099. December 15, 1997 to January 31, 1997.

Merck & Co. A 5-Year, Double-Blind, Randomized, Placebo-Controlled Extension Study to Examine the Long-Term Safety & Efficacy of Oral Alendronate In Postmenopausal Women Who Previously Received Alendronate in Conjunction with the Fracture Intervention Trial (FLEX) UCSD #98-9051. January 3, 1998 to October 30, 2003.

National Institutes of Health, Soy Health Effects (SHE). 1RO1 HL57790-01, April 1, 1997 to March 31, 2000.

National Institutes of Health/NIDDK, Diabetes Primary Prevention Program (DPP). 5UO1 DK48339-04, September 10, 1994 to June 30, 2001.

National Institutes of Health, Comparison of Medical and Surgical Treatment for Abnormal Uterine Bleeding Post-Menopausal Women (Ms?). September 30, 1996 to September 29, 2001.

Eli Lilly & Co. Raloxifene Hydrochloride or Placebo in Postmenopausal Women At Risk for Major Cardiovascular Events. UCSD #98-9146. September 4, 1998 – September 30, 2005.

National Institutes of Health, NIA. Gender Differences in Osteoporosis (OSTEO III) UCSD #98-6285. December 1, 1998 to November 30, 2002.

National Institutes of Health, Osteoporotic Fractures in Men (MR.OS). UCSD #98-6088. December 10, 1998 to November 30, 2003.

MEDICAL QUALIFICATIONS:

Licensure, Florida, 1965
Licensure, California, 1970 (#C-32076)
Diplomate, American Board of Internal Medicine, 1968
Diplomate, National Board of Medical Examiners

PROFESSIONAL SOCIETY MEMBERSHIPS:

Fellow, American College of Physicians (Publications Committee, 1988-90)
Fellow, Council on Cardiovascular Epidemiology, America Heart Association (Chair, 1989)
Fellow, Royal Society of Health
Fellow, American College of Preventive Medicine
Fellow, American College of Nutrition
Fellow, The Royal Society of Medicine
Member, American Venereal Disease Association (Vice-President, 1977-1978)
Member, American Federation for Clinical Research
Member, Association of Teachers of Preventive Medicine (Board of Directors, 1987-90)
Member, Infectious Disease Society of America

Member, International Epidemiological Association
Emeritus Member, American Society of Tropical Medicine and Hygiene
Member, Society for Epidemiologic Research (President, 1983)
Member, Association for Practitioners in Infection Control
Member, California Academy of Preventive Medicine
Member, Western Association of Physicians
Member, American Epidemiological Society (President, 1993-94)
Member, American Diabetes Association
Consultant, Veterans Administration Hospital, Miami, 1969
Consultant/Lecturer in Internal Medicine (Infectious Diseases), U.S. Naval Hospital, San Diego, 1970-85
Consultant, Mercy Hospital, San Diego, 1970-85
Consultant, American Medical Association Department of Drugs, Chicago, 1976
Member, Hospital Infection Control Committee, University Hospital, San Diego, 1970-1972 (Chairman 1975-1977)
Member, Hospital Infection Control Committee, Veterans Administration Hospital, La Jolla, 1971-85
Member, Research Committee, Zoological Society of San Diego, 1978-86
Member-at-Large, Research Peer Review Sub-Committee, American Heart Association, California Affiliate, 1977-1981
Member, Advisory Committee for Genetic Disorders, California Department of Health, 1974-1975
Ad hoc member, Study Section, Center for Disease Control, Atlanta, 1971-1972
Member, Expert Advisory Committee, Food & Drug Administration, Rockville, 1972-1977
Member, Advisory Council on Immunization Practices, Center for Disease Control, Atlanta, 1973-1977
Member, Preventive Medicine and Public Health Test Committee, National Board of Medical Examiners, Philadelphia, 1974-1980 (Chair, 1977-1980)
Member, Epidemiology Working Group, National Commission on Arthritis and Musculoskeletal Diseases, Boston, 1975-1976
Ad hoc Member, National Institute of Allergies and Infectious Diseases Committee, HEW/NIH, 1977
Member, Consultant Task Force for the Study of Health in Egypt and Future U.S. Development Assistance Alternatives, National Institute of Medicine, 1978
Member, National Institute of Allergies and Infectious Diseases

Committee, 1978-1982
Member, American Tropical Medicine Delegation to China, American Society of Tropical Medicine and Hygiene, 1978
Member, The American Geriatrics Society, 1987-present
Member, Medical Research and Development Advisory Panel, Review Group Concerned with Parasitic Diseases, Walter Reed Army Institute of Research, Department of the Army, 1979-1982
Member, Special Consultants to Department of Defense Overseas Medical Research Laboratories, US Department of Defense, 1980
Consultant, Task Force, Institute of Medicine, Division of International Health, Health in Egypt: Recommendations for U.S. Assistance, January, 1979
Member, Core Faculty, Annual Seminars on Epidemiology of Cardiovascular Disease, American Heart Association, 1978-present
Member, California Medical Association Scientific Advisory Panel; Preventive Medicine and Public Health, 1982-present
Member, American Epidemiological Society Membership Committee 1987-present
Member, Advisory Committee, Role of BCG Vaccinations in the United States, Research Foundation, 1983-1985
Member, (San Diego) Mayor's Task Force for Acquired Immunity Deficiency Syndrome (AIDS), 1983-1985
Member, Epidemiology Research Unit, University of Texas, 1983-1986
Member, National Advisory Committee on Vital and Health Statistics, May 30, 1984 - February 28, 1987
Member, American Public Health Association, Epidemiology Section, (Chair, 1989-91)
Member, European Diabetes Epidemiology Study Group, 1984- present
Member, NHANES III Advisory Committee (FACEB), 1985
Member, Preventive Medicine Residency Advisory Committee, San Diego (Chair, 1985)
Member, Epidemiology and Biometry Program Working Group, Subcommittee of the Clinical Applications and Prevention Advisory Committee (CAPAC), National Heart, Lung, and Blood Institute, Bethesda, Maryland, 1985-1987
Member, Burroughs-Wellcome Fund/American College of Preventive Medicine Pharmacoepidemiology Award Advisory Committee, 1986-1989
Member, San Diego Foundation for Medical Care, 1986-present
Member, Resource Advisory Committee on the Epidemiology of the

Chronic Diseases of Aging of the National Archives of Computerized Data on Aging, 1988-1994
Member, Technical Advisory Committee for Diabetes Translation and Community Control Programs, Centers for Disease Control, February 6, 1989 - June 30, 1991.
Member, International Epidemiological Association (North American Councillor, 1990-present)
Member, International Scientific Committee for the 3rd International Conference on Preventive Cardiology, 1989-1990
Member, U.S. Army Research and Development Advisory Committee, Ft. Detrick, Frederick, Maryland 1990-1993
Member, International Society and Federation of Cardiology, Section on Epidemiology, 1990-present
Member, National Heart, Lung, and Blood Institute Task Force on Hypertension 1990-93
Member, National Diabetes Advisory Board, National Institutes of Health, 1990-1994
Member, The Royal Society of Medicine, 1992-present
Member, Advisory Board of the HERITAGE Study, 1992-present
Member, Faculty, WHO Postgraduate Seminar on Diabetic Epidemiology (Krakow, Poland), 1992
Member, Data and Safety Monitoring Board, Women's Health Initiative, 1993-present
Member, Faculty of International Society & Federation of Cardiology Teaching Seminar 1993-present
Councilor, Western Association of Physicians, 1994-97
Member, Human Subjects Program Review Committee, UCSD, 1994-present
Member, The New York Academy of Sciences, 1995-present
Member, Scientific Advisory Board, Ostex International, Inc., 1995-present
Member, Raloxifene Advisory Board, Eli Lilly and Company, 1995-present
Member, American Federation for Aging Research, National Scientific Advisory Committee, 1996
Member, Membership Committee, Institute of Medicine, 1996-1999
Member, Armed Forces Epidemiology Board, 1996 -
Member, Advisory Council, National Instiurte of Aging-1996-
Member, Advisory Council, National Institute of Aging, 1997 –
Board of Directors, North American Menopause Society, 1997-
National Institues of Health/Women's Health Initiative: Data and Safety Monitoring Board, 1997-

Member, Editorial Board, American Journal of Preventive Medicine, 1998-
Sigma Xi – The Scientific Research Society, 1998 –
Member, National Lipid Education Council, 1998-
Member, Science Advisory Board, County of San Diego, 1999-
Member, Medical Committee, Royal Netherlands Academy of Arts and Sciences, 1999-
Member, Endocrine Society, 1999-

REVIEWER:

Annals of Internal Medicine, 1974-present
Review of Respiratory Diseases, 1974-present
New England Journal of Medicine, 1974-present
Journal of American Medical Association, 1975-present
Public Health Reports, 1975-1985
Emergency Medicine, 1975-1980
Western Journal of Medicine, 1975-present
American Journal of Tropical Medicine and Hygiene, 1979-present
Arthritis and Rheumatism, 1981-present
American Journal of Epidemiology, 1981-present
Reviews of Infectious Diseases, 1982-present
Arteriosclerosis, 1984-present
Circulation, 1985-present
Journal of Chronic Disease, 1982-present
Preventive Medicine, 1988-present
International Journal of Gynecology & Obstetrics, 1994-present

EDITORIAL BOARDS:

American Journal of Epidemiology
American Journal of Infection Control, 1981-1986
American Journal of Preventive Medicine
Annals of Epidemiology
Annals of Internal Medicine, 1979-82
Cardiovascular Risk Factors, 1995-present (Member of Advisory Board)
Circulation
International Journal of Epidemiology
Journal of Clinical Investigation (Consulting Editor), 1995-1997
Reviews in Clinical Gerontology
Sexually Transmitted Diseases, 1977-81
The Women's Letter
Menopause

November 1999

CURRICULUM VITAE

Name: Philip J. Landrigan, M.D., M.Sc., D.I.H.
SSN: 022-32-0504

Born: Boston, Massachusetts, June 14, 1942

Wife: Mary Florence

Children: Mary Frances
Christopher Paul
Elizabeth Marie

Education:

High School:	Boston Latin School, 1959
College:	Boston College, A.B. (magna cum laude), 1963
Medical School:	Harvard - M.D., 1967
Internship:	Cleveland Metropolitan General Hospital, 1967-1968
Residency:	Children's Hospital Medical Center, Boston, (Pediatrics), 1968-1970
Post Graduate:	London School of Hygiene & Tropical Medicine, 1976-77 Diploma of Industrial Health (England), 1977 Master of Science in Occupational Medicine, University of London (with distinction), 1977

Positions Held:

Current:

Mount Sinai School of Medicine, Ethel H. Wise Professor of Community and Preventive Medicine and Chairman of the Department of Community and Preventive Medicine, 1990-Present.

Mount Sinai School of Medicine, Director, Division of Environmental and Occupational Medicine, Department of Community and Preventive Medicine, 1985-Present.

Mount Sinai School of Medicine, Professor of Pediatrics, 1985-Present.

Previous:

U.S. Environmental Protection Agency, Senior Advisor to the Administrator on Children's Health and the Environment, 1997-1998.

National Institute for Occupational Safety and Health, Director, Division of Surveillance, Hazard Evaluations and Field Studies, 1979-1985.

Centers for Disease Control, Chief, Environmental Hazards Activity, Cancer and Birth Defects Division, Bureau of Epidemiology, , 1974-1979.

Centers for Disease Control, Director, Research and Development, Bureau of Smallpox Eradication, 1973-1974.

Centers for Disease Control, Epidemic Intelligence Service (EIS) Officer, 1970-1973.

Adjunct Positions:

University of Washington School of Public Health and Community Medicine, Clinical Professor of Environmental Health, 1983 - Present.
Harvard Medical School, Visiting Lecturer on Preventive Medicine and Clinical Epidemiology, 1982 - Present.
Harvard School of Public Health, Visiting Lecturer on Occupational Health, 1981 - Present.
University of Cincinnati, Department of Environmental Health, College of Medicine, Assistant Clinical Professor of Environmental Health, 1981 - 1986.
London School of Hygiene and Tropical Medicine, Visiting Fellow, TUC Institute of Occupational Health, 1976 - 1977.
Harvard Medical School, Clinical Instructor in Pediatrics, 1969 - 1970.

Memberships:

American Academy of Pediatrics, Fellow
Society for Epidemiologic Research, Member
American Public Health Association, Member
Occupational Health Section, Chair, 1989-90
Royal Society of Medicine, Elected Fellow
International Commission on Occupational Health, Member
Scientific Committee on Epidemiology
American College of Epidemiology, Fellow
Board of Directors, 1990 - 1993.
American Epidemiological Society, Elected Member
Collegium Ramazzini, Fellow
President, 1997-present
Herman Biggs Society, Member
New York Academy of Sciences, Fellow
New York Occupational Medicine Association, Member
Board of Directors, 1988 - 1990.
American College of Occupational and Environmental Medicine, Fellow
New York Academy of Medicine, Elected Fellow
Physicians for Social Responsibility, Member
Board of Sponsors, 1994-95; Board of Directors 1996-1999

Specialty Certifications:

American Board of Pediatrics - 1973
American Board of Preventive Medicine:
General Preventive Medicine - 1979
Occupational Medicine - 1983

Awards and Honors:

Institute of Medicine, National Academy of Sciences, Elected to membership, 1987
U.S. Department of Health, Education and Welfare ,Volunteer Award, 1973
U.S. Public Health Service, Career Development Award, 1976
Centers for Disease Control, Group Citation as Member of Beryllium Review Panel, 1978
U.S. Public Health Service, Meritorious Service Medal, 1985
New York Committee for Occupational Safety and Health, Annual Honoree, 1985
New England College of Occupational and Environmental Medicine, Harriet Hardy Award, 1993
United Brotherhood of Carpenters, William Sidell Presidential Award, 1995
American Public Health Association, Herbert L. Needleman Medal and Award for Scientific Contributions and Advocacy on Behalf of Children, 1995.
International Association of Fire Fighters, Occupational Health and Safety Award, 1995
Physicians for Social Responsibility, Broad Street Pump Award in Environmental Health, 1996
Mayo Clinic, Department of Pediatrics, Amberg-Heimholtz Lecturer in Pediatrics, 1998
International Society for Occupational and Environmental Health, Vernon Houk Award, 1998
Centers for Disease Control and Prevention, Langmuir Memorial Lecturer, 1999
American College of Preventive Medicine, Katherine Boucot Sturgis Award, 1999
Mothers & Others for a Livable Planet, Award for Advocacy on Behalf of the Health of Children, 1999
Earth Day New York, Award for Excellence in Environmental Medicine, 1999

Visiting Professorships:

University of Tokyo, Visiting Professor of the Faculty of Medicine, September 1989
University of Tokyo, Visiting Professor of the University, July 1990
University of Cape Town Medical School, Visiting Professor, Department of Community Health, March 1992
Medical College of Pennsylvania, Catherine Boucot Sturgis Visiting Professor in Community and Preventive Medicine, March 1992
National University of Singapore, Visiting External Examiner in Occupational Medicine, 1994
Duke University Medical School, Visiting Professor, NIEHS Clinical Training Program in Environmental Medicine, 1995

Committees:

The White House
Presidential Advisory Committee on Gulf War Veterans' Illnesses, 1995-1996.

American Academy of Pediatrics
Committee on Environmental Hazards, 1976 - Present. Chairman, 1983-1987.

National Research Council

National Academy of Sciences, Assembly of Life Sciences. Board on Toxicology and Environmental Health Hazards, 1978-1987; Vice-Chairman, 1981-1984.
National Academy of Sciences, Assembly of Life Sciences, 1981-1982; Commission on Life Sciences, 1982-1984.
Institute of Medicine, Committee for a Planning Study for an Ongoing Study of Costs of Environment-Related Health Effects, 1979-1980.
National Academy of Sciences, Panel on the Proposed Air Force Study of Herbicide Agent Orange, 1979-1980.
National Academy of Sciences, Committee on the Epidemiology of Air Pollutants, Vice-Chairman, 1984-1985.
National Academy of Sciences, Committee on Neurotoxicology in Risk Assessment, 1987-1989.
National Academy of Sciences, Committee on the Scientific Issues Surrounding the Regulation of Pesticides in the Diets of Infants and Children, Chairman, 1988-1992.
National Academy of Sciences, Board on Sustainable Development, 1995-1998.

National Institutes of Health/U.S. Public Health Service

National Institutes of Health, Study Section on Epidemiology and Disease Control, 1986-1990.
National Institute of Environmental Health Sciences, Third Task Force for Research Planning in the Environmental Health Sciences; Chairman, Subtask Force on Research Strategies for Prevention of and Intervention in Environmentally Produced Disease, 1983-1984.
National Institute for Occupational Safety and Health, Board of Scientific Counselors, 1995-1997.

State and Local Government

State of New York, Governor's Blue Ribbon Committee on the Love Canal, 1978-1979.
State of New Jersey, Meadowlands Cancer Advisory Board, Chair, 1987-1989.
State of New York, Asbestos Advisory Board, Chair, 1987 - Present.
State of New York, New York State Advisory Council on Lead Poisoning Prevention, Chairman, 1993 - Present.
City of New York, Mayor's Lead Paint Poisoning Advisory Committee, 1991-1993.
State of New York, Public Health Priorities Committee, 1996.
State of New York, Health Research Science Board, 1997 - Present.

Academic

Harvard School of Public Health, Occupational Health Program, Residency Review Committee, 1981-1983; Chairman, 1981.
New York Academy of Medicine, Working Group on Housing and Health, 1987-1989; Chairman, 1989.
Association of University Programs in Occupational Health and Safety, 1985 – Present; President, 1986-1988.
New York Lung Association, Research and Scientific Advisory Committee, 1986-1989. Board of Directors, 1987-1990.
Milbank Memorial Foundation, Technical Board, 1986-1988.
Mickey Leland National Urban Air Toxics Research Center, National Advisory Committee, 1994-1995.
Cornell University, Dean's Advisory Council in Veterinary Medicine, 1996-1997.

International Organizations

World Health Organization. Contributor to the WHO Publication: "Guidelines on Studies in Environmental Epidemiology" (Environmental Health Criteria, No. 27), 1984.

International Agency for Research on Cancer, Working Groups on Cancer Assessment, October 1981 and June 1986. (IARC Monographs No. 29 and No. 42).

Environmental Organizations

INFORM, Board of Directors, 1991 - Present.

Environmental Health Foundation, Board of Directors, 1993 - Present.

Colette Chuda Environmental Fund, Scientific Advisory Committee, 1994 - Present.

Children's Health Environment Coalition, Board of Directors, 1996 - Present.

Children's Environmental Health Network, Board of Directors, 1995 - Present.

Labor Unions

United Automobile Workers (UAW) - Chrysler Corporation, Joint Scientific Advisory Committee, Member, 1990 - Present.

United Brotherhood of Carpenters, National Health and Safety Fund, Medical Advisory Committee, 1990 - Present; Chairman, 1994 - Present.

International Association of Fire Fighters, John Redmond Foundation, Medical Advisory Committee, 1989 - Present.

International Brotherhood of Teamsters, National Health and Safety Advisory Committee, 1994 - Present.

George Meany Center for Labor Studies, Board of Trustees, 1994-1997.

Other Organizations

Health Insurance Plan (HIP) of Greater New York, Board of Directors, 1992-1994.

American Legion, Science Panel, Chairman, 1988 - Present.

Editorial Boards:

Editor-in-Chief: *American Journal of Industrial Medicine*, 1992 - Present; Consulting Editor, 1979-1992.

Editor-in-Chief: *Environmental Research*, 1987-1994.

Consulting Editor: *Archives of Environmental Health*, 1982 - Present.

Editorial Board: *Annual Review of Public Health*, 1984-1990.

Senior Editor: *Environmental Research*, 1985-1987.

Editorial Board: *American Journal of Public Health*, 1987 - Present.

Editorial Board: *New Solutions*: A Journal of Environmental and Occupational Health Policy, 1990 - Present.

Editorial Board: *The PSR Quarterly*: A Journal of Medicine and Global Survival, 1990-1994.

Editorial Board, *Journal of Public Health Management and Practice*, 1995-1996.

National Service:

United States Public Health Service, Commissioned Corps, 1970-1985. LCDR (04) to CAPT (06).

United States Naval Reserve, Medical Corps, 1996 - Present.

LCDR (0-4) 1996-98; CDR (0-5) 1 April, 1998 - Present.

ACCUSATIONS– SQUALENE

1. What is squalene?

Squalene is a naturally occurring substance found in plants, animals, and humans. It is manufactured in every human body as part of the process of making cholesterol and hormones. Squalene is also found in a variety of foods, cosmetics, health supplements, and over-the-counter medications. (Links to commercial squalene sources)

Squalene has been used as an adjuvant (a substance used to improve the body's response to a vaccine) in some investigational vaccines manufactured in the U.S., including vaccines to protect against HIV disease. Squalene is approved by European health agencies for use in an influenza vaccine. Whatever the arguments for or against squalene as a vaccine adjuvant, the fact is that none of the vaccines that were administered to U.S. troops during the Gulf War contained squalene as a vaccine adjuvant. This includes the anthrax vaccine, which does not contain squalene and never has contained squalene. The FDA has licensed only aluminum salts (e.g., aluminum hydroxide, aluminum phosphate, aluminum potassium sulfate) as adjuvants.

The Department of Defense (DoD) has never exposed any military member or civilian to any squalene-containing investigational product without the person's informed consent, abiding by FDA regulations. The DoD has conducted five human clinical trials using investigational vaccines containing squalene (investigational vaccines for the prevention of malaria and HIV infection) in FDA-approved vaccine studies. Two of the malaria vaccine studies involving a total of 17 human volunteers were conducted before or during the Persian Gulf War. Although it is unlikely, some of these subjects may have been involved in the Gulf War. Nevertheless, these investigational vaccines were part of FDA-approved studies that followed FDA guidelines for the use of investigational vaccines, including the informed consent of the participants.

2. Did DoD have anthrax vaccine tested for the presence of squalene?

Yes, and the vaccine was found to contain no squalene. To determine whether squalene was present in the anthrax vaccine, the DOD recently contracted with an independent civilian laboratory, Stanford Research Institute (SRI) International of Menlo Park, California, to test for the presence of squalene in every lot of the anthrax vaccine released to DOD. SRI International tested 14 lots of anthrax vaccine and formally reported that no squalene was detected in any of the 14 lots. The test they used is sensitive enough to detect the squalene naturally present in the oil in a human fingerprint. The DOD will test all other lots of anthrax vaccine in the stockpile when the allegations arose. Graphic images of the test results are posted at http://www.anthrax.osd.mil/Site_Files/lot_documents/lot_documents_menu.htm.

3. Has DoD ever requested that MBPI change the formula for licensed anthrax vaccine or develop a new anthrax vaccine to include squalene?

No. DoD never requested MBPI to change the formula for the licensed vaccine or to develop a new anthrax vaccine with any adjuvant, including squalene.

4. What are the facts behind the accusations about squalene?

In their effort to explain the health problems of some Gulf War veterans, a few investigators have theorized, and the press has amplified their theories, that a vaccine adjuvant may have caused an autoimmune disease in veterans. A recent *Vanity Fair* article "The Pentagon's Toxic Secret" (May 1999) alleges that the DoD possibly used "an illicit and secret anthrax vaccine" on its own soldiers. The writer's interpretation and presentation of the facts regarding the Department's use of anthrax vaccine are speculative, inflammatory, and wrong. His allegations and the reported "clinical evidence" are not new. Since 1997, reports in the *Washington Times* and its magazine *Insight on the News* have made similar allegations regarding an experimental "anti-HIV vaccine."

The investigators cited in the Vanity Fair and Insight on the News articles (Pamela Asa, Ph.D., Memphis, TN and Robert Garry, Ph.D., Tulane University School of Medicine, New Orleans, LA) report that they have developed and patented a test for anti-squalene antibodies. Autoimmune Technologies, LLC, of New Orleans, has an exclusive license on the use of the test. With their test the investigators report that they have detected anti-squalene antibodies in the blood of ill Gulf War veterans. Their method was published in the February 2000 issue of the journal "Experimental and Molecular Pathology." Whether or not this test has any clinical meaning will be settled by medical experts over time. For now, it is sufficient to recognize the conclusions of the authors: "It is important to note that our laboratory-based investigations do not establish that squalene was added as adjuvant to any vaccine used in military or other personnel who served in the Persian Gulf War era."

5. What did the GAO say about squalene testing and what are DoD researchers doing?

The U.S. General Accounting Office (GAO) has released a report "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" (GAO/NSIAD-99-5). The Department of Defense disagreed with the GAO's opinion that "the first step is to determine the extent to which they [antibodies to squalene] are present in a larger group of sick Gulf War-era veterans."

To investigate the squalene hypothesis, a scientifically proven test for squalene antibodies is needed to assess whether Gulf War veterans have antibodies to squalene. In response to a DoD solicitation for research on illnesses among Gulf War veterans, a DoD investigator and nationally recognized expert on antibodies to cholesterol and other lipids submitted a research proposal to determine the feasibility of developing a test for antibodies to squalene. The funded research project to determine whether antibodies to squalene exist has five main objectives: 1) Development and validation of an enzyme-linked immunosorbant assay (ELISA) for antibodies against squalene. 2) Evaluation and potential development of other assays for antibodies to squalene. 3) Development of a positive control antibody to squalene. 4) Production of the positive control antibody to squalene for use in the assays. 5) Testing of normal human serum for antibodies to squalene by ELISA and other methods. This study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and can be detected in human serum. Only if this kind of preliminary evidence indicates that it is possible to create and measure anti-squalene antibodies can one contemplate the next step. The next step would be to determine whether the presence of anti-squalene antibodies differs between two groups. For example, one might want to compare (1) deployed vs. nondeployed veterans, (2) veterans with vs. without symptoms attributed to Gulf War illnesses, or (3) some other comparison. These steps will take a couple years to work through.

The proper first step is to show that the test measures what the test claims to measure. Further, the medical significance and the origin of antibodies to squalene, even if their existence is corroborated, remain unknown. Without such information, Gulf War veterans get only speculation about the meaning of the test result and its implication for their health. Gulf War veterans deserve objective evidence and recommendations based on sound science.

6. What does the U.S. Senate say about squalene?

In its investigations of illnesses among Gulf War veterans, the Senate Special Investigations Unit (SIU) found no credible information indicating that vaccines used during the Gulf War contained squalene (1998, page 123). In its report, the SIU stated that according to the Food and Drug Administration (FDA), squalene can be contained in a vaccine due to two different processes: 1) as an adjuvant, which is an agent to enhance the immune response; or 2) in minute quantities in vaccines manufactured using eggs, since eggs are rich in squalene and cholesterol. The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant.

7 May 1999

William Y. Ellis
Chief, Department of Chemical Information
Division of Experimental Therapeutics
Walter Reed Army Institute of Research
Washington, DC 20307-5100

Dear Sir:

This letter reports our preliminary findings on the determination of squalene in vials of an anthrax vaccine preparation.

Three vials of ANTHRAX VACCINE ADSORBED, Manufactured By MICHIGAN DEPARTMENT OF PUBLIC HEALTH, Lansing, Michigan, 48909, U.S. License No. 99, LOT FAV020, EXP 6 FEB 99, were received on 23 April 1999.

We have developed a sensitive, rapid assay method for squalene using high performance liquid chromatography. The assay specificity is based on chromatographic retention time and on the uv absorption characteristics of the analyte. The method sensitivity is ~0.7 nanogm squalene/10 microL injection, based on squalene in 2-propanol. The method linearity is 0.7 nanogm to 225 nanogm/10 microL injection with $r^2 = .999$, also based on squalene in 2-propanol. The method is currently undergoing validation.

We find no measurable amount of squalene in the vials. If any squalene were present, it would be less than 70 nanogm per 0.5 milliL vaccine preparation, which volume is the label dose.

We will prepare and submit our final report as soon as the study is completed.

Sincerely yours,

Peter Lim, Ph.D.
Principal Investigator
Catalysis and Anal. Chem. Dept.
Pure and Applied Phy. Chem. Div.

Ronald J. Spanggord, Ph.D.
Assistant Principal Investigator
Catalysis and Anal. Chem. Dept.
Pure and Applied Phy. Chem. Div.

SRI International
333 Ravenswood Ave • Menlo Park, CA 94025

JACK METCALF
2D DISTRICT, WASHINGTON

COMMITTEE ON TRANSPORTATION AND INFRASTRUCTURE
SUBCOMMITTEES
AVIATION
GROUND TRANSPORTATION

COMMITTEE ON SCIENCE
SUBCOMMITTEE
ENERGY AND ENVIRONMENT

Congress of the United States
House of Representatives
Washington, DC 20515–4702

FINANCIAL SERVICES
SUBCOMMITTEES
HOUSING
FINANCIAL INSTITUTIONS
DOMESTIC AND INTERNATIONAL MONETARY POLICY

CHAIR, REPUBLICAN HOUSING OPPORTUNITY CAUCUS

REPUBLICAN POLICY COMMITTEE

January 31, 2000

Jane E. Henney M.D., Commissioner
Food and Drug Administration
Room 1555
5600 Fishers Lane
Rockville, MD 20857

re: Department of Defense (DOD)
Report To Congress: Gulf War Illness
"Development and Validation of an Assay
To Test for the Presence of Squalene Antibodies"

Dear Commissioner Henney:

In its report provided to Congress this month, the DOD made the following statement in its Executive Summary: "The FDA verified that none of the vaccines used during the Gulf War contained Squalene as an adjuvant."

Unfortunately, the DOD report did not provide a site reference for their statement. Please provide copies of the written documents in which your verification was provided to the DOD.

Specifically, please provide answers to the following questions:

1. What vaccines were tested?
2. What lot numbers of those vaccines were tested?
3. Who did the testing?
4. Where was the testing done?
5. What specifically was being looked for during the testing?
7. Were any additional adjuvants identified during the testing?

Please respond within 14 days. Thank you for your attention to this matter.

Sincerely,

Jack Metcalf

Jack Metcalf

cc: Kathryn c. Zoon, Ph.D.

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BELLINGHAM, WA 98225
(360) 733-4500

DEPARTMENT OF HEALTH & HUMAN SERVICES

MAR 2 2 RECD

RECEIVED

Food and Drug Administration
Rockville MD 20857 MAR 23 2000

MAR 20 2000

The Honorable Jack Metcalf
House of Representatives
Washington, D.C. 20515-4702

Dear Mr. Metcalf:

Thank you for your letter dated January 31, 2000, addressed to Dr. Jane E. Henney, requesting information from the Food and Drug Administration (FDA) concerning squalene and vaccines used during the Gulf War. We apologize for the delay in responding.

Your letter referenced a Department of Defense (DOD) Report to Congress which you indicated had included the statement that "The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant." Your letter requested both that verification to DOD and responses to a number of questions. FDA was unfamiliar with the DOD report you cited. On March 9, Ms. Jarilyn Dupont of my staff discussed this with Ms. Norma Smith of your district office and she provided FDA with the DOD Executive Summary referred to in your letter. In reviewing the DOD Executive Summary, it appears that the statement DOD made was in reference to a statement contained in a report from the Senate Special Investigation Unit (SIU) of the Senate Veterans' Affairs Committee which conducted a comprehensive review of Gulf War illnesses. That report indicated that the FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant. (*Report of the Special Investigation Unit on Gulf War Illnesses*, page 123, footnote 331).

In fact, FDA did verify to the Senate Special Investigations Unit on July 23, 1997, in a telephone conversation with Committee staff of the SIU, not with DOD, that neither the licensed vaccines known to be used in the Gulf War, nor the one investigational product known to have been used, contained squalene as an adjuvant in the formulations on file with FDA. FDA also has provided this information, and the information provided below, to the General Accounting Office (GAO) as part of an audit on squalene and Gulf War illness.

Currently, the only adjuvant in licensed vaccine formulations are aluminum compounds. Squalene, an intermediate in the

biosynthesis of cholesterol, is not approved for use as an adjuvant in licensed vaccines. Vaccines are not routinely tested for the presence or absence of squalene by the manufacturer or by FDA's Center for Biologics Evaluation and Research (CBER). Manufacturers perform specific tests as outlined in their license application. The tests for Anthrax Vaccine Adsorbed include Sterility, General Safety, Potency, Aluminum, Formaldehyde, and Benzethonium Chloride. Samples for the Anthrax lots and corresponding protocols containing the test results are submitted to CBER. CBER has the option to perform additional testing on lots submitted for lot release.

Very limited testing of Anthrax Vaccine, Adsorbed, conducted by CBER in 1999 determined that there were only trace amounts of squalene in the lots tested. After an article appeared in the May 1999 issue of Vanity Fair entitled "The Pentagon's Toxic Secret," CBER tested in its laboratories the two lots mentioned in the article (FAV020 and FAV030) for squalene. Three other Anthrax lots (FAV038, FAV043, FAV047) and two other lots of other bacterial vaccines (Wyeth Diphtheria and Connaught Tetanus) containing alum adjuvants were randomly selected for comparative purposes. Due to the inability to detect trace amounts of squalene parts per million, CBER developed a test to detect the substance in parts per billion. The trace amounts of squalene were determined by gas chromatography with flame ionization detection. The squalene content of the lots was determined to be in the level of low parts-per-billion and was comparable to levels determined in three other lots of the anthrax vaccine and the other biological products that were tested. In addition to squalene, lots FAV020 and FAV030 were also tested for aluminum, formaldehyde and benzethonium chloride.

We trust this information responds to your concerns. If we may be of any further assistance, please contact us again.

Sincerely,

Melinda K. Plaisier
Associate Commissioner
of Legislation

BAYLOR COLLEGE OF MEDICINE

Department of Immunology
One Baylor Plaza, BCMM-M929
Houston, TX 77030-3498
Tel: 713-798-6054
Fax: 713-798-3700

September 22, 2000

Congressman Jack Metcalf
2930 Wetmore Avenue, Suite 9-E
Everett, WA 98201

Dear Congressman Metcalf:

As you know, squalene is not approved for use as an immune adjuvant; however, there is evidence that very small amounts of the Anthrax Vaccine given to Gulf War participants contained this compound.

The tests done by SRI International were performed using a fairly sensitive technique called High Pressure Liquid Chromatography(HPLC). This technique is commonly used to find trace chemicals of drugs in a test specimen compared to a control specimen. However, as I understand this case, a much more sensitive test using gas chromatography, which instead of examining the test specimen as a liquid, vaporizes it which makes it a much more sensitive technique, found low levels of squalene in Anthrax vaccine samples.

The real issue is whether squalene in parts per billion was added to the vaccine preparations given to the military, as well as whether this concentration of squalene could alter the immune response.

More research needs to be done to answer these questions, but it is possible that very small amounts of a biologically active product could induce an immune response, either to the molecule itself or it could boost immune responses to other agents in the mixture. In any case, the discrepancy between the SRI test and that done by CBER needs to be investigated.

Sincerely,

Dorothy E Lewis

Dorothy E. Lewis, Ph.D.
Associate Professor of Immunology

DEL/tfs

(43)

Congressional

CMAT Control #
1999295-0000001

	SECRETARY OF DEFENSE ROUTING SLIP	ACT COPY	INFO COPY			ACT COPY	INFO COPY
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	EXECUTIVE SECRETARY						
	UNDER SEC FOR ACQUISITION & TECHNOLOGY				CHAIRMAN, JOINT CHIEFS OF STAFF		
	Director, Defense Research & Engineering				Director, Joint Staff		
	UNDER SECRETARY FOR POLICY						
	ASD (International Security Affairs)				BALLISTIC MISSILE DEFENSE ORGANIZATION		
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	ASD (Strategy &Threat Reduction)				DEFENSE COMMISSARY AGENCY		
	UNDER SECRETARY (COMPTROLLER)				DEFENSE CONTRACT AUDIT AGENCY		
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	DIR, OPERATIONAL TEST & EVALUATION						
	DIR, ADMINISTRATION & MANAGEMENT						
					GWI		X

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	PREPARE REPLY FOR DEP SEC OF DEF SIGNATURE		INFORMATION AND RETENTION
1	REPLY DIRECT *(Forward copy of reply to CCD, Room 3A948)*	X	COORDINATE REPLY WITH LA
	APPROPRIATE ACTION		

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COMMITTEES:
ARMED SERVICES
COMMERCE
GOVERNMENTAL AFFAIRS
SMALL BUSINESS

United States Senate

WASHINGTON, DC 20510-1005

September 13, 1999

The Honorable William Cohen
Secretary of Defense
Department of Defense
The Pentagon
Washington, 20310

Dear Mr. Secretary:

I have taken the opportunity to forward to you an email I recently received from one of my constituents. (b)(6) is concerned with possible exposure to chemical agents during his service in the Gulf War. I have keen interest in the questions that (b)(6) has raised. I would appreciate specific answers to his three questions and look forward to hearing from you soon.

Most respectfully,

Max Cleland

Max Cleland
United States Senator

MC:arv

U14780 /99

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Savannah, GA 31406-4823
(912) 352-0283

154463
DC PDR

Sen. Cleland - GA

From: Nobody[SMTP:nobody@ftp5.senate.gov]
Sent: Tuesday, June 22, 1999 11:49 PM
To: Sen. Cleland - GA
Subject: www_email

(b)(6)

Other
Honorable M. Cleland:
I hope you can understand what I am writing about since you are a vet also.

I realize there is a lot going on at this time with the Kosovo peace fiasco, Clinton's Chinagate (hopefully an investigation) and other important domestic issues like keeping the Liberals from watering down the First and Second Amendement, but this issue personally involves me [and thousands of my fellow veterans] and I don't hear or read about any one in Congress doing anything to find out what has happened and/or what can be done.

Before the actual war (Desert Storm) and during Desert Shield, my unit, the 11th Signal Brigade received several series of injections. We received routine injections and flu shots and Anthrax and an unknown injection. I know it was unknown because I was part of the immunization team. The immunization team assisted the medics and nurses from the nearby Air Force MASH. We had no medics in our unit because of a shortage and what there was had to be used in the front line attack units. So anyone with medical experience was sent to the MASH unit and given refresher courses. I was part of that team. I also was the only one in almost the entire brigade who was qualified to operate large passenger vehicles (PAX) like the 66-passenger bus they acquired. I picked up the nurses and the supply of vaccine in this bus and shuttled them back and forth. I also assisted administering vaccines by filling disposable hypodermics so they were ready for the nurses to inject the soldier!
s. We did the whole brigade in this manner, about 2400 soldiers and attached units. After preparing the injections I would then sit at a table and fill out the soldiers' shot records (a small yellow folded "book") they carried with them. This would later be transcribed (supposed to be) to their permanent medical records.

Everyone was worried about the Antrhax shot because of it being so new. But many of us, especially those who were in charge of administration wondered why were told it was a classified substance on a particular injection. I asked what I was supposed to put in their shot record as to what they were receiving (and then the date is entered) and the head nurse said write in "Vaccine A".

Well, the ground war began and one hundred days later it ended. Sometime before it was my time to leave with my unit's headquarters company I began getting chronic diarreha. It would happen for no reason. Then I would get flu symptoms that would come and go and joint pain. I had found out I had a light case of arthritis previously, so attributed the joint pain to that - although calcium pills had seem to be helping that. Then I would get these strange light-headed feelings, etc.

Well, I came back home and they did some tests on me. They checked me for illness and also for parasites I might have picked up (which would account for the diarreha). Nothing. Not explainable. Now remember, this was before this Gulf War Syndrome was getting around as to the explanation. They even gave me a diabetes test because my cholesterol was skyrocketing for no apparent reason. I was active and doing my physical training and going to the gym at that time, so it was not explainable.

Then I mustered out in 1994 and was going through my VA physical and the doctor gave me a Persian Gulf medical questionaire. It asked me if I was near the burning oil fields, which I was for only about three days. Then there were other questions which I answered. I have not been called back since and I don't remember them taking blood samples at that time.

The diarreha has been chronic ever since and I will get tired for no apparent reason. I have had some serious bouts of "flu" and a case of pneumonia, but nothing else. I don't know whether this is from the Gulf, but the spontaneous moments of having to relieve myself is frustrating. I have always had good health and it is discomforting and I wonder about it.

The continual investigations have revealed that squalene has been found in the blood samples of soldiers and vets and this can only be received by injection. It is an adjuvant for the immune system to speed up the antibody process - but has never been approved for humans. I was worried about the same thing about the Anthrax shots at the time it was administered to us but was told this was approved for humans. Everyone knew that was why it was a biological weapon because previously it was only found in cows.

So, on behalf of myself and the thousands of others, I would like to ask the following questions and wonder if anyone in Congress is going to push this matter to the front of the table.

1) Why do antibodies for the experimental immune system adjutant - squalene - and not approved for human use beyond highly controlled experimental use - show up in the bloodstreams of gulf-war veterans who are sick with a variety of illnesses apparently not related to any known biological or chemical agent?

2) What inoculation was administered was administered to the gulf-war veterans that may have contained squalene, was it the "secret" injection?

3) Why have thousands of gulf-war veterans told investigators that they have been administered shots of secret contents which have not been identified 4 Whya have military doctors, nurses and medics told investigators that they were ordered to administer shots of "secret" contents to soldiers and then ordered to destroy the records? (I was not ordered to destroy my personal shot records, but it never showed up in my permanent official records, to include the anthrax - the injection known as "Vaccine A")

4) Where are the shot records and why didn't they show up in our personal medical records? (When I mustered out the VA couldn't find any such vaccine I described - to include the Anthrax vaccine and date(s) given).

This subject is a critical concern. My son was conceived after returning from the Gulf War and he was born with a mild birth defect - hypospatia. It was surgically corrected and I had always wondered if all of this "syndrome" and secret vaccines didn't have something to do with it. Fortunately it was correctable, but I will always wonder.

Soldiers, sailors, marines and airmen know they are taking chances when fullfilling their military obligation, especially when our duty calls to serve in a combat zone. But we were never meant to be guinea pigs for some weird science project at Walter Reed hospital.

When is someone going to quit trying to hide this matter and get down to helping those of us who have any of these symptoms. I count myself lucky because they also issued us "anti-nerve agent" pills and were told not to take them until ordered to do so. My unit was fortunate to have a level-headed commander who cared a great deal for those under his command. He never ordered us to take them and when the appropriate time came he ordered us to flush them down the toilet.

Tragically, there were some commanders who went ahead and ordered this new drug to be taken and the result was horrible. I knew an officer from one of those units whose hair fell out and a rash developed and other terrible symptoms. Those of us with NBC (Nuclear-Biological-Chemical) training know that there is nothing know so far that will cure or prevent harm by nerve agents. The only thing the military has is something that will keep the soldier going for a little bit longer, and I believe they even discontinued that recently.

Please find out what is going on with this.

Thank you for your time, (b)(6)

(44)

JACK METCALF
2d District, Washington

TEE ON TRANSPORTATION
ND INFRASTRUCTURE
SUBCOMMITTEE
Aviation
Ranking Transportation

COMMITTEE ON SCIENCE
SUBCOMMITTEE
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CHAIR, REPUBLICAN HOUSING
OPPORTUNITY CAUCUS

REPUBLICAN POLICY COMMITTEE

Congress of the United States
House of Representatives
Washington, DC 20515–4702

January 31, 2000

Jane E. Henney M.D., Commissioner
Food and Drug Administration
Room 1555
5600 Fishers Lane
Rockville, MD 20857

re: Department of Defense (DOD)
Report To Congress: Gulf War Illness
"Development and Validation of an Assay
To Test for the Presence of Squalene Antibodies"

Dear Commissioner Henney:

In its report provided to Congress this month, the DOD made the following statement in its Executive Summary: "The FDA verified that none of the vaccines used during the Gulf War contained Squalene as an adjuvant."

Unfortunately, the DOD report did not provide a site reference for their statement. Please provide copies of the written documents in which your verification was provided to the DOD.

Specifically, please provide answers to the following questions:

1. What vaccines were tested?
2. What lot numbers of those vaccines were tested?
3. Who did the testing?
4. Where was the testing done?
5. What specifically was being looked for during the testing?
7. Were any additional adjuvants identified during the testing?

Please respond within 14 days. Thank you for your attention to this matter.

Sincerely,

Jack Metcalf

Jack Metcalf

cc: Kathryn c. Zoon, Ph.D.

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(360) 733-4500

Arthur Brand

MAR 2 0 2000

The Honorable Jack Metcalf
Rouse of Representatives
Washington, D.C. 20515-4702

Dear Mr. Metcalf:

Thank you for your letter dated January 31, 2000, addressed to Dr. Jane E. Henney, requesting information from the Food and Drug Administration (FDA) concerning squalene and vaccines used during the Gulf War. We apologize for the delay in responding.

Your letter referenced a Department of Defense (DOD) Report to Congress which you indicated had included the statement that "The FDA verified that none of the vaccines used during the Gulf War contained squalene as au adjuvant." Your latter requested both that verification to DOD and responses to a number of questions. FDA was unfamiliar with the DOD report you cited. On March 9, Ms. Jarilyn Dupont of my staff discussed this with Ms. Norma Smith of your district office and she provided FDA with the DOD Executive Summary referred to in your letter. In reviewing the DOD Executive Summary, it appears that the statement DOD made waa in reference to a statement contained in a report from the Senate Special Investigation Unit (SIU) of the Senate Veterans' Affairs Committee which conducted a comprehensive review of Gulf War illnesses. That report indicated that the FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant. (*Report of the Special Investigation Unit on Gulf War Illnesses,* page 123, *footnote* 331).

In fact, FDA did verify to the Senate Special Investigations Unit on July 23, 1997, in a telephone conversation *with* Committee staff of the SIU, not with DOD, that neither the licensed vaccines known to be used in the Gulf War, nor tha one investigational product known to have been used, contained squalene as an adjuvant in the formulations on file with FDA. FDA also has provided this Information, and tha Information provided below, to the General Accounting Office (GAO) as part of an audit on squalene and Gulf War illness.

Currently, the only adjuvant in licensed vaccine formulations are aluminum compounds. Squalene, an intermediate in the

biosynthesis of cholesterol, is not approved for use as an adjuvant in licensed vaccines.. vaccines are not routinely tested for the presence or absence of squalene by the manufacturer or by FDA's Center for Biologics Evaluation and Research (CBER). Manufacturers perform specific torts as outlined in their license application. The tests for Anthrax Vaccine Adsorbed include Sterility, General safety, Potency, Aluminum, Formaldehyde, and Benzethonium Chloride. Samples for the Anthrax lots and corresponding protocols containing the teat results are submitted to CBER. CBER has the option to perform additional testing on lots submitted for lot release.

Very limited testing of Anthrax Vaccine, Adsorbed, conducted by CBER in 1999 determined that there were only trace amounts of squalene in the lots tested. After *an article* appeared in the May 1999 issue of Vanity Fair entitled "The Pentagon's Toxic Secret," CBER tested in its Laboratories the two lots mentioned in the article (FAV020 and FAV030) for squalene. Three other Anthrax lots (FAV038, FAV043, FAV047) and two other lots of other bacterial vaccines (Wyeth Diphtheria and Connaught Tetanus) containing alum adjuvants were randomly selected For comparative purposes. Due to the inability to detect trace amounts of squalene parts per million, CBER developed a test to detect the substahcs in parts par billion. The trace mounts of squalene were determined by gas chromatography with flame ionization detection. The squalene content of the lots was determined to be in the level of low parts-per-billion and was comparable to levels determined *in* three other lots of the anthrax vaccine and the other biologic81 products that were tested. In addition to squalenc,lots FAV020 and FAV030 wero also tested for aluminum, formaldehyde and benzethonium chloride,

We trust this information responds to your concerns. If we may be of any further assistance, please contact us again.

Sincerely,

Melinda K. Plaisier
Associate Commissioner
of Legislation

2001100-0000004 **Congressional** 6W1 CMAT Control # 2001100-0000004 (45)

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Suspense Date: **April/5/2001**	Routing Date: **March/30/2001**	OSD CONTROL #: **U06509-01**

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Congress of the United States

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March 29, 2001

The Honorable Donald H. Rumsfeld
Secretary of Defense
The Pentagon
Washington, DC 20301-1000

Dear Mr. Secretary:

I am writing regarding the Defense Department's Anthrax Vaccination Immunization Program (AVIP) and my continuing serious reservations regarding DOD's implementation and management of the program. During the Last Congress, the Committee issue a report entitled, The *Department of Defense Anthrax Vaccine Immunization Program: Unproven Force Protection,* and held two hearings on this issue. On May 16.2000, I joined 34 of my colleagues in writing a letter to former Secretary Cohen outlining our concerns. We asked former Secretary Cohen to suspend the AVIP program until a comprehensive re-examination occurred in light of growing evidence questioning the safety and efficacy of the vaccine, as well as significant legal and production irregularities in the manufacturing process by BioPort Corporation, the sole-source supplier of the vaccine. DOD declined to suspend the program, or at a minimum, to make it voluntary until such time as the irregularities and inadequacies could be addressed. Since that time, DOD has had to restrict mandatory immunization of the Total Force to only those personnel assigned *to* Southwest Asia for more than 30 days because of continuing problems at the BioPort facility.

I have recently been informed that the Centers for Disease Control and Prevention (CDC) will conduct two research studies on the Anthrax vaccine used by DOD. These studies could lead to a better understanding of the vaccine's capabilities and changes in the way it is administered. These are exactly the types of studies that should have been conducted prior to DOD's implementation of the program in the spring of 1998. It is my understanding that the current supply of vaccine will be exhausted this fall and the program will have to be suspended until BioPort is certified by the Food and Drug Administration (FDA). It is uncertain when, or if, the FDA will certify BioPort.

The Honorable Donald H. Rumsfeld
Secretary of Defense
March 29, 2001

Since the implementation of the AVIP program, approximately 450 servicemembers have declined to be immunized out of a firm and sincere beliefthat to do so would harm them. Most of these personnel arc acknowledged by their commanders to be superior performers, and are individuals who want to continue to serve their country. However, in almost all of the cases, the military has felt compelled to punish them for their well-founded fear of the Anthrax vaccine, many with prison terms, and then separate them with unfavorable discharges. Two prominent recent examples are:

1. Captain John Buck, USAF – Captain Buck is a physician stationed at the base hospital at Keesler APB, MS. He is to bc tried by general court-martial in early May 2001 for declining immunization with the current Anthrax vaccine. Based upon his medical background, training and experience he hasserious reservations regarding its safety. A conviction could result in a dismissal from the Air Force, imprisonment, and fines. Additionally, a felony conviction could jeopardize his ability to practice medicine.

2. Petty Officer 3rd Class David Ponder, USN – PO Ponder is assigned to Naval Construction Battalion 74 ("SeaBee") and is stationed at Gulfport, MS. He was trird by special court-martial for declining to receive the Anthrax vaccination. He was sentenced to 60 days confinement and a reduction in rank. He testified before the Committee last fall. He was acknowledged to be a superior performer by his commander.

The Defense Department currently holds the position that there is no evidence of significant adverse health complications attributable to the Anthrax vaccine. At the same time, DOD is unable to provide any compelling medical explanation to hundreds of servicemembers who have complained of serious ailments immediately after taking the shot.

I recommend that DOD's AVIP program be suspended, at a minimum, pending the results of the CDC's studies of the current vaccine, and a comprehensive re-examination by you of how the Services have implemented and administered the program to date. I would appreciate the opportunity to meet with you at the earliest possible date to discuss this issue. If you have any questions, please have your staff contact Thomas G. Bowman, Senior Counsel, at (202) 225-5074.

Sincerely,

Dan Burton
Chairman

ONE HUNDRED SEVENTH CONGRESS

Congress of the United States

House of Representatives

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To: The Honorable Donald H. Rumsfeld **From:** Chairman Dan Burton

Fax: (b)(6) **Pages:** 3

Phone: **Date:** March 29, 2001

- **Comments:**

1100 - 004

Routing Sheet – Information Only

Office of the Special Assistant to the Under Secretary of Defense (Personnel & Readiness) for Gulf War Illnesses, Medical Readiness, and Military Deployments

Date

Coord/ Routing	Position/Organization		Comments
2	Deputy Special Assistant	(DSA)	✓ 4.12
3	Chief of Staff	(CoS)	4-12
7	☒ Director, Investigation & Analysis _____ (IAD) ☐ C/B __ ☐ ENV __ ☐ PAG __ ☐ VDM _____		13 1480 Apr 01
6	Dir Lessons Learned Implementation	(LLI)	13 April
5	Dir Public Affairs & Outreach	(PA)	by 12 Apr 01
4	Dir Medical Readiness	(MR)	12 Apr 01
	Legal Advisor	(LGL)	
	Info Technology & Security	(ITS)	
1	PM, Support	(PM)	11 April
	☐ CMAT__ ☐ OPNS__ ☐ DMT__		
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Congressional

CMAT Control #
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(46)

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OSAGWI

MAY 25 2000

May 12, 2000

The Honorable William Cohen
Secretary of Defense
Washington, DC 20301

Dear Secretary Cohen:

I appreciate that the United States Air Force was compassionate enough to allow Major Sonnie Bates to resign his commission after the retaliation he suffered for testifying before the Government Reform Committee in October 1999. Although this decision was slow in coming, the Air Force did the right thing.

I continue to be disturbed about the manner in which individuals in all services who refuse the anthrax vaccine are being disciplined. Navy E-4 (b)(6) who declined to take the vaccine earlier this year, has been shipped to Okinawa to face court-martial charges instead of allowing him to remain in Louisiana. The practical effect is that he is placed thousands of miles from his family, and it is virtually impossible for him to obtain civilian legal counsel. The estimated up-front cost for civilian legal counsel to assist in his defense in Okinawa is $50,000. Of course, such counsel is now out of his reach as an enlisted man.

Last year Captain (b)(6), an Air Force Academy graduate and pilot of the 457th Airlift Squadron, Andrews Air Force Base, refused the vaccine, and accepted an Article 15, for which he was fined over three thousand dollars. He has since faced severe retaliation. He requested to resign his commission and leave the Air Force with an honorable discharge and was rejected. Immediately following the refusal of his Commanders to process his request, he received notification that he was being discharged by means that may include other than honorable. This after a year of severe retallation, including denying him the opportunity to continue serving as a mentor to young children in an established service program at Andrews. Just as you did the right thing by Sonnie Bates, I ask the Secretary of the Navy and the Secretary of the Air Force to do the right thing by (b)(6) and (b)(6). Please return (b)(6) to the U.S. There is no justification for forcing him to face a court martial in Okinawa. Please allow both men to resign and receive honorable discharges.

U06914 /00

Given all that has been learned about the lack of science, the admission that between 5 and 35 percent of individuals will have a systemic reaction to the vaccine, which can include muscle aches, joint aches, headaches, malaise, rashes, chills, low-grade fever, and nausea, as well as the experimental nature of utilizing the anthrax vaccine for prophylactic protection against inhalation exposure of biological warfare anthrax, members of the armed services are justified in their concerns for the preservation of their own health. These concerns are justified given the large number of Gulf War Veterans who have suffered from Gulf War Syndrome, for which we do not yet have conclusive evidence of cause and have not been able to conclusively rule out the anthrax vaccine as a culprit.

The concerns of members of the military have been confirmed both the Committe's report which recommends suspending the mandatory anthrax vaccine immunization program, and the interim report of the Institute of Medicine (IOM). The IOM reported:

> "There is a paucity of published peer-reviewed literature on the safety of the anthrax vaccine.... The published studies have found transient local and systemic effects...of the anthrax vaccine. There have been no studies of the anthrax vaccine in which the long-term health outcomes have been systematically evaluated with active surveillance... The committee concludes that in the peer-reviewed literature there is inadequate/ insufficient evidence to determine whether an association does or does not exist between anthrax vaccination and long-term adverse health outcomes."

On Friday, Canada's Chief Military Judge, Col. Guy Brais, threw out a court-martial action and ruled that an Canadian Air Force Sergeant who refused the (U.S. manufactured) anthrax vaccine during the Gulf War because he felt it was unsafe was acting within his rights, saying that "evidence indicated the vaccine was "unsafe and hazardous."

The May 9 DOD response to our letter requesting information on the treatment of refusals in entirely inadequate. It shows a clear decision by the Department to subvert the oversight jurisdiction of the Government Reform Committee.

I again reiterate to you that the mandatory anthrax vaccine immunization program should be suspended. Too many lives have been adversely affected through the loss of health, the loss of military careers, and maybe saddest of all the loss of trust in the military leadership because of the misinformation campaigns that have been waged to enforce this program.

Sincerely,

Dan Burton
Chairman

Cc: Honorable Richard Danzig, Secretary of the Navy
Honorable F. Whitten Peters, Secretary of the Air Force

(47)

CMAT Control #
1999196-0000004

Directorate for Freedom of Information and Security Review (DFOISR)
Coordination Record

Date: 15-JUL-1999

To: [redacted] GWI attn Bob Mein EXPEDITE

Case No: 99-C-1075

DESCRIPTION

Number of Pages: 20 Classification: U

Type of Document: STATEMENT Requestor: CLAYPOOL, G

Subject: *ANTHRAX VACCINE IMMUNIZATION PROGRAM*

Source: OSD(LA) Event Date: 21-JUL-1999

Purpose: NATIONAL SECURITY VETERANS AFFAIRS & INTERNATIONAL RELATIONS COMMITTEE

The attached material is forwarded for review and comment in accordance with the following guidelines. Questions concerning this case should be directed to : (b)(6), Rm 2C757, (b)(c-mail: (b)(6) @osd.pentagon.mil, unclassified Fax (b)(6)

REVIEWERS: HEALTH AFFAIRS, GWI, JOINT STAFF

A reply is requested by: 16-JUL-1999

CONGRESSIONAL

COORDINATION OFFICE ACTION

To: Directorate for Freedom of Information and Security Review, DFOISR, Room 2C757.
Review by this office in accordance with the guidelines below, result in the following recommendation concerning clearance for publication.

(Check One):

- ☐ No Objection as Received.
- ☐ No Objection Subject to Amendments made by this office (in black pencil). Ammendments and rationale (security and policy) are annotated on page numbers listed below.
- ☐ Objection. Amendments to permit publication are impracticable. Reasons stated below.

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RECORD VERSION

DRAFT

ANTHRAX VACCINE IMMUNIZATION PROGRAM

STATEMENT BY

Major General G. Robert Claypool
Medical Corps, United States Army
Deputy Assistant Secretary for Health Operations Policy

Submitted To

SUBCOMMITTEE ON NATIONAL SECURITY,
VETERANS AFFAIRS AND INTERNATIONAL RELATIONS
COMMITTEE ON GOVERNMENT REFORM

FIRST SESSION, 106TH CONGRESS

JULY 21, 1999

DRAFT

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VETERANS AFFAIRS AND INTERNATIONAL RELATIONS

99-C-1075

INTRODUCTION

Chairman Shays, Representative Blagojevich and Distinguished Committee Members, I am honored to appear before your Committee today to address your questions about the Department of Defense (DOD) Anthrax Vaccine Immunization Program (AVIP). I am Major General G. Robert Claypool, Deputy Assistant Secretary for Health Operations Policy. I am accompanied today by Rear Admiral Michael L. Cowan, Deputy Director for Medical Readiness, Joint Staff; Colonel Frederick E. Gerber, Director, Health Care Operations, Office of the Army Surgeon General; and Colonel Renata J. M. Engler, Chief Allergy Immunology Service, Walter Reed Army Medical Center. At your request, our testimony will specifically address AVIP implementation, communication and medical protocols for deferrals and adverse events.

THE BIOLOGICAL WARFARE AGENT ANTHRAX: A CLEAR AND PRESENT DANGER

Our National Security Strategy places our Service Members in a posture of global engagement to **Shape** the international environment; **Respond** to the full spectrum of crises; and **Prepare Now** for an uncertain future. The strategic deployability of our Armed Forces places our men and women at significant risk from the proliferation of biological weapons. Anthrax clearly tops the annual intelligence threat lists from a host of hostile countries known to have stockpiles and the offensive ways and means to deploy anthrax against our forces. Regional, transnational, asymmetric threats and proliferation of biological weapons grows each year. We face a clear and present danger from anthrax.

Death is the predictable outcome of inhalational anthrax in unvaccinated persons. Once clinical symptoms appear, death is assured, despite the most heroic, state of the art, post-exposure medical intervention and treatment given.

The good news is — death from anthrax is vaccine preventable. Immunization with Anthrax Vaccine Adsorbed, licensed as safe and effective by the Food & Drug Administration (FDA) in 1970, provides our men and women with their only chance of survival. Experienced reviewers at the FDA found Anthrax Vaccine Adsorbed (AVA) safe and effective in preventing anthrax in human beings. Furthermore, DOD now has a stockpile of anthrax vaccine enabling us to begin vaccinating our Armed Forces.

KEY IMPLEMENTATION PRINCIPLES: SAFETY, COMMUNICATION, & INDIVIDUALIZED CARE

Chairman Shays, as you requested, my testimony will focus on the DOD's programs to assess and assure the safe delivery of anthrax vaccination. I will review our multi-faceted vaccine safety surveillance programs and discuss our comprehensive communication programs to explain the value of anthrax vaccination to Service Members and their families. Additionally, I will describe our consensus medical protocols for diagnosis, evaluation and disposition of persons who develop physiologic reactions after receiving a dose of anthrax vaccine.

COORDINATED SURVEILLANCE FOR ANTHRAX VACCINE SAFETY

The Department of Defense conducts an aggressive, multi-faceted surveillance program to assess vaccine safety. In fact, the safeguards of vaccine administered to DOD personnel meets or exceed every standard for vaccine administration to the civilian population. Table A clearly outlines over 14 discrete safety initiatives DOD implements compared to those required by Federal programs. Our program includes a wide variety of activities that can be grouped into three main scientific method categories: clinical studies of vaccine recipients themselves; database analysis of vaccine recipient automated medical records; and spontaneous reports. I will summarize each category for you, as well as describe the adverse events that have been reported to either DOD or FDA or both.

Table A: Comparison of Federal Vaccine Safety Programs

	Vaccines for the Civilian Populace	Vaccines for Armed Forces & Essential Civilians
Responsible Parties	- Centers for Disease Control & Prevention (CDC) - Food & Drug Administration (FDA) - other Federal Agencies	- Department of Defense (DOD), Anthrax Vaccine Immunization Program (AVIP)
A. Manufacturing Quality Standards	FDA's Center for Biologics Evaluation & Research (CBER)	- FDA's Center for Biologics Evaluation & Research (CBER) - Collaboration with BioPort to update product labeling ("package insert") with recent experience
B. Clinical Standards	Vaccine Information Statements (VIS)	- Trifold fact sheet (Quad-fold version under development) - VIS based on Quad-fold sheet under development, to mimic CDC VIS format - Education of leadership - Education of troops and families - Quality of health care delivery (e.g., epinephrine availability) - Automated anthrax vaccination registry
C. Vaccine Safety Surveillance		
Clinical Studies		- Clinical immunogenicity trials (different routes of administration, different dosing schedules) - Vaccine-vaccine, vaccine-drug interaction studies - Long-term studies
Database Studies (i.e., large-linked databases)	Vaccine Safety Datalink (VSD) project	Defense Medical Surveillance System (DMSS), Army Medical Surveillance Activity (AMSA)
Spontaneous Reports	Vaccine Adverse Event Reporting System (VAERS)	Vaccine Adverse Event Reporting System (VAERS)
D. External Advisory Panels	Advisory Committee on Immunization Practices (ACIP)	- Armed Forces Epidemiological Board (AFEB) - Anthrax Vaccine External Committee (AVEC)
E. Compensation Programs	Vaccine Injury Compensation Program (VICP) (for damages)	- Military Health Service System (direct care delivery) - Medical retirement process

Each of these scientific methods has advantages and disadvantages. As the Centers for Disease Control & Prevention (CDC), the FDA and trained epidemiologists

over time discovered, these methods need to be used in tandem, to fully understand whether or not an adverse event was caused by a vaccine or merely coincided in time with the vaccination. Coincidental events are sometimes referred to as temporal (pertaining to or limited in time) associations.

DOD follows the convention of CDC, FDA, and the nation's public health and epidemiologic specialists in distinguishing adverse events and adverse reactions. Adverse events are adverse outcomes, for which a cause-and-effect relationship with an exposure (to a medication or vaccine) has not yet objectively been determined. An ***adverse event*** becomes an ***adverse reaction*** once objective evidence is available to establish a cause-and-effect link between an exposure and an adverse outcome. Table B lists some of the criteria proposed many years ago by famed epidemiologist Sir Austin Bradford Hill that help us make the determination of causal association.

Table B: Causal Association Criteria

1. How strong is the association between the exposure and the outcome?
2. What is the quality of the evidence for an association?
3. Is there a dose-response relationship?
4. Is there consistency among several studies?
5. Is there a specific cause for the effect observed?
6. Did the cause exist before the effect occurred?
7. Is the outcome plausible, given what we know about biology?

Adapted from: Rothman KJ, Greenland S. Modern Epidemiology, 2nd ed. Philadelphia: Lippincott-Raven, 1998:24-28.

Let me now review the three scientific method categories of evaluations.

CLINICAL STUDIES

Clinical studies are active studies that have the advantage of compiling data that is valid and reliable. They are expensive and time-consuming. Good clinical studies are often narrowly focused. Great care must be taken in designing clinical studies to avoid pitfalls that epidemiologist experts call *selection bias* and *recall bias*, among others. The challenge is to design a study that eliminates *alternative explanations*. As described below, numerous clinical studies have been conducted on the safety of the anthrax vaccine.

BRACHMAN STUDY

Some of the original safety data on anthrax vaccine was collected through *active monitoring* of vaccine recipients from the Brachman study of 1,330 mill workers in the northeastern United States (*Am J Publ Health* 1962;52:632-45). Brachman showed that *mild local reactions*, consisting of 1 to 2 cm of redness, plus slight local tenderness, occurred in about 30% of recipients. *Moderate* local inflammation (a defensive reaction to irritation) (> 5 cm in diameter), occurred in 4% of recipients. More *severe* local reactions occurred less frequently and consisted of extensive swelling of the forearm, in addition to local inflammation. *Systemic reactions* (reactions beyond the limb into which the vaccine was injected) occurred in fewer than two per thousand (< 0.2%) recipients. These reactions included malaise, and even less frequently, fever and chills.

LICENSURE SAFETY STUDY

Studies on the safety of four lots of anthrax vaccine in the late 1960s, involving approximately 16,000 doses administered to approximately 7,000 people, were submitted in support of vaccine licensure to the National Institute of Health (NIH) Division of Biological Standardization (now the Center for Biologics Research & Review of the FDA) by the Communicable Disease Center (now the Centers for Disease Control & Prevention). With *active querying* and examination of vaccine recipients, *mild local reactions* (<= 3 cm) were reported after 3% to 20% of doses administered. *Moderate reactions* (> 3 cm to < 12 cm) were reported after 1% to 3% of doses. *Severe reactions* (>= 12 cm) were reported after fewer than 1% of doses. *Systemic reactions*, reported in four individuals (fewer than 6 per 10,000 doses), consisted of fever, chills, nausea and general body aches, which resolved spontaneously.

FT. DETRICK MULTI-DOSE SAFETY STUDY

Starting as far back as the 1950s, 99 male laboratory workers at Fort Detrick, Maryland, were followed for up to 25 years, after being vaccinated against multiple diseases, including anthrax. Regrettably, these studies did not include control groups considered adequate by today's standards. While there were some minor elevations in liver and kidney function tests and white blood cell counts in these men (which cannot reliably be distinguished from the simple effects of aging), none of these men developed any unusual diseases or unexplained symptoms that could be attributed to the repeated doses of multiple vaccines [*Annals of Internal Medicine* 1965;63:44-57; 1974;81:594-600; *Bulletin of the Johns Hopkins Hospital* 1958;103:183-98].

SPECIAL IMMUNIZATION PROGRAM SAFETY STUDY

In another clinical study begun in 1973, a study group of 1,590 people working in the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), received 10,451 doses of anthrax vaccine, as part of USAMRIID's Special Immunization Program (SIP). Based on visits to an occupational health clinic (the USAMRIID Special

Immunizations Clinic), 4% of doses resulted in a *local reaction* consisting of redness, induration (an area of hardened tissue), itching, and soft or puffy swelling (edema) at the injection site. *Systemic reactions* of headache, fever, chills, malaise (discomfort, uneasiness), muscle and joint aches occurred after 4 per 1,000 doses. All *local* and *systemic* reactions resolved without any lost time from work, hospitalization or long-term effects. These employees continue to be examined and tested annually for medical conditions since their last visit, yet no diseases or unexplained symptoms have been observed that would not be expected in an unvaccinated group of comparable age and other demographic characteristics.

FT. BRAGG BOOSTER STUDY

In yet another DOD sponsored clinical study, USAMRIID investigators actively assessed the safety of booster doses of anthrax vaccine in 1992-93, given to 486 U.S. Army soldiers at Fort Bragg, North Carolina who had been previously vaccinated against anthrax during the Persian Gulf War 1990-91. Of these soldiers, 21% had local redness and/or swelling in the arm where the booster vaccination was administered. In 5%, the redness and/or swelling was >= 5 cm. No reaction caused lost time from work or hospitalization and all reactions resolved without lasting consequences. One or more *systemic reactions* occurred in 44% of recipients during the first 30 days after vaccination, most commonly muscle aches (30%), malaise (16%), headache (16%), rash (16%), or joint aches (12%). We should note that these troops were engaged in a field exercise at the time of this study. Therefore, the role of the anthrax vaccination cannot reasonably be separated from the rigorous physical exertion (*alternative explanation*) commonly associated with Special Forces field deployments.

CANADIAN SAFETY STUDY

A Canadian sponsored, actively monitored study of vaccine reactions in 576 Canadian Service Members who received anthrax vaccine in 1998 revealed that *mild local reactions* (<= 5 cm) after 9.5% of doses, *moderate local reactions* (> 5 to 12 cm) after 0.5%, with no *severe local reactions* occurring. *Systemic reactions* occurred after 1.4% of doses. Five people developed a fever with or without chills, two reported transient (temporary) indigestion. One vaccine recipient developed a transient nerve disorder. One individual reported having a persistent lump (nodule) at the injection site and multiple nodules at several distant sites, but it is unknown whether those lumps existed unnoticed before the vaccination.

USAMRIID REDUCED DOSE STUDY

In another DOD sponsored pilot study, USAMRIID actively collected safety data during a pilot study to evaluate a reduced schedule for administering the anthrax vaccine (the current protocol requires administration of six doses, given at 0, 2 and 4 weeks and 6, 12 and 18 month intervals with an annual booster). The safety of the standard schedule of the first three doses (0, 2, 4 weeks) into the subcutaneous fat layer under the skin (a subcutaneous injection) was compared to two doses given

subcutaneous and also compared to two injections into the muscle in the upper arm (an intramuscular deltoid injection), in a study totaling 173 people. *Systemic adverse events* were uncommon and their incidence did not differ among the three groups. After the first dose, the side effects noted were headache (14%); malaise (9%); loss of appetite (3%); nausea or vomiting (3%); muscle ache (3%); itching (3%) and low grade fever (3%). Redness and swelling at the injection site occurred more commonly among those given subcutaneous injections, compared to intramuscular injections. Male vaccine recipients developed injection-site reactions less frequently after subcutaneous injection (5% to 32%) than female vaccine recipients (39% to 66%), but the rates were comparably low for both genders when the vaccine was given by intramuscular injection (5% to 7%). Subcutaneous nodules, which resolved spontaneously, were common among recipients of subcutaneous injections, but were not observed among recipients of intramuscular injections. Subcutaneous nodules were usually not noticed by the vaccinee and resolved spontaneously. This pilot study provides compelling evidence that *local adverse events* are less common when the intramuscular route is used to administer anthrax vaccine.

USAMRIID presented these preliminary findings to the FDA in December 1998, showing fewer doses by a less reactive route produce comparable levels of protective antibodies. The FDA requires an additional study of more than 900 anthrax vaccine recipients before it will consider to definitively assert the change in route and schedule is comparably safe and effective as the current route and schedule. This confirmatory trial is being planned at this time, under the sponsorship of the Joint Program Office for Biological Defense.

The difference in injection site reactions between men and women is interesting. The biological explanation for this phenomenon may involve chemicals that transmit signals between cells in the blood or hormonal variations. This is intriguing to biological scientists in both civilian and military health care and needs to be assessed further. The pursuit of answering this question under the support of the AVIP or another agency is the subject of ongoing discussions.

TAMC-600 Study

The next study collecting data on the safety of the anthrax vaccine that I will describe is a prospective, population-based survey conducted at the Tripler Army Medical Center (TAMC), Honolulu, Hawaii. Called the TAMC-600 Study, the survey included 603 TAMC personnel who are physicians, nurses, medics and other medical support personnel who augment U.S. medical forces in Korea in the event of military contingencies. Note that the people surveyed are a highly educated, medically experienced population who would be more able than the norm to describe any adverse events that might occur (and introduces a potential *population bias*). The objectives of this study were to compare the TAMC data to previous studies and to evaluate the TAMC data against spontaneous reports submitted through DOD and FDA channels. Overall, the incidence of *local* reactions, specifically subcutaneous nodules and muscle soreness, are higher than previous surveys or studies, approximately 70% and 65%,

respectively. *Systemic reactions* were not remarkably different from previous clinical experience. About 55% of vaccine recipients reported no *systemic* symptoms; about 20% reported symptoms that they personally judged could be ignored; 15% reported symptoms that affected their activity for a short time but did not limit their ability to perform duties; 8% reported symptoms that affected their activity for a short time that was relieved by self-treatment with nonprescription medication; and fewer than 2% reported that their symptoms were unrelieved by medication and that their ability to perform their duties was limited for a short time. In this group of vaccine recipients, the relative frequency of side effects for each of the first four doses was measured. The frequency of reports of muscle aches was roughly 15%, which represented the most frequently reported *systemic* complaint. The results for all *systemic* complaints did not substantially vary between dose #1, dose #2, dose #3, and dose #4. Muscle aches typically lasted between 7 hours and 3 days. In this group, three spontaneous reports (the FDA Form VAERS-1) were submitted and only one person lost more than one day of work and none were hospitalized.

USAF Vision Study

United States Air Force researchers are finalizing a multicenter pilot study of the effects of anthrax vaccine on visual acuity. The first phase of this study assessed 354 aircrew members vaccinated against anthrax and 363 unvaccinated aircrew members. Vision changes over the course of one year occurred in 12% of vaccinated crewmembers compared to 16% of unvaccinated crewmembers. Additional data are being accrued to increase the precision of this analysis.

Comparison of Anthrax Vaccine with Other US Vaccines

The safety data on anthrax vaccine compare very favorably with safety data for other vaccines licensed in the United States. For hepatitis A vaccine, soreness at the injection site was reported by 56% of adult vaccine recipients. Headache was reported by 14%. For the typhoid polysaccharide vaccine, local tenderness was reported by 98%, pain by 56%, malaise by 24% and headache by 11%. The pneumococcal vaccine has a 71% rate for localized soreness. The recently licensed Lyme disease vaccine produced localized pain in 93% of recipients and fever in 2.5%. The hepatitis B vaccine reports a *local reaction rate* of 17% and a *systemic reaction rate* of 15% in adults.

Each of these nine clinical safety studies alone, as well as all the studies in aggregate (totaling 12,599 people), confirm that the principle *adverse reactions* associated with anthrax vaccine involve the injection site or minor, transient systemic events like malaise or headache. It is important to note all the events that did not occur during the surveillance described above. No deaths occurred following doses of anthrax vaccine, nor any cases of severe allergic hypersensitivity reactions (known as anaphylaxis). The anthrax vaccine clearly has a more favorable side-effect profile, compared to other vaccines commonly used by the civilian population.

Additional Long-Term Study

On July 29, 1999, the Anthrax Vaccine Immunization Program will convene a team of civilian and military medical experts to design a set of studies to assess the long-term safety of anthrax vaccine, in response to requests from Service Members, their families and recommendations of the General Accounting Office. In designing these studies, we will draw from the accumulated experience of some of the nation's best vaccine researchers at CDC, FDA, and civilian universities.

This section summarizes the clinical studies performed to date and those anticipated in the near term. Recall that clinical studies are limited in their ability to detect rare events. Thus, I would like to discuss the next category of scientific study method, database analyses.

Database Analyses

Database studies are active inquiries that can be completed more quickly than clinical studies, if data of interest have already been compiled in electronic databases. Database studies are only as valid and reliable as the quality of the data in the database. They are relatively inexpensive, after the investment in compiling the database is taken into account and they are the one of the best means of assessing rare adverse events.

The Defense Medical Surveillance System (DMSS) is coordinated by the Army Medical Surveillance Activity (AMSA), under the supervision of the U.S. Army Center for Health Promotion & Preventive Medicine (USACHPPM). The DMSS offers the capability to analyze hospitalizations, outpatient visits and other automated records. We intend to use the DMSS to measure the impact of anthrax vaccine, if any, on health outcomes among vaccinated Service Members, to see if it differs from unvaccinated Service Members. Plans are being developed now for more studies of this type, assessing both short-term and long-term questions of vaccine safety, as discussed in the previous sections.

Having discussed the various *active* studies already accomplished and those we are planning, I will now explain our solicitation and analysis of spontaneous reports of *adverse events*, a *passive* form of surveillance.

Spontaneous Reports

Spontaneous reports are unedited reports of individual patient-clinician experiences. But clearly, spontaneous reports are rarely sufficient to assert that the risk of an *adverse event* is higher in a group of vaccine recipients than in a comparable group of unvaccinated people. CDC and FDA agree that spontaneous reports are important for generating signals of issues to address further, but spontaneous reports cannot determine cause-and-effect directly. Spontaneous reports are uncontrolled,

lacking comparison groups. Spontaneous reports are an important part of the national information-gathering effort to assess vaccine safety in general.

VACCINE ADVERSE EVENT REPORTING SYSTEM

The Department of Defense takes advantage of a world class program for collecting spontaneous reports of *adverse events* coincidentally associated with vaccination. This program was developed collaboratively by the FDA and CDC and is called VAERS, the "Vaccine Adverse Event Reporting System".

VAERS is known as a *passive surveillance system.* Passive in this case means VAERS relies on the initiative of health care professionals and patients to report adverse events after immunization. I should note that VAERS reports, by definition, will include a combination of events caused by the vaccine and coincidences that are only temporally associated with immunization and have no cause-and-effect relationship with the vaccine.

Military health care professionals have been instructed repeatedly in multiple media and over many years to report *adverse events.* Naturally, we are most interested in serious adverse events, but we are also interested in reactions at the injection site, what are often called "local reactions." Let me say again, DOD encourages our health care professionals to report all *adverse events* that they consider important and clinically relevant.

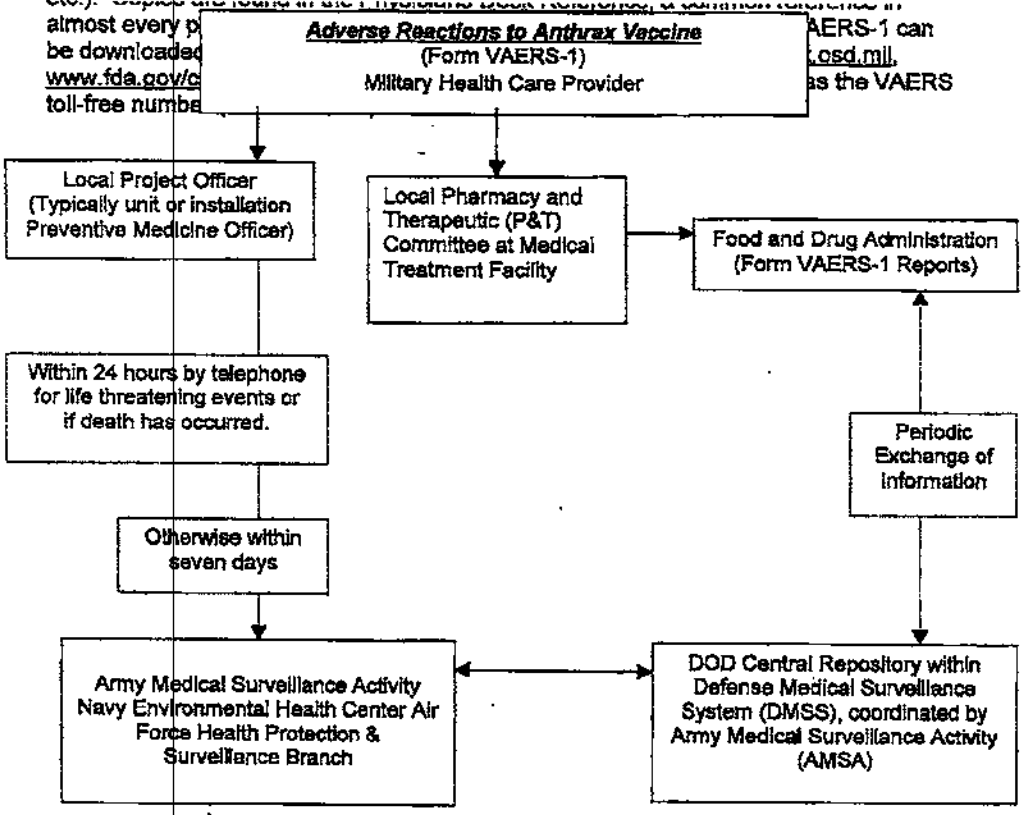
DOD JOINT IMMUNIZATION REGULATION

The duty to report adverse medication events has been codified for many years in the joint immunization instruction (Army Regulation 40-562, Bureau of Medicine & Surgery Instruction 6230.15, Air Force Joint Instruction 48-110, Coast Guard · Commandant Instruction M6230.4E, dated November 1, 1995). The joint regulation requires submission of a Form VAERS-1 for all adverse events resulting in more than 24 hours of lost duty time or any period of hospitalization. These requirements represent a higher standard than in comparable civilian community health care settings. VAERS reporting is strictly voluntary for civilian health care providers. DOD VAERS reporting channels are depicted in Figure 1, below.

DOD has have been consistent with CDC instructions to civilian health care professionals for VAERS reports and MedWatch (for reporting adverse events related to medications other than vaccines). Full and complete reporting of VAERS, MedWatch, and their predecessor programs has been the DOD policy for decades.

Copies of Form VAERS-1 are readily available at the pharmacy of every military medical treatment facility, as well as from multiple clinics and departments within the facility (e.g., pediatrics, internal medicine, immunization clinics, emergency department,

Figure 1: DOD Reporting Channels for Adverse Events to Anthrax Vaccine



DOD FORM VAERS-1 INITIATIVES

Additionally, DOD emphasizes/encourages Form VAERS-1 reporting in the following publications/policies/initiatives:

◆ The Apr 99 updated DOD "Force Health Protection Against Anthrax Leaders Briefing", required to be given for all Service Members and DOD Emergency Essential Civilians by supervisors/commanders prior to receiving the anthrax immunization. Slides 12, 13, 14 clearly state for example, for both the AC and RC, "any vaccine associated adverse event may be reported through VAERS by either the patient of provider...in writing or by calling 1.800.822.7869...reporting instructions are available on the Internet at www.fda.gov/cber/vaers.htm."

◆ The Apr 99 updated DOD "Anthrax Vaccine Immunization Program Health Care Providers Briefing", slides 31, 32, 33 provide clear clinical guidelines for VAERS reporting in addition to the guidance provided in the Leaders Briefing above.

◆ DOD Policy Memorandum "Policy for Reporting Adverse Reactions Associated with the Anthrax Vaccine Immunization Program (AVIP)" created 30 Jun 98, issued 21 Apr 99 for Service coordination/implementation outlines clinical protocols and algorithms for submitting VAERS. This policy also requires submission of an "Anthrax Vaccine Adverse Reaction Supplemental Form" in addition to the VAERS.

◆ DOD Policy Memorandum "Ensuring Reservists Have Full Access to Department of Defense (DOD) Medical Treatment Facilities (MTF) for Treatment of Adverse Events from DOD Directed Immunizations" staffed May 99, clearly outlines patient or provider submission of Form VAERS-1. The Memo will be accompanied by a Patient Information 'walk-away' brochure outlining facts about the anthrax vaccine, local and systemic reactions and adverse event reporting options, phone numbers, instructions, Internet access, etc.

◆ DOD Clinical Practice Guidelines for the Management of Anthrax Vaccine Adsorbed Adverse Events, were finalized during the 25-27 May 99 Annual DOD Conference for Biological Warfare Defense Immunizations. Over 150 personnel attended this AVIP Agency sponsored conference from the Services and Interagency participants (CDC, DHHS, Johns Hopkins University, FDA, George Washington University, AFEB, JVAP, CHPPM, USAMRIID, GAO, etc. The Guidelines outline clinical protocols, pre-treatments, specialty referral processes, contraindications, categorization of local and systemic reactions and associated treatment algorithms. The Guidelines clearly outline patient or provider reporting of Form VAERS-1 with all associated phone and Internet access numbers. In addition to normal Service distribution of the Guidelines, they can also be found on the www.anthrax.osd.com web site.

◆ Form VAERS-1 reporting options, sources of information, downloaded copies of the form are a prominent feature of our newly revised anthrax website www.anthrax.osd.mil with separate hot button access to adverse reporting.

◆ The AVIP Agency's 1.877.GETVACC hotline, scheduled for 1 Aug 99 implementation will prominently feature patient or provider reporting of adverse events.

◆ The AVIP Open House/Speakers Bureau effort routinely addresses adverse event reporting, sources of information, etc.

◆ The AVIP Agency continues to encourage advertising VAERS reporting awareness on each of the Services automated Immunization Tracking Systems. The Army's Medical Protection System (MEDPROS) began such advertisements on 7 Jun 99.

◆ The AVIP Agency highlights VAERS reporting in their silent training aids product line in addition to other key themes such as dosing schedule, recording all vaccinations, threat, safety, efficacy, etc.

NON DOD SUBMISSION OF FORM VAERS-1

Individual Service Members or their family members are free to submit VAERS reports directly to FDA if they wish. However, this procedure has a number of disadvantages I would like to make you aware of. First, reports submitted by lay people may not be sufficiently detailed to allow grouping with similar reports causing potentially missed trends. Second, reports that go to FDA first, shared later with DOD, have information redacted. This redaction prevents DOD from categorizing demographic or geographic factors that otherwise helps us assess trends.

As you are well aware, several groups of reports of adverse events associated with anthrax vaccination have been reported Dover Air Force Base, Delaware and the 110th Fighter Wing, Battle Creek, Michigan. In each case, local medical officers redoubled their efforts to assure optimal VAERS reporting at their facilities. Reports from these facilities and all other DOD medical treatment facilities are included in the Form VAERS-1 Summary below.

ANTHRAX VACCINE EXTERNAL COMMITTEE

Once the VAERS reports are received at the central offices, an independent external review panel we call the Anthrax Vaccine External Committee (AVEC) evaluates each report received. The AVEC represents a special panel of experts commissioned by the AVIP Agency in early 1998 to review and identify any signaling event that would identify problems stemming from the anthrax vaccine. These experts come from the Health Resources & Services Administration (HRSA), a component of the Department of Health & Human Services sponsored Vaccine Injury Compensation Program (VICP). To date, the AVEC has found no problems stemming from the anthrax vaccine. The AVEC uses explicit criteria for attributing causality to adverse events coincidentally associated with anthrax vaccination, based on work begun by the

Canadian Advisory Committee on Causality Assessment (http://www.hc-sc.gc.ca/main/lcdc/web/bid/di/acca_e.html).

FORM VAERS-1 SUMMARY

VAERS reports flow steadily and reliably through our analytic processes. To be consistent, we will report our findings as of July 1, 1999. As of that date, FDA received a total of 215 VAERS reports. Note that the number 215 are the number of Form VAERS-1 submitted. It does not correspond to a number of people in whom an event occurred. Nor does it refer to 215 events, because the same event may have been submitted through duplicate channels on separate pieces of paper by different reporters or advocacy groups encouraging mass reporting. Recognizing that the number 215 properly refers to Form VAERS-1 submitted, we will simply refer to them as 'Reports' or 'VAERS Reports' for the remainder of this discussion.

Of the 215 reports, 174 have been reviewed by the AVEC, up through their most recent meeting on 29 Jun 99. Of these 174 fully reviewed reports, 50 reported *local reactions* at the injection site only; 95 reported various *systemic reactions* only; 29 reported both *local* and *systemic reactions.*

You specifically asked about the frequency of VAERS reports among Service Members in the active (AC) and reserve (RC) components. As of 1 Jul 99, 153 VAERS reports involved AC members, 17 reports involved RC members, and four involved civilians. We report this data with a high degree of confidence although there is no block on Form VAERS 1 to specifically record AC or RC status. You recall that VAERS reports submitted directly to FDA have personal information redacted. These direct FDA submissions limit our ability to fully categorize the AC or RC component of the person reporting. Thus, 88% were from the AC and 10% were from the RC. The reporting rates were 153 reports from the 285,164 AC personnel vaccinated against anthrax (54 reports per 100,000 vaccine recipients). And 17 reports arose from the 26,662 RC personnel vaccinated (64 reports per 100,000 vaccine recipients). The total reporting rate among RC personnel is only slightly higher than among active-duty personnel, a difference that could easily be explained by the slight imprecision of our ability to attribute reports to AC or RC personnel. None of the 17 RC generated involved hospitalization. Six of those 17 reports involved lost duty time. As expected, there is no indication that reservists are burdened with a greater risk of adverse events than their active-duty colleagues.

Eight reports discussed Service Members hospitalized with an illness coincidentally related to anthrax vaccination. Five have recovered completely. Among the five Service Members who recovered, the reports described the events as one case each of *Guillain-Barre' syndrome*, *multiple sclerosis*, *angioedema* involving the left jaw, *aseptic meningitis*, and severe *injection site inflammation*. Three of the eight Service Members hospitalized with an illness coincidental to anthrax vaccination have ongoing conditions: *bipolar psychiatric disorder*, *diabetes mellitus* and *systemic lupus erythematosus*. You will notice that the serious adverse events reported to date are all isolated cases. Only one of each condition was reported, with each condition being an

event that also occurs among unvaccinated people. There are no reports of outbreaks of multiple cases of same disease, other than allergic-type (hypersensitivity) reactions, described below, that are expected with all vaccines and many medications.

The AVEC judged that there was no evidence that the ongoing conditions or the *angioedema* were caused by anthrax vaccination. The AVEC found evidence submitted through VAERS in the case of the alleged *Guillain-Barre' syndrome* was insufficient to reach a conclusion and they are awaiting receipt of additional information. For the cases of *multiple sclerosis*, *aseptic meningitis*, the AVEC judged the events were incompatible with a causal association and unrelated to anthrax vaccination. Notably, the AVEC judged the *injection site inflammation* event as the only case likely caused by the vaccine.

There have been three reports of serious illness coincidentally associated with vaccination that required loss of duty time greater than 24 hours. These reports involved *urticaria* (generalized itching) with hypersensitivity pneumonia, *spondyloarthropathy* (a vertebra joint disease) and *urticaria* with dizziness. The AVEC members judged the cases of *urticaria*, an allergic-type reaction similar to that seen in other vaccine studies, likely caused by the vaccine. The case of aggravation of pre-existing *spondyloarthropathy* was judged to be unclassifiable, not worthy of further review.

The DOD uses a broader definition of serious adverse events, as we cast a broader net than the FDA definition of "serious." Twelve VAERS reports were submitted for Service Members who lost duty time greater than 24-hours, but were not hospitalized. These 12 reports outlined some of the following temporary symptoms: dizziness, nausea, fatigue, diarrhea, double-vision, abdominal pain, "flu"-like symptoms, urticaria, neck stiffness, abdominal cramps, inflammation at the injection site, migraine headache, mood swings and hair loss. Some of these events have been seen in other anthrax vaccine studies and are fully expected. Some are caused by multiple factors. The AVEC judged all these events "not serious".

FORM VAERS-1 RECAPITULATION

To recapitulate, the AVEC reviewed 174 reports; eight reports reflected hospitalization and 15 reflected other "serious" events by either FDA or DOD definition. All the remaining 151 VAERS reports reviewed by the AVEC through 29 Jun 99 were not serious. That is to say, the remaining 151 reports were a mixture of expected skin reactions or transient flu-like symptoms due to the vaccine, or coincidental events the AVEC judged to be unrelated to vaccination.

The eight reports of hospitalization came from eight different geographic locations. Obviously, there is no geographic clustering of adverse events severe enough to warrant hospitalization. Similarly, the 15 other "serious" events by either FDA or DOD definition were not clustered by geographic location.

No VAERS reports were submitted regarding microbial contamination of vaccine lots. When the VAERS reports were compared to the lot of vaccine administered, there were no correlations between lot and number of reports received.

EDUCATION & COMMUNICATION

The Department of Defense is committed to fully educating our Service Member population and their families on the purpose and value of anthrax vaccination in an unprecedented manner. We use each of the following communications media to accomplish this goal:

- A sophisticated anthrax specific website www.anthrax.osd.mil with multiple layers of information and methods for communicating with our Service Member population, their families, other DOD beneficiaries and concerned members of the American public.

- Three Service specific anthrax websites hyper-linked to all known military and civilian websites discussing anthrax, biological weapons, health care, domestic preparedness, terrorism, VAERS reporting, preventive medicine, infectious disease, etc.

- Three Tri-fold information sheets individually tailored for Service Members, Family Members and Civilians. DOD issued Tri-folds to each Service Member since administering the first doses of anthrax vaccine in March 1998. The Tri-fold explains the threat of biological weapons, the benefits of anthrax vaccination and the known risks from the vaccine. The Tri-fold is currently under revision to become a Quad-fold to include RC specific information on accessing care.

- DOD Leaders Briefing required to be given to all Service Members prior to receiving the anthrax immunization. Distributed by each Service and prominently posted on the www.anthrax.osd.mil website.

- DOD Health Care Providers Briefing given to all DOD health care providers who then serve as teachers, coaches, mentors for supervisors, commanders, Service Members and their families. Distributed by each Service and prominently posted on the www.anthrax.osd.mil website.

- Open House/Speakers Bureau briefings and open educational forums for all Service Members and their families.

- A 1.877.GETVACC telephone hotline scheduled for 1 Aug 99 implementation.

- A variety of anthrax vaccine 'silent training aids'. These highly visible training aids emphasize the key themes of the anthrax threat, safety and efficacy of the vaccine, adverse event reporting, etc.

◆ Armed Forces Information Service news media; local installation print, radio and television news service initiatives.

◆ A state of the art Anthrax Education CD-ROM which provides Service Members, families, supervisors, commanders and health care providers with tailored, multimedia information on the anthrax threat; safety and efficacy of the vaccine; signs, symptoms and prevention of anthrax. Under development for over none months, the CD is scheduled for release in Sep 99.

◆ An Anthrax Vaccine Immunization Program Videotape explaining the threat, safety, efficacy of the vaccine. The video features prominent civilian and Government scientists and vaccine experts explaining and endorsing the vaccine. Under development for over six months, the Videotape is scheduled for release 19 Jul 99.

◆ DOD is currently collaborating with CDC to array this information in the format of Vaccine Information Statements (VIS) that civilian health care providers around the country give America's children, adolescents, and adults during routine vaccinations. Our DOD VIS is currently in draft with an expected implementation date of 1 Sep 99.

THE BEST INDIVIDUALIZED CARE

"Consensus Clinical Practice Guidelines For the Management of Anthrax Vaccine Adsorbed Adverse Events" is our DOD written and produced document providing diagnostic and treatment protocols for adverse events coincidentally associated with anthrax vaccine. These Guidelines help individual health care providers who see and treat Service Members in their practice of medicine. The Guidelines enable consistent care and medical work-ups to best serve the individual health needs of Service Members, as well as providing guidance about when to issue medically appropriate waivers or deferrals from further doses of anthrax vaccine.

Clinical Guidelines were issued in draft form in May 1999, based on a consensus panel of civilian and military physicians experienced both in immunology and the general provision of health care. The finalized Guidelines were electronically transmitted to all military medical treatment facilities in early July 1999, as well as being posted on the www.anthrax.osd.mil AVIP website. Guidelines represent DOD's concerted effort to standardize the evaluation and care of people who have adverse events after vaccination against anthrax.

WAIVERS, DEFERRALS AND REPORTING

We define a waiver as a long-term postponement from receiving additional doses of anthrax vaccine. A deferral is a temporary delay, such as during the course of an acute illness, pregnancy or similar short-term condition. Although the Services collaborate in designing the administrative and medical criteria for waivers and deferrals, each Service reports waivers or deferrals according to the needs of the individual Services. The U.S. Army can identify locally and centrally all doses

administered, as well as all administrative and medical waivers and deferrals, in its Medical Protection System (MEDPROS) database. The U.S. Navy and U.S. Marine Corps can identify local doses administered using the Shipboard Non-tactical Automatic Program/Automated Medical System (SNAP/SAMS), but does not collect information about waivers or deferrals. The U.S. Air Force tracks local doses administered, as well as waivers and deferrals, using its Military Immunization Tracking System (MITS). All four services transmit data to the central Defense Enrollment Eligibility Reporting System (DEERS) database.

MONITORING AND COMPLIANCE REPORTING

Monitoring and compliance using guidelines discussed in the preceding paragraphs are an ongoing quality assurance/quality improvement responsibility of both individual medical treatment facilities and the DOD military health system. Overarching guidance is established in a variety of ways, including standards printed in the joint immunization instruction, "Immunization and Chemoprophylaxis Regulation" (Army Regulation 40-562, Bureau of Medicine & Surgery Instruction 6230.15, Air Force Joint Instruction 48-110, Coast Guard Commandant Instruction M6230.4E), dated 1 November 1995. This regulation represents the current standard for immunizations and chemoprophylactic practices within the military health system. In addition to this joint regulation, each Service formal anthrax immunization implementation plan addresses clinical aspects of vaccine administration. Furthermore, we have begun additional programs to train health care providers before the next major expansion of the anthrax vaccine immunization program. In May 1999, the AVIP Agency sponsored the "First Annual DOD Conference for Biological Warfare Defense Immunizations" at Fort Detrick, Maryland, to train clinical experts in anthrax immunization. These trainers will further train and advise medical treatment facilities within their Service specified geographic areas or regions.

DOCUMENTATION

There are several other quality assurance/quality improvement measures commonly adopted in medical treatment facilities to ensure the highest clinical standards are fulfilled. All clinical encounters (e.g. immunizations administered, sick call visits, hospitalizations, etc.) are documented in the patient's health record (HREC). Each dose of anthrax vaccine is recorded in service-specific and DOD-wide tracking systems. The service-specific tracking system reports when a service-member is due the next dose or has been waived or deferred.

CLINICAL PANELS

At the facility level, health care providers use panels called morbidity-&-mortality committees to discuss and investigate negative outcomes such as death (none of which have been reported to date from anthrax vaccination). Medical treatment facilities have pharmacy & therapeutics (P&T) committees to review and encourage reporting of all medication-related adverse events (including those involving vaccines). Treatment

facilities submit reports of their quality assurance/quality improvement programs to each Service medical headquarters for corporate review and analysis. To monitor and assure compliance, all Services report any adverse events weekly to their higher medical headquarters.

INSPECTOR GENERAL STUDY

A DOD inspector general (IG) study begun Nov 98 is still underway to measure compliance with requirements to document anthrax vaccination. Data is still being collected and a final IG report is scheduled for October 1999.

DEPLOYMENT ELIGIBILITY GUIDANCE

Guidance to Service Members, Emergency Essential Civilians and contractor personnel regarding deployment eligibility involving anthrax vaccine is found in each Service anthrax immunization implementation plan; in the DOD Country/Theater Clearance Guide; and the "One Day Policy" issued 30 Mar 99 by the Secretary of Defense establishing a policy requiring anthrax immunization for duty in any of the current high-threat areas of one day duration or more. According to the Service implementation plans for anthrax immunization, DOD force-protection policy states a Service Member will be considered deployable if he or she received the first dose of the six-dose series, regardless of whether or not the series is complete. In those rare instances when an individual is unable to start or continue the anthrax vaccination series due to medical or administrative reasons, as with all DOD vaccines required for worldwide deployment, the Service Member is still deployable, but is the clear exception to the rule. The DOD goal is to receive the first three immunizations (at 0, 2 and 4 weeks) before entry into high threat areas because of the high degree of protective antibodies conferred. This alleviates some of the complexities of having to vaccinate personnel in a high threat area while trying to focus on contingency operations. Anyone unable to comply with vaccination prior to deployment begins or continues the vaccination series upon arrival. Clearly the DOD objective is to begin Total Force vaccinations once the anthrax vaccine stockpile is assured in order to eliminate these deployment confounders.

Our National and Military Security Strategies are founded on a posture of global engagement and emergency response, often requiring no-notice or short-notice deployment of AC and RC units and individuals who deploy, fight and support as teams. DOD is committed to protecting Service Members and Emergency Essential Civilians and contractors with a full anthrax vaccination series. Our program is sufficiently flexible to allow for individual waivers and deferrals when in the individual's best interests, based on objective scientific, clinical expertise and operational requirements.

RESERVE COMPONENT RETENTION

As of July 1, 1999, our records reflect 311,826 Service Members received at least one dose of anthrax vaccine. These include 285,164 members of the AC (91%) and

26,662 members of the RC (9%). Most of the reservists vaccinated to date are in rapid response units, primarily Air Force units. We consider it much too early in the process of vaccinating people in the Reserve Component to assess the effect, if any, of the Anthrax Vaccine Immunization Program on Reserve Component retention.

Isolating the effect of anthrax vaccination on RC retention in a turbulent environment, when so many variables are simultaneously changing, is very difficult to achieve. As you know, Mister Chairman, reserve units are experiencing unprecedented high levels of operations tempo (OPTEMPO), personnel tempo (PERSTEMPO), consolidation of units, changes in missions and equipment (e.g. sea, ground, air major combat platforms), downsizing, deactivations, realignments and other factors. The Assistant Secretary of Defense for Reserve Affairs is currently conducting a series of exit surveys of individuals leaving reserve service to identify trends about which you inquired.

CONCLUSION

DOD conducted serious studies to assess the safety and efficacy of the anthrax vaccine. We have found no serious, long-lasting adverse reactions due to anthrax vaccine. An independent panel of civilian academic experts, from some of America's best clinical institutions confirms our findings. I assure you, the Department of Defense is and will continue to be vigilant in our surveillance for any rare, unexpected reactions to anthrax vaccine. We are committed to fully investigating all allegations against the safety of anthrax vaccine and continuing full and complete disclosure of all risks, based on objective evidence.

We know anthrax kills and vaccination protects. We know death from anthrax is vaccine preventable and that DOD has a safe and effective vaccine to protect its Service Members. Vaccinating men and women we place in harms way to prevent death or serious injury is our moral and ethical duty — a leadership responsibility we perform with full and unfettered confidence.

Thank you for listening. I am now prepared to answer your questions.

(48)

C*O*N*G*R*E*S*S*I*O*N*A*L

CMAT Control #
2000244-00000[illegible]8

CHIEF OF LEGISLATIVE LIAISON
CONGRESSIONAL INQUIRY DIVISION
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August 29, 2000

OFC OF THE SPEC ASS'T FOR GULF WAR ILLNESSES
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FALLS CHURCH VA 22041

Control ID: **00803682** Task Officer: (b)(6)

Tasked Agency: **GULF** Action: **Direct Reply**

Suspense Date: 05-SEP-2000

Constituent: (b)(6)

Subject: Gulf War Ilness

Member of Congress: Senator Don **Nickles**

Remarks:

Keyword: GULF WAR SYNDROME

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REMINDER: Direct replies require a courtesy copy be provided to OCLL

DON NICKLES
OKLAHOMA

SECRETARY OF THE SENATE

2000 AUG 14 AM 7:50

United States Senate

WASHINGTON, DC 20510-3602

COMMITTEES
FINANCE
ENERGY AND NATURAL RESOURCES
BUDGET
RULES AND ADMINISTRATION

August 4,2000

Respectfully referred to

Department of Veteran's Affairs

for such consideration as the communication herewith submitted may warrant, and for a report thereon, in duplicate to accompany return of enclosure.

By direction of

DON NICKLES
U.S. Senator

Please reply to G.T. Bynum of my staff.

DEPT OF VETERANS AFFAIRS
SENATE CONG LIAISON SVC
321 SENATE HART BLDG

00 AUG -7 AM 10:31

U11340 /00

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OKLAHOMA CITY, OK 73102

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409 SOUTH BOSTON
TULSA, OK 74103-4007

601 SW D AVENUE
SUITE 206
LAWTON, OK 73501

1914 LAKE ROAD
PONCA CITY, OK 746

Author: (b)(6) at Internet
Date: 7/20/2000 9:44 PM
TO: senator at Nickles-DC
Subject: Gulf War Illnesses and Co A 402d TSB, 95th DIV, Lawton, OK
---------- Message Contents

Dear Senator Nickles; You may remember me, I am (b)(6) former IRS Revenue Officer in the (b)(6) office. I helped resolve several congressionals filed by SW OK. taxpayers who felt they had been mistreated by certain employees of the Lawton office's Collection Division. YOU may also recall helping me secure a medical (workman's Comp) retirement from the IRS/Dept. of Labor. This is to make you aware that several members of Co A have and or displaying symptons of the GWI. Our Commander, MAJ (b)(6) USAR, died of cancer last year. Several have displayed chronic fatigue syndrome,lower back pains(severe), joint problems and various types of sexual dysfunctions.
Only A Company
recived the full vaccinations/inoculations as we were 11Bravos, Infantrymen. To the best of my knowledge no one in the other MOS's has had any of these problems. The reason we received the full compliment of shots,vaccines, etc is that it is common knowledge that the reservist infantrymen were going to fulfill any levy Ft. Sill received for infantrymen. "Vaccine A" was an unapproved vaccine Desert Storm soldiers have received. This vaccine was suspended in an animal protein to be administered. The effects of this appears to be mycoplasma and an auto-immune disorder. The auto-immune disorder has been theorized to cause AIDS among veterans. Have you seen the pictures of soldiers who are dying, have turned purple and have tubes in every orafice? I have and it is a terrible thing to see. I have read on various sites that Lawton/Ft Sill has a very high rate of GWI. My own health has deteriorated since my retirement. Doctors say that I have the heart and eyes of a 70 year old, col
on of a 65 year old.

(b)(6)

Reply by: US_Mail

August 9, 2000

The Honorable Don Nickles
United States Senate
Washington, DC 20510

(b)(6)

Dear Senator Nickles:

This is in reference to your inquiry on behalf of (b)(6).

Since this matter falls under the jurisdiction of the Department of Defense, we have referred your inquiry to that Agency for appropriate response.

If we can assist in any other way, please let us know.

Sincerely yours,

PHILIP R. MAYO
Director, Congressional Liaison Services
321 Hart Senate Office Building
Washington, DC 20510

DEPARTMENT OF VETERANS AFFAIRS
OFFICE OF CONGRESSIONAL AFFAIRS
WASHINGTON DC 20420

August 9, 2000

(b)(6)

Assistant Secretary for Legislative Affairs
Department of Defense
1300 Defense, The Pentagon
Washington, DC 20301-1300

CONGRESSIONAL REFERRAL

The enclosed correspondence from Senator Don Nickles on behalf of (b)(6) comes under your jurisdiction and it would be appreciated if you would provide the appropriate response. The Senator has been advised of this referral.

Sincerely,

PHILIP R. MAYO
Director, Congressional Liaison Services
321 Hart Senate Office Building
Washington, DC 20510

Enclosures
LJ/jcl

(b)(6)

09/20/2000 12:58 PM

To: (b)(6) @hqda.army.mil
cc: (b)(6) OSAGWI@OSAGWI

Subject: CONTROL ID 00603662
Document is set for Permanent Archival

(b)(6)

Our reply to MOC Nickles regarding (b)(6) is in coordination, awaiting Dr. Rostker's signature as of 9/19. I will fax you a copy of the signed letter for your files.

(b)(6)

(b)(6)

Office of the Special Assistant to the Secretary of Defense for Gulf War Illnesses, Medical Readiness and Military Deployments

CMAT #: 0244-018

Date: SEP 07 2000

Action Tasking // Internal Routing Sheet

			Action	Info	Comments
7	Special Assistant	(SA)			signature
5	Deputy Special Assistant	(DSA)	V 9/8		
6	Executive Assistant to SA	(EA)			
	Executive Assistant to DSA	(EADSA)			
	☐ Director, Investigation & Analysis ___ (IAD) ☐ C/B __ ☐ ENV __ ☐ PAG __ ☐ VDM __				
	Dir Lessons Learned Implementation	(LLI)			
3	Dir Public Affairs & Outreach	(PAO)	for signature		
2	Dir Medical Readiness	(MR)	BAR	9/19/00	
	Legal Advisor	(LGL)			
	Info Technology & Security	(ITS)			
4	PM, Gulf War Illnesses Support	(PM)	WMA	9 Sep	
1	Editorial Review	(ER)	Dow	9/7/00	amend as indicated, esp. by adding comparative statistics, if available
8	☐ COMEBACK COPY TO: MOI ☐ GET CMAT NUMBER WHEN SIGNED&SENT ☐ READING FILE ☒ CHRON FILE				

SUSPENSE:

Prepare reply for signature of:

☐ Special Assistant ☐ Deputy Special Assistant

Response to Senator Nichles

re: (b)(6)

☐ Congress ☐ Oversight ☐ FOIA ☐ OSD ☐ WBM ☐ VSO/MSO ☐ Outgoing

☐ Ltr to SA ☐ IR ☐ E-Mail ☐ OGA ☐ Other ☐ veteran

KEYWORDS:

08/25/00 Issuance

****
*** TX REPORT ***
****

TRANSMISSION OK

TX/RX NO	**2052**
CONNECTION TEL	(b)(6)
SUBADDRESS	
CONNECTION ID	
ST. TIME	**09/27 12:25**
USAGE T	03'21
PGS. SENT	9
RESULT	OK

Office of the Special Assistant for Gulf War Illnesses,
Medical Readiness and Military Deployments
5 113 Leesburg Pike, Suite 901
Falls Church, Virginia 22041
(b)(6)
Fax: (b)(6)

FACSIMILE TRANSMITTAL SHEET

TO: (b)(6) ***FROM:*** (b)(6)

ORGANIZATION: ICCD

FAX NUMBER: (b)(6) ***TOTAL NO. OF PAGES INCLUDING COVER:*** 9

PHONE NUMBER: (b)(6) ***SENDER'S PHONE NUMBER:*** (b)(6)

SUBJECT: Hon. Don Nickles Congressional

☒ URGENT ☐ FOR REVIEW ☐ PLEASECOMMENT ☐ PLEASEREPLY ☐ PLEASERECYCLE

NOTES/COMMENTS:

This action was given to us by the Army, since it dealt with [illegible]

09/27/00 12:21 FAX (b)(6) OSAGWI/MR/MD 001

****
*** TX REPORT ***
****

TRANSMISSION OK

TX/RX NO	2051
CONNECTION TEL	(b)(6)
SUBADDRESS	
CONNECTION ID	
ST. TIME	**09/27 12:18**
USAGE T	03'03
PGS. SENT	4
RESULT	OK

Office of the Special Assistant for **Gulf War** Illnesses,
Medical Readiness and Military Deployments
5113 Leesburg Pike, Suite 901
Falls Church, Virginia 22041
(b)(6)
Fax: (b)(6)

FACSIMILETRANSMITTALSHEET

TO: (b)(6) ***FROM:*** (b)(6)

ORGANIZATION: Army Legislative Affairs

FAX NUMBER: (b)(6) **TOTAL NO. OF PAGES** ***INCLUDING COVER:***

PHONE *NUMBER:* (b)(6) ***SENDER'S*** **PHONE *NUMBER:*** (b)(6)

SUBJECT: Hon. Don Nickles Congressional

X URGENT X FOR REVIEW ☐ PLEASECOMMENT ☐ PLEASEREPLY ☐ PLEASE RECYCLE

NOTES/COMMENTS:

SECRETARY OF DEFENSE CORRESPONDENCE ACTION REPORT

This farm must be completed and forwarded to the Correspondence Control Division (CCD), WHS Room 3A948. Suspense Desk: (b)(6) FAX Number: (b)(6) Email: (b)(6) @osd.pentagon.mil

Action Agency: GWI

Suspense Date: 20000905

1. ACTION TAKEN (Check one)

- [x] a. ACTION HAS BEEN COMPLETED (Copy attached)
- [ ] b. REQUEST EXTENSION OF SUSPENSE DATE TO *(Justify below)*
- [ ] c. INTERIM REPLY HAS BEEN SENT (Copy attached) EXTEND SUSPENSE TO *(Justify below)*
- [ ] d. REQUEST CANCELLATION *(Justify below)*
- [ ] e. REQUEST TRANSFER TO *(Justify below /include POC Name & Phone Number)*
- [ ] f. REQUEST DOWNGRADE TO *(Justify below)*

2. JUSTIFICATION

Reply to the Honorable Don Nickles on the behalf of his constituent (b)(6)
The Army asked that we respond to this action related to Gulf War illnesses; Army POC is (b)(6) (b)(6)

3. REPORTING AGENCY

a. ACTION AGENCY: OSAGWI

b. NAME OF ACTION OFFICER: CAPT (b)(6)

c. TELEPHONE NO.: (b)(6)

d. DATE: 09/27/2000

4. CCD CONTROL #:

e. APPROVING AUTHORITY
(Service Secretary/Under Secretary/ASD/Military/Executive Assistant Level)

Signature: for (b)(6)

Date Signed: 9/27/00

5. ACTION TAKEN (For EXSEC Correspondence Control Division Use Only)

a. EXT	Approved	Disapproved
b. CANX	Approved	Disapproved
c. DWNGRD	Approved	Disapproved
d. TRANSFER	Approved	Disapproved
e. OTHER (Specify)		

Signature

Date Signed

SD FORM 391, JAN 2000

OFFICE OF THE SECRETARY OF DEFENSE
1000 DEFENSE PENTAGON
WASHINGTON, DC 20301-I 000

SPECIAL ASSISTANT
FOR
GULF WAR ILLNESSES

SEP 2 7 2000

Honorable Don Nickles
United States Senate
Washington, D.C. 205 10

Dear Senator Nickles:

I have received your recent inquiry on behalf of your constituent, (b)(6) . In his letter he expressed the belief his health and that of those who served in his Gulf War unit has been adversely affected by vaccines they received. In the past three years, my office has extensively investigated this issue. I hope the following information is useful to you and (b)((b)(6)

In particular, (b)(6) referred to "Vaccine A" administered to him before Operation Desert Storm. He believes it was not an FDA-approved vaccine. Two vaccines, anthrax and botulinum toxoid, were administered to those at greatest risk for exposure to biological warfare agent attack. Because the vaccine supply was very limited, approximately 150,000 servicemembers received the anthrax vaccine and 8,000 botulinurn toxoid. Operational leaders were particularly concerned that Saddam Hussein not know which units were vaccinated, therefore, the information was protected. In some cases, units protected the information by using codes, such as "Vacc A" and "Vaccine A, " as shorthand for the anthrax vaccine. Many veterans have talked to us about receiving "Vaccine A."

Given the safety and security risks, it was common to withhold vaccination-associated information from servicemembers in theater. Many didn't know what vaccine they received or why. Even after the war, when the information should have been fully entered into individual shot records, this wasn't routinely done. Consequently, many Gulf War veterans incorrectly believe they received unapproved vaccines,

The anthrax vaccine is a cell-free filtrate, produced by a strain of anthrax that does not cause disease. The vaccine contains no whole bacteria, dead or alive. The vaccine was developed in the United States during the 1950s and 1960s for humans and was licensed by the FDA in 1970. Since then, it has been safely and routinely administered to at-risk wool mill workers, veterinarians, laboratory workers, livestock handlers and military personnel in the United States. The anthrax vaccine is not suspended in an animal protein for administration and has not been scientifically connected to mycoplasma, autoimmune disorder or AIDS. Additional information about the anthrax vaccine is available on-line at *http://www.anthrax.osd.mil.*

(b)(6) also is concerned about cancer. The information we have available on cancer related to Gulf War veterans comes from evaluating data collected from the Department of

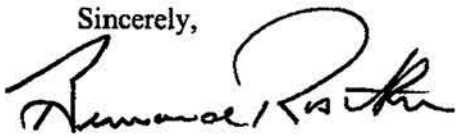
Defense Comprehensive Clinical Evaluation Program (CCEP). Cancer is rare among CCEP enrollees and persons in the Department of Veterans Affairs' (VA) Registry. Physicians have diagnosed cancer in 52 individuals (.3 percent). According to American Cancer Society published data, this rate is far lower than the general population rate of cancer occurrence (1.65 percent for men and 1.95 percent for women) in the 20- to 40-year age group. The majority of Gulf War veterans are in this age group. In the general population, as age increases, the risk of cancer rises correspondingly. Gulf War veterans are no different in this respect. Lymphomas are the most frequent cancer diagnosed in CCEP participants; lymphomas also are the most common types of cancer among the 20- to 40-year age group in the general U.S. population. The second most frequent cancer diagnosis for CCEP participants is skin cancer – again, one of the most common malignancies in the age-matched U.S. general population. Cancer also is rare among individuals in the VA's Registry. The Gulf War veteran population does not appear to have incurred an unusual incidence of any specific type of cancer. Deaths due to illness and disease are lower in Gulf War veterans than the general population, including a lower incidence of cancers.

(b)(6) also expressed his belief that the Fort Sill/Lawton, Oklahoma area has a higher-than-usual rate of undiagnosed illnesses. In reviewing CCEP admissions records, we found the number of Gulf War veterans reporting symptoms in the Lawton/Fort Sill, Oklahoma area is typical of other military communities.

Finally, (b)(6) mentioned his unit, A Company, was experiencing symptoms other units' members did not report. Much of what we have learned about the events of the Gulf War comes from the eyewitness accounts of veterans like (b)(6). To date, we have spoken by telephone with more than 13,000 veterans. We would like to incorporate (b)(6) observations into our database. My staff members are available Monday through Friday from 7 a.m. to 11 p.m. If he is willing to assist our investigation, please ask him to contact us at his convenience using the toll-free number, (800) 497-6261.

Thank you for the opportunity to address your constituent's concerns. I hope this information is helpful to you.

Sincerely,



Bernard Rostker

(49)

SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS,
AND INTERNATIONAL RELATIONS
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http://www.house.gov/reform/ns/

Statement of Rep. Christopher Shays

February 17, 2000

Today we release an oversight report entitled, "The Department of Defense Anthrax Vaccine Immunization Program: Unproven Force Protection." Based on testimony from more than 50 witnesses at six subcommittee hearings and many thousands of pages of DOD and FDA documents, we conclude the program is not sustainable in its present form. It is an unrealistically broad undertaking built on a dangerously narrow scientific, medical and industrial base.

Plagued by unstable supplies, uncertain safety and unproven efficacy against the anthrax threat, the mandatory, force-wide immunization program should be suspended until DOD gets approval to use an improved vaccine. Meanwhile, except in very limited circumstances, the current vaccine would be used only when service members give their informed consent.

The recommendation to suspend the program should come as no surprise. Due to the inability of the vaccine manufacturer to pass Food and Drug Administration (FDA) inspection, DOD has already been forced to defer the next two phases of the program. In this report, we are simply asking DOD to end the mandatory inoculations while focusing on the research and testing that should have been done before the program began.

Designed in the 1950s and 60s, the vaccine was licensed in 1970 for protection against cutaneous (under the skin) anthrax infection. Before the Gulf War, it had not been widely used. After the war, DOD scientists acknowledged the vaccine caused adverse reactions and contained inconsistent amounts of the desired antigenic protein.

They also knew it was unsuitable for broad military use due to the elaborate, arbitrarily established inoculation schedule of six shots over 18 months, plus annual boosters. DOD began, but did not aggressively pursue, research and testing on a purer, safer vaccine and an optimal shot course.

We would not ask our armed forces to fight a battle using rifles and tanks designed in the 1950s. We should not ask them to risk their lives by relying on 1950s vintage medical technology, when modern science has the capacity to produce a safer, more effective vaccine.

When Defense Secretary William Cohen announced the Anthrax Vaccine Immunization Program (AVIP), he set four explicit conditions on implementation of what he apparently knew then would be a complex and controversial program. They were the right conditions. Had they been more than cosmetically addressed, there might be no need for a report like this.

First, to address concerns about vaccine safety raised by deficiencies at the manufacturing plant uncovered by Food and Drug Administration (FDA) inspections, Secretary Cohen

ordered supplemental testing of stockpiled vaccine lots. But when more than half the lots failed the supplemental review, DOD exempted 9 lots from the tests even though they had been produced under the same deficient conditions as all the others.

Second, to address concerns about lax medical record keeping, such as occurred in the Persian Gulf War, Secretary Cohen required an accurate inoculation tracking system to assure compliance with the vaccine's lengthy dosing schedule. But we found the unified tracking system unreliable. Even the Secretary of Defense got his fourth shot three weeks early. Many others missed scheduled shots, sometimes by weeks or months, particularly members of Reserve and National Guard units.

Third, the Secretary required each military service branch to finalize AVIP operations and communication plans. But witnesses testified AVIP operational protocols, particularly with regard to vaccine waivers and adverse event reporting, were not being followed. A DOD witnesses acknowledged communication to reserve component members had not been effective.

Finally, Secretary Cohen assured service members the program would be subjected to an independent medical and scientific review. But we discovered only a cursory review of DOD materials by a friend of the Department who, while well meaning, acknowledged he had no expertise in anthrax.

Because the anthrax vaccine is still being studied as a possible causative or contributing factor in Gulf War veterans' illnesses, its use in a vastly expanded and demographically diverse population should be monitored carefully. Women report adverse events after receiving the vaccine at twice the rate among men. But we found DOD's reliance on a passive reporting system very likely, if not predisposed, to understate the true health effects of the vaccine.

To address that problem we recommend DOD enroll all vaccine recipients in a comprehensive clinical evaluation and treatment program for long term study. Because DOD has concluded the vaccine is essential "body armor" that cannot be removed, we concluded it ought to come with a health insurance policy just as permanently attached.

The strength of this report flows from the personal courage and sacrifice of the men and women of the military who testified before our Subcommittee.

Some had taken the vaccine and become ill. Captain Michelle Piel, a C-5 Galaxy pilot from Dover Air Force Base lost her flying status when she developed chronic fatigue, dizziness joint pain and other debilitating symptoms after taking the vaccine. She doesn't care what made her sick. She just wants to get better and start flying again. But the resistance she encountered to the mere suggestion her illness was related to the vaccine frustrated her, hurt her, and discouraged others from reporting post-inoculation symptoms.

Capt. Jon Richter, another C-5 pilot at Dover AFB, suffered chronic joint pain after receiving two anthrax inoculations. Because doctors could not definitively attribute his condition to the vaccine, no waiver was offered and he was ordered to take another shot. For the sake of his health, it was an order felt he could not follow.

Others had refused the vaccine and given up a career of service they loved. Major Thomas Rempfer, an Air Force Academy graduate and active duty veteran, was an A-10 pilot with the Connecticut Air National Guard. When his questions about the vaccine program could not be answered, and his chain of command stopped trying, he felt betrayed. He and several of his colleagues left the Guard or transferred to non-mobility positions not requiring the vaccine yet. To this day, DOD leadership refuses to acknowledge any impact of the AVIP on National Guard retention or morale.

Still others shared their struggle to decide which path to take. Major Cheryl Hansen, an Air

Force Reserve nurse, found DOD communications about the risks and benefits of the vaccine one sided. She wanted to finish her career in the Air Force reserves. But she expressed a legitimate fear of being ignored or abandoned in the event she suffered a serious, albeit rare, reaction to the vaccine.

These people were not troublemakers or conspiracy theorists. They were not malingerers looking to duck tough duty. They are among the most level-headed, dedicated and patriotic Americans it has ever been my privilege to meet. They deserve a better vaccine, and a better vaccination program.

CMAT Control #
2000067-0000007

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29 February 2000

DOD RESPONSE TO THE STAFF REPORT OF THE HOUSE GOVERNMENT REFORM'S SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS, AND INTERNATIONAL RELATIONS ENTITLED, "THE DEPARTMENT OF DEFENSE ANTHRAX VACCINE IMMUNIZATION PROGRAM: UNPROVEN FORCE PROTECTION."

REPORT SUPPOSITION	DOD POSITION	RATIONALE
Because the anthrax vaccine is still being studied as a potential causative or contributing factor in Gulf War veterans' illnesses... (Pg. 1, par. 1)	There is no established connection between the anthrax vaccine and the Gulf War illness. A connection between the two is unlikely.	Several independent national-renowned scientific groups have found no evidence of a link between the anthrax vaccine and Gulf War veterans' illnesses. The Institute of Medicine (1995) concluded that there is no evidence that vaccines caused the non-specific complaints associated with service during Operation Desert Storm. The Presidential Advisory Committee on Gulf War Veterans' Illnesses (1996) concluded that it is unlikely that the health effects reported by Gulf War veterans resulted from anthrax vaccine used alone or in combination with botulinum toxoid vaccine. NIH and Defense Science Board also concluded that the anthrax vaccine did not explain the reported chronic effects associated with GWI.
Against the so-called "asymmetric" threats to U.S. conventional military superiority posed by a growing range of chemical and biological weapons, the anthrax vaccine program represents a medical Maginot	DoD, DIA and CIA believe that this is a valid and serious threat. Several former and potential adversary nations possess weaponized anthrax in several forms - enough to destroy the world's population several times.	As identified by the Chairman of the Joint Chiefs of Staff, anthrax is a major threat to our troops. Anthrax is the primary biological warfare threat faced by U.S. forces. More than 7 countries, including Iraq, Iran, Syria,

Line, a fixed fortification protecting against attack from only one direction. (Pg. 1, par. 3)		and Russia have or are suspected of developing this biological warfare capability. Anthrax is the biological weapon most likely to be utilized because it is highly lethal, easy to produce in large quantities, and remains viable over long periods of time. It is colorless, tasteless, odorless and very difficult to detect. One deep breath is enough to kill an unprotected person. Our vaccine protects against all known strains and all three forms of the disease. To not use it because it only protects against anthrax - the CIA and DIA identified Bio-Weapon of choice - would be ill advised. Protective gear is used in conjunction with vaccination. Research is ongoing to improve and develop detection equipment.
The AVIP lacks a consistent standard of care.(Pg. 1, par 2)	DoD has very sound Clinical Practice Guidelines and standards of care as well as a sophisticated tracking system. It also has a responsive and effective adverse reaction reporting and follow-up system. This includes an independent civilian review committee.	Clinical Practice Guidelines for administering the vaccine and for managing adverse events after vaccination, are in place and very comprehensive. Our system is designed to tell what person received what shot on what day and from what lot. Unlike other vaccines that afford protection after a single dose, anthrax vaccination requires 6 doses over 18 months. So, we must begin administering the vaccination to the entire force early, in

		order to protect the active and reserve forces for future conflicts.
The AVIP... is designed to reach far beyond those at risk. (pg. 1, par 2)	All of our servicemen and women are potentially at risk.	In at least two major theatres, thousands of troops go to work every day under the threat of weaponized anthrax. Many others fly or sail in and out of these areas. Many more are listed as first responders and as reinforcing units. All of our force is subject to terrorist attack by anthrax. At least two groups have it. One has tried to use it. It is strategically unwise to wait for an attack before implementing the program.
Heavy handed, one-sided informational materials only fuel suspicions the program understates adverse reaction risks in order to magnify the relative, admittedly marginal, benefits of the vaccine (Pg. 2, par. 3)	DoD's informational materials are straightforward and fact based. Adverse reaction risks are stated exactly as we know them and as recorded by FDA and VAERS. The benefits are anything but marginal.	"With respect to risk communications, again a major change is taking place. For this and future such programs, the troops are being clearly advised, up front, why the vaccination is needed, what vaccination they are receiving, the safety and efficacy of the vaccine, and what potential adverse effects could occur. It is important that the troops understand the benefits as well as the risks, though very low, of anthrax immunization. When the program starts in a particular unit, troops are given the opportunity to ask questions of the Commanders and medical personnel." *Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DoD, NSVAIR Anthrax Hearing (1).* The statements in our informational materials are

		medically responsible, scientifically accurate and professionally ethical. Although suspicions have certainly been fueled, we would contend they have been motivated by opponents of AVIP, of vaccines in general, of strong national defense, etc., and not by our informational materials. Education of commanders and medical personnel is accomplished through standardized briefings and other informational materials. These educational materials were a major component of AVIP execution from the beginning of the program in Mar 98.
The decision to use the 1950's era vaccine, which requires an elaborate inoculation regime of six shots over 18 months, presents daunting, perhaps insurmountable, logistical challenges to reach a force of 2.4 million active duty and reserve component members. (Pg. 2, par. 5)	There are many vaccines that were developed in the 1950's and earlier that are currently still in use in the United States. This one was, for the record, actually licensed in 1970 and represents an improvement over the 1950's vaccine. It was re-evaluated in 1980 when biomedicine responsibility was transferred from NIH to FDA. At that time it was re-certified safe and effective. DoD is aware of the logistical challenge with the dosing schedule. Services use automated tracking systems to manage the administration in accordance with the FDA approved dosing schedule. Shipping and distribution of	"The only known effective prevention against anthrax is the anthrax vaccine. Treatment of cutaneous anthrax infection involves administration of antibiotics. In the case of pulmonary anthrax infection, therapy has been of limited benefit, except when given immediately after exposure". *Statement by Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999*

		the anthrax vaccine is a world-class successful operation.	"Prior to use of the anthrax vaccine, cases of human anthrax infection in the United States were much more prevalent. According to data from the Centers for Disease Control and Prevention, (CDC) there were approximately 130 reported cases of anthrax infection per year at the start of this century. In the past decade, there have been years with no reported cases of human anthrax infection in the United States. It is difficult to assess exactly how much of this dramatic reduction is due to the vaccine, but immunization with the anthrax vaccine of people at risk, along with vaccination of animals against anthrax, have likely contributed to this favorable decline. Elsewhere in the world, human anthrax cases continue to be reported, especially in countries with predominately agricultural economies." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* "Based upon their review of available data, the Advisory Review Panel recommended

		that the anthrax vaccine manufactured by Michigan Department of Public Health be classified as a Category I product and that appropriate licenses be continued based upon substantial evidence of safety and effectiveness of this product. The safety data from the CDC trials and the efficacy data from the Brachman et al. trials were the basis for these findings. These findings were published in the *Federal Register* on December 13, 1985." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* The GAO recognized the DoD's "well designed and administered packing and shipping" of anthrax vaccine in its Oct 99 report: "DoD Faces Challenges in Implementing Its Anthrax Vaccine Immunization Program."

The sole-source procurement strategy leaves the program vulnerable to supply shortages and price increases. (Pg., 2, par. 6)	The cost of AVA is one of the lowest for any vaccine. Several foreign countries have offered to pay from 2 to 5 times the DoD contracted price.	Sole-source vaccine production is common in the US. Many vaccines licensed in the US are from sole-source vendors: Japanese encephalitis, Lyme borreliosis, Measles, Mumps, Plague, Poliovirus inactivated, Rubella, Typhoid (oral), Chicken Pox, and Yellow Fever. DoD is aware of possible vaccine shortages and designed a phased implementation to address this challenge. Phased implementation is directed in each Service Implementation Plan CDC's web site lists the cost of many vaccines. Adult vaccine costs range from $16 to $35 per dose. AVA increased from $4.44 per dose, in the first contract, to $10.64 per dose in the second contract. *CDC Pricetable, 2 August 1999.*

As a result (of sole-source procurement) DoD and the sole vaccine maker are locked in a mutually dependent relationship. (Pg. 2, par. 6)	DoD has entered in a **contractual** basis with BioPort Corporation to produce AVA. Anthrax vaccine is a key element in protecting service members against the lethal threat of anthrax. DoD is working with BioPort, the only licensed anthrax vaccine manufacturer to ensure there is a supply of this safe and effective vaccine. *Statement by Brigadier General Eddie Cain, Joint Program Manager, Joint Program Office for Biological Defense, Falls Church, Virginia, Before the National Security, Veterans Affairs and International Relations Subcommittee on Government Reform, First Session, 106th Congress, Anthrax Vaccine Immunization Program (AVIP) April 29, 1999.* We are also pursuing a second source, but in order to meet FDA requirements at a new facility, this effort will require several months to years to complete.	"The BioPort Corporation facility in Lansing, Michigan is the only manufacturer licensed by FDA to manufacture anthrax vaccine. Originally, the facility was operated by the Michigan Department of Public Health. In 1996, the facility became known as the Michigan Biologics Products Institute (MBPI), an entity controlled by the State Government of Michigan Currently, the facility is known as BioPort Corporation based upon the September 1998 transfer of ownership from MPBI to BioPort Corporation." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* A second manufacturer would be required to submit a supplemental application and pass detailed FDA approval inspections.

The manufacturer, struggling to reopen a plant with a checkered regulatory history, clings to a captive customer. (Pg. 2, par. 7)	MBPI began, and BioPort Corporation continued and completed renovation of the AVA production suite and is now in the normal process of FDA certification under a Biologics License Application (BLA) Supplement. BioPort Corporation produces four other products sold to domestic and international markets so they are not dependent on a single customer.	In their 26 Nov 99 written response addressed to Congressman Dan Burton, FDA stated, "A review of inspection reports from 1972 to 1998 shows the Anthrax Vaccine Adsorbed was covered as part of the inspection on 12 separate occasions either by record review, observation of manufacturing areas or interview with engineering and manufacturing staff." This FDA letter is never acknowledged in the Subcommittee's Report. "The FDA conducted an inspection of MBPI in November 1996. During that inspection, FDA investigators documented numerous significant deviations from the Federal Food, Drug, and Cosmetic Act, FDA's regulations and the standards in MBPI's license. Based upon the documented deviations, FDA issued a Notice of Intent to Revoke Letter (NOIR) to MBPI in March 1997. The NOIR letter did not mandate the closure of the facility or lead to seizure of finished product. The letter, however, did state that if MBPI's corrective actions proved to be inadequate, they would run the risk of having their license revoked. MBPI responded to the NOIR with a "Strategic Plan for Compliance" presented to FDA in April 1997. This plan

		called for the periodic submission of data to FDA that would serve as evidence of MBPI's progress towards achieving compliance with FDA's regulations. Under the plan, FDA would review this data and then monitor MBPI's progress through follow-up inspections. In February 1998, FDA conducted a follow-up inspection of the MBPI facility to evaluate MBPI's compliance with its strategic plan. The February 1998 inspection disclosed significant deviations from FDA's regulations. These deviations included, but were not limited to, the manufacture of the anthrax vaccine. In addition, the inspection resulted in a request by FDA that MBPI quarantine 11 lots of anthrax vaccine held in storage, pending review of additional information to be submitted by BioPort... These lots are still in quarantine, and will remain in quarantine until the company submits required information to the Agency. FDA noted that MBPI had made progress in achieving its compliance goals, but additional work remains in order to correct the deviations related to the manufacture of the anthrax vaccine. Pursuant to its purchase of the MBPI facility in September 1998, BioPort agreed to abide by the strategic plan and other

		commitments for corrective actions made by the management of MBPI. It should be noted that MBPI halted production of anthrax vaccine sublots in January 1998 to begin a comprehensive renovation of the anthrax production facilities." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* BioPort now has a very modern production suite run by knowledgeable professionals. They have satisfactorily resolved the majority of noted discrepancies. The others are in work. Approval for new production is expected by fall of 2000. BioPort Corporation also produces Diphtheria-Tetanus (DT) Pediatrics, Rabies Vaccine Adsorbed, Immune Globulin (Human), as well as Albumin (Human), which target domestic and international markets.
Adverse events following vaccination are reported by women at twice the rate among men. (Pg. 3, par. 1)	This was found to be true in two DoD studies, however, a significant number of the reactions reported were minor	Adverse events (local reactions) following vaccination are reported by women at twice the rate

		local reactions and readily spontaneously resolved.	compared to men. "With regard to safety data, FDA and CDC jointly operate a system called the Vaccine Adverse Event Reporting System (VAERS). FDA uses this system to track adverse events possibly associated with licensed vaccines. Reporting of adverse events associated with the use of anthrax vaccine is voluntary for individual healthcare providers. The vaccine manufacturer, however, must report to FDA all reports of adverse events of which they are aware. The report of an adverse event to VAERS is not documentation that a vaccine caused the event, only that the event occurred after the vaccine was administered. Doctors and other healthcare providers are encouraged to report serious or unexpected adverse events following vaccination, whether or not they believe that the vaccination was the cause of the adverse event. Since it is difficult to distinguish a coincidental event from one truly caused by a vaccine, the VAERS database contains events of both types. It should be emphasized that adverse event reports can be made by a health care professional, a patient or anybody else. If a patient's physician does not file a VAERS report, the patient can do so. FDA encourages individuals to report to VAERS any

		clinically significant adverse event occurring after the administration of any vaccine licensed in the United States. Reports to VAERS may be made in writing or by calling a toll-free number, 1-800-822-7967. Reporting instructions are available on the Internet at www.fda.gov/cber/vaers.html." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999.* A CDC-supervised study is in progress to determine gender differences and, if appropriate, to recommend, to the FDA, a reduced shot regimen, as female immunity appears to increase faster than male immunity.
Preposterously low adverse report rates generated by DoD point to a program far more concerned with public relations than effective force protection or the practice of medicine. (Pg. 3, par. 1)	We disagree. VAERS reports can be filled out by any medical person giving the shots, any person receiving a shot, or any person treating a suspected reaction. There is no time limit in when they can be submitted and they are not discouraged in any way. DoD updates all educational materials regularly, reflecting the most up-to-date side effect	"From the time the VAERS system started operating in 1990 until April 1, 1999, there have been 101 reports of adverse events associated with use of the anthrax vaccine reported to the VAERS system. Of those, 87 were non-serious events and 14 were considered serious events. Non-serious events included the following symptoms: injection site

		and adverse event data available in order to keep its patients fully informed.	edema (swelling with fluid in tissue), injection site hypersensitivity, rash, headache and fever. Of the 11 serious reactions reported during the current anthrax vaccination program, most individuals have recovered. Three patients were hospitalized for injection site reactions. One individual experienced a more widespread allergic reaction. One individual was hospitalized with a confirmed case of aseptic meningitis nine days after vaccination. Another individual experienced Guillain-Barré syndrome within 24 hours of the third dose. He was unable to walk for nine days. He gradually recovered and his symptoms resolved within five months of the vaccination. Three weeks after receiving the vaccine, another individual experienced a bipolar disorder and thus for has not recovered. It should be emphasized, once again, that it is not always possible to attribute a cause and effect relationship between a reported event and a vaccination. With the exception of injection site reactions, all of the adverse events noted above do occur in the absence of immunization. While the data gathered from the VAERS system can serve

		as a useful tool in spotting potential problems, the data gathered from the VAERS reports on anthrax vaccine, thus far, do not signal concerns about the safety of the vaccine. As more people receive the vaccine, the numbers of adverse events reported will increase." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999.*
Administration of the anthrax vaccine for mass prophylaxis against biological warfare should be considered an off-label use of the product to treat an indication for which it is not explicitly licensed. (Pg. 3, par. 3)	FDA has confirmed repeatedly that AVA use against biological warfare is not an off-label use. DoD requested in writing an opinion on this issue from the FDA prior to the announcement of the program.	Immunization with Anthrax Vaccine Adsorbed is recommended for individuals who may come in contact with animal products such as hides, hair, or bones which come from anthrax endemic areas and may be contaminated with *Bacillus anthracis* spores; and for individuals engaged in diagnostic or investigational activities which may bring them into contact with *B. anthracis* spores. It is also recommended for high-risk persons such as veterinarians and others handling potentially infected animals. Since the risk of exposure to anthrax infection in the general population is slight, routine immunization is not

			recommended. If a person has not previously been immunized against anthrax, injection of this product following exposure to anthrax bacilli will not protect against infection. *Anthrax Vaccine Adsorbed Package Insert, BioPort Corporation, Lansing, Michigan U.S. License No. 1260.* Letter from Dr. Michael A. Friedman, Lead Deputy Commissioner, Food and Drug Administration to Dr. Stephen C. Joseph, The Assistant Secretary of Defense of Health Affairs, March 13, 1997 reads: "While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert does not preclude this use. The original efficacy trial clearly showed that the vaccine conferred a high level of protection against cutaneous exposure. None of the 5 inhalation cases in this trial occurred in Anthrax Vaccine recipients, but these data alone are insufficient to allow definitive statistical conclusions. Results from animal challenge studies have also indicated that pre-exposure administration of Anthrax Vaccine protects against inhalation anthrax. Therefore, I believe your interpretation is not inconsistent with the current

		label." From the FDA's 26 Nov 99 letter addressed to Congressman Dan Burton, "Use of the vaccine for protection against both cutaneous and inhalation anthrax exposure is not inconsistent with the labeling for Anthrax Vaccine Absorbed." Further, "There is presently no basis for concluding that the anthrax vaccine, a licensed product, when used in accordance with current labeling, should be used pursuant to an IND application or, as requested in your letter, that FDA 'place the anthrax vaccine back under IND status'." The contents of this letter are never referenced in the Subcommittee's report.
DoD's operational use of a standard of "functional protection" after three inoculations constitutes a *de facto* alteration of the approved six shot regimen. (Pg. 3, par. 3)	DoD's service implementation plans and all subsequently published policies direct and emphasize the adherence to the FDA approved dosing schedule of six doses over 18 months. We do not, have not and do not plan to intentionally deviate from FDA's approved dosing schedule.	At risk individuals who start the series of anthrax vaccinations are required to continue them. After receiving the first three doses, studies indicate that 93-95 % of the individuals will have an immune response. That does not mean that DoD deviates from the protocol. It is only a sign that if one were exposed before completing the protocol, he or she would have a better chance of survival than an unvaccinated person would. For individuals remaining under the program, the FDA protocol is only interrupted due to events such as illness, absence from duty

		or an adverse reaction. This point was made several times during sworn testimony. DoD does not understand how this allegation can continue to show up in subcommittee documents.
The AVIP is a well-intentioned but over-broad response to the anthrax threat. (Pg. 4, par. 1)	AVIP is an appropriate response to the threat.	Force health protection encompasses both preventive and medical intervention as well as personal protective equipment and procedures. We have good protective clothing and equipment, but you cannot fight in it for long periods of time. In addition, our troops might not be wearing the gear when the invisible spore-containing aerosol is dispersed. We may not know an attack has occurred until members become ill or symptomatic. We have some early state of the art detectors, but they lack the sensitivity and quick analytical capability to be effective. Anthrax kills and kills quickly. The enemy has it and it is easy to employ. If you breathe it, and are not vaccinated, you will die. The lethality of inhalation anthrax was impressively demonstrated by the numerous fatalities that occurred after the unintentional release of anthrax spores from the factory in Sverdlovsk, Russia in 1979.

		Vaccination will save the lives of our service men and women if exposed. It is also a huge deterrent to the use of weaponized anthrax and to other bio-weapon development. It would be a dereliction of duty not to provide such protection.
The AVIP is vulnerable to supply shortages and price increases. (Pg. 4, par. 2)	DoD has confidence that the manufacturer will comply with the contract. The cost of AVA is one of the lowest for any vaccine. The DoD constructed the implementation of the program in three phases to accommodate a stockpile of vaccine and knowledge that a new production suite would require FDA certification.	Research and development on a second-generation, recombinant vaccine would take years to accomplish and would not have as much safety history as the current licensed vaccine. A second source of production is being pursued, as well as a second site for testing, certification, storage and shipping.
The AVIP is logistically too complex to succeed... Using an artificial standard that counts only shots more than 30 days overdue, DoD tolerates serious deviations from the Food and Drug Administration (FDA) approved schedule. (Pg. 4, par. 3)	DoD policy is to adhere to the FDA schedule. DoD is aware of the logistical challenge with the dosing schedule and had the Services have designed automated tracking systems to manage the administration in accordance with the FDA approved dosing schedule.	Management tools are used as predictive, current and trailing indicators of performance and timeliness of vaccinations. Protocols are not always precise to the hour and the day, but they are very close. The number of vaccination sites has been increased to ease this challenge, by using VA and civilian hospitals and clinics. Deployable medical teams are also available when required.
Safety of the vaccine is not being monitored adequately. (Pg. 4, par. 4)	Recognizing that this is the largest use of AVA, a safety program was designed by DoD and articulated during the multiple Subcommittee hearings.	The DoD Safety program was described in detail during testimony to the Subcommittee on National Security, Veterans Affairs and International Relations. None of this testimony is reflected

		in the Subcommittee's report. As reported by Major General Claypool, "DoD conducts an aggressive, multi-faceted surveillance program to assess vaccine safety. In fact, the safeguards of vaccine administered to DoD personnel meets or exceeds every standard for vaccine administration to the civilian population. The DoD program uses three scientific methods to evaluate safety, clinical studies, database studies and spontaneous reports (passive surveillance). The extent of this safety surveillance far exceeds any vaccine program in the United States for both childhood and adult vaccines."
...DoD institutional resistance to associating health effects to the vaccine. (pg. 4, par. 4)	There is no institutional resistance to associating health effects with the vaccine.	Every person taken ill either before or after vaccination receives treatment, diagnosis and follow-up. It is unfounded slander against our doctors, nurses, and other medical professionals to make such a statement.
Efficacy of the vaccine against biological warfare is uncertain. (Pg. 4, par. 5)	The FDA and many prominent groups have sited AVA as efficacious against inhalational anthrax bacillus.	"With respect to efficacy, a FDA Advisory Panel stated in 1985 that there is sufficient evidence to conclude that the anthrax vaccine is effective under the limited circumstances for which this vaccine is employed. In a March 13, 1997 memorandum, the FDA confirmed that the pre-exposure administration of the FDA-licensed anthrax vaccine for the prevention of inhalation anthrax is not

		inconsistent with the current product label. In addition, the Committee on Infectious Diseases, American Academy of Pediatrics (1994), states that 'the vaccine is effective in preventing or significantly reducing the occurrence of cutaneous and inhalation anthrax in adults'." *Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DoD, NSVAIR Anthrax Hearing (I).* "Several studies performed at the USAMRIID have demonstrated the efficacy of the FDA-licensed anthrax vaccine against inhalation anthrax in rhesus monkey challenge studies. These animal studies showed that the FDA-approved anthrax vaccine provided greater than 95% protection against high-dose aerosol challenge with anthrax in the monkey model. Human antibody response to the FDA-licensed vaccine provides further suggestive evidence that the FDA-licensed anthrax vaccine will protect against inhalation anthrax." *Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DoD, NSVAIR Anthrax Hearing (I).* The Brachman study (1962) involving four mills in the northeastern United States reported of 5 cases of inhalation anthrax (4 fatal) that occurred in the

		unvaccinated population. The vaccinated population, working in the same mills, had no cases of inhalation anthrax and no deaths. In the Soviet Union, at Sverdlovsk a release of aerosolized anthrax caused at least 68 deaths in an unvaccinated population.
A physician reviewed the AVIP program plans. (Pg. 8, par. 4)	DoD conducted a "detailed, deliberative process" spanning almost four years, prior to approval of this program. It then requested an independent expert to review the health and medical aspects of the program.	Dr. Gerald Burrow, who conducted the independent review, was Dean of Yale University Medical School, special advisor to the President for Health Affairs, David Page Smith Professor of Medicine, a professor of Obstetrics and Gynecology and was a noted participant in other studies and research.
Communication plans were approved centered around a "tri-fold" brochure to be given to service personnel. (Pg. 8, par. 4)	Communication plans are detailed in the service plans and are much more elaborate than distribution of a single "tri-fold".	Communication plans were developed and implemented within each Service. DoD Commanders and Health Care Provider briefings and brochures were developed through working groups representative of all of the Services and DoD. All service plans and training material have been distributed electronically, in written format or via the web site www.anthrax.osd.mil. In addition, lectures have been given, films have been produced and a "1-800" hotline phone number was established to provide 24 hour-a-day question and answer capability (1-877-GET VACC).

On May 18, 1998, Secretary Cohen pronounced the four conditions fulfilled and approved the total force program, which began in September with troops in Korea. (Pg. 8, par. 5)	Supplemental testing is on going. Only anthrax vaccine lots both released by the FDA and supplementally tested are used in the DoD AVIP.	"The Secretary of Defense (SecDef) announced in his December 15, 1997 press release that the Anthrax Vaccine Immunization Program (AVIP) would start only after several conditions were met. One of those conditions was 'supplemental testing to assure sterility, safety, potency and purity of the vaccine'. FDA had previously released these anthrax vaccine lots for use. DoD, however, for added assurance directed JPO-BD to contract with BioPort, formerly Michigan Biologic Products Institute (MBPI), to conduct supplemental testing, with external oversight, on all lots of anthrax vaccine in the DoD stockpile. The supplemental testing is based on tests required by FDA for lot release, and provides an added level of confidence in the potency and purity of the anthrax vaccine in our stockpile. BioPort has performed, and continues to perform supplemental testing on all licensed lots of anthrax vaccine that were in DoD's original stockpile. Mitretek Systems Inc. performs independent oversight and provides a quality assurance function for DoD within the BioPort production facility. Mitretek's staff observes all aspects of the supplemental testing and provides a written report to JPOBD on the acceptability of the testing and test results. JPOBD reviews

		all data prior to releasing any lot for shipment and use. Supplemental testing began in January 1998, and originally was scheduled for completion in November 1998. As of April 1999, eight licensed lots have passed all supplemental testing requirements. JPOBD has approved these eight lots for use." *Statement by Brigadier General Eddie Cain, Joint Program Manager, Joint Program Office for Biological Defense, Falls Church, Virginia, Before the National Security, Veterans Affairs and International Relations Subcommittee on Government Reform, First Session, 106th Congress, Anthrax Vaccine Immunization Program (AVIP) APRIL 29, 1999*
Subsequent FDA review of the studies in 1985 concluded the vaccine was safe, "fairly well tolerated," and effective against cutaneous anthrax, but that data from both human and animal tests was insufficient to support a finding of efficacy with regard to airborne exposure (Pg. 10, par. 3)	Efficacy is based in part on the Brachman study and further substantiated in Rhesus monkey trials.	"Conducting lethal challenge studies in humans is considered unethical and, since there is no study population identified as being at high risk for inhalation anthrax, directly determining the efficacy of the vaccine in humans against aerosol exposure to anthrax spores is not possible. There have been numerous studies of the anthrax vaccine involving animal models. Several studies performed at the USAMRIID have demonstrated the efficacy of the FDA-licensed anthrax vaccine against inhalation anthrax in rhesus monkey challenge studies. These animal studies showed that the

		FDA-approved anthrax vaccine provided greater than 95% protection against high-dose aerosol challenge with anthrax in the monkey model. Human antibody response to the FDA-licensed vaccine provides further suggestive evidence that the FDA-licensed anthrax vaccine will protect against inhalation anthrax." *Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DoD, NSVAIR Anthrax Hearing (I).* The Brachman study indicating that NO cases of inhalation anthrax have occurred in fully vaccinated subjects while the risk of infection continued. These observations lend further support to the effectiveness of this product. "This vaccine is recommended for a *limited, high-risk of exposure population* along with other industrial safety measures designed to minimize contact with potentially contaminated material. The benefit-to-risk assessment is satisfactory *under the prevailing circumstances of use." Federal Register, 21 CFR Part 610, December 13, 1985.* In the nonhuman primate studies, a total of 62 (94%) of the 65 animals vaccinated with AVA survived a highly lethal challenge of aerosolized anthrax. Whereas, of the 18 controls (unvaccinated

		animals) that were challenged with the anthrax aerosol, NONE survived. Rabbits have also been used to evaluate AVA. 114 (97%) of 117 rabbits vaccinated with AVA survived lethal aerosol challenge, while none of 88 controls survived the challenge. The rabbit, in contrast with the guinea pig, resembles the nonhuman primate in that AVA vaccination confers excellent protection against aerosol challenge.
In March 1997, the FDA warned MBPI that steps would be taken to revoke production licenses, including anthrax vaccine, unless immediate actions were taken to correct longstanding deficiencies. (Pg. 11, par. 1)	The Subcommittee's report leaves out information that would clarify the FDA's intention. DoD supports FDA actions to ensure the quality of vaccine production by MBPI.	The statement in the Subcommittee report left out a sentence, which would have clarified the FDA's intention. Based upon the documented deviations, FDA issued a Notice of Intent to Revoke Letter (NOIR) to MBPI in March 1997. The NOIR letter did not mandate the closure of the facility or lead to seizure of finished product. The letter, however, did state that if MBPI's corrective actions proved to be inadequate, they would run the risk of having their license revoked. MBPI responded to the NOIR with a "Strategic Plan for Compliance" presented to FDA in April 1997.
Vaccine production resumed in May 1999, but neither the renovated facility nor any newly produced vaccine lots have been approved by the FDA. (Pg. 11, par. 1)	BioPort is currently undergoing the normal FDA certification process.	Vaccine must be produced as part of the FDA's process validation. Its use is subject to FDA release. If it is not proven to be potent, sterile safe or effective, it will not be

		used.
In 1992, Secretary of the Army Togo West, Jr. approved a request to indemnify the anthrax vaccine manufacturer, the Michigan Biologics Product Institute (MBPI), against all liability... (Pg. 15, par. 2)	Indemnification of a vaccine manufacturer is for reasons quite similar to those that led Congress to establish the Vaccine Injury Compensation Program (VICP) and is an appropriate, cost-effective method to address potential liability issues for vaccines not covered by the VICP.	The U.S. federal government first indemnified vaccine manufacturers in 1976, to enable production of the swine influenza vaccine that year. Since 1986, the federal government has limited the liability exposure of manufacturers of the most commonly used vaccines in America, primarily those given to children. The Vaccine Injury Compensation Program (VICP) accomplishes this. The 1999 Secretary of the Army memo indemnifies BioPort Corporation for claims arising from administration of anthrax vaccine to service members. Indemnification of BioPort Corporation for potential claims related to anthrax vaccine ensures the availability of anthrax vaccine to protect the nation's Armed Forces against the threat of biological weapons. It does not indicate a lack of faith, confidence or compliance.
...DoD supplemental testing program have raised questions regarding the validity of test procedures and the selection of reference lots. (Pg. 13, par. 1)	There is no problem regarding the validity of test procedures and selection of reference lots.	Additional testing needed to meet the supplemental testing schedule put increased demand on the animal colony resulting in aberrant results and in response. DoD sent a team of external experts to assist BioPort in identifying the cause of these unexpected results. They found the animal colony was too small in number so that smaller animals had to be used for testing which caused the aberrant results. At the same

		time FDA requested BioPort develop a new evaluation method for the potency test. The FDA and BioPort are currently finalizing the approval process for a new evaluation method. It will not reflect a compromise of either quality assurance or compliance with standards.
Following the Gulf War, and prior to adoption of the DoD immunization policy in 1993, and the mandated AVIP in 1998, Pentagon officials considered and rejected alternative anthrax vaccine production sites. Instead, an acquisition strategy was adopted focusing solely on the MBPI/BioPort vaccine. (Pg. 17, par. 1)	Prior to and during Desert Storm/ Desert Shield, DoD investigated the possibility of alternative production sites to meet requirements for a sustained conflict. The conflict resolved before this became necessary.	The process to develop AVA by another manufacturer would require that manufacturer to obtain a FDA license, which would take several years to accomplish. This cannot be accomplished quickly, as it is a very demanding process, negating the immediate or near term use of a second source.
The Army Anthrax Vaccine Immunization Plan directs medical personnel to report severe adverse reactions (resulting in hospitalization or more than 24 hours lost from duty)... (Pg. 19, par. 3)	DoD maintains that the **minimum** reporting would be anyone hospitalized or loss of duty for 24 hours or longer. This does not inhibit others from initiating VAERS reports.	This message has been disseminated in the Policy for Reporting Adverse Events, dated 15 Oct 99 as well as in the educational mediums of the 'trifolds', health care providers briefing, leaders briefing and individual briefings.
VAERS guidance recommends recording any clinically significant symptoms occurring subsequent to vaccine administration, whether or not a causal relationship has been established between the vaccine and the adverse reaction. (Pg. 19, par. 3)	DoD continues to address this issue of "clinically significant" symptoms. DoD encourages anyone to submit a Form VAERS-1 no matter what the symptom or temporal relationship.	This message has been disseminated in the Policy for Reporting Adverse Events, dated 15 Oct 99 as well as in the educational mediums of the 'trifolds', health care providers briefing, leaders briefing and individual briefings. Members are encouraged to report any symptom they feel could be an adverse reaction.
Once the testing problems became apparent, vaccine lots	All lots have been subjected to supplemented testing. This	After the SecDef's 15 Dec 97 press announcement, DoD

not technically in the stockpile when the AVIP was announced were not subjected to the supplemental assays under the rationale the FDA was requiring the same tests for lot release. All the lots submitted for supplemental testing had also undergone the same FDA lot release protocols. (Pg. 24, par. 3)	testing was established to verify that there were no changes in approved vaccine since FDA certification. It was an extra step to ensure safety.	contracted for 32 lots of the existing vaccine in the stockpile, owned by DoD but stored by BioPort, to be supplementally tested even though they had passed the FDA lot release test. DoD subsequently awarded another, new contract to purchase additional lots of newly manufactured vaccine after MBPI's sale to BioPort in Sep 98. Because these lots still had to be tested and meet FDA lot release criteria, redundant supplemental testing is not necessary and was never contracted.
Without a proven model in animals that is known to correlate to protection in humans, animal data remains only suggestive. (Pg. 25, par. 2)	When a disease is fatal, the use of drug or vaccine animal data is the only way to demonstrate protection in humans. Obviously, it would be unethical to conduct them on humans. In circumstances of this kind, reliance on animal data is necessary and appropriate	"Today, it would be difficult to repeat the efficacy studies because there are no evident populations in the United States where prophylactic vaccine protection could be evaluated in a clinical field trial." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999.* Even according to the testimony prepared by Dr. Nass, "data suggests that the vaccine can protect humans against inhaled anthrax". *Subcommittee on National Security, Veterans Affairs and*

		International Relations Report dated 15 February 2000.
Vaccine-acquired anthrax immunity may also be limited or overwhelmed when the subject is challenged with variant anthrax stains. (Pg. 26, par. 1)	Our vaccine has proven effective against every strain of anthrax against which it has been tested, including the Ames Strain, which is one of, if not the most, lethal strain.	Its use of protective antigen suggests effectiveness against other existing strains as well.
When one U.S. laboratory studying the release of anthrax at Sverdlovsk implied the Russian mixtures of anthrax strains might overcome the protection afforded by the anthrax vaccine, DoD persuaded the author "to correct the press release to make it more accurate. (Pg. 26, par. 5)	The author of the press release corrected the release to make it more accurate after normal scientific discourse with researchers from the US Army Medical Research Institute of Infectious Disease (USAMRIID). It is inaccurate to describe this normal scientific discourse among research professionals as an unethical persuasion.	Scientists from Los Alamos National Laboratory described identification, using gene probes, of multiple strains of anthrax in tissue specimens obtained from victims of the 1979 Sverdlovsk anthrax incident. The laboratory press release implied that mixtures of anthrax strains might overcome the protection afforded by the US anthrax vaccine. After discussions with USAMRIID researchers, the author of the press release, Dr. Walt Kirchner, DoD Programs Office, Los Alamos National Laboratory, agreed to correct the press release to make it more accurate. The modification stated, in part, "...there is no experimental data or evidence to suggest that such a mixture is resistant to the FDA-licensed anthrax vaccine used by the US military."
Hearing testimony and correspondence from Reservists and National Guard members suggests up to 30 percent of some units would resign or seek to transfer due to the anthrax program. (Pg. 28, par. 1)	Admittedly, even one is too many, but there have been no failures of mission accomplishment in any of our units.	"Except in a very small number of cases, Anthrax Vaccination Program is not the determining factor behind a member's decision to withdraw from military service." *Statement by Charles L. Cragin, Principal Deputy Assistant Secretary of Defense for Reserve Affairs, to the Subcommittee on*

		National Security, Veterans Affairs, and International Relations Committee on Government Reform, September 29, 1999. Mr. Cragin also provided a written statement to the Sub-Committee. Many units have retention that is in fact better than the five years prior to implementation of AVIP.
Safety is also an issue for some because the anthrax vaccine is one of the exposures under study by the National Academy of Science's Institute of Medicine (IOM) pursuant to the Persian Gulf War Veterans Act of 1998, enacted as Title XVI of the 1998 Omnibus Appropriations Act, P.L. 105-277. The law directs IOM to review associations between illnesses and wartime exposures that warrant a presumption of service-connection for sick Gulf War veterans. That study is ongoing. (Pg. 28, par. 2)	There is no known link between AVA and Gulf War Illness and no reason to believe one will be found.	When Persian Gulf War veterans returned and started reporting symptoms, some people asked if vaccines administered during the Gulf War might have caused the symptoms. Several independent expert panels addressed this and other questions head-on. These panels consisted of Veterans, civilian academic experts, scientists, health-care professionals, and policy specialists. Each of these panels included some of the nation's best scientists, who spent months or even years listening to veterans, reviewing the evidence, and deliberating the issues. In each case, the independent expert panels found that there was no evidence of any link between any vaccines and any Gulf War illness. To let you read these reports for yourself, hot links appear below. Some of these documents are rather lengthy, so we listed page numbers that refer to vaccines, to speed your

		search. • Presidential Advisory Committee (PAC) on Gulf War Illnesses Final Report, December 1996: p. 114, states: "The committee concludes it is unlikely that health effects reported by Gulf War veterans today are the result of exposure to the botulinum toxoid or anthrax vaccines, used alone or in combination." <http://www.gwvi.ncr.gov/toc-f.html> Pages of Interest: second page, Executive Summary, plus pages 112-114 of the original document (Chapter 4 in the web version). • Health Consequences of Service During the Persian Gulf War: Recommendations for Research and Information Systems, National Academy of Science Institute of Medicine (IOM) 1996: p. 55, 2nd paragraph: concerning adverse interactions due to multiple exposures... "All of these possible drug interactions (and others not mentioned) cause acute and short-term problems. The committee knows of no evidence of any chronic effect." <http://books.nap.edu/books/0309055369/html/1.html> Pages of Interest: 49-

		52, 55, 100. • The Persian Gulf Experience and Health, NIH Technology Assessment Workshop Panel, JAMA, August 3, 1194-Vol 272, No. 5, p.391-395, p. 394, vaccines: general discussion including botulinum and anthrax vaccines...."No long-term adverse effects have been documented." <http://text.nlm.nih.gov/ftrs/tocview/ Select report #14. See the third section, under the caption "Vaccines." • Defense Science Board Task Force on Persian Gulf War Health Effects, June 1994. <http://www.gulflink.osd.mil/dsbrpt/index.html> See chapter VIII, section E.2. • The postwar hospitalization experience of U.S. veterans of the Persian Gulf war. New England Journal of Medicine 1996;335:1505-1513. <http://www.nejm.org/content/1996/0335/0020/1505.asp> This study concluded that "During the two years after the Persian Gulf War, there was no excess of unexplained hospitalization among

		Americans who remained on active duty after serving in that conflict." • The risk of birth defects among children of Persian Gulf war veterans. New England Journal of Medicine 1997;336:1650-1656. <http://www.nejm.org/content/1997/0336/0023/1650.asp> The authors concluded "This analysis found no evidence of an increase in the risk of birth defects among the children of Gulf War veterans." • Mortality among U.S. veterans of the Persian Gulf war. New England Journal of Medicine 1996;335:1498-1504. <http://www.nejm.org/content/1996/0335/0020/1498.asp> The authors concluded: "Among veterans of the Persian Gulf War, there was a significantly higher mortality [death] rate than among veterans deployed elsewhere, but most of the increase was due to accidents rather than disease, a finding consistent with patterns of postwar mortality among veterans of previous wars."
Problems with supplemental testing underscore vaccine safety and production issues. The failure to test all lots	The promise of supplemental testing is being fulfilled on the original stockpile.	The Secretary of Defense ordered supplemental testing of all lots of anthrax vaccine in the Lansing stockpile, when

produced before the plant closed suggests to some the promise of supplemental testing was not fulfilled. (Pg. 29, par. 3)		he authorized the Anthrax Vaccine Immunization Program in December 1997. Supplemental testing repeats the original FDA tests for sterility, purity, potency, and general safety. Supplemental tests are performed by the manufacturer and overseen by an independent contractor (Mitretek, Inc., McLean, Virginia). Supplemental tests are not performed on lots 040 or higher, because these lots were not part of the DoD stockpile in Dec 97, in fact, were not purchased by DoD until after the MBPI sale to BioPort. These newer anthrax vaccine lots have undergone (or will undergo) the same tests for sterility, purity, potency, and general safety required by the FDA to determine whether the lots meet approval criteria for FDA release. Supplemental testing results may be accessed at the AVIP web site: http://www.anthrax.osd.mil/scanned/articles/articles.htm Supplemental testing problems were identified and corrected with testing resumed on the 32 lots in the original stockpile. *Statement provided by Dr. Robert Myers to the Subcommittee on National Security, Veterans Affairs, and International Relations, April 29, 1999.*

An informal Survey of Reserve and Guard units shows more than 700 current or likely departures due to the AVIP. The survey can be found at: http://www/dallasnw.quik.com /cyberell/Anthrax/Chron_Info. html (Pg. 28, Footnote)	Except for a small number of cases, AVIP is not the determining factor behind a member's decision to withdraw from military service. *Statement by Charles L. Cragin, Principal Deputy Assistant Secretary of Defense for Reserve Affairs, to the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, September 29, 1999.*	Even one serviceman or woman who resigns as a result of not taking a vaccine that was designed to be good for him or her, is one too many. DoD seeks the cooperation of the Congress and the "No Group" to stop encouraging individuals to disobey orders A review of current units who have lost members due to the anthrax vaccine indicate that they are mission capable. There is normally a waiting list to join most units.
Contrary to subsequent DoD characterizations, the promised outside, expert, scientific review of the program was only very general in nature. Others question the necessity of the program, asking whether it betrays a lack of confidence in deterrence and other force protection elements, and suggesting a vaccine program makes anthrax attack more, not less, likely. (Pg. 30, par. 3,4)	DoD reviewed all data prior to Secretary of Defense's announcement to start this program. AVA in conjunction with other force protection elements is used as a deterrent. Vaccination was unanimously recommended by the Joint Chiefs and specifically requested by two Theatre CINCs. We are satisfied with the outside expert scientific review and the credentials of those who participated.	A civilian medical advisory panel to the Food & Drug Administration reviewed all bacterial vaccines in the early 1980s, revoking a few licenses for lack of evidence of safety or efficacy. When that panel considered anthrax vaccine, they reaffirmed all previous NIH and FDA decisions about the vaccine. The report can be found in the 1985 edition of the *Federal Register*, volume 50, pages 51002-117. Second, the Armed Forces Epidemiological Board (AFEB), a civilian body of scientists and physicians, provides recommendations regarding vaccination use and other medical issues to the Assistant Secretary of Defense for Health Affairs (ASD(HA)). AFEB has specific responsibilities in DoD Directive 6205.3, Immunization Program for Biological Warfare Defense.

		The AFEB assists in providing recommendations on vaccines and immunization protocols necessary to enhance protection against validated BW threats. The external Department of Defense Anthrax Vaccine Adverse Event Task Force reviewed adverse events on 3 August 1998 and provided a report on 10 August 1998. The Task Force recommended that reviews of adverse event reports, received as a result of the anthrax immunization program, be performed at 3 to 6 month intervals. Based on a review of the adverse events reported to date and the apparent safety of the anthrax vaccine, the Task Force recommended no other change in the current DoD anthrax immunization program. They also recommended a review of Vaccine Adverse Event Reporting System (VAERS) reports at service level for completeness. AFEB also suggested a small prospective study ("a small records review study") to record all reactions. This led to the survey performed at the Tripler Army Medical Center that involved 603 medical personnel and collected data on symptoms, side effects and reactions subsequent to vaccination. Third, an independent review

		of the health and medical aspects of the program was completed by Dr. Gerard Burrow. Dr Burrow was immensely qualified for this review. He is currently Special Advisor for Health Affairs to the President of Yale University, and he previously served as Dean of the Yale University Institute of Medicine, Vice Chancellor for Health Services of the University of California (San Diego), Dean of the School of Medicine of the University of California (San Diego), and Member of the Institute of Medicine, National Academy of Sciences. He completed his review on 19 February 1998. Fourth, the Anthrax Vaccine Expert Committee (AVEC) is a panel of civilian physicians convened by the Health Resources & Services Administration of the Department of Health & Human Services to review all VAERS reports submitted to the FDA. This independent external review panel meets every 6 weeks or so. To date, the committee has identified no unexpected events after anthrax vaccination. Today, there is a broad consensus that the FDA-licensed anthrax vaccine is safe and effective for people at high risk of exposure. Recent publications of the CDC [ftp://ftp.cdc.gov/pub/

			Publications/mmwr/wk/mm4804.pdf] and the Johns Hopkins Center for Civilian Biodefense Studies [http://www.ama-assn.org/sci-pubs/journals/archive/jama/vol_281/no_18/jst80027.htm] recognize the anthrax vaccine as part of the national preparedness against biological terrorism. Anthrax vaccination is needed because the threat is real and lethal. The Chairman of the Joint Chiefs of Staff named anthrax as the #1 biological threat. The current world threat environment and the unpredictable nature of terrorism make it prudent to include biological warfare defense as part of our force protection planning. Weapons inspectors discovered during the Gulf War that Saddam Hussein maintained an anthrax arsenal sufficient to kill every man, woman and child on the face of the earth. By 1992, U.S. intelligence sources recognized that the former Soviet Union maintained a capability that dwarfed Iraq's. Inhalation anthrax following a biological warfare attack is almost invariably lethal to those who become infected, if not treated quickly. Even with prompt treatment, the likelihood of death is 80%. Bio-weapon attacks would probably not be detected until large numbers of people

		become ill. The anthrax vaccination program is a critical component of DoD's multi-component Force Health Protection Strategy to protect the force from the threat of this bio-weapon.
Some who testified are experiencing serious illnesses they associate with the anthrax vaccine. (Pg. 31, par. 2)	While the overwhelming majority of reactions will be minor, the Department is aware that serious reactions are a possibility. Because of that possibility, each service member who reports an illness subsequent to a dose of this vaccine, or any other, is evaluated and treated for his or her illness or symptom. Some of those testifying were later found to have had pre-existing medical conditions vice reactions. Some are still under study.	The Anthrax Vaccine Expert Committee (AVEC) is a panel of civilian physicians convened by the Health Resources & Services Administration of the Department of Health & Human Services to review all VAERS reports submitted to the FDA. This independent external review panel meets every 6 weeks or so. To date, the committee has identified no unexpected events after anthrax vaccination. There are many more individuals who have taken the AVA without any reactions. These individuals were not asked to provide statements to the Subcommittee. Over 1.4 million shots have been given to over 400,000 personnel. Reactions reported to date are below those of almost all other vacciness.
Entitled, "Anthrax Vaccine Adverse Reactions," the hearing focused on the program's willingness to recognize and ability to treat adverse reactions to the vaccine in military personnel. Issues discussed included the	Recognizing that this is the largest use of AVA, a safety program was designed by DoD and articulated during the multiple Subcommittee hearings. DoD medical professionals are	The DoD Safety program was described in detail during testimony to the Subcommittee on National Security, Veterans Affairs and International Relations. None of this testimony was reflected in the Subcommittee's report.

extent the main adverse event surveillance system used by DoD, the joint FDA/CDC Vaccine Adverse Event Reporting System (VAERS), under-reports adverse events and adverse vaccine reactions. (Pg. 31, par. 4)	well trained and are capable of treating adverse events presented by service members for a multitude of reasons.	As reported by Major General Claypool, "DoD conducts an aggressive, multi-faceted surveillance program to assess vaccine safety. In fact, the safeguards of vaccine administered to DoD personnel meets or exceed every standard for vaccine administration to the civilian population. The DoD program uses three scientific methods to evaluate safety, clinical studies, database studies and spontaneous reports (passive surveillance). The extent of this safety surveillance far exceeds any vaccine program in the United States for both childhood and adult vaccines."
Rep. Walter Jones (NC) introduced HR 2543 on July 16, 1999. Entitled "The American Military Health Protection Act," the bill would instruct the DoD to make the anthrax military vaccination immunization program voluntary for all members of the Armed Forces until the FDA has approved a new anthrax vaccine for humans or the FDA has approved a new, reduced course of shots for the current anthrax vaccine. This bill was referred to the Committee on Armed Services. (Pg. 32, par. 4)	DoD opposes having the vaccinations voluntary.	It could leave part of our force unprotected and result in mass casualties. It would also interrupt the established FDA protocol for any participating service member who elected not to continue the protocol.
The FY2000 Defense Appropriations Act (HR 2561) contained a provision directing the Comptroller General to report on: effects on morale, retention and	This is correct and action is ongoing to meet the Act's provisions.	DoD will fully cooperate and looks forward to the results of these new studies. We believe these studies will validate the many studies which have already done and will support

recruiting; the civilian costs and burdens associated with adverse reactions for members of the reserve components; adequacy of long and short term health monitoring; assessment of the anthrax threat, including but not limited to foreign doctrine, weaponization, quality of intelligence, and other biological threats. DoD was directed to contract with the National Research Council to conduct studies on: vaccine adverse events and adverse reactions, particularly among women; vaccine efficacy against inhalation anthrax; correlation of animal models to safety and efficacy in humans; research gaps; and other matters. (Pg. 32, par. 6)		our ongoing efforts.
AVIP represents a doctrinal departure overemphasizing the role of pre-exposure medical intervention in force protection. (Pg. 34, par. 1)	DoD utilizes vaccines as pre-exposure for prevention of all types of disease that service members may encounter during deployment.	Vaccination is a cornerstone to fighting disease in the United States. A major difference between this and other mandatory vaccines is that the decision to begin the series came late in our careers as opposed to being given in initial training. There are several mandatory vaccines.
But in the absence of proven capability and intent to use biological weapons, vulnerability alone does not constitute a validated threat for purposes of determining appropriate and effective countermeasures. (Pg. 22, par. 3)	DoD has determined that there is a valid threat. CIA and DIA agree. Even the Subcommittee's report mentions that clearly there is a real and imminent threat.	There is some evidence that anthrax was used as a biological weapon (BW) on a limited basis by the Japanese in China during World War II (Christopher GW, et al. Biological warfare: A historical perspective. *JAMA* 1997; 278(Aug 6): 412-17). Since then, several countries are believed to have incorporated anthrax into

		biological weapons. Intelligence analysts believe that at least seven potential adversaries have an offensive BW capability to deliver anthrax - twice the number of countries compared to when the 1972 Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Construction (commonly called the Biological Weapons Convention) took effect. The Biological Weapons Convention was designed to prohibit such activity. Iraq admitted to the United Nations in 1995 that it loaded anthrax spores into warheads during the Gulf War. In the post-cold war era, the former Soviet Union admitted to having enough anthrax on hand to kill every person on the planet several times over. The accidental aerosolized release of anthrax spores from a military microbiology facility in Sverdlovsk in the former Soviet Union in 1979 resulted in at least 79 cases of anthrax infection and 68 deaths and demonstrated the lethal potential of anthrax aerosols.
So the threat remains tactically limited and regional. The AVIP is universal. (Pg. 39, par. 3)	Conflicts have traditionally been regional not global. Worldwide deployability of all forces, active and reserve component, mandates universal vaccination with the	The following concept is expressed in the instructions entitled, Joint Instruction, Immunizations and Chemoprophylaxis, AFJI 48-110, AR 40-562,

	anthrax vaccine.	BUMEDINST 6230.15, and CG COMDTINST M6230.4E: Current health threat assessments based on disease prevalence in specific geographic regions are maintained by each Service preventive medicine authority using federal, DoD, and other relevant sources of information and are disseminated appropriately to all units within their respective jurisdictions. Specific immunization requirements are based on special disease threat assessment. Full protection against anthrax is afforded only after the 6 doses are administered over 18 months, so anthrax vaccination must begin now to protect our forces in the future and to prepare members who will be rotating through the units.
That study was conducted, for the most part, behind closed doors. However, the documentation provided to the subcommittee by DoD describes a process more predetermined than deliberative, as the obvious operational benefits of passive, pre-exposure protection ... (Pg. 40, par. 1)	DoD undertook a detailed, deliberative process over more than three years that culminated in the decision to implement a mandatory, force-wide AVIP.	This was conducted in the normal business processes that DoD uses to determine decisions and policy. It included input and research from medical, scientific, university research laboratory and many other activities. DoD believes that if members of the Committee and Subcommittee had conducted the same research that we had, they would agree with the program we have implemented.
The mission profile for the improved vaccine called only	This statement in the Subcommittee report was	Conceptually, a new anthrax vaccine could provide

for inoculation of deployed and rapid deployment units based on intelligence estimates of the potential for use of specific BW agents against U.S. forces. ... Other military personnel will be vaccinated prior to departure to BW threat areas. An accelerated immunization program will be conducted under certain alert or mobilization conditions. (Pg. 41, par. 3)	lifted from a DoD "Operational Requirements Document (ORD) for Improved Anthrax Vaccine"; report dated 2 Oct 1995. It was an evolving step to an evolving threat.	protection after only a single dose. If this were true, this new vaccine could be administered like other vaccines DoD administers, just prior to deployment to forces at risk. This has no bearing on the current AVIP which uses the currently FDA licensed vaccine requiring 6 doses given over 18 months for full protection.
Shortcomings of the currently licensed vaccine were seen as the "serious logistical obstacles, especially for reserve force "posed by the approved six-shot schedule and reports that suggest "this vaccine may not provide universal protection against all anthrax strains." (Pg. 41, par. 4)	DoD recognizes that the FDA approved dosing schedule represents a challenge. To this end, we mandated use of automated immunization tracking systems to manage the program. For Reserve Component (RC) forces in particular, DoD established several initiatives through the Public Health Service, the VA, and a private sector contract to increase access for vaccination and treatment. DoD believes that the current anthrax vaccine would be effective against all strains of anthrax because of its incorporation of protective antigen.	DoD now maintains agreements with the Division of Federal Occupational Health, Public Health Service; the Department of Veterans Affairs; and Arora Group, Inc to provide vaccinations and treatment to military personnel through a preferred provider network at more than 12,000 locations throughout the US. This greatly facilitates RC adherence to the dosing schedule. The current U.S. licensed anthrax vaccine is considered to be highly effective against naturally occurring strains of anthrax, including antibiotic-resistant strains. This is because anthrax vaccine targets the key disease-causing protein common to all strains of anthrax. DoD is aware of the Russian research effort recently reported in a British scientific journal. Russian scientists reported using technology to introduce two foreign genes

		into anthrax. The potential for a genetically altered virulent organism is of concern to us and we are anxious to learn more about this organism. Hamsters, vaccinated with the Russian live attenuated anthrax vaccine were not resistant to challenge with their engineered strain. There are substantive scientific questions about this report. First, the validity of the animal model that the Russians used needs to be addressed, because hamsters may not be predictive of results in other animals and humans. Second, the strain produced may not be stable, a fact the Russians admit. An unstable organism would not be a candidate for weaponization. There have been ongoing efforts by OSD Cooperative Threat Reduction Program, the National Academy of Sciences, and the International Science and Technology Center to evaluate the possibility of a potential threat from genetically modified strains, and to ensure that our vaccine is effective against them. We believe that the current anthrax vaccine would be effective against altered genetic strains based on the biologic principles of the U.S. vaccine, which is different from the Russian vaccine.
Briefing materials produced by the U.S. Army Medical Research Institute of	During the normal course of DoD decision-making, all pros and cons are assessed,	Concurrent with the AVIP using the currently FDA-licensed anthrax vaccine, DoD

Infectious Disease (USAMRIID) in 1994 listed the following problems with the current vaccine: Prolonged immunization schedule Reactogenicity: Systemic reactions: .7 - 1.3% Significant local reactions: 2.4 -3.9% (5.9%) Vaccine components completely undefined in terms of characterization and quantitation of the PA, and other bacterial products and constituents present Significant lot-to-lot variation in the PA immunogen content Human trials with similar but not identical vaccine showed protection against cutaneous anthrax but insufficient data to show efficacy against inhalation anthrax Made from spore-forming strain requiring dedicated production facility. (Pg. 41, par. 5)	evaluated, and debated. The DoD decision to implement the AVIP considered all these factors.	is pursuing research to produce a new anthrax vaccine using recombinant technology that hopefully will result in fewer required doses and fewer side effects than the currently licensed product. This is responsible pursuit of better medicine technology. It does not, however, exist today. Unfortunately, the threat does exist. It would be irresponsible not to use the available protection - an FDA licensed and approved, safe and effective vaccine.
At the same time, DoD interest in an improved anthrax vaccine diminished sharply. Reservations about the suitability of the old vaccine were put aside once it was made the centerpiece of the proposed immunization effort. (Pg. 42, par. 6)	DoD does not have reservations concerning the suitability of anthrax vaccine adsorbed and it has not kept us from pursuing a better vaccine for the future.	"In completing an Industrial Capabilities Assessment, it was determined that while a series of alternatives were available, only two options were realistic in meeting DoD's requirement: 1) Seek alternative manufacturing sources and 2) maintain current capability... the only viable alternative that will support the current policy of total force vaccination is to continue with the current manufacturer. In evaluating the industrial base in the

		biological defense area, DoD found little interest by U.S. commercial firms." *Statement by Honorable John J. Hamre, Deputy Secretary of Defense to Subcommittee on Military Personnel House Committee on Armed Services, First Session, 106th Congress, 30 September, 1999.* None of Mr. Hamre's statement was included in the subcommittee's report. Concurrent with AVIP using the currently FDA-licensed anthrax vaccine, DoD is pursuing research to produce a new anthrax vaccine using recombinant technology that hopefully will result in fewer required doses and fewer side effects than the currently licensed product.
One statement of chem/bio defense doctrine ranks force protection strategies as follows: "... The most effective and singularly most important prophylaxis in defense against biological warfare agents is physical protection. Preventing exposure of the respiratory tract and mucous membranes ... to infectious and/or toxic aerosols through use of a full-face respirator will prevent exposure, and should, theoretically, obviate the need for additional measures. Chemical protective masks effectively filter biological hazards. ... All medical	DoD policy maintains vaccination, as disease prevention, is but one pillar of force protection. At this point in time, it is the best protection available.	The first protection we rely on is deterrence. We hope it is successful, but we know it will not always work. Next we rely on intelligence and hope to thwart the attack before it occurs. Our intelligence is not perfect. We cannot always count on it. We have good protective clothing, but we cannot wear it 24 hours a day and cannot fight in it for long periods of time. We have detectors and warning devices, but we only have a few and they are early state-of-the-art. The best and most effective piece of the Bio-Protection suite is our FDA licensed, safe and effective vaccine.

prophylactic modalities described should be viewed only as **secondary** (i.e. backup), and are not to be relied upon as primary protective measures. Agent exposures near the source of dissemination will be high, and likely to overwhelm any medical protective measure." The AVIP makes medical prophylaxis is a primary aspect of force protection and CBW deterrence. (Pg. 44, par. 1)		The vaccine would protect our servicemen and women in the instance of an unannounced, undetected release of anthrax aerosol. The aerosol is tasteless, odorless and invisible and could infect our forces at a time when they are not wearing protective gear.
The vaccine policy also reflects a lack of confidence in current force protection equipment. (Pg. 46, par. 5)	DoD uses vaccination as one prong in the policy of force protection. Our mask, suits and detectors continue to be improved.	Early warning detection equipment is in its developmental stages. Service members would be unable to wear protective gear twenty-four hours a day, seven days a week. This leaves service members vulnerable to attacks with biological agents and points to the need for vaccination as a prong of force protection. Use of the vaccine provides an avenue of protection that more gear and intelligence cannot provide in an unannounced silent attack.
Even this doctrinal reliance on the primacy of medical protection does not necessarily demand the universal, pre-deployment inoculation that characterizes the AVIP. (Pg. 48, par. 1)	Deployment possibilities are worldwide and **do** require universal vaccination.	Many vaccinations, for example hepatitis A, are given universally to service members during basic training to prepare them for worldwide deployment.
Other inoculations are required pursuant to medical, not military command authority, and they are required primarily to maintain and protect the health of	The Armed Forces Epidemiology Board (AFEB) recommends vaccinations that are necessary for force health protection in the DoD.	Medicine is a support function for the line units. Anthrax shots are as safe and effective as other vaccines and are accompanied by

personnel from naturally occurring diseases or pathogens endemic to specific duty or deployment areas. (Pg. 50, par. 1)		comparable adverse reactions.
Although the threat of natural anthrax "remains a significant problem in numerous countries throughout Africa, the Middle East, Europe and Asia," the general military immunization policy contains no reference to the anthrax vaccine. (Pg. 50, par. 1)	DoD policy is currently being revised to include anthrax vaccine. It just wasn't part of our program when the policy was last published.	The following concept is expressed in the instructions entitled, Joint Instruction, Immunizations and Chemoprophylaxis, AFJI 48-110, AR 40-562, BUMEDINST 6230.15, and CG COMDTINST M6230.4E, dated Nov 1995: Current health threat assessments based on disease prevalence in specific geographic regions are maintained by each Service preventive medicine authority using Federal, DoD, and other relevant sources of information and are disseminated appropriately to all units within their respective jurisdictions. Specific immunization requirements are based on special disease threat assessment. The 1995 policy included FDA licensed vaccines for endemic diseases worldwide. No vaccines for bio-warfare were listed or in use at that time.
"Deploying civilian employees who decline to participate in the DTRA-AVIP will be required to execute a "Statement of Informed Declination" attesting to the Agency's offer of anthrax immunization and the individual's decision to decline. (Pg. 50, par. 4)	The Defense Threat Reduction Agency rescinded this policy.	Emergency-Essential civilians and contractors who perform mission essential services are part of our war-fighting team and as such are expected to take the vaccine when deploying with our forces. The applicable documents include the following: - DoD Directive Number

		1404.10, April 10, 1992, Emergency-Essential (E-E) DoD U.S. Citizen Civilian Employees. - DoD Instruction Number 3020.37, November 6, 1990, Continuation of Essential DoD Contractor Services During Crises.
DoD concluded, but cannot prove, that individual antibody response to the vaccine equals protection from anthrax attack. (Pg. 50, par. 5)	Vaccine is known to be safe and effective against anthrax. This is not just a DoD opinion.	"The only known effective prevention against anthrax is the anthrax vaccine. Treatment of cutaneous anthrax infection involves administration of antibiotics. In the case of pulmonary anthrax infection, therapy has been of limited benefit, except when given immediately after exposure." *Statement by Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* Antibiotics must be given before symptoms develop to be effective. Since the spores are colorless, odorless and tasteless, normally one would not know they had been exposed until symptoms developed. <u>Animal studies</u>: – In support of the clinical studies, two

		rabbit animal protocols were completed to develop an in vitro correlate of immunity in a relevant animal model. These studies also accomplished a comparative pathology evaluation between rabbit and non-human primate models. References: (1) Protocol Number F96-17. Development of an in vitro correlate of immunity for anthrax in the rabbit model (2) Protocol Number F97-08. Confirmation of an in vitro correlate of immunity for anthrax in the rabbit model using AVA Lot FAV032. In the nonhuman primate studies, a total of 62 (94%) of the 65 animals vaccinated with AVA survived a highly lethal challenge of aerosolized anthrax. Whereas, of the 18 controls (unvaccinated animals) that were challenged with the anthrax aerosol, NONE survived. Rabbits have also been used to evaluate AVA. 114 (97%) of 117 rabbits vaccinated with AVA survived lethal aerosol challenge, while none of 88 controls survived the challenge. The rabbit, in contrast with the guinea pig, resembles the nonhuman primate in that AVA vaccination confers excellent protection against

		aerosol challenge.
Nevertheless, DoD concludes enrollment in the AVIP equals protection for purposes of satisfying the need for uniform force protection. (Pg. 52, par. 1)	DoD policy is to follow the approved FDA dosing schedule to gain the proven protection needed.	Numerous studies support this finding. No studies disprove it.
In tactical terms, the protection afforded by vaccination would be needed only during the time between detection and the order to deploy individual and collective physical protective measures (suits, masks, tents, etc.). Better detection capability, improved masks and a battlefield doctrine to deploy protective measures earlier could limit or eliminate the need even for that small window of protection provided by the vaccine. (Pg. 52, par. 2)	DoD utilizes vaccines as pre-exposure prevention of many types of disease that Service Members may encounter during deployment.	Vaccination is a cornerstone to fighting disease in the United States and has been for many years. The anthrax attack that would endanger our members would be disseminated in a manner to best utilize its colorless, odorless, tasteless and difficult-to-detect character. Therefore, it is not guaranteed that members will be afforded the opportunity to use the physical protective measures available to them. "Post-exposure vaccination following a biological attack with anthrax [vaccine] would be recommended with antibiotic administration to protect against residual retained spores..." *Journal of the American Medical Association, May 12, 1999, Vol. 281, No. 18, p 1740.* Such treatment is helpful if given within 24-48 hours of exposure, and prior to the development of symptoms. Once a member becomes symptomatic, however, such treatment would likely be too late and not be lifesaving.
The sole-source procurement of a vaccine that requires a dedicated production facility	BioPort Corporation renovated and modernized the AVA production suite and now is	The anthrax vaccine works. No one who has taken the vaccine is known to have

leaves DoD captive to old technology and a single, untested company. (Pg. 53, par. 1)	involved in the normal process of FDA certification under a Biologics License Application (BLA).	contracted inhalational anthrax; Whether one considers it old or current, the vaccine is effective. The new BioPort facility is one of the more modern of its kind in the country.
Research and development on a second-generation, recombinant vaccine would allow others to compete. (Part 53, par. 1)	This may be true, but it would be years away, and the threat is now. We are pursuing the second-generation vaccine as well.	"In completing an Industrial Capabilities Assessment, it was determined that while a series of alternatives were available, only two options were realistic in meeting DoD's requirement. 1) Seek alternative manufacturing sources and 2) maintain current capability...the only viable alternative that will support the current policy of total force vaccination is to continue with the current manufacturer. In evaluating the industrial base in the biological defense area, DoD found little interest by U.S. commercial firms." *Statement by Honorable John J. Hamre, Deputy Secretary of Defense to Subcommittee on Military Personnel House Committee on Armed Services, First Session, 106th Congress, 30 September, 1999.* None of Mr. Hamre's statement was included in the subcommittee's report.
DoD has built a force-wide program on the narrowest possible industrial base. (Pg. 53, par. 2)	The same is true for most other vaccines. However, a second source will be pursued.	Such a solution is months to years away, while the threat is real now.
FDA inspection findings on the renovated facility contain a number of observations repeated from the February 1998 inspection. (Pg. 55, par.	BioPort Corporation renovated the AVA production suite and is now involved in the normal process of FDA certification under a Biologics License	"The February 1998 inspection disclosed deviations from FDA's regulations. These deviations included, but were not limited

1) GAO also found the dependent relationship between DoD and BioPort unusual and risky. While sole-source procurements for vaccines may be common, those producers usually have other product lines generating income from other customers. (Pg. 59, par. 1) One vaccine producer operating a single production site also points to security risks. (Pg. 59, par. 2) GAO observed, "But if we are relying upon this vaccine as part of the backbone of our defensive biological program, the question of vulnerability to a single site becomes an issue. If you made a decision with respect to that vulnerability that led you to want to have an alternative site, then we probably should be looking at establishing a second source." (Pg. 59, par. 2)	Application (BLA).	to, the manufacture of the anthrax vaccine. In addition, the inspection resulted in a request by FDA that MBPI quarantine 11 lots of anthrax vaccine held in storage, pending review of additional information to be submitted by BioPort... These lots are still in quarantine, and will remain in quarantine until the company submits required information to the Agency. FDA noted that MBPI had made progress in achieving its compliance goals, but additional work remains in order to correct the deviations related to the manufacture of the anthrax vaccine. Pursuant to its purchase of the MBPI facility in September 1998, BioPort agreed to abide by the strategic plan and other commitments for corrective actions made by the management of MBPI. It should be noted that MBPI halted production of anthrax vaccine sublots in January 1998 to begin a comprehensive renovation of the anthrax production facilities." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives,*

		April 29, 1999 As previously stated, a second source will be pursued, however, this cannot be accomplished immediately. BioPort Corporation also produces Diphtheria-Tetanus (DT) Pediatrics, Rabies Vaccine Adsorbed, Immune Globulin (Human), as well as Albumin (Human), which target domestic and international markets.
Rather than risk long term health impairment, some service members would be willing to consider the vaccine-preventable risk of anthrax among the inherent, unavoidable risks of military service. They do not have that option, an opportunity to assume risk made available to essential civilian employees of the Defense Threat Reduction Agency. (Pg. 97, par. 3)	The DTRA agency policy was rescinded. All DoD immunizations are mandatory.	If an FDA certified, safe and effective protective vaccine did not exist, such a choice might be prudent. Given the availability of safe and effective protection, it would be highly irresponsible to send troops into battle without it.
Others view this force protection effort as an untested medical solution to a purely mechanical problem - contamination prevention and avoidance - better solved by physical rather than pharmacological technology. (Pg. 97, par. 4)	DoD uses vaccination as one prong in the policy of force protection.	Early warning detection equipment is in its developmental stages. Service members would be unable to wear protective gear twenty-four hours a day, seven days a week. This leaves service members vulnerable to attacks with biological agents and points to the need for vaccination as a prong of force protection.
But DoD is unwilling to wait for the research, development and FDA approval processes, even though DoD believes within a year we will get FDA approval for reduced dose	The threat of this biological agent is now; therefore, DoD has an urgent need to protect the force now and cannot wait for the reduced dose study, which will take at least a year	DoD will make the appropriate changes to the AVIP, if and when the FDA approves changes to the licensed dose schedule and vaccination route, subsequent

based on the science. (Pg. 100, par. 3)	or two to complete.	to the completion of the necessary clinical studies.
To address the domestic bioterrorism threat, the Department of Health and Human Services' National Institute of Allergy and Infectious Diseases formed a working group to develop and test a second-generation anthrax vaccine, and the Institute has funded some research. DoD should support those efforts. (Pg. 100, par. 4)	DoD works with and does actively support the DHHS in this endeavor.	DoD is participating in and will be anxious to have the results of this effort.
With regard to an improved anthrax vaccine, the American Public Health Association adopted a policy statement in November 1999 urging DoD to "delay any further immunization against anthrax using the current vaccine or at least to make immunization voluntary" and to convene a commission of military and non-military public health experts to review safety and efficacy evidence for the current vaccine, attempt to determine when an improved vaccine might be available, and make recommendations about continuation of the current program. (Pg. 101, par. 1)	DoD Force Health Protection cannot effectively be a voluntary program, and the threat is now.	The APHA policy was adopted after a presentation that only covered the opposing viewpoint. DoD offered to present our views and findings but the offer was declined. Adopting a policy after hearing only one side of an issue is inappropriate.
DoD expended significant time and resources in 1994 and 1995 on plans and programs to demonstrate the safety and efficacy of a shorter anthrax inoculation regime, and a different route of administration, but appears to have all but abandoned those efforts when planning for the AVIP began. Support for the	DoD and the manufacturer pursued this research in the past and continue this effort now.	The Comparative Study to Determine the Best Two-Dose Schedule and Route of Administration of Human Anthrax Vaccine, by Dr. Phillip Pittman, sponsored by Dr. Robert Myers, MBPI (now BioPort) was submitted to the FDA in Fall 1998. The results were favorable but the FDA requires a larger pivotal

FDA application to reduce the shot course seems to have been redirected to vaccine acquisition and AVIP logistics. (Pg. 105, par. 1)		study. Funding has been obtained and DoD is working in conjunction with the CDC, NIH and the sponsor (BioPort) to complete this study.
"In November 1971, the Division of Biologics Standards, NIH, noted an apparent increase in reports of adverse reactions after individuals received booster shots. The Division considered it advisable to reevaluate the need for annual boosters and possibly the amount of the booster dose. Although the record is unclear as to whether or not NIH requested a reevaluation, to date, no such reevaluation has been done." (Pg. 102, par. 5)	A study of immunogenicity is currently being conducted under CDC oversight.	DoD will anxiously await these results.
For this purpose, "suitable" should not just mean FDA approved, but demonstrably as safe and effective as possible for the intended military use. A vaccine that takes 18 months, and annual boosters, to confer immunity should not be considered suitable under the policy. (Pg. 103, par. 1)	DoD disagrees given the threat.	FDA is Congressionally charged with the mission of approving for licensure only those drugs, vaccines and devices that are safe and effective and thus suitable for human use.
In terms of increased safety, there is also some evidence an intravenous injection would produce fewer side effects and adverse reactions than subcutaneous administration. (Pg. 104, par. 5) (emphasis added)	The term *intravenous* is incorrectly used in this sentence: the correct term is intramuscular. In the past, the DoD and the manufacturer have pursued research on using alternate routes of administration and continue in this research effort now.	The Comparative Study to Determine the Best Two-Dose Schedule and Route of Administration of Human Anthrax Vaccine, by Dr. Phillip Pittman, sponsored by Dr. Robert Myers, MBPI (now BioPort) was submitted to the FDA in Fall 1998. The results were favorable but the FDA requires a larger pivotal study. Funding has been obtained and DoD is working in conjunction with the CDC,

		NIH and the sponsor (BioPort) to complete this study.
DoD only recently began "to design a set of studies to better evaluate the long term safety of the anthrax vaccine ... to conform with present-day, post-marketing practice" (Pg. 106, par. 2)	In 1970 when the vaccine was licensed, the FDA did not require post-marketing studies. FDA changed this requirement to improve product information and safety. This said, there exists more long-term safety data on the anthrax vaccine than many other vaccines currently routinely administered to populations in the U.S., such as hepatitis A and B and chicken pox (varicella).	To date, at least 12 human studies have assessed the safety of anthrax vaccination. These studies, some stretching back almost 50 years, reported adverse events after vaccination, in varying degrees of detail. The following paragraphs list the studies. Among the studies listed below, one of two vaccine formulations was used. The Brachman study and the early Fort Detrick studies used anthrax vaccine manufactured according to the original 1950s formula developed at Fort Detrick, Maryland. In the 1960s, the production process for anthrax vaccine was improved to increase the concentration of the active ingredient, protective antigen, (thus increasing the vaccine's potency) and to decrease the amount of other bacterial components in the vaccine (thus increasing purity). This purer, more potent vaccine, manufactured in Lansing, Michigan, was licensed by the FDA in 1970. The CDC observational study involved people who received either the original vaccine or the improved vaccine, or both. The other studies described below used anthrax vaccine manufactured according to the improved 1960s formula, the

		same vaccine used throughout the United States today. Details of each study appear on following pages. The twelve studies include: a. The Brachman Study (the pivotal field trial evaluating the safety and efficacy of anthrax vaccination). b. The CDC Observational Study (the follow-on study between the Brachman Study and vaccine licensing in 1970). c. The Fort Detrick Multi-Dose, Multi-Vaccine Safety Studies (evaluations of Army laboratory workers vaccinated hundreds of times with dozens of vaccines). d. The Fort Detrick Special Immunization Program (SIP) Safety Study (a continuation of the previous study among more workers into modern times). e. The Fort Bragg Booster Study (an evaluation of additional doses of anthrax vaccine among soldiers vaccinated several years earlier during the Persian Gulf War). f. The USAMRIID Reduced-Dose / Route-Change Study (a study of anthrax vaccine administered by two different injectable routes of administration).

		g. The Canadian Forces Safety Survey (a study of Canadian Service Members). h. The TAMC-600 Survey (a study of adverse events after anthrax vaccination of medical personnel at Tripler Army Medical Center). i. The U.S. Forces Korea Records Study (a study of adverse events among service members serving in Korea). j. The USAF Vision Study (a study of visual acuity among vaccinated and unvaccinated aircrew members). k. The USAF Air Combat Command Study, Langley Air Force Base (a study of outpatient medical care among Air Force personnel after return from Southwest Asia). l. The reports involving Anthrax Vaccine submitted to the FDA/CDC Vaccine Adverse Event Reporting System (VAERS). SUMMARY: Like all vaccines, anthrax vaccine may cause soreness, redness, itching, swelling, and lumps (a subcutaneous nodule) at the injection site. About 30% of men and 60% of women report mild local reactions, but these reactions usually last only a few days. Lumps can persist for a few weeks, but

		eventually completely resolve. For both genders, between 1% and 5% report moderate reactions of 1 to 5 inches in diameter. Larger reactions occur after about one in a hundred vaccinees or less. Beyond the injection site, from 5% to 35% will notice muscle aches, joint aches, chills, fever, headaches, nausea, loss of appetite, malaise, or related symptoms. Again, these symptoms usually go away after a few days. To monitor rare or unexpected adverse events associated in time to any vaccine, DoD health care providers have participated in the Vaccine Adverse Event Reporting System (VAERS) since its inception in 1990, when it was established by the Department of Health and Human Services. In addition, each VAERS report is reviewed by an independent panel of civilian physicians. To date, this panel has detected no patterns of unexpected adverse events related to anthrax vaccination. There are no known long-term patterns of side effects from the anthrax vaccine, based on an ongoing series of studies at Fort Detrick, Maryland, and elsewhere. The first report in this series was published in 1958. Despite the extensive body of

		knowledge regarding the safety of anthrax vaccine, safety monitoring continues, as is prudent for all vaccines and medications.
Therefore,"a member of the Reserve Component may present themselves for initial treatment and evaluation at any military treatment facility, after vaccination during a period of duty. The member will be examined and provided necessary medical care. Once treatment is rendered or the individual's emergent condition is stabilized a Line of Duty and/or Notice of Eligibility status will be determined by the member's unit, as required. No treatment beyond that justified to stabilize the condition or emergency is authorized until Service connection is validated." (Pg. 106, par. 4)	Adverse events linked to DoD-directed immunizations are treated the same as any other line of duty injury or illness per Title 10, United States Code for the Armed Forces.	*Office of the Assistant Secretary of Defense for Health Affairs memorandum subject: Ensuring Reserve Component Have Full Access to Department of Defense (DoD) Military Treatment Facilities (MTF) for Treatment Evaluation of Adverse Events from DoD Directed Immunizations, dated 20 Jul 1999, states:* "Title 10, United States Code for the Armed Forces directs that members of the Reserve components who incur or aggravate any injury, illness, or disease while performing active duty for less than 30 days, or inactive duty training are entitled to medical care appropriate for the treatment of the injury, illness or disease. Adverse reactions from DoD-directed immunizations are line of duty illnesses. Therefore, when a member of the Reserve component presents for treatment at an MTF, expressing a belief that the condition for which treatment is sought is related to receiving an immunization during a period of duty, the member must be examined and provided necessary medical care." The Department has initiated a network of health care

		facilities to support Reserve Component (RC) personnel, not only for anthrax vaccination and/or vaccine-related reactions, but also for medical care.
But requiring an immediate determination of service-connection for vaccine related health effects means many short term, and most long term, adverse reactions will not be monitored by DoD physicians. (Pg. 107, par. 1)	Line of Duty and/or Notice of Eligibility will be determined as soon as possible. Commanders initiate the investigation process once he/she has been notified by the service member.	*Office of the Assistant Secretary of Defense for Health Affairs memorandum subject: Ensuring Reserve Component Have Full Access to Department of Defense (DoD) Military Treatment Facilities (MTF) for Treatment Evaluation of Adverse Events from DoD Directed Immunizations, dated 20 Jul 1999, states:* "Title 10, United States Code for the Armed Forces directs that members of the Reserve components who incur or aggravate any injury, illness, or disease while performing active duty for less than 30 days, or inactive duty training are entitled to medical care appropriate for the treatment of the injury, illness or disease. Adverse reactions from DoD-directed immunizations are line of duty illnesses. Therefore, when a member of the Reserve component presents for treatment at an MTF, expressing a belief that the condition for which treatment is sought is related to receiving an immunization during a period of duty, the member must be examined and provided necessary medical care."
Enrollment of every vaccine recipient in a clinical	Enrollment of 2.4 million people in a comprehensive	Through its automated immunization tracking

evaluation and treatment protocol would allow DoD to capture a unique and valuable data set for use in their longitudinal studies, avoiding disputes over cohort selection bias and other methodological issues. (Pg. 107, par. 2)	treatment protocol is not warranted by the adverse reaction data collected and evaluated to date. Neither the FDA, CDC, AVEC, nor the Longitudinal Studies Concept Committee have found any adverse events, not otherwise expected, nor have made a recommendation for such an evaluation and treatment protocol. Such a protocol at this time is neither standard medical practice, recommended, or cost effective.	systems, DoD captures all vaccine recipients and each anthrax vaccine immunization event in an automated database. This information is being used in database and potential cohort studies, and will facilitate any evaluation and treatment protocols that may be recommended in the future.
While an improved vaccine is being developed, use of the current anthrax vaccine for force protection against biological warfare should be considered experimental and undertaken only pursuant to FDA regulations governing investigational testing for a new indication. (Pg. 10 8, par. 1)	FDA has confirmed that AVA use against biological warfare is not an off-label use, nor is it subject to FDA's Investigational New Drug (IND) regulations.	Letter from Dr. Michael A. Friedman, Lead Deputy Commissioner, Food and Drug Administration to Dr. Stephen C. Joseph, The Assistant Secretary of Defense of Health Affairs, March 13, 1997 reads: "While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert does not preclude this use. The original efficacy trial clearly showed that the vaccine conferred a high level of protection against cutaneous exposure. None of the 5 inhalation cases in this trial occurred in Anthrax Vaccine recipients, but these data alone are insufficient to allow definitive statistical conclusions. Results from animal challenge studies have also indicated that pre-exposure administration of Anthrax Vaccine protects

		against inhalation anthrax. Therefore, I believe your interpretation is not inconsistent with the current label." Furthermore, a FDA 26 Nov 99 letter from Melinda K. Plaisler, Associate Commissioner for Legislation, in response to a letter from Congressman Dan Burton states, "Use of the vaccine for protection against both cutaneous and inhalation anthrax exposure is not inconsistent with the labeling for Anthrax Vaccine Absorbed." and "There is presently no basis for concluding that the anthrax vaccine, a licensed product, when used in accordance with current labeling, should be used pursuant to an IND application or, as requested in your letter, that FDA 'place the anthrax vaccine back under IND status'."
Under FDA regulations, use of an FDA-approved product in an unapproved way, or for an unapproved purpose, can only be undertaken pursuant to clinical trial protocols contained in Investigational New Drug (IND) applications. (Pg. 108, par. 2)	The anthrax vaccine is a FDA-licensed vaccine and is being used per the indications and usage on the package insert. The FDA in repeated testimony to Congress last year and in written communications continues to maintain that DoD's use of the anthrax vaccine for protection against inhalation anthrax is an appropriate use of the vaccine and is in accordance with the package insert.	"Immunization with Anthrax Vaccine Adsorbed is recommended for individuals who may come in contact with animal products such as hides, hair, or bones which come from anthrax endemic areas and may be contaminated with *Bacillus anthracis* spores; and for individuals engaged in diagnostic or investigational activities which may bring them into contact with *B. anthracis* spores. It is also recommended for high-risk persons such as veterinarians

		and others handling potentially infected animals. Since the risk of exposure to anthrax infection in the general population is slight, routine immunization is not recommended. If a person has not previously been immunized against anthrax, injection of this product following exposure to anthrax bacilli will not protect against infection." *Anthrax Vaccine Adsorbed Package Insert, BioPort Corporation, Lansing, Michigan U.S. License No. 1260.* Letter from Dr. Michael A. Friedman, Lead Deputy Commissioner, Food and Drug Administration to Dr. Stephen C. Joseph, The Assistant Secretary of Defense of Health Affairs, March 13, 1997 reads: "While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert does not preclude this use. The original efficacy trial clearly showed that the vaccine conferred a high level of protection against cutaneous exposure. None of the 5 inhalation cases in this trial occurred in Anthrax Vaccine recipients, but these data alone are insufficient to allow definitive statistical conclusions. Results from animal challenge studies have also indicated that pre-

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Despite the fact the vaccine was approved as safe and subsequently deemed effective only against cutaneous anthrax infection, DoD asserts use of the FDA-approved AVA as prophylaxis against weaponized, inhalation anthrax does not constitute an off-label use against a new indication because while the package insert for this vaccine is nonspecific as to the route of exposure, DoD has long interpreted the scope of the license to include inhalation exposure, including that which	The package insert does not specify or limit the use of the vaccine for exposure to only the cutaneous form of anthrax. The FDA in repeated testimony to Congress last year and in written communications continues to maintain that DoD's use of the anthrax vaccine for protection against inhalation anthrax is an appropriate use of the vaccine and is in accordance with the package insert.	"Immunization with Anthrax Vaccine Adsorbed is recommended for individuals who may come in contact with animal products such as hides, hair, or bones which come from anthrax endemic areas and may be contaminated with *Bacillus anthracis* spores; and for individuals engaged in diagnostic or investigational activities which may bring them into contact with *B. anthracis* spores. It is also recommended for high-risk persons such as veterinarians

would occur in a biological warfare context. (Pg. 108, par. 4)		and others handling potentially infected animals. Since the risk of exposure to anthrax infection in the general population is slight, routine immunization is not recommended. If a person has not previously been immunized against anthrax, injection of this product following exposure to anthrax bacilli will not protect against infection." *Anthrax Vaccine Adsorbed Package Insert, BioPort Corporation, Lansing, Michigan U.S. License No. 1260.* Letter from Dr. Michael A. Friedman, Lead Deputy Commissioner, Food and Drug Administration to Dr. Stephen C. Joseph, The Assistant Secretary of Defense of Health Affairs, March 13, 1997 reads: "While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert does not preclude this use. The original efficacy trial clearly showed that the vaccine conferred a high level of protection against cutaneous exposure. None of the 5 inhalation cases in this trial occurred in Anthrax Vaccine recipients, but these data alone are insufficient to allow definitive statistical conclusions. Results from animal challenge studies have also indicated that pre-exposure administration of

		Anthrax Vaccine protects against inhalation anthrax. Therefore, I believe your interpretation is not inconsistent with the current label." Further, FDA 26 Nov 99 letter from Melinda K. Plaisler, Associate Commissioner for Legislation to Congressman Dan Burton states, " Use of the vaccine for protection against both cutaneous and inhalation anthrax exposure is not inconsistent with the labeling for Anthrax Vaccine Absorbed." and "There is presently no basis for concluding that the anthrax vaccine, a licensed product, when used in accordance with current labeling, should be used pursuant to an IND application or, as requested in your letter, that FDA 'place the anthrax vaccine back under IND status'."
Since 1997, the *Department of Defense Nuclear/Biological/Chemical (NBC) Defense – Annual Report to Congress* has referred to medical CBW countermeasures proven safe because they have "been widely used to treat other medical conditions." The report cites pyridostigmine, bromide, the botulinum toxoid vaccine, both used for CB prophylaxis only pursuant to INDs, and the anthrax vaccine. (Pg. 109, par. 5)	Anthrax vaccine is not investigational. It is an FDA-approved vaccine and has been licensed since 1970.	Covered extensively above.
So the AVIP's cumbersome logistics, additional costs, and	The threat of weaponized anthrax to our troops is real	The new vaccine study, which is a tech-based effort to

increased risk of adverse reactions all flow directly from an unwillingness to do the research and testing to develop a better vaccine or improve the safety and efficacy of the current AVA. (Pg. 111, par. 4)	and is now. The AVIP's use of the current FDA-licensed anthrax vaccine is an appropriate, timely response to the current threat. Meanwhile, DoD continues to pursue a new, hopefully better vaccine through ongoing research, and continues an unprecedented program to monitor safety of the current vaccine.	develop a new vaccine candidate against anthrax, includes the following aspects: • Genetically engineering a new vaccine candidate based on Protective Antigen. The new vaccine candidate is called rPA. • Evaluating, selecting and optimizing an expression system. • Developing purification schemes. • Evaluating and selecting a vaccine adjuvant. • Demonstrating efficacy in animal models.
If DoD were to concede administration of AVA against inhalational battlefield exposure is an off label use, informed consent would be required. (Pg. 112, par. 3)	Anthrax vaccine is a licensed product and is not investigational.	Covered extensively above.
"A distinction must be made between treatment and experimentation. It may be asserted that anthrax vaccine (unlike pyridostigmine bromide as used in the Gulf War or anti-botulinum vaccine) constitutes 'treatment,' or that it is not experimental because of being declared safe and effective by FDA. ... In fact, the anthrax vaccine was licensed by the FDA before efficacy studies were required. Its efficacy against inhalational anthrax has been questioned.... British epidemiologist suggested that troops be publicly randomized to receive active vaccine or placebo, clearly implying that	The FDA in repeated testimony to Congress last year and in written communications continues to maintain that DoD's use of the anthrax vaccine for protection against inhalation anthrax is an appropriate use of the vaccine and is in accordance with the package insert.	In addition to the Department of Defense, other agencies and groups advocate or support the use of the anthrax vaccine. The Food and Drug Administration licensed the anthrax vaccine in 1970. The Centers for Disease Control & Prevention, the World Health Organization, the Armed Forces Epidemiological Board, and many other respected public health organizations support the use of the vaccine in persons at risk for exposure to *Bacillus anthracis*. Information about the AVIP and the anthrax vaccine is available on the Internet in a

many consider the vaccine to be experimental." (Pg. 113, par. 2)		variety of DoD web sites and in web sites such as the Center for Disease Control & Prevention and the Food and Drug Administration web sites. The web sites include facts about the vaccine, its history, side effects, purpose and more. Evidence for the efficacy of the anthrax vaccine is sufficient for it to be included in standard medical reference books in the United States and around the world. These references include: • *Control of Communicable Diseases Manual*, 16th ed. Abram S. Benenson, ed. "An official report of the American Public Health Association," Washington, DC, 1995. • *Guide for Adult Immunization*, Philadelphia: American College of Physicians, 1994 edition. • *Immunisation Against Infectious Disease*. Her Majesty's Stationery Office, London: British Joint Committee on Vaccination and Immunisation, 1996. • *Report of the Committee on Infectious Diseases*, 24th edition, Elk Grove Village, IL: American Academy of Pediatrics, 1997.

		• *ImmunoFacts: Vaccines & Immunologic Drugs.* Saint Louis: Facts and Comparisons, Inc., 1999. • *Merck Manual on Drugs & Therapeutics.* West Point, PA: Merck and Company, 1999. Anthrax vaccine is a prominent part of the World Health Organization's 1998 *Guidelines for the Surveillance and Control of Anthrax in Humans and Animals* (www.who.int/emc-documents/zoonoses/whoemczdi986c.html). Similarly, anthrax vaccination is specifically endorsed in the Working Group on Civilian Biodefense position paper on preparedness against anthrax (Inglesby et al. Anthrax as a biological weapon. *Journal of the American Medical Association)* 1999;281:1735-45; (www.ama-assn.org/sci-pubs/journals/archive/jama/vol_281/no_18/jst80027.htm). Officials at the CDC confirmed the validity of the vaccination guidelines in Inglesby's paper (MMWR 1999;48(Feb 5):69-74). ftp://ftp.cdc.gov/pub/Publications/mmwr/wk/mm4804.pdf The U.S. Department of Agriculture lists anthrax vaccine as a condition of employment for personnel of the Animal & Plant Health Inspection Service (APHIS),

		if potentially exposed on the job.
The AAPS recommended a careful examination of the medical ethics involved in military, and civilian, vaccination efforts, noting the entire point of informed consent in combat is 'not to prevent soldiers from obtaining whatever protection may be afforded them by an investigational agent that has not been adequately tested, but rather, it is to give them the choice of whether they think the 'protection' is worth the risks of adverse effect'" (Pg. 72, par. 1)	Anthrax vaccine is not an investigational new drug (IND).	Covered extensively above.
Although DoD's track record administering INDs or informed consent waivers is not exemplary, current procedural safeguards, adopted since the Gulf War, provide far more protection to service members receiving investigational products than the AVIP now provides. (Pg. 72, par. 3)	Anthrax vaccine is not an IND. This has no bearing and should be deleted from the report.	Covered extensively above.
In November 1997 the Subcommittee proposed, and the full Government Reform and Oversight Committee approved, an oversight report on Gulf War veterans' illnesses containing 18 findings and 18 recommendations. Among them was the finding that "the FDA was passive in granting and failing to enforce the conditions of a waiver to permit use of PB by DoD" and the recommendation that	This portion of the report has to do with PB as an IND and not with the anthrax vaccine. This portion of the report should be deleted since anthrax vaccine is not experimental, is not an IND, but is an FDA-licensed vaccine.	Covered extensively above.

"FDA should grant a waiver of informed consent requirements for the use of experimental or investigational drugs by DoD only upon receipt of a Presidential finding of efficacy and need." (Pg. 72, par. 4)		
Legislation reflecting that recommendation was introduced in both chambers of Congress. The 1999 Defense Authorization Act contained provisions, codified at 10 USC 1107(f), implementing the recommendation by strengthening notice requirements and by requiring a presidential authorization for any waiver of informed consent. (Pg. 73, par. 2)	This has to do with IND drugs and anthrax vaccine is not an IND.	Covered extensively above.
In view of the new statutory provision, FDA on October 5, 1999 revoked the 1990 interim final rule and issued a new regulation to govern DoD compliance with IND conditions and informed consent waivers. (Pg. 73, par. 3)	Anthrax vaccine is not an IND so this portion of the Subcommittee report does not apply.	Covered extensively above.
On September 30, 1999 the White House issued Executive Order 13139 establishing the procedures by which the president would comply with the new law. The EO says "[w]aivers of informed consent will be granted only when absolutely necessary " and only upon a written determination by the president that obtaining consent is not feasible, is contrary to the best interest of the service member	Anthrax vaccine is not an IND. This Executive Order 13139 is for granting permission to use an IND drug or vaccine; therefore, it does not apply to anthrax vaccine	Covered extensively above.

or is not in the interest of national security. In the event a waiver is granted, the DoD Secretary must notify Congress and publish a notice in the Federal Register. No waiver may last more than one year. Waivers may be renewed based on a new, fully documented request." (Pg. 73, par. 4)		

CMAT Control #
2000098-0000003

51

(b)(6) @otsg.amedd.army.mil on 03/09/2000 12:13:04

To: (b)(6) /OSAGWI
cc:
Subject: GW Records Question

LCDR (b)(6),

As discussed, #27 is the question I mentioned. The entire document is attached.

27. Please explain the administrative lapses that occurred during the Gulf War, which conveniently deleted shot and medical record information pertaining to anthrax and other vaccinations received.

<<CurryAnthrax Questions1.doc>>

Thank you,

(b)(6)

http://www.anthrax.osd.mil
1-877-GETVACC

- CurryAnthrax Questions1.doc

27. Please explain the administrative lapses that occurred during the Gulf War, which conveniently deleted shot and medical record information pertaining to anthrax and other vaccinations received.

Answer:

*There were **NO** DoD or Service-directed policies or administrative procedures intended to have "conveniently deleted shot and medical record information pertaining to anthrax and other vaccinations received."*

POLICY: In January 1991, USCENTCOM and Army messages, originally classified as SECRET and since declassified, provided policy guidance for the theater-wide anthrax and botulism immunization programs. Both messages cautioned recipients of these vaccines not to discuss them with anyone, then stated that the vaccinations may be recorded on the yellow shot record (PHS 731), or on the Immunization Record (SF 601) as: Vacc A and Vacc A-2 (for the anthrax series), and Vacc B and Vacc B-2 (for the botulinum toxoid series).[1] If shot records were not available, medical units were to create rosters of those who received the shots.[2] A later memorandum indicated these vaccines may also have been recorded as "Anthrax," "A Vaccination," "A-Vax," "Botulinum," "Bot-Tox," "B-Vax," or something similar.[3]

In the case of botulinum toxoid, personnel were required to sign an information sheet about the vaccine, indicating that they had read and understood the information and had voluntarily submitted to this immunization.[4] This information sheet appears to have been designed to serve as a roster for vaccine recipients, as well as a "consent form" for this investigational vaccine.

There were no specific guidelines in the original messages for the maintenance or forwarding of the rosters and information sheets for official recording of the information while the personnel were in theatre. After the conflict was over, the Army Surgeon General ordered a copy of all rosters be sent to the Office of the Surgeon General (Army) in order to create an audit trail of where the vaccines were given.[5] Not all units complied with this order. A Marine Corps message, released in March 1991, directed that, if feasible, entries of anthrax and botulinum toxoid vaccines should be recorded in the individual health record "...before personnel depart the AOR," and that units that had already returned back to the US should have their entries made at the earliest possible date.[6]

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[1] USCENTCOM Message, USCINCCENT/CCSG to COMUSARCENTMAIN/SG et al., Subject: "Biological Warfare Vaccination Guidelines," 171832Z Jan 91; Army Message, from ARCENT/CG, Subject: "Biological Warfare Vaccination Guidelines," 06007002 Jan 91.
[2] Army Message, CRDUSATWO to AIG 12153, Subject: "Medical Records and Rosters Related to Immunization Against Biological Warfare (BW) Agents," 091300Z July 1991, www.gulflink.osd.mil/declassdocs/otsg/19970107/970107_sep96_decls32_0001.html.
[3] Army Memorandum, from OTSG/SGPS-PSP, Subject: "Medical Records and Rosters Related to Vaccination Against Biological Warfare Agents," May 21, 1991, www.gulflink.osd.mil/declassimages/otsg/19961028/100896_sep96_decls13_0001.html.
[4] CENTCOM Message, USCINCCENT/CCSG to COMUSARCENTMAIN/SG et al., Subject: "Biological Warfare Vaccination Guidelines," 171832Z Jan 91.
[5] Army Memorandum, from OTSG/SGPS-PSP, Subject: "Medical Records and Rosters Related to Vaccination Against Biological Warfare Agents," May 21, 1991, www.gulflink.osd.mil/declassimages/otsg/19961028/100896_sep96_decls13_0001.html.
[6] Marine Corps Message, CG FIRST MARDIV/CG to ALL FIRST MARDIV, Subject: "Biological Warfare Vaccination Program," 1009327MAR91Z

PRACTICE: Vaccine documentation in theater varied from good to poor. Although some service members' records were properly annotated with regard to anthrax and botulinum toxoid immunizations, many were not. Some were not transcribed from rosters into the permanent health records because of unit movement and the records not being in the area of operation.[7] While there are reports that personnel signed the botulinum toxoid vaccine consent forms, there are also cases of no consent forms being available, and cases where the botulinum toxoid vaccine was ordered to be given without informed consent.[8, 9] This lack of documentation has left many Gulf War veterans confused and upset over which shots they actually received.

In an effort to ascertain what practices occurred in the field, telephone interviews of some health care personnel from the Gulf War Era were conducted. The health care personnel included all ranks, services, and components (Reserves, active duty, National Guard, those personnel who had left the service, were retired, and those who are still serving). The interviews yielded a wide range of comments about the immunization program in the Gulf region. Some medical providers recalled that the program posed no problem, that records were updated, service members were informed of the botulinum toxoid vaccine and had the option to refuse it, and signed copies of these documents were retained. Others spoke of the problems involved and the rushed nature of the programs. In general it was felt that the secretive conduct of the immunization program for anthrax and botulism was just as confusing to some of the medical personnel as it was to many of the non-medical service members.

In many cases the vaccine documentation policy was followed. The DoD recognized the problem with immunization documentation and tried to rectify the problem with messages to the units to properly document the special immunizations in July 1991.[10] Many military personnel have sent to the Office of the Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses copies of their shot records and medical records, showing the correct recording of vaccines given during ODS/S, in accordance with CENTCOM guidance.

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[7] Special Assistant for Gulf War Illnesses, "Military Medical Recordkeeping During and After the Gulf War," Information Paper, August 11, 1999.

[8] Lead Sheet #14808, Interview of ANG Clinic Manager, May 13, 1998.

[9] Lead Sheet #14806, Interview, of flight Surgeon, May 6, 1998.

[10] Army Message, from CDRFORSCOM, "Medical Records And Rosters Related To Immunization Against Biological Warfare Agents." 091300Z Jul 91.

AVIP full response

POLICY

1. If Anthrax is the threat that DOD is telling us it is, then it is a logical weapon for terrorists to use here in the U.S. Why are we not requiring the emergency personnel, police, hospitals, firefighters, etc., to take this series of shots? Additionally, all of our embassies are potential targets for terrorism, so why is the State Department making this shot voluntary and not mandatory for personnel assigned there.

   THE DEPARTMENT OF STATE (DOS) AND THE DEPARTMENT OF DEFENSE (DOD) ARE TWO DIFFERENT US GOVERNMENT AGENCIES AND HAVE DIFFERENT MISSIONS. THE DOS ANTHRAX VACCINATION PROGRAM IS VOLUNTARY, AS ALL THEIR VACCINATIONS ARE VOLUNTARY, BECAUSE THEIR EMPLOYEES WILL BE EVACUATED PER INTERAGENCY AGREEMENTS AS THE THREAT INCREASES. THE DOD ANTHRAX VACCINATION PROGRAM IS MANDATORY, AS ALL THEIR VACCINATIONS ARE MANDATORY, BECAUSE THEIR MISSION REQUIRES FORCES TO STAY IN HIGH-THREAT AREAS DURING CONTINGENCIES AND FIGHT THE NATIONS' WARS. THE CENTERS FOR DISEASE CONTROL & PREVENTION (CDC) IS CONSIDERING RECOMMENDATIONS FOR CIVILIAN EMERGENCY PERSONNEL, BUT MANDATORY RECOMMENDATIONS ARE UNLIKELY.

2. One more thing that I would like to remind you off is that President Clinton signed an Executive Order the end of September 1999 authorizing the use of non FDA approved experimental drugs on our troops without their consent.

   EXECUTIVE ORDER (EO) 13139 DOES NOT APPLY TO "EXPERIMENTAL" DRUGS, BUT ONLY TO "INVESTIGATIONAL NEW DRUGS (INDs)" USED FOR FORCE HEALTH PROTECTION. THE DISTINCTION IS IMPORTANT. THE EO SIMPLY IMPLEMENTS EXISTING LAW PASSED BY CONGRESS (10 US CODE 1107). SECTION 1107 REFLECTS A CONGRESSIONAL RECOGNITION THAT WHEN AN IND IS THE ONLY MEANS AVAILABLE TO PROTECT AGAINST A LETHAL CHEMICAL OR BIOLOGICAL WEAPON, THE LIVES OF INDIVIDUAL MEMBERS, THE SAFETY OF THEIR COMRADES WHO RELY ON THEM, AND THE SUCCESS OF THE MILITARY MISSION MAY REQUIRE UNIFORM USE OF MEDICAL PROTECTION. USE ON ANY IND REQUIRES THE INFORMED CONSENT OF THE INDIVIDUAL UNLESS THE PRESIDENT UNDER A NONDELEGABLE AUTHORITY AUTHORIZES A WAIVER UNDER THE STRINGENT PROVISIONS OF SECTION 1107 AND THE EO. WAIVERS OF INFORMED CONSENT WILL BE GRANTED ONLY WHEN ABSOLUTLEY NECESSARY. (THE ANTHRAX VACCINE IS FULLY LICENSE BY THE FDA FOR THE PURPOSE DOD IS USING IT; ACCORDINGLY, ANTHRAX VACCINE IN NEITHER EXPERIMENTAL NOR AN IND).

ANTHRAX VACCINE IS 180 DAYS FOR THOSE INDIVIDUALS WHO ARE SEPARATING OR RETIRING FROM THE MILITARY SERVICE AND ARE NOT CURRENTLY ASSIGNED, DEPLOYED, OR SCHEDULED TO DEPLOY TO A HIGH THREAT AREA. COMMANDERS MAY OVERRIDE ADMINISTRATIVE EXEMPTIONS TO MEET MISSION REQUIREMENTS.

5. The Nuremberg Code requires informed consent prior to being injected with experimental or investigational new drugs. Why the need for Executive Order 13139, which allows for experimental and investigational new use drugs to be used without informed consent under the guise of Force Protection?

   EO 1107 SIMPLY IMPLEMENTS THE INTENT OF CONGRESS. INDs ARE NOT EXPERIMENTAL. DRUGS AND VACCINES THAT HAVE NOT BEEN APPROVED BY THE FDA FOR GENERAL COMMERCIAL MARKETING FOR THE SPECIFIC USE INVOLVED ARE CLASSIFIED AS INDs. TYPICALLY INDs ARE FDA-APPROVED FOR SOME USE. THE ONLY INDs THAT WILL BE USED FOR FORCE HEALTH PROTECTION ARE THOSE WITH SAFETY RECORDS COMPARABLE TO APPROVED DRUGS AND VACCINES, AND FOR WHICH THE EVIDENCE FOR EFFICACY CLEARLY SUPPORTS USE OF THE IND. IN NO UNCERTAIN TERMS, USE OF INDs UNDER EO 13139 WILL BE FOR FORCE HEALTH PROTECTION, NOT "UNDER THE GUISE" OF IT.

6. Why is DOD ignoring the Congressional Reform Committee's report urging the AVIP program to be suspended until a safer vaccine is developed?

   DOD REVIEWED THE CONGRESSIONAL REFORM COMMITTEE'S REPORT AND RESPONDED TO THE SUPPOSITIONS CONTAINED IN THE REPORT. DOD REMAINS COMMITTED THAT THE ANTHRAX VACCINE IMMUNIZATION PROGRAM IS BASED ON SOLID SCIENCE AND MEETS THE TEST OF MEDICAL RESPONSIBILITY. SUSPENDING THE PROGRAM WOULD LEAVE THE FORCE UNPROTECTED FROM THIS GRAVE BIOLOGICAL WARFARE THREAT WITH THE POTENTIAL FOR LARGE NUMBERS OF VACCINE PREVENTABLE CASUALTIES. THE DOD REBUTTAL MAY BE FOUND AT WWW.ANTHRAX.OSD.MIL

7. Secretary Cohen has repeatedly likened the use of the anthrax vaccine as sending a soldier into battle with a helmet. Would you be willing to wear a helmet 24 hours a day for the rest of your life? What if the helmet mysteriously swelled to 6 times its normal size 20 years later?

   VACCINATIONS ARE NOT WITHOUT RISK, HOWEVER, THE BENEFIT OF BEING PROTECTED FROM A LETHAL BIOLOGICAL AGENT FAR OUTWEIGHS ANY RISK OF VACCINATION. ANTHRAX IS HIGHLY LETHAL TO AN UNVACCINATED, UNPROTECTED INDIVIDUAL IF NOT TREATED IMMEDIATELY AFTER EXPOSURE. BECAUSE ANTHRAX

INHALATIONAL ANTHRAX IS 99% FATAL IN UNPROTECTED, UNVACCINATED INDIVIDUALS, LEFT UNTREATED. ONCE SYMPTOMS DEVELOP IN INFECTED INDIVIDUALS, EVEN IF TREATED AGGRESSIVELY IN THE FINEST MEDICAL FACILITY, INHALATIONAL ANTHRAX VICTIMS' DEATH RATE EXCEEDS 80%.

EFFECTS

12. Given the apparent correlation between systemic and/or chronic symptoms and anthrax (healthy before the shots, unhealthy after the shots based on Dover AFB testimonies), why is the burden of proof in favor of proving the symptoms were caused by the shots instead of caused by something other than the shots?

    IN BRIEF, THE ANSWER IS BECAUSE THE ADVERSE EVENTS OR SYMPTOMS REPORTED ALSO OCCUR AMONG PEOPLE WHO HAVEN'T BEEN VACCINATED; THE KEY ISSUE IS WHETHER THESE ADVERSE EVENTS (AE) OCCUR MORE COMMONLY AMONG VACCINE RECIPIENTS THAN THOSE NOT VACCINATED. MONITORING VACCINE SAFETY IS A COMPLEX AND SHARED RESPONSIBILITY BETWEEN THE INDIVIDUAL WHO REPORTS HAVING AN AE AND COMMITTEES CONVENED TO REVIEW THE INFORMATION FOR CAUSALITY. CAUSALITY ASSESSMENT IS DETERMINED BY EVALUATING SEVERAL IMPORTANT FACTORS: FREQUENCY OF OCCURANCE OF THE AE; SIMILAR EVENTS KNOWN TO OCCUR WITH OTHER DISEASES; WHETHER THE EVENT IS KNOWN TO BE RELATED TO A PARTICULAR VACCINE; WHETHER THE EVENT IS EXPLAINABLE BY THE BIOLOGICAL PROPERTIES OF THE VACCINE; WHETHER THE INTERVAL BETWEEN THE VACCINATION AND THE EVENT IS COMPATIBLE; WHETHER THE PERSON HAD A SIMILAR EVENT IN THE PAST PRIOR TO GETTING VACCINATED; CONCOMITANT DRUG THERAPY; AND/OR DID THE INDIVIDUAL HAVE A PRECEDING MEDICAL CONDITION POSSIBLY RELATING TO THE EVENT. KNOWLEDGABLE PHYSICIANS MUST COMPLETE THE ABOVE EVALUATION. THAT IS WHY THE BURDEN OF PROOF IS DETERMINED USING A SOUND, SCIENTIFIC, LOGICAL APPROACH RATHER THAN INDIVIDUAL STORIES OF UNDEFINED ILLNESSES.

13. How can DOD state that they have found no evidence of long term effects when they also admit that there are no studies of long term effects?

    DOD HAS CONDUCTED LONG-TERM STUDIES. THERE IS MORE LONG-TERM DATA ON ANTHRAX VACCINE THAN HEPATITIS A, LYME

PRIVATE HEALTH CARE SECTOR, DOD HAS ALWAYS MADE IT MINIMALLY MANDATORY FOR (NOT LIMITED TO) EVENTS RESULTING IN EITHER HOSPITALIZATION FOR ANY LENGTH OF TIME OR LOSS OF DUTY GREATER THAN 24 HOURS. VAERS IS OUR NATIONAL REPORTING SYSTEM AND HAS ALWAYS ALLOWED ANYONE TO FILE A FORM. TO EMPHASIZE AND CLEAR UP THIS POSITION, DOD INCREASED ITS EDUCATION EFFORTS IN THIS REGARD. VAERS REPORTS ACT AS SIGNALING EVENTS FOR ASSOCIATED RARE ADVERSE EVENTS FOR ANY VACCINES AND SHOULD NOT BE USED TO DETERMINE REACTION RATES. IN THE LAST SEVERAL QUARTERS, THE FDA RECEIVED A GREATER NUMBER OF REPORTS OF MILD, PREDOMINANTLY LOCAL INJECTION SITE EVENTS, BUT THE SAME VERY LOW NUMBER OF SERIOUS EVENTS.

16. If very few of the severe reactions are judged by the AVEC to be caused by anthrax vaccine, what are the rest of the reactions caused by?

THE EVENTS DETERMINED UNRELATED TO THE VACCINE ARE SIMPLY TEMPORALLY RELATED. A GENERAL STATEMENT CANNOT BE MADE ABOUT WHAT CAUSED THOSE REACTIONS. THERE ARE A WIDE VARIETY OF SYMPTOMS REPORTED ON THE FORMS AND EACH ONE IS CONSIDERED INDIVIDUALLY.

17. If both vaccinated and unvaccinated are exposed to anthrax, why do both have to undergo the same intensive antibiotic treatment?

PROMINENT PHYSICIANS CONSIDERING THE MEDICAL MANAGEMENT OF PATIENTS AFTER THE USE OF THE BIOLOGICAL AGENT ANTHRAX RECOMMEND THE VACCINE AS PRE-EXPOSURE PREVENTION OF DISEASE AND THE VACCINE AND ANTIBIOTIC THERAPY AS POST-EXPOSURE TREATMENT. VACCINE ADMINISTRATION EVOKES THE IMMUNE RESPONSE AND WORKS TO PROTECT AGAINST RESIDUALLY RETAINED SPORES AND SHORTENS THE LENGTH OF ANTIBIOTIC TREATMENTS.

GWS

18. If no correlation between GWS and the anthrax vaccine exists, explain why troops who were vaccinated but did not deploy show signs of GWS and French troops who deployed but were not vaccinated do not show signs of GWS. Also, British and Canadian troops who received US anthrax vaccine have sufferers of GWS.

this in subsequent congressional hearings, and I have repeated my opinion on numerous occasions.

More often than not, opponents of the program choose to ignore my current opinion because it does not suit their purposes. Let me repeat myself one more time to clear up any remaining doubt about my position: There is no rational evidence to lead any responsible person to conclude there is a connection between the anthrax vaccine and the medical problems reported by Desert Storm veterans."

LTG BLANCK IS RETIRING AFTER 32 YEARS OF SERVICE IN THE ARMY, AFTER FULFILLING HIS FULL FOUR-YEAR TERM AS ARMY SURGEON GENERAL. HIS RETIREMENT IS NOT "EARLIER THAN EXPECTED."

TESTING

20. Why did DOD stop independent testing of the vaccine?

DOD HAS NOT STOPPED INDEPENDENTLY MONITORED SUPPLEMENTAL TESTING. SUPPLEMENTAL TESTING OF VACCINE LOTS IN THE ORIGINAL STOCKPILE AT THE TIME OF THE SECDEF'S 17 DEC 97 PRESS RELEASE CONTINUES TODAY. SUPPLEMENTAL TESTS ARE NOT PERFORMED ON LOTS 040 OR HIGHER, BECAUSE THESE LOTS WERE MORE RECENTLY MANUFACTURED AND NOT PURCHASED BY DOD UNTIL SEP 98, SO WERE NOT PART OF THE SUPPLEMENTAL TESTING CONTRACT. RATHER, THESE VACCINE LOTS HAVE UNDERGONE (OR WILL UNDERGO) THE SAME TESTS FOR STERILITY, PURITY, POTENCY, AND GENERAL SAFETY, AND THE DATA HAVE BEEN (OR WILL BE) REVIEWED BY THE FDA TO DETERMINE WHETHER THE LOTS MEET APPROVAL CRITERIA FOR FDA RELEASE.

21. Why doesn't DOD destroy anthrax vaccine that failed supplemental testing? Secretary of defense William Cohen referred to approximately 1 million doses that failed testing but were still being stored.

DOD DOES NOT PLAN TO REQUEST BIOPORT DESTROY THE ANTHRAX VACCINE IN THE "EMERGENCY" STOCKPILE. THE VACCINE REMAINS SAFE, POTENT, AND EFFECTIVE. THE ISSUES RELATED TO THE VACCINE IN THE "EMERGENCY" STOCKPILE ARE NOT RELATED TO SUPPLEMENTAL TESTING, BUT RATHER DIFFICULTY RECONSTRUCTING SOME OF THE REGULATORY DOCUMENTATION. IN THE CASE OF A NATIONAL EMERGENCY, THIS VACCINE COULD BE OFFERED IF NO OTHER LICENSED VACCINE IS AVAILABLE. THIS WOULD REQUIRE CLOSE COORDINATION WITH THE FDA AND

24. Given DOD's track record with regards to radioactive testing, Agent Orange, Swine Flu, nerve agent and chemical agent testing during the 50's and 60's, etc., why should anyone believe DOD's claims of product safety? Why should service member concerns get them labeled as a troublemaker? (Latest is the fielding of faulty chemical protective gear.)

DOD IS VERY CONCERNED WITH THE SAFETY OF THE ANTHRAX VACCINE AND THE AVIP. TO VALIDATE BOTH, DOD HAD THE VACCINE AND THE PROGRAM CAREFULLY SCRUTINIZED AND VALIDATED BY INDEPENDENT EXPERTS. THE VACCINE HAS BEEN SAFELY ADMINISTERED IN THE U.S. TO AT-RISK VETERINARY AND LABORATORY WORKERS, LIVESTOCK HANDLERS, AND SERVICE MEMBERS SINCE LICENSURE BY THE FOOD & DRUG ADMINISTRATION (FDA) IN 1970. WE HAVE NOT AND WILL NOT LABEL SERVICE MEMBERS AS "TROUBLEMAKERS". SOME SERVICE MEMBERS HAVE GENUINE CONCERNS ABOUT THE VACCINE AND THE PROGRAM; OUR GOAL IS TO EDUCATE THEM AND ANSWER THEIR CONCERNS.

PRESCRIPTION

25. Given that FDA approval is only applicable when following the prescribed shot regimen and its strict schedule, how can deviations from the schedule be justified? (They were going to send Shawn with only 1 shot (at least 3 preferred).)

IT IS DOD POLICY TO ADHERE TO THE FDA DOSING SCHEDULE FOR THE ANTHRAX VACCINE. ANY DEVIATION FROM THE DOSING SCHEDULE IS THE EXCEPTION RATHER THAN THE RULE.

26. Please explain the administrative lapses that occurred during the Gulf War, which conveniently deleted shot and medical record information pertaining to anthrax and other vaccinations received.

*There were **NO** DoD or Service-directed policies or administrative procedures intended to have "conveniently deleted shot and medical record information pertaining to anthrax and other vaccinations received."*

POLICY: In January 1991, USCENTCOM and Army messages, originally classified as SECRET and since declassified, provided policy guidance for the theater-wide anthrax and botulism immunization programs. Both messages cautioned recipients of these vaccines not to discuss them with anyone, then stated that the vaccinations may be recorded on the yellow shot record (PHS 731), or on the Immunization Record (SF 601) as: Vacc A and Vacc A-2 (for the

In an effort to ascertain what practices occurred in the field, telephone interviews of some health care personnel from the Gulf War Era were conducted. The health care personnel included all ranks, services, and components (Reserves, active duty, National Guard, those personnel who had left the service, were retired, and those who are still serving). The interviews yielded a wide range of comments about the immunization program in the Gulf region. Some medical providers recalled that the program posed no problem, that records were updated, service members were informed of the botulinum toxoid vaccine and had the option to refuse it, and signed copies of these documents were retained. Others spoke of the problems involved and the rushed nature of the programs. In general it was felt that the secretive conduct of the immunization program for anthrax and botulism was just as confusing to some of the medical personnel as it was to many of the non-medical service members.

In many cases the vaccine documentation policy was followed. The DoD recognized the problem with immunization documentation and tried to rectify the problem with messages to the units to properly document the special immunizations in July 1991.[10] Many military personnel have sent to the Office of the Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses copies of their shot records and medical records, showing the correct recording of vaccines given during ODS/S, in accordance with CENTCOM guidance.

[1] USCENTCOM Message, USCINCCENT/CCSG to COMUSARCENTMAIN/SG et al., Subject: "Biological Warfare Vaccination Guidelines," 171832Z Jan 91; Army Message, from ARCENT/CG, Subject: "Biological Warfare Vaccination Guidelines," 0600700Z Jan 91.
[2] Army Message, CRDUSATWO to AIG 12153, Subject: "Medical Records and Rosters Related to Immunization Against Biological Warfare (BW) Agents," 091300Z July 1991, www.gulflink.osd.mil/declassdocs/otsg/19970107/970107_sep96_decls32_0001.html.
[3] Army Memorandum, from OTSG/SGPS-PSP, Subject: "Medical Records and Rosters Related to Vaccination Against Biological Warfare Agents," May 21, 1991, www.gulflink.osd.mil/declassimages/otsg/19961028/100896_sep96_decls13_0001.html.
[4] CENTCOM Message, USCINCCENT/CCSG to COMUSARCENTMAIN/SG et al., Subject: "Biological Warfare Vaccination Guidelines," 171832Z Jan 91.
[5] Army Memorandum, from OTSG/SGPS-PSP, Subject: "Medical Records and Rosters Related to Vaccination Against Biological Warfare Agents," May 21, 1991, www.gulflink.osd.mil/declassimages/otsg/19961028/100896_sep96_decls13_0001.html.
[6] Marine Corps Message, CG FIRST MARDIV/CG to ALL FIRST MARDIV, Subject: "Biological Warfare Vaccination Program," 1009327MAR91Z
[7] Special Assistant for Gulf War Illnesses, "Military Medical Recordkeeping During and After the Gulf War," Information Paper, August 11, 1999.
[8] Lead Sheet #14808, Interview of ANG Clinic Manager, May 13, 1998.
[9] Lead Sheet #14806, Interview, of flight Surgeon, May 6, 1998.
[10] Army Message, from CDRFORSCOM, "Medical Records And Rosters Related To Immunization Against Biological Warfare Agents," 091300Z Jul 91.

27. Why is DOD allowed to redate vaccine that has expired?

DOD DOES NOT RE-DATE VACCINE THAT HAS EXPIRED. ONCE THE VACCINE IS LABELED WITH THE EXPIRATION DATE, THAT DATE DOES NOT CHANGE. VACCINE RELEASED TO DOD IS HANDLED ACCORDING TO MANUFACTURER'S INSTRUCTIONS AND PROPERLY STORED VIALS MAY BE USED AFTER OPENING UNTIL THE LABELED EXPIRATION DATE. LOTS CAN HAVE THEIR POTENCY EXTENDED BY THE FDA IF

[10] Army Message, from CDRFORSCOM, "Medical Records And Rosters Related To Immunization Against Biological Warfare Agents," 091300Z Jul 91.

QUALITY AND PURITY CHARACTERISTICS THAT THEY ARE REPRESENTED TO HAVE.

MISCELLANEOUS

30. As recent Hill testimony shows, the Tricare system is woefully inadequate to take care of the troops. Obviously they are not prepared to provide for treatment of folks with problems from the Anthrax vaccination that DOD is pushing regardless of the congressional recommendations.

    TRICARE IS FULLY CAPABLE OF PROVIDING HEALTH CARE TO THE ACTIVE FORCE, FAMILY MEMBERS AND RETIREED BENEFICIARIES.

31. It was disclosed recently that all of the military's chemical warfare suits are being recalled for defects, however this has been known for more than 5 years. Why the lapse in action and how long to secure new suits for all military personnel? Shouldn't this be the first line of defense?

    CHEMICAL PROTECTION SUITS ARE BUT ONE PART OF THE ARSENAL OF COMPLIMENTARY MEASURES DESIGNED TO PROVIDE THE FORCE PROTECTION NECESSARY TO ACCOMPLISH THE MISSION. FOR ALL THE PROTECTION SUITS OFFER, THEY ARE NOT COMFORTABLE TO WEAR FOR LONG PERIODS AND ARE VERY DIFFICULT TO FIGHT IN EFFECTIVLEY. BECAUSE ANTHRAX IS COLORLESS, ODORLESS, AND TASTELESS, EXPOSURE CAN OCCUR WITHOUT PRIOR WARNING. IF UNVACCINATED, ONCE EXPOSED TO ANTHRAX SPORES IN THE LUNGS AND AFTER THE ON-SET OF SYMPTOMS, DEATH IS VIRTUALLY CERTAIN.

Congressional Questions

POLICY

1. If Anthrax is the threat that DOD is telling us it is, then it is a logical weapon for terrorists to use here in the U.S. Why are we not requiring the emergency personnel, police, hospitals, firefighters, etc., to take this series of shots? Additionally, all of our embassies are potential targets for terrorism, so why is the State Department making this shot voluntary and not mandatory for personnel assigned there.

The Department of State (DoS) and the Department of Defense (DoD) are two different US Government Agencies and have different missions. The DoS program is voluntary because their employees will be evacuated per interagency standards to address a continuing threat. The DoD mission whose program is mandatory is to stay in high-threat areas during contingencies.

2. One more thing that I would like to remind you off is that President Clinton signed an Executive Order the end of September 1999 authorizing the use of non FDA approved experimental drugs on our troops without their consent.

3. Anthrax is apparently among the first vaccines to combat biowarfare or bioterrorism. I understand that there are dozens of additional vaccines under development. Does this mean that service members will be receiving dozens more vaccination shots, and are they being investigated for interrelated side effects caused by receiving multiple injections at the same time?

Immunizations are essential to protect against biological warfare threats for US personnel and therefore, as potential biological warfare threats are identified, DoD is working with the FDA to determine appropriate protection mechanisms. Vaccines are being developed, whenever appropriate, for all validated biological threat agents. Anthrax vaccine can be administered concurrently with other vaccines, using separate syringes and different anatomic sites. Expected reactions to vaccines may be additive when anthrax vaccine is given along with other immunizations.

4. In some pilot's units, up to 30% of members have quit or transferred - leaving manpower critically short. The cost to train new pilots exceeds 1 million dollars each. Probably more costly is the loss of combat experience with 10 to 20 years of service. Why continue a program that threatens military readiness and negatively impacts morale and retention so much more than the perceived threat of anthrax.

By continuing the Anthrax Vaccine Immunization Program, our service members are afforded the best protection available. Vaccination will save the lives of our service men and women if exposed to anthrax. It is also a huge deterrent to the use of weaponized anthrax and to other bio-weapon development. It would be a dereliction of duty not to provide such protection.

5. DOD is finalizing exemptions based on previous reactions to the vaccine. What are the proposed thresholds for the exemptions?

The proposed threshold for exemption to the anthrax vaccine is 180 days for those individuals who are separating or retiring from the military service and are not currently assigned or deployed to a high threat area. Commanders may override exemptions to meet mission requirements.

6. The Nuremberg Code requires informed consent prior to being injected with experimental or investigational new drugs. Why the need for Executive Order 13139, which allows for experimental and investigational new use drugs to be used without informed consent under the guise of Force Protection?

7. Why is DOD ignoring the Congressional Reform Committee's report urging the AVIP program to be suspended until a safer vaccine is developed?

DoD has reviewed the Congressional Reform Committee's report and has responded to the suppositions contained in the report. DoD believes that the Anthrax Vaccine Immunization Program is based on solid scientific studies and meets the test of medical responsibility. Suspending the program would leave the force unprotected from a deadly threat with the potential for massive casualties as a result.

8. Secretary Cohen has repeatedly likened the use of the anthrax vaccine as sending a soldier into battle with a helmet. Would you be willing to wear a helmet 24 hours a day for the rest of your life? What if the helmet mysteriously swelled to 6 times its normal size 20 years later?

Vaccinations are not without risk, however, the benefit of being protected from a lethal biological agent far outweighs any risk of vaccination. Anthrax is 99% lethal to an unvaccinated individual.

9. One of the things that DOD is telling you is that only a small percentage of folks are refusing the shots. My son refused the shot and received a general discharge under honorable conditions. Reason given was for minor infractions and not refusal of the shot.

GEOPOLITICS

10. In 1990, a DOD threat report stated that there were 9 or 10 countries with the ability to wage biowarfare. This is the same number of countries in the report represented as the impetus for the AVIP program. Why the change in attitude to the same level of threat?

11. Didn't the US supply Iraq with a significant portion of its biowarfare equipment during its war with Iran?

12. The Japanese cult Aum Shinriyko has released anthrax as a terrorist act at least 8 times, yet no illnesses or deaths have been reported. This doesn't seem to substantiate DOD's claims of anthrax toxicity.

EFFECTS

13. Given the apparent correlation between systemic and/or chronic symptoms and anthrax (healthy before the shots, unhealthy after the shots based on Dover AFB testimonies), why is the burden of proof in favor of proving the symptoms were caused by the shots instead of caused by something other than the shots?

14. How can DOD state that they have found no evidence of long term effects when they also admit that there are no studies of long term effects?

15. Dr. Pam Asa recently released a report in which she found conclusive evidence of squalene antibodies in GWS and anthrax vaccines, but not in control groups. If we assume that DOD's statements that they never used squalene as an adjuvant, shouldn't DOD at least investigate whether the anthrax vaccine (possibly combined with other vaccines received at the same time) causes natural production of squalene antibodies?

16. Initially, VAERS forms were only accepted for review if the service member was hospitalized or missed more than 24 hours of duty time. After severe criticism of these extreme requirements, the VAERS policy was amended to allow anyone to file a VAERS report for any reason. Are there current statistics showing more accurate reaction rates after the threshold was reduced that exclude the previous skewed data?

17. If very few of the severe reactions are judged by the AVEC to be caused by anthrax vaccine, what are the rest of the reactions caused by?

18. If both vaccinated and unvaccinated are exposed to anthrax, why do both have to undergo the same intensive antibiotic treatment?

GWS

19. If no correlation between GWS and the anthrax vaccine exists, explain why troops who were vaccinated but did not deploy show signs of GWS and French troops who deployed but were not vaccinated do not show signs of

GWS. Also, British and Canadian troops who received US anthrax vaccine have sufferers of GWS.

20. Army Surgeon General Ron Blanck stated in Senate Report 103-97, 8 Dec. 1994 that "although the anthrax vaccine had been considered approved prior to the Persian Gulf War, it was rarely used. Therefore, its safety, particularly when given to thousands of soldiers in conjunction with other vaccines, is not well established. Anthrax vaccine should continue to be considered as a potential cause for undiagnosed illnesses in Persian Gulf military personnel because many of the support troops received the anthrax vaccine, and because DOD believes that the incidence of undiagnosed illnesses in support troops may be higher than in combat troops." Why the change of heart by General Blanck and has he announced his reasons for retiring earlier than expected?

TESTING

21. Why did DOD stop independent testing of the vaccine?

22. Why doesn't DOD destroy anthrax vaccine that failed supplemental testing? Secretary of defense William Cohen referred to approximately 1 million doses that failed testing but were still being stored.

23. Didn't the DOD testing, which only shows effectiveness in animals and not humans, only use a single strain of the approximately 2 dozen naturally occurring strains and none of the bio-engineered strains? In some follow-up independent testing, some of the other strains killed virtually all of the vaccinated animals. Any comments?

24. Life magazine reported in November 1995 that Gulf War vets in both US and England were having babies with severe unexplainable birth defects at a rate exceeding 4 times the national average. No studies have been done on the reproductive side effects for anthrax vaccine. Comments?

25. Given DOD's track record with regards to radioactive testing, Agent Orange, Swine Flu, nerve agent and chemical agent testing during the 50's and 60's, etc., why should anyone believe DOD's claims of product safety? Why should service member concerns get them labeled as a troublemaker? (Latest is the fielding of faulty chemical protective gear.)

PRESCRIPTION

26. Given that FDA approval is only applicable when following the prescribed shot regimen and its strict schedule, how can deviations from the schedule be

justified? (They were going to send Shawn with only 1 shot (at least 3 preferred).)

It is DoD policy to adhere to the FDA dosing schedule for the anthrax vaccine. Deviation from the dosing schedule are the exception rather than the rule and must be documented by bonafide reasons such as pregnancy, active infection, etc. According to USAMRIID, new studies show that the vaccine induces an antibody response in almost all of the recipients after 2 doses. Even with 100% antibody response, your defense system can be overwhelmed given exposure to sufficient number of spores.

27. Please explain the administrative lapses that occurred during the Gulf War, which conveniently deleted shot and medical record information pertaining to anthrax and other vaccinations received.

28. Why is DOD allowed to redate vaccine that has expired?

DoD does not re-date vaccine that has expired. Once the vaccine is labeled with the expiration date that date does not change. Vaccine released to DoD is handled according to manufacturer's instructions and properly stored vials may be used after opening until the labeled expiration date.

SUPPLY

29. What happens to AVIP if Bioport is unable to gain FDA certification before current stockpiles run out?

The AVIP can continue with the program through CY00 on the remaining stockpiles. DoD is confident that BioPort, Corp. will gain FDA certification before current stockpiles run out.

30. The production plant MBPI was not examined by the FDA from 1970 until 1993. In 1996 FDA found significant quality control problems. In 1997, FDA issued a 'Notice of Intent to Revoke' due to continued problems and in 1998 finally halted production. Bioport took over and built a larger facility on site. This new facility was inspected in November 1999 and the FDA found more than 30 significant problems including quality control, sterility, potency, temperature monitoring and other issues. How can service members be assured that every dose isn't contaminated, doesn't contain too much protective antigen (testing indicated as much as 4000% variation between samples), hasn't previously expired, hasn't at some point exceeded its storage temperature, is given following the proper protocols (shaking the bottle before each dose, swabbing the bottle cap, asking questions before giving the shot, etc.), etc., given the fact that all Phase 1 doses were manufactured during the time of the quality control problems. Can you understand the apprehension service members have about the shot?

Service members can be confident about the safety, sterility, potency, and purity of every dose they receive. The Food and Drug Administration ensures manufacturers of vaccines conform to the Federal Register on Human and Veterinary Drugs: Good Manufacturing Practices and Proposed Exemptions for Certain OTC Products. The FDA ensures that drugs and vaccines meet the safety requirements of the act and have the identity and strength and meet the quality and purity characteristics that it is represented to have.

MISCELLANEOUS

31. As recent Hill testimony shows, the Tricare system is woefully inadequate to take care of the troops. Obviously they are not prepared to provide for treatment of folks with problems from the Anthrax vaccination that DOD is pushing regardless of the congressional recommendations.

32. It was disclosed recently that all of the military's chemical warfare suits are being recalled for defects, however this has been known for more than 5 years. Why the lapse in action and how long to secure new suits for all military personnel? Shouldn't this be the first line of defense?

CONGRESSIONAL or SPECIAL CORRESPONDENCE

CMAT:

Date: MAR 10 2000

Office of Special Assistant for Gulf War Illnesses
Internal Routing/Tasking Sheet

Coord/ Routing	Position/Organization		Action	Comments
	Special Assistant	(SA)		Done 4/5
5	Deputy Special Assistant	(DSA)	JHV 3-10	answer to Sec copy for Kelly Reporter
	Executive Assistant to SA	(EA)		
	Executive Assistant to DSA	(EADSA)		
3	☒ Director, Investigation & Analysis ____ (IAD) ☐ DepDir ____ ☒ MED ____ ☐ VDM ____ ☐ C/B ____ ☐ ENV ____ ☐ PAG ____		MTA approved	Typo - ? Do not use. Should be Conjunctive suppress
	Dir Lessons Learned Implementation	(LLI)		
	Dir Public Affairs & Outreach	(PA)		
	Dir Legislative Outreach	(LA)		
2	Dir Medical Outreach & Issues	(MOI)		
	Legal Advisor	(LGL)		
4	PM, Gulf War Illnesses Support	(PM)		
1	Editorial Review ☒ AMB ____ ☒ Editors ____	(ER)		
	CMAT	(CMAT)		
6	Action Management Call 845-8369 ☒ COMEBACK COPY TO: Leda [redacted] and MOI ☒ GET CMAT NUMBER WHEN SIGNED & ☐ READING FILE ☐ THANK YOU FILE ☒ CHRON FILE ☐ ADD TO GulfNEWS			

SUSPENSE:

Prepare reply for signature of:

☐ SA/GWI ☐ SD ☐ DSD ☐ DepSA/GWI

INPUT TO ASIP CONGRESSIONAL ON GW USE OF ANTHRAX & BOTULINUM VACCINES

☐ Congress	☐ Oversight	☐ FOIA	☐ OSD	☐ WBM	☐ VSO/MSO	☐ Outgoing
☐ Ltr to SA	☐ IR	☐ E-Mail	☐ OGA	☐ Other		☐ Veteran

KEYWORDS:

03/07/00 Issuance

CMAT Control #
1999281-0000001

(52)

(b)(6) @osdgc.osd.mil on 10/07/99 04:08:39 PM

To: (b)(6)

cc:

Subject: NonD/DTest 1710, Safety and Efficacy of the Anthrax Vaccine – HH S Proposed Testimony

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DEPARTMENT OF DEFENSE
OFFICE OF THE GENERAL COUNSEL
LEGISLATIVE REFERENCE SERVICE

DATE: October 7, 1999

MEMORANDUM FOR: ACTION AGENCY - ASD(HA)

STAFFING FOR: ARMY, NAVY, AIR FORCE, JCS, USD(P&R), SpecAss'tGWI

INFORMATION FOR: ASD(LA), ASD(PA), IG, DGC(P&HP), GC

SUBJECT: LRS DESIGNATOR NonD/DTest 1710, Safety and Efficacy of the Anthrax Vaccine -- HEALTH & HUMAN SERVICES Proposed Testimony

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SUSPENSE: 1300, FRIDAY, 8 OCTOBER 1999

OMB has requested the views of the Department of Defense on the enclosed subject matter.

ACTION AGENCY: Please advise upon receipt of name of action officer and phone number. Action agency must prepare a draft proclamation. Please respond by the suspense date or request an extension. OSD agency comments require DGC coordination.

STAFFING AND INFORMATION AGENCIES: Please review the enclosed request and respond appropriately. If staffing agencies do not respond by the suspense date or request an extension, we will assume you have no interest. Information agencies need not respond unless comments are necessary. OSD agency comments require DGC coordination. Please advise us in advance if comments will be provided.

A response sheet is enclosed for your convenience.

DO NOT CALL OMB. LRS will consolidate all responses and notify OMB of the

Department of Defense response.

LRM ID: RJP190
EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF MANAGEMENT AND BUDGET
Washington, D.C. 20503-0001

Thursday, October 7, 1999

LEGISLATIVE REFERRAL MEMORANDUM

TO: Legislative Liaison Officer - See Distribution below

FROM: (b)(6) (for) Assistant Director for Legislative Reference
OMB CONTACT: (b)(6)

SUBJECT: HEALTH & HUMAN SERVICES Oversight Testimony on the safety
and efficacy of the anthrax vaccine

DEADLINE: 1:00 P.M. Friday, October 8, 1999
In accordance with OMB Circular A-19, OMB requests the views of your agency on the above subject before advising on its relationship to the program of the President. Please advise us if this item will affect direct spending or receipts for purposes of the "Pay-As-You-Go" provisions of Title XIII of the Omnibus Budget Reconciliation Act of 1990.

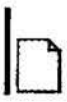
COMMENTS: Hearing is before the House Committee on Government Reform on Tuesday, October 12th. Dr. Kathryn Zoon is the HHS witness.

DISTRIBUTION LIST

AGENCIES:
29-DEFENSE - (b)(6)
83-National Security Council - (b)(6)
95-Office of Science and Technology Policy - (b)(6)

<<hearing>> <<hearing.doc>> <<hearing.wpd>> <<NDT1710.doc>>


- hearing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Draft 10/6/99

Introduction

Mr. Chairman and Members of the Committee, I am Dr. Kathryn Zoon, Director, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration (FDA or Agency). I appreciate this opportunity to discuss with you vaccine licensing generally, and specifically, the safety and efficacy of the anthrax vaccine, currently manufactured by BioPort Corporation (previously known as Michigan Biologics Product Institute (MBPI) or prior to that, Michigan Department of Public Health (MDPH)). Let me begin with a brief overview of the process for a vaccine to be licensed.

Background

CBER is responsible for evaluating the safety, purity, efficacy and potency of the products we regulate. These products include biological products such as vaccines, products derived from human blood, and many products produced by recent advances in biotechnology. The scope of regulatory responsibility extends to both licensed or approved products and unlicensed products under investigation.

From a regulatory perspective, there are four stages in vaccine development:
1) the pre-Investigational New Drug (IND) stage (before the product is used in people);
2) the IND stage (where human use occurs under limited study conditions);
3) the license application stage for vaccines (where FDA reviews the results of the clinical studies and the manufacturing process); and,
4) the post-licensure stage (following approval of the product for marketing).

Before a new vaccine can be studied in people, a sponsor must submit an IND application to FDA[1]. In the application, the sponsor:
1) describes the composition, source, and method of manufacture of the product and the methods used in testing its safety, purity, and potency;
2) provides a summary of all laboratory and pre-clinical animal testing performed; and,
3) provides a description of the proposed clinical study and the names and qualifications of each clinical investigator.

[1] Sponsors may be individual physicians, a university, a hospital, or a commercial firm, as well as Government agencies, such as the Department of Defense or one of the institutes of the National Institutes of Health.

Once the sponsor submits the IND, FDA has 30 days to review the application to determine whether or not the study may proceed. FDA may prohibit a sponsor from conducting a study for a number of reasons, including when the study volunteers will be exposed to unwarranted risks, by putting the IND on "clinical hold".

The IND process generally is described as having three phases prior to product approval; however, the distinctions between these phases are not absolute. Phase 1 trials are focused on basic safety and, for vaccines, Phase 1 trials also usually evaluate the immune response elicited by the vaccine. These trials are usually small – generally between 20 and 100 subjects – and they frequently are done in healthy "normal volunteers" and may last just several months. Phase 2 trials often include several hundred subjects, are often randomized, and last anywhere from several months to several years. These trials usually include individuals who are at high risk for the infectious disease of interest. Unless severe reactions or a lack of effectiveness surface during the first two phases, the sponsor may decide to perform one or more Phase 3 studies that can include up to several thousands of people. These Phase 3 trials are intended to provide the definitive measure of effectiveness, as well as continue the evaluation of the product's safety. The size of the efficacy trial will be affected by the expected incidence of disease that the vaccine is intended to prevent. If at the end of Phase 3 trials the manufacturer believes there are adequate data to show the vaccine is safe and effective for its intended use, the manufacturer submits a license application to the Agency.

Licensing a new vaccine is only one stage of FDA's oversight of vaccine safety. Following issuance of the license, there is continued postmarketing surveillance of the product by monitoring adverse events, e.g., the Vaccine Adverse Events Reporting system (VAERS), and of the manufacturer's production activities, including compliance with good manufacturing practices. Manufacturers generally submit samples of each licensed vaccine lot and the results of their own tests for potency, safety, and sterility to the Agency before release of each lot of the licensed product, because of the complex manufacturing processes for most biological products. In addition, licensed establishments are inspected regularly by FDA.

Let me now turn to anthrax.

Anthrax Disease

Anthrax is a highly infectious disease caused by spores of a bacterium known as *Bacillus anthracis*. These spores resist destruction and may be present in the soil for decades, occasionally infecting grazing animals that ingest the spores.

Goats, sheep and cattle are examples of animals that may become infected. Human infection may occur by three routes of exposure to anthrax spores: cutaneous, gastrointestinal, and pulmonary. Skin contact with live infected animals, or with the hide, hair or bones of an infected animal may lead to infection of a person's skin, known as cutaneous anthrax infection. This is the most common manifestation of anthrax in humans, accounting for more than 95 percent of cases. Untreated cutaneous anthrax infection is associated with a death rate estimated to be approximately 20 percent. Eating undercooked or raw, infected meat can cause gastrointestinal anthrax infection. Breathing in airborne spores may lead to pulmonary anthrax, also known as inhalation anthrax. Experience has shown that inhalation anthrax has a very high mortality rate, with estimates ranging from 80 percent to 90 percent or higher.

Inhalation anthrax infection has two phases. During the first phase, which occurs within one to five days after inhalation of the spores, the patient has influenza-like symptoms, such as a cough, malaise, fatigue and mild fever. Several days later these symptoms may subside, but are rapidly followed by the second, more severe stage of disease. During the second phase, the patient experiences sudden onset of severe respiratory distress, and sometimes chest pain accompanied by fever. Chest x-rays may show fluid in the lung. Within a day, septic shock and death will likely occur.

Treatment of cutaneous anthrax infection involves administration of antibiotics. In the case of pulmonary anthrax infection, therapy has been of limited benefit, except when given immediately after exposure. Prior to use of the anthrax vaccine, cases of human anthrax infection in the United States were much more prevalent. The only known effective prevention against anthrax is the anthrax vaccine. According to data from the Centers for Disease Control and Prevention, (CDC) there were approximately 130 reported cases of anthrax infection per year at the start of this century. In the past decade, there have been no confirmed reports of human anthrax in the United States. It is difficult to assess exactly how much of this dramatic reduction is due to the vaccine, but immunization with the anthrax vaccine of people at risk, along with vaccination of animals against anthrax, have likely contributed to this favorable decline. Elsewhere in the world, human anthrax cases continue to be reported, especially in countries with predominately agricultural economies.

History of the Anthrax Vaccine

Philip S. Brachman et al. conducted clinical trials on the anthrax vaccine during

the 1950s [2]. This controlled field study involved workers in four mills in the northeastern United States that processed imported animal hides. This selected population was at risk because the mill workers routinely handled anthrax-infected animal materials. Prior to vaccination, the yearly average number of human anthrax infection was 1.2 cases per 100 employees in these mills.

For this trial, employees who had not previously contracted anthrax were selected and divided into two groups. The groups were balanced with regard to their age, length of employment, department at the mill, and the particular job they performed. The trial was a single-blinded study, in which the participants were not told whether they received the vaccine or placebo. Individuals who did not participate in the controlled study [because they were ineligible (i.e., had a history of prior anthrax) or chose not to receive the injections] were also monitored for anthrax. These individuals who did not receive vaccine or placebo were referred to as the observational group.

During the trial, 26 cases of anthrax infection were reported at the mills - five inhalation and 21 cutaneous. Of the five inhalation cases, two individuals had received the placebo, while three individuals were in the observational group. Four of the five people who developed inhalation anthrax died. No cases of inhalation anthrax occurred in anthrax vaccine recipients. Of the 21 cutaneous cases, 15 individuals had received the placebo, three individuals were in the observational group, two individuals were partially immunized and one individual was fully immunized. Based upon a comparison between the populations completely vaccinated versus the populations receiving placebo, the authors calculated a vaccine efficacy level of 92.5 percent.

On April 14, 1966, CDC submitted an IND for the anthrax vaccine to the Division of Biologics Standards, which was then part of the National Institutes of Health (NIH), later transferred to FDA. The method of preparing this vaccine was similar, but not identical, to the vaccine used in the Brachman et al. study. The vaccines in both studies were based on the immunity induced by the protective antigen (PA). Persons receiving the vaccine made by the two different methods demonstrated similar peak immune responses (antibody concentration) following the initial three doses. Textile employees and laboratory workers were immunized under this IND. A number of lots of investigational vaccine used by CDC under this IND were manufactured by the MDPH.

[2] Brachman, P.S., H. Gold, S.A. Plotkin, F.R. Fekety, M. Werrin & N.R. Ingraham. 1962. Field evaluation of a human anthrax vaccine. Am. J. Public Health 52:632-645.

The data submitted to the Division of Biologic Standards described CDC's experience with approximately 16,000 doses of anthrax. This vaccine was administered to approximately 7,000 study participants. Reported local reactions at the immunization site ranged between 3 percent to 36 percent of the initial series of doses, and 3 percent to 33 percent of the booster doses, depending on the lot. Reported mild reactions were 3 percent to 20 percent of all doses. Reported moderate local reactions were 1 percent to 3 percent of doses. Severe reactions were reported for less than 1 percent of doses. Systemic reactions were reported in four cases during the five-year reporting period. These reactions included fever, chills, nausea and general body aches, and were reported to have been transient.

The Division of Biologics Standards determined that the data submitted by CDC supported licensure of the vaccine. On November 10, 1970, the Division of Biologics Standards issued a product license to MDPH to manufacture anthrax vaccine.
Approved labeling for the anthrax vaccine states that immunization with this product is recommended for individuals who may come in contact with animal products that may be contaminated with *Bacillus anthracis* spores, and for individuals engaged in diagnostic or investigational activities which may bring them in contact with *Bacillus anthracis* spores. It is also recommended for persons at high risk, such as veterinarians and others handling potentially infected animals.

The approved labeling also states that anthrax vaccine is to be administered subcutaneously (injected under the skin). After the initial dose of 0.5ml, further doses of 0.5ml are administered at two weeks, four weeks, six months, 12 month and 18 months, thereafter, with yearly boosters.

The Panel Review

The Public Health Service Act, under which biologicals such as vaccines were licensed, required evidence of safety, purity and potency. After the Division of Biologic Standards was transferred from NIH to FDA, expert panels were assigned to review information on biological products, including vaccines that had been on the market prior to the transfer. The review was initiated in order to verify whether existing data supported the safety and efficacy of marketed biological products.

Biological products were divided into one of six categories. FDA assigned responsibility for initial review and recommendation for all products in these six categories to separate independent advisory panels of outside scientific experts,

collectively known as the Advisory Review Panel. The Advisory Review Panel also was charged with advising FDA, in the form of a report, on classification of these products into one of the following categories: Category I - safe, effective and not misbranded; Category II - unsafe, ineffective or misbranded; Category III - insufficient information, further testing required.

Based upon their review of available data, the Advisory Review Panel recommended that the anthrax vaccine manufactured by MDPH be classified as a Category I product and that appropriate licenses be continued based upon substantial evidence of safety and effectiveness of this product. The safety data from the CDC trials and the efficacy data from the Brachman et al. trials were the basis for these findings. These findings were published in the *Federal Register* on December 13, 1985.

Today, it would be difficult to repeat the efficacy studies. This is because there are no evident populations in the United States where prophylactic vaccine protection against natural exposure to anthrax could be evaluated in a clinical field trial, such as was done in the Brachman et al. study. Specifically, the incidence of naturally occurring anthrax in humans is low and sporadic in occurrence, making identification of a trial target population difficult. Likewise, it would be unethical to perform challenge/protection studies in humans. In addition, human immunogenicity and safety data would be required. The safety database obtained by CDC under the IND would be considered a reasonable pre-licensure database for evaluating a safety study today.

Post-Marketing Experience

Since licensure in November 1970, livestock workers, veterinarians, lab workers and researchers who are at risk for infection have used the anthrax vaccine. The manufacturer provided FDA the following information regarding distribution. From 1974 to 1989, approximately 68,000 doses were distributed. In 1990, approximately 268,000 doses were distributed. Between 1991 and the present, we understand that approximately 1,200,000 doses were distributed.

It is not possible to give a precise number of persons who received the vaccine prior to use in Operation Desert Shield and Operation Desert Storm. We estimate that approximately 7,000 subjects received approximately 16,000 doses of the vaccine during clinical trials conducted by the CDC. In addition, between 1974 and 1989, our files show approximately 68,000 doses were distributed. This is sufficient to vaccinate about 11,000 people with the full six-dose regimen of the currently approved anthrax vaccine. It is possible that some doses distributed were not used, or that some individuals did not receive the full course

of the vaccine. Thus, it is not possible to accurately report the precise number of people vaccinated between 1974 and 1989.

According to the CDC, from 1962 to 1974, 27 cases of anthrax occurred in the "at-risk" populations in the United States. Of those, 24 cases occurred in unvaccinated individuals, one case after the person had been partially immunized with one dose of the vaccine and two cases after individuals had been partially immunized with two doses of the vaccine. No documented cases of anthrax were reported for individuals who had received the recommended six doses of the vaccine.

Vaccine Adverse Event Reporting – Anthrax

With regard to safety data, FDA and CDC jointly operate VAERS. FDA uses this system to track adverse events possibly associated with licensed vaccines. Reporting of adverse events associated with the use of anthrax vaccine is voluntary for individual healthcare providers. The vaccine manufacturer, however, must report to FDA all reports of adverse events of which they are aware.

The report of an adverse event to VAERS is not documentation that a vaccine caused the event, only that the event occurred soon after the vaccine was administered. Doctors and other healthcare providers are encouraged to report serious or unexpected adverse events following vaccination, whether or not they believe that the vaccination was the cause of the adverse event. Since it is difficult to distinguish a coincidental event from one truly caused by a vaccine, the VAERS database contains events of both types.

It should be emphasized that adverse event reports can be made by a health care professional, a patient or anybody else. If a patient's physician does not file a VAERS report, the patient can do so. FDA encourages individuals to report to VAERS any clinically significant adverse event occurring after the administration of any vaccine licensed in the United States. Reports to VAERS may be made in writing or by calling a toll-free number, 1-800-822-7967. Reporting instructions are available on the Internet at www.fda.gov/cber/vaers.html.

[Will update these data to Oct. 1 when available] Since the beginning of VAERS operations in 1990, through July 1, 1999, 215 reports of adverse events associated with use of the anthrax vaccine have been reported to VAERS. Of those, FDA considers 22 serious events. These reports are for diverse conditions, with no clear patterns emerging at this time. Some of these events

are described below. The remaining 193 reports describe a variety of symptoms, including injection site edema (swelling with fluid in tissue), injection site hypersensitivity, rash, headache and fever.

The 22 serious events were reported to have occurred or been diagnosed at times ranging from 45 minutes to 4 ˝ months after vaccination. Some individuals experienced adverse events following the first dose; others received up to 5 doses before event onset. Most of these individuals reporting adverse events during the current anthrax vaccination program have recovered. Five patients were hospitalized for severe injection site reactions. One individual experienced a more widespread allergic reaction. One individual was hospitalized with a confirmed case of aseptic meningitis nine days after vaccination. Two individuals experienced Guillain-Barré syndrome. Three weeks after receiving the vaccine, another individual was diagnosed with bipolar disorder and has not recovered. One individual experienced onset of multi-focal inflammatory demyelinating disease and has since recovered. Another individual experienced onset of lupus and has not recovered.

None of these events, except for the injection site reactions, can be attributed to the vaccine with a high level of confidence, nor can contribution of the vaccine to the event reported be entirely ruled out. It should be emphasized once again that it is not always possible to attribute a cause and effect relationship between a reported event and a vaccination. With the exception of injection site reactions, all of the adverse events noted above do occur in the absence of immunization.

While the data gathered from the VAERS system can serve as a useful tool in identifying potential problems, the reports on anthrax vaccine received thus far do not raise any specific concerns about the safety of the vaccine. As more people receive the vaccine, the numbers of adverse events reported will increase. FDA continues to view the anthrax vaccine as safe and effective for individuals at risk of exposure to anthrax.

Lot Release

As mentioned above, because of the complex manufacturing processes for most biological products, each product lot undergoes thorough testing for purity, potency, identity, and sterility. The anthrax vaccine is subject to lot release. FDA reviews the lot release protocols showing results of applicable tests and lot samples are submitted for possible testing by FDA. The manufacturer may not distribute a lot of the product until FDA's Center for Biologics Evaluation and Research releases it. The lot release program is part of our multi-part strategy that helps assure product safety by providing a quality control check on product specifications.

Memorandum of Understanding (MOU) with the Department of Defense (DOD)

On May 21, 1987, FDA entered into the current MOU with DOD. This replaced the previous MOU signed in 1974. The 1987 agreement established procedures to be followed by DOD and FDA regarding the investigational use of drugs, biologics and medical devices. The MOU affirms that clinical testing of new drugs will be done in accordance with application regulations concerning INDs and IRBs.

The MOU addressed the possibility of a need for expedited review of an IND by FDA to meet DOD requirements concerning National defense considerations. Under the MOU, DOD is responsible for classifying medical research and development as it relates to information that may be made public under Freedom of Information Act regulations. It should be stressed that this agreement, however, does not allow DOD to perform research on humans without submitting an IND and it requires DOD to comply with all FDA regulations.

FDA's Consultation with DOD
Regarding the Anthrax Vaccine Immunization Program

FDA has not had an official role in the development or operation of the Department of Defense's Anthrax Vaccine Immunization Program, including the AVIP tracking system or the program's adverse event reporting system. In March 1997, DOD briefed FDA about their draft plan for the possible use of the anthrax vaccine to inoculate U.S. military personnel according to the FDA approved labeling for six doses administered on a specified schedule over eighteen months. Subsequently, FDA learned that the DOD plan had been adopted.

In July 1998, CDC requested that Health Resources Services Administration, National Vaccine Injury Compensation Program (VICP) organize and coordinate a program to evaluate VAERS reports for the anthrax vaccine. In response to the request by DOD, a group of non-government medical experts was convened by the VICP in the fall of 1998 as the Anthrax Vaccine Expert Committee (AVEC). AVEC, coordinated by VICP, has met eight times since 1998. These experts have been reviewing all VAERS reports for the anthrax vaccine. Representatives of VICP, FDA, CDC and DOD have attended meetings, and FDA has provided information to assist the committee in its deliberations.

AVEC is unique in that it provides an independent civilian expert assessment of adverse events reported for the anthrax vaccine.

Upon learning that some DOD personnel may be receiving their anthrax vaccine doses significantly later than the FDA approved schedule, both Dr. Jane E. Henney, Commissioner of Food and Drugs, and I, sent letters to DOD. In the letters we asked DOD to expeditiously investigate this matter as we are unaware of any data demonstrating that any deviation from the approved intervals of doses found in the approved labeling will provide protection from anthrax infection. We have not yet received a response from DOD on this matter. Although we are aware of some ongoing studies conducted by DOD on the Anthrax Vaccine Adsorbed, FDA has not received data for these studies nor do we have the authority to require DOD to submit such data.

Conclusion

Mr. Chairman, we believe the anthrax vaccine is a safe and effective vaccine for the prevention of anthrax disease – an often-fatal disease – when used according to the FDA approved label. Our confidence in this vaccine, like all vaccines, is based upon four components: first - the review of manufacturing and clinical trials and subsequent clinical laboratory experience with the vaccine; second – ongoing inspections of the manufacturing facility; third – our lot release requirements; and fourth – our ongoing collection and analysis of adverse event reports. So far, the data gathered from VAERS reports on anthrax vaccine do not signal concerns about the safety of the vaccine. The Agency will continue to closely monitor and investigate reports of serious adverse events received on all vaccines, including anthrax, to assure that only safe products are on the market.

I appreciate the Committee's interest in this very important topic and would be happy to answer any questions.

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Rd: (b)(6) 10/2/99
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1999238-0000009

(b)(6) @osdgc.osd.mil on 08/26/99 12:00:18 PM

To: (b)(6)

cc:

Subject: HR 2543, Make the Department of Defense Anthrax Vaccination Immun ization Program Voluntary for All Members of the Armed Forces

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DEPARTMENT OF DEFENSE
OFFICE OF THE GENERAL COUNSEL
LEGISLATIVE REFERENCE SERVICE

DATE: August 26, 1999

MEMORANDUM FOR: ACTION AGENCY - ASD(HA)

STAFFING FOR: ARMY, NAVY, AIR FORCE, JCS, USD(P&R), SpecAss'tGWI

INFORMATION FOR: ASD(LA), ASD(PA), IG, DGC(P&HP), GC

SUBJECT: LRS DESIGNATOR H.R. 2543, To Make the Department of Defense Anthrax Vaccination Immunization Program Voluntary for All Members of the Armed Forces

---

SUSPENSE: 1700, TUESDAY, 7 SEPTEMBER 1999

The views of the Department of Defense have been requested on the enclosed bill by the House Armed Services Committee.

ACTION AGENCY: Please advise upon receipt of name of action officer and phone number. Action agency must prepare a views report following the enclosed sample format. Please respond by the suspense date or request an extension. OSD agency reports require DGC coordination.

STAFFING AND INFORMATION AGENCIES: Please review the enclosed bill and respond appropriately. If staffing agencies do not respond by the suspense date or request an extension, we will assume you have no interest. Information agencies need

not respond unless
comments are necessary. If comments are provided, they will be forwarded to the action
agency. OSD agency comments require DGC coordination. Please advise us in advance if
comments will be provided.

A response sheet is enclosed for your convenience.

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- HR2543ih.txt

DEPARTMENT OF DEFENSE
OFFICE OF THE GENERAL COUNSEL
LEGISLATIVE REFERENCE SERVICE

DATE: August 26, 1999

MEMORANDUM FOR: **ACTION AGENCY - ASD(HA)**

STAFFING FOR: ARMY, NAVY, AIR FORCE, JCS, USD(P&R), SpecAss'tGWI

INFORMATION FOR: ASD(LA), ASD(PA), IG, DGC(P&HP), GC

SUBJECT: **LRS DESIGNATOR H.R. 2543, To Make the Department of Defense Anthrax Vaccination Immunization Program Voluntary for All Members of the Armed Forces**

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A response sheet is enclosed for your convenience.

The views (reports) on Bills letter should follow the following format:

The Honorable _____
Chairman, _____
House of Representatives (United States Senate)
Washington, DC 20515 (House)
20510 (Senate)

Dear Mr. Chairman:

This is in response to your request for the views of the Department of Defense on H.R. _____ (S. _____), 106th Congress, a bill "(give entire title of bill _____)."

The Department of Defense has no objection to (supports, objects to, opposes, etc.) The legislation. (With one or two sentences summarizing rationale.)

H.R. _____ (S. _____) would (explain very generally what the purpose of the bill is and what it would do.

This legislation would (explain the effects of the bill on the Department, or state that it has no effect should that be the case. This is the core of your views from the perspective of the committee. They want our opinion as to how the legislation will influence our operations).

Detailed rationale for Department of Defense position. (If you object to or oppose the bill, specific rationale must be set forth for the position. You may want to emphasize some specific consequences referring to the paragraph above where you set forth what the legislation would do).

(If you object to or oppose the bill, specific rationale must be set forth for the position. You may want to emphasize some specific consequences referring to the paragraph above where you set forth what the legislation would do).

(If there is a substantial cost to the Government or Department, that should be noted--some committees specifically ask for this--see their request attached.)

The Office of Management budget advises that, from the standpoint of the Administration's program, there is no objection to the presentation of this report for the consideration of the committee. (Boilerplate for each report.)

Sincerely,

RESPONSE TO DOD LEGISLATIVE REFERENCE SERVICE

You may respond to this request in one of the following ways:

1. Call (b)(6) with your response.

2. Fax this response sheet to (b)(6) with or without attachments.

3. Send or deliver your written response to OSD/DLSA-LRS, Room 3D282, Pentagon, Washington, D.C. 20301-1600, with copy of response on disk in WordPerfect format.

4. E-mail your response to (b)(6) @OSDGC.OSD.MIL with action officer name and individual who cleared response.

If you are using/returning this response sheet

Complete the following information:

Date:
LRS Designator:
Your Name:
Your Agency:
Your Telephone Number:

Mark your response on the appropriate line following:

Concur
No Objection
No Comment
Defer To:
Comments/Edits Attached
Comments Coming - Please Wait
Other

HR 2543 IH

106th CONGRESS

1st Session

H. R. 2543

To make the Department of Defense anthrax vaccination immunization program voluntary for all members of the Armed Forces.

IN THE HOUSE OF REPRESENTATIVES

July 16, 1999

Mr. JONES of North Carolina introduced the following bill; which was referred to the Committee on Armed Services

---

A BILL

To make the Department of Defense anthrax vaccination immunization program voluntary for all members of the Armed Forces.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the `American Military Health Protection Act'.

SEC. 2. FINDINGS.

Congress finds the following:

(1) All branches of the Armed Forces are faced with severe challenges in recruiting and retaining quality military personnel.

(2) Time and again military personnel are asked to place their lives on the line and to ultimately sacrifice themselves and their families in defense of the United States.

(3) The Department of Defense has initiated an anthrax vaccination program, which a rapidly growing number of military personnel believe may jeopardize their long-term health and safety as well as that of their families.

(4) The lack of a single, conclusive independent study regarding

the long-term health effects of the anthrax vaccine on humans has created additional concerns among military personnel.

(5) Despite assurances by the Secretary of Defense of minimal adverse reactions to the anthrax vaccine, the standards which the Secretary uses to determine adverse reactions are insufficient to support such claims.

(6) As a result of the lack of conclusive data on the long-term effects of the anthrax vaccine, many military personnel are being forced to make decisions between the safety and security of their families and their dedication and commitment to serving the United States.

SEC. 3. REQUIREMENT TO MAKE THE DEPARTMENT OF DEFENSE ANTHRAX VACCINATION IMMUNIZATION PROGRAM VOLUNTARY FOR ALL MEMBERS OF THE ARMED FORCES.

The Secretary of Defense shall require that the anthrax vaccination immunization program be voluntary for all members of the Armed Forces until--

(1) the Food and Drug Administration has approved a new anthrax vaccine for humans; or

(2) the Food and Drug Administration has approved a new, reduced course of shots for the anthrax vaccine for humans.

END

[redacted]

CONGRESSIONAL or SPECIAL CORRESPONDENCE

CMAT:

Date: 9/7/99

Office of Special Assistant for Gulf War Illnesses
Internal Routing/Tasking Sheet

Coord/ Routing	Position/Organization		Action	Info	Comments
	Special Assistant	(SA)			
2	Deputy Special Assistant	(DSA)	OK 9/7		For approval.
	Executive Assistant to SA	(EA)			
	Executive Assistant to DSA	(EADSA)			
	☐ Director, Investigation & Analysis _____ (IAD) ☐ DepDir _____ ☐ MED _____ ☐ VDM _____ ☐ C/B _____ ☐ ENV _____ ☐ PAG _____				
	Dir Lessons Learned Implementation	(LLI)			
	Dir Public Affairs & Outreach	(PA)			
	Dir Legislative Outreach	(LA)			
	Dir Medical Outreach & Issues	(MOI)	Originator		
	Legal Advisor	(LGL)			
1	PM, Gulf War Illnesses Support	(PM)			
	Editorial Review ☐ AMB _____ ☐ Editors _____	(ER)			
	CMAT	(CMAT)			
	Action Management Call 845-8369 ☐ COMEBACK COPY TO: _____ ☐ GET CMAT NUMBER WHEN SIGNED & SENT ☐ READING FILE ☐ THANK YOU FILE ☐ CHRON FILE ☐ ADD TO GulfNEWS				

SUSPENSE: OK BW

Prepare reply for signature of:

☐ SA/GWI ☐ SD ☐ DSD ☐ DepSA/GWI

Greg Simon, enclosed are 2 proposed bills regarding anthrax. HA has lead for DoD comment -- we are a staffing agency; as such our comments are optional. Col O'Donnell has proposed comments for each bill. With your concurrence I will pass comments to HA for their consideration. Bob.

☐ Congress ☐ Oversight ☐ FOIA ☐ OSD ☐ WBM ☐ VSO/MSO

☐ Ltr to SA ☐ IR ☐ E-Mail ☐ OGA ☐ Other ☐ Veteran

KEYWORDS:

07/23/99 Issuance

1. The following text provides OSAGWI comment on HR 2543, 106th Congress, for your office to consider in preparing the views of the Department of Defense. The comments are organized in the sequence requested by Office of the General Counsel.

2. a. The Department of Defense opposes the legislation. The bill grievously undermines not only the anthrax vaccination program itself, but also some fundamental principles of responsibility which guide the exercise of command in the U.S. armed forces. The bill is illogically conceived and based on a misapprehension of the relevant science.

b. This legislation (unless repealed by another act) would seriously interfere with the Department of Defense's ability to meet its responsibility to protect its service members from the biological weapon (anthrax) most likely to be employed against our armed forces during conflict and against U.S. citizens by acts of domestic terrorism.

c. Rationale:

(1) The bill impugns the safety of the anthrax vaccine while paradoxically affirming that it meets the usual standards of safety to such a degree that it is safe for both military personnel and civilians, including the family members of military personnel, to receive the vaccine on a voluntary basis.

(2) The repeated references to the lack of data on the long-term effects of the vaccine betray the naiveté of the drafters. Such data is lacking for virtually all vaccines except for the efficacy of the vaccines in providing long term protection against the intended disease. Information on long-term adverse effects is generally lacking for all vaccines.

(3) This bill might embolden terrorists and rogue states to advance their weaponization of anthrax, since the bill will result in very low levels of protection of military personnel with anthrax vaccine.

(4) The bill imposes a sham condition, namely the approval by the FDA of a new anthrax vaccine for humans. It seems highly improbable that any such new vaccine will be approved in the U.S., given the ethical barriers to demonstrating human efficacy. The inclusion of this condition in the bill suggests either scientific ignorance or unfortunate cynicism on the part of the drafters.

(5) The legislative precedent being attempted by this bill ties the hands of the military in trying to protect all service members with any available means in anticipation of the risks of military service.

(6) The bill demeans the integrity of the members of the Department of Defense by suggesting that the anthrax program was the result of ignorance, carelessness, or maliciousness.

3. POC for this action is COL O'Donnell, (b)(6)

(54)

CMAT Control #
20020422-0000039
20020422-0000039

MCHL-YOUR OFFICE SYMBOL **(40-38a)** *DATE:* 1 November 2001

MEMORANDUM FOR CHIEF, DEPARTMENT OF CLINICAL INVESTIGATION, WALTER REED ARMY MEDICAL CENTER

SUBJECT: Request for Review of Research Activity Involving Human Subjects
Request for Exemption from IRB Review

Table 1 : Please answer the questions in this table to help us decide if your proposed research activity will qualify for exempt review procedures. A 'yes" answer does not automatically disqualify a project from exempt review (with the exceptions of questions E, F, I, and M). **However, "yes" answers will require explanation in the description of the study section to ensure the study is eligible for exempt review.** Use instruction file, ExemptReview-Ins.doc, to fill out questions in this application.

	Yes	No
A. Will this project involve collaborators outside Walter Reed Army Medical Center?		x
B. Does the research involve contacting subjects in any manner?		x
C. Does the project require the use of direct patient identifiers (like names or social security numbers)?		x
D. Does the project require the use of indirect patient identifiers (such as a coding system that uses a unique subject identification number and master list of names)?	x	
E. Does the project involve prisoners, fetuses, or pregnant women?	Not Exempt	x
F. Does the project involve activities which expose the subject to discomfort or harassment beyond levels encountered in daily life?	Not Exempt	x
G. Does the research involve the collection of sensitive information (such as illegal conduct, sexual behavior, drug or alcohol use) from research subjects?		x
H. Does the research involve the prospective collection of data or specimens?		x
I. Does the research involve the use of investigational drugs or devices (IND)?	Not Exempt	x
J. Are all of the samples/data already existing?	x	
K. Does the project involve genetic testing?		x
L. Will data or samples be used by investigators outside WRAMC?	x	
M. Does the research require DCI funding support other than travel?	Not Exempt	x

1. PROTOCOL TITLE:

Vaccine Temporally Associated Adverse Events: Review of Clinical Cases Referred To A Tertiary Medical Center

2. PRINCIPAL INVESTIGATOR:

LTC Bryan L. Martin, MC
Asst. Chief, Co-Program Director Allergy-Immunology Fellowship
Allergy-Immunology Department
Phone (b)(6)
FAX:

Associate Investigators:
COL Renata J.M. Engler, MC
Tara E. King
Mary C. Minor
Jeannette F. Williams
John E. Grabenstein
Robert Labutta
Kristen Bamer

3. **I am requesting that the research project described herein be considered exempt fromIRB review based on the following AR 40-38 exemption category:**

_____ **B-6 Existing Records and Specimens**

4. **Provide a brief description of the project:**
Joint Commission for Accreditation of Hospitals (JCAHO) requirements and continuous quality improvement programs for immunization health care delivery include monitoring the rates of adverse events temporally associated with vaccines. Improved Vaccine Adverse Events Reporting System (VAERS) submissions with prescription vaccines have become an even greater requirement. Concerns have been raised that service members who have received anthrax vaccine are experiencing temporally associated persistent adverse events without adequate visibility to the VAERS system. Questions have been raised at congressional hearings that the Department of Defense has not adequately reported or evaluated systemic illness in this setting. National criticisms of the Vaccine Adverse Events Reporting System (VAERS) have been linked with recommendations for quality improvement in VAERS reports to include follow-up VAERS on individuals with prolonged illness and/or disability. Specific case definitions for adverse events temporally related to any vaccination have been problematic. There is currently a Center for Disease Control and Prevention (CDC) funded international collaborative effort called the Brighton Collaboration, which is designed to develop international consensus on definitions for

common clinical symptoms. Although the focus of this Collaboration is on pediatric vaccine related problems, there is a call to develop a similar effort for adult immunizations. In this context, a retrospective records review is being conducted of patients referred to the Walter Reed Allergy-Immunology Department between May of 1998 and September of 2001 for vaccine related adverse events or requests for medical exemptions.

It is the goal of this project to document the spectrum of medical problems that have presented as adverse events temporally associated with anthrax vaccination as well as other standard immunizations. By detailing the frequency and timing of symptom patterns within the evaluated population, case definitions for improved reporting can be developed.

5. **List the research objectives of the project:** To characterize the clinical features of vaccine related adverse events referred to a center of excellence in vaccine safety assessment

6. **Describe the characteristics of the subject population such as gender, age ranges, ethnic background, and health status. Indicate any special classes of subjects that might be included in the subject population (e.g., prisoners, minors, mentally disabled):** The subjects involved service members andDoD beneficiaries referred to the Allergy-Immunology Department at Walter Reed Army Medical Center. Research clinical records and quality assurance documents are available within the clinic and the Walter Reed National Vaccine Healthcare Center. There are no prisoners, minors or mentally disabled subjects involved.

7. **Describe plans (sources and methods) for data collection or specimen acquisition to include the following issues:**

A. The retrospective data review for the period extending from1 August 1998 to 30 September 200 1.

B. Data regarding subjects will be entered in a spreadsheet with unique identifiers. Any indirect linkages will be destroyed after compilation of data is completed.

Cases with neurologic symptoms will be reviewed by Neurology staff participating in the project for input on which neurologic clinical data elements should be included in the analysis. Descriptive statistics will be generated using SPSS.

8. **List all variables to be included in the study (Please include Data Collection Sheets):** The following variables are included in the analysis:

a. Demographic data including gender, age and ethnicity.

b. Large local reactions including mild (< 5 cm), moderate (5-12 cm), and severe (> 12 cm), pain, subcutaneous nodules, loss of range of motion, duration of reactions.
c. Systemic reactions to include malaise, fever, and chills and those listed in the DoD Clinical Guidelines at the AVIP web-site (see attached algorithm).
d. Detailed neurologic manifestations to include both focal and generalized and any associated diagnostic test results.
e. Time lost from work or hospitalization temporally associated with the vaccine.
f. Data regarding quality of life impact of the illness: e.g., change in physical training status.

9. **Describe any potential risks to subjects (physical, social, legal, or other):** None

10. **Are you requesting travel funding from DCI? YES (x) NO ( ) If "Yes", please list the number of protocols that you have received funding for this fiscal year:** None

11. **Is there be any Federal funding approved for this research project? Yes ( ) No (x) (If yes, provide detailed information or submit a budget page about the transfer of funds.) Funding from non-Federal sources may not be considered under the Exempt mechanism.**

12. **Provide the proposed starting date: 1 November 2001**
And completion date of the research activity: 1 November 2002

13. **Have you completed the WRAMC Research Course? YES(x) NO( ) When?** September 1999.

PRINCIPAL INVESTIGATOR
LTC (p) Bryan L.Martin, MC
Assistant Chief
Allergy/Immunology Department

DEPARTMENT CHIEF
COL Renata J.M. Engler, MC
Chief
Allergy/Immunology Department

ANTHRAX VACCINE TEMPORALLY ASSOCIATED SYSTEMIC ADVERSE EVENTS REFERRED TO A TERTIARY MEDICAL CENTER

Bryan L. Martin, Michael R. Nelson, Robert Labutta, Tara E. Ring, Jeannette F. Williams, Mary C. Minor, John E. Grabenstein, Renata J. M. Engler, Walter Reed Army Medical Center

Background: There is increasing public interest in adverse events temporally associated with immunizations and the need for improved reporting of these events through the Vaccine Adverse Events Reporting System (VAERS). Walter Reed Army Medical Center Allergy-Immunology (AI) Department has initiated an immunization quality improvement program that includes follow-up VAERS reports for patients with anthrax vaccine related medical exemptions, particularly if symptoms are chronic and'impact on quality of life. **Method:** Clinical guidelines for categorizing and managing adverse events after vaccination have been developed within the DoD in order to educate providers and develop a standardized approach. These guidelines are available on the web (www.anthrax.osd.mil) and are used to categorize patients referred to the AI Department for evaluation of a vaccine related adverse event. This information was reviewed in order to prioritize patient re-evaluations for follow-up VAERS and validation of the original VAERS reporting. **Results:** Between May 1998 and July of 2001, 82 patients were evaluated for complaints of prolonged systemic clinical problems whose onset was associated or attributed to anthrax vaccine exposure by the patient, referring provider or family member. Twenty-two (27%) experienced moderate to severe large local reactions along with a variety of systemic symptoms. The spectrum of systemic symptoms in this group is heterogenous with the reasons for referral including (but not limited to) one or more of the following features: non-injection site skin rashes (15%); persistent headaches (12%); tinnitus (16%); other neurologic disease or symptoms (21%); prolonged fatigue with 50% functional loss for > 60 days (21%). Specific diagnoses are diverse with some patients manifesting prolonged disability. Conclusion: Concerns about serious adverse reactions to anthrax vaccine continue despite the fact that the majority of 520,000 vaccinated service members (757,540 person-years January 1998 to December 2000) have tolerated the vaccine without persistent systemic symptoms. Epidemiologic evidence shows no population-based increased risk of disease in those who received anthrax vaccine compared to those who did not(3,430,459 person-years, Army, Navy, Marines, Air Force, and Coast Guard). However, for rare individual cases, causality cannot be proven nor disproved and there continues to be a need to improve our understanding of these clinical scenarios.

From the desk of RJM Engler, MD

Anthrax Vaccination and Antibiotic Distribution Daily Report																	
Updated: 1/5/02 1:00 p.m.																	
		12/20 *	12/22	12/27	12/28	12/29	12/30	12/31	1/2	1/3	1/4	1/5 **	1/6	1/7	Total		
Education	CT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0		
	DC	126	0	209	337	267	99	26	65	84	224	68			1504		
	FL	0	62	0	0	0	0	0	0	0	0				62		
	NJ	0	0	0	293	50	59	35	78	76	39				630		
	NYC	0	0	0	0	2165	0	0	85	0	46				2296		
	Total	125	62	209	630	2482	158	62	228	159	309	68	0	0	4492		
Enrollment	CT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0		
	DC	48	0	168	191	108	701	201	311	75	471	15			771		
	FL	0	42	0	0	0	0	0	0	0	0				42		
	NJ	0	0	0	98	24	31	18	52	54	43				320		
	NYC	0	0	0	0	165	0	0	0	0	0				165		
	Total	48	42	168	289	295	101	38	83	129	90	15	0	0	1298		
Antibiotics	CT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0		
	DC	0	0	159	193	104	63	20	31	70	44	15			699		
	FL	0	38	0	0	0	0	0	0	0	0				38		
	NJ	0	0	0	92	23	25	16	45	45	37				283		
	NYC	0	0	0	0	156	0	0	0	0	0				156		
	Total	0	38	159	285	283	88	36	76	115	81	15	0	0	1176		
Vaccine	CT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0		
	DC	48	0	9	8	2	7	0	0	5	3	0			82		
	FL	0	4	0	0	0	0	0	0	0	0				4		
	NJ	0	0	0	6	1	6	2	7	9	6				37		
	NYC	0	0	0	0	7	0	0	0	0	0				7		
	Total	48	4	9	14	10	13	2	7	14	9	0	0	0	130		

* - Capitol Hill Clinic on 12/20

** - DC totals for 1/5/02 are preliminary totals reported at 1:00 p.m. 1/5/02. Final report for 1/5 DC will be available at noon 1/6.

CMAT Control #
2000202-0000004 55

PLEASE EXPEDITE RESPONSE BY, July 26, 2000

Response to Member of Congress request for further objective analysis of an article published in the February 2000 issue of Experimental and Molecular Pathology

If you have any questions, please call LtCol (b)(6) Please call (b)(6) (b)(6), when coordination is completed or fax back at (b)(6)

Signed 7/21 coordination sheet

DEPARTMENT OF DEFENSE
ARMED FORCES EPIDEMIOLOGICAL BOARD
5109 LEESBURG PIKE
FALLS CHURCH VA 22041-3258

AFEB (15-1a) 00-6 11 July 2000

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)
THE SURGEON GENERAL, DEPARTMENT OF THE ARMY
THE SURGEON GENERAL, DEPARTMENT OF THE NAVY
THE SURGEON GENERAL, DEPARTMENT OF THE AIR FORCE

SUBJECT: Armed Forces Epidemiology Board (AFEB) Recommendations Regarding Review of the Paper, "Antibodies to Squalene in Gulf War Syndrome by P. B. Asa, Y. Cao and R. F. Garry."

1. The AFEB was tasked by the Department of Defense (Health Affairs) to conduct an objective analysis of the above paper following a request by Congressman Jack Metcalf to Health Affairs.

2. A Special Subcommittee was formed to review the paper. Results of the review and the paper were distributed to the rest of the Board prior to the AFEB meeting. The Subcommittee's findings were presented to the whole Board at the AFEB Meeting held 28-29 February 2000 at Fort Sam Houston, Texas. After discussions and several additional reviews, the report was finalized.

3. The AFEB has thoroughly reviewed the paper by Dr. Asa and colleagues who describe a laboratory test they feel may identify individuals ill with "Gulf War Syndrome." The following is a summary of the findings:

a. **THE RESEARCH REPORTED IN THIS PAPER DOES NOT SUPPORT THIS CLAIM.**

b. **THE PAPER CONTAINS NUMEROUS SHORTCOMINGS, SEVERAL OF THEM SERIOUS, THAT COMBINE TO INVALIDATE THE AUTHORS' CONCLUSIONS.**

c. **IT REMAINS UNCLEAR IF THE ASSAY ACTUALLY MEASURES ANTIBODIES TO SQUALENE, AS THE AUTHORS ASSERT; THE ASSAY MAY MEASURE SOMETHING ELSE OR THEIR FINDINGS MAY BE A NON-SPECIFIC CHEMICAL REACTION.**

AFEB (15-1a) 00-6 11 July 2000

SUBJECT: Armed Forces Epidemiology Board (AFEB) Recommendations Regarding Review of the Paper, "Antibodies to Squalene in Gulf War Syndrome by P. B. Asa, Y. Cao and R. F. Garry."

4. The Board unanimously endorses and approves the above findings and the enclosed report. Details of their findings can be found in the enclosed report.

FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD:

F. MARC LAFORCE, M.D.
AFEB President

BENEDICT M. DINIEGA
Colonel, USA, MC
AFEB Executive Secretary

3 Encls
1. Report
2. Tasking Letter
3. CVs

Copies Furnished:
Board Members
DASG-ZH
OASD(HA)/HOP, Prog. Dir.,
Prev. Med. & Surveillance
AFMOS/SGOP
DASG-HS-PM
HQ, USMC, PMO, CAPT Kenneth W. Schor
Dep. Dir. Occup Hlth & Prev Med Div, BUMED-DN
CDR, WRAIR
CDR, USACHPPM, ATTN: MCHB-DC-C
CDR, USAMRMC
Navy Env. Health Center
Dir, Med Resources, Plans & Policy Div. (N931)
CDR Mark Tedesco, USPHS
COL Andrew S. Warde,
BvetMed Msc MRCVA
LCol Maureen Fensom, CFMS

REVIEW OF THE PAPER

ANTIBODIES TO SQUALENE IN GULF WAR SYNDROME
by PB Asa, YCao and RF Garry

published in
***Experimental and Molecular Pathology*, Volume 68, pp 55-64 (2000)**

A REPORT FROM
THE ARMED FORCES EPIDEMIOLOGICAL BOARD
JUNE 22, 2000

SUMMARY OF FINDINGS

The Armed Forces Epidemiological Board has thoroughly reviewed the paper by Dr. Asa and colleagues who describe a laboratory test they feel may identify persons ill with "Gulf War Syndrome." The AFEB has concluded unanimously that the research reported in this paper does not support this claim. The paper contains numerous shortcomings, several of them serious, that combine to invalidate the authors' conclusions. It remains unclear if the assay actually measures antibodies to squalene, as the authors assert; the assay may measure something else, or their findings may be a non-specific chemical reaction.

BACKGROUND

The Armed Forces Epidemiological Board (AFEB) was tasked by the Department of Defense (Health Affairs) to conduct an objective analysis of the above captioned paper by Asa *et al*. The tasking letter is enclosed.

A special subcommittee[1] of the AFEB was formed to initiate the task. The Special Subcommittee read the above captioned paper by Asa *et al*. The subcommittee fully discussed its impressions, questions and concerns, and developed a consensus document. The chair of the subcommittee then formally presented the subcommittee's findings to the entire AFEB[2] which had been supplied with the paper and the consensus document in advance of the meeting. After input from the entire AFEB, this final report is offered to the requester by the AFEB president.

FINDINGS

The AFEB reviewed the paper with great interest. However, the AFEB found the paper to contain a large number of scientific flaws, some of which are extremely grave. These flaws invalidate to an almost complete degree the conclusions regarding squalene and the implications that proceed from them. The major flaws include the following:

Controls: Despite assertions and disclaimers in the paper, there are no valid controls.

- For a valid positive control, one needs serum previously proven to contain antibodies to squalene; only this can validate that the assay can detect antibodies to squalene. What the authors use as and assert is a positive control are two sera from individuals reportedly vaccinated (either once or three times) with an NIH trial vaccine containing squalene. The authors provide no pre-vaccination data to demonstrate that the activity detected in their assay was not present before vaccination with a squalene adjuvant.
- Negative controls are essential to prove that the assay is not detecting something other than anti-squalene antibodies. Missing are controls which omit serum containing the presumed antibodies or which omit the avidin-conjugated horse radish peroxidase. Also missing is a negative specificity control to rule out non-specific binding of normal IgG molecules to squalene.

Blinding: It is unclear if the researchers were blind as to illness/wellness status of study participants.

- The paper asserts at several points that this is a blinded study, but it remains possible that the critical element of knowing the illness/wellness status or category may have been known, even if, as the paper states, "...The identities or exact number of samples from each category were not made available..."

---

[1] S Music, Chair; E Barrett-Connor, P Landrigan, Members; *curricula vitae* attached per written request of Congressman Metcalf to Defense Secretary Cohen, as "...objective analysis...including identification of those who are providing the analysis and their professional credentials."

[2] During the 30-31 May 2000 meeting of the AFEB at Ft. Detrick, MD.

- Thus, the authors' assertions, that they did not know which subjects had "Gulf War Syndrome" and which did not, are not convincing. If the authors knew which blood samples came from Gulf War veterans, this could have biased their interpretation of their test findings.

Specificity: Does the ASA Assay actually measure antibodies to squalene?

- In this type of blotting experiment, one normally demonstrates specificity of the reaction by blocking (or adsorbing) the antibody with the antigen (in solution). This is not demonstrated.
- Hence, it is not possible to know what the ASA assay detects. It is a Western-blot type assay, and is either positive (+) or negative (–). Since the paper describes it being used in only one dilution of patient serum (1:400), it seems the assay can determine only whether "something" was detectable or not, and this "something" is not presently definable.
- Antibodies to squalene, or to any other substance for that matter, should be detectable across a range of concentrations, so antibody assays are normally constructed to demonstrate this, the most common form today being an enzyme-linked immunoassay (ELISA). The actual level or concentration of antibody, ranging from undetectable to just detectable through high concentration, should have medical/biological correlations and implications, with some threshold point that correlates with the development of symptoms or disease.
- Nitrocellulose is a highly reactive substance that binds many materials. The paper does not show that the squalene deposited on the membrane is actually still there at the end of the assay. For example, one could imagine that squalene could "block" the nitrocellulose membrane long enough to protect the "dot" from the milk treatment and then be washed out, as polyoxyethylene sorbitan laurate is a detergent that could remove a lipid like squalene. This could leave a naked spot of nitrocellulose to react with some other protein.
- If this were a valid assay it should work with another substrate (other nylon membranes, like Immobilon).
- Given the relationship between squalene and cholesterol, do these sera react with cholesterol? The authors raise the question but don't answer it.
- Can one actually raise antibodies, deliberately, to squalene? It is a common component of cells and should be present in amounts that would swamp out any squalene-specific antibodies.

Dose response: None is apparent.

- In the figures of the Asa *et al* paper, there is no obvious dose response in relation to the amount of antigen (squalene) deposited on the nitrocellulose membrane.
- A dose-response should be seen with respect to antigen and antibody concentration; neither is shown.

CONCLUSIONS

In summary, the clear failure to provide positive controls and negative controls as well as unambiguous blinding, invalidates the authors' ability to argue for the meaningfulness of their test and any conclusions they might draw from these results. This is true even before one gets to the more technical issue of the specificity of the ASA assay.

Therefore, the AFEB has little confidence that the patent-pending ASA assay actually measures antibodies to squalene, though we cannot entirely eliminate this possibility.

Whatever the paper's flaws and since the AFEB cannot exclude the remote possibility that the authors have identified a laboratory means of distinguishing persons with possible Gulf War Syndrome (GWS) from all others, replicability becomes the major unresolved issue. The AFEB recognizes the difficulties inherent in defining a possible case of GWS since there is no standardized case definition. However, the AFEB feels that the symptom list in the Asa *et al* paper is a good potential starting point, and that, for example, cases might be selected from tertiary referral centers for GWS such as the one at Walter Reed, with controls from a civilian, non-exposed workforce. Therefore we recommend that a suitable test of replicability be done in cooperation with the authors and with attention to the following design elements:

- selection of participants - cases and control subjects - by an independent *ad hoc* body or committee, chaired by a tenured academic from a well-known medical research institution
- establishing clear *a priori* selection and exclusion criteria for cases and for controls
- serological testing done in a secure and absolutely blind manner with strict chain of custody rules and documentation in place
- a sufficient number of subjects to have statistical power to detect a true difference, if one exists, with 80% likelihood and with a 5% chance or less of finding a difference due to random chance alone.
- a study design with at least two arms – testing done as in the paper by the people who have licensed this patent-pending technique, versus testing done by one or more lipid laboratories using more standard antibody techniques such as enzyme-linked immunoassay to detect antilipid antigens

We wish to be clear that we are not discussing a study to validate whether the ASA assay can detect antibodies to squalene. Rather, we are trying to leap over this intermediate obstacle and get quickly and inexpensively to a more meaningful bottom line: does the ASA assay clearly, reliably and unequivocally distinguish people with GWS from all others, and, if so, with what specificity and sensitivity? Many caveats and qualifiers would have to be in place to assure meaningfulness, and the preceding bulleted list can (and probably should) be usefully expanded and further refined to help assure that any ensuing serological study be definitive.

The AFEB is extremely doubtful that the assay reported by Asa *et al* is a valid or accurate test for illness among Gulf War veterans. However in an effort to leave no stone unturned in evaluating veterans' complaints, the AFEB feels it may be worthwhile to repeat the study, using appropriate scientific methods as outlined above. This recommendation should definitely not be considered an endorsement of the paper by Asa *et al* that we have herewith reviewed.

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

09 MAR

MEMORANDUM FOR EXECUTIVE SECRETARY, ARMED FORCES EPIDEMIOLOGICAL BOARD

SUBJECT: Objective Analysis of Article "Antibodies to Squalene in Gulf War Syndrome"

I request that the Armed Forces Epidemiological Board (AFEB) convene a subcommittee and review and provide OASD(HA) with an objective analysis of the attached article, "Antibodies to Squalene in Gulf War Syndrome" published in the February 2000 issue of *Experimental and Molecular Pathology*. Congressman Jack Metcalf requested this objective analysis. Congressman Metcalf would also like the curriculum vitas of the reviewers.

OASD(HA) will provide Congressman Metcalf with this critique and the curriculum vitas of the reviewers when complete. Please provide this review NLT 15 May 2000. To assist in this review, I have attached an extensive review of the work on squalene as a cause of illnesses among Gulf War veterans by the interagency Research Working Group of the Persian Gulf Veterans Coordinating Board prior to publication of the article and previous correspondence with Congressman Metcalf's office on this topic.

My point of contact is (b)(6) LtCol, USAF, BSC, (b)(6), fax (b)(6), or email (b)(6)@ha.osd.mil.

John F. Mazzuchi

John F. Mazzuchi, Ph.D.
Deputy Assistant Secretary of Defense
Clinical and Program Policy

Attachments:
As Stated

CURRICULUM VITAE

I. PERSONAL DATA

A. Name: Stanley I. Music, M.D., DTPH (Lond.)

B. Home Address: (b)(6)

C. Home Telephone:

II. EDUCATION

Institution	Date	Major/Minor Courses	Degree
University of London; London School of Hygiene and Tropical Medicine	1975-1976	Tropical Public Health	Diploma
Centers for Disease Control and Prevention – Atlanta, GA	1972-1973	Preventive Medicine	Resident
University of Maryland School of Medicine; Baltimore, MD	1966-1970	Fellow in Infectious Disease; Assistant Resident in Internal Medicine; Junior Assistant Res in Internal Medicine; Intern in Internal Medicine	Fellow, Resident, Intern
University of Maryland School of Medicine; Baltimore, MD	1962-1966	Doctor of Medicine	MD
George Washington University Washington, DC	1962	Invertebrate zoology and entomology	BS
George Washington University Washington, DC	1961	Liberal arts	AA

III. MERCK/MRL EMPLOYMENT HISTORY

Title	From – To
Director, Report Evaluation and Safety Surveillance Worldwide Product Safety and Epidemiology Department Merck Research Laboratories, Blue Bell, PA	May 1999 to present

IV. NON-MERCK EMPLOYMENT HISTORY

Title	From - To
Medical Epidemiologist Division of Women's and Children's Health, Department of Health and Human Services; State of North Carolina; Raleigh, NC	June 1998 to May 1999
Chief, Occupational and Environmental Epidemiology Division of Epidemiology, Department of Health and Human Services; State of North Carolina; Raleigh, NC	November 1996 – May 1998
Senior Regional Advisor for the Caucasus and Embassy Physician; United States Agency for International Development and American Embassy; Tbilisi, Republic of Georgia	1995 - 1996
Administrator, Division of Preventive Medicine and State Epidemiologist; then State Health Officer (last 6 months) Department of Health, State of Wyoming; Cheyenne, WY	1991 - 1994

Director, Global EIS Program; CDC, USPHS; Atlanta, GA	1988 - 1990
Deputy Director, Global EIS Program; CDC, USPHS; Atlanta, GA	1983 - 1988
Staff Epidemiologist, Policy Unit Population, Health and Nutrition Department, World Bank; Washington, DC	1982 – 1983
Deputy Director; Field Services Division, Atlanta, GA	1977-1982
Assistant Director; Field Services Division, Atlanta, GA	1976-1977
Full Time Internal Student, CDC Career Development; University of London, School of Hygiene and Tropical Medicine	1975 – 1976
Smallpox Eradication Advisor; Dacca, Bangladesh	1973 – 1975
Epidemic Intelligence Service Officer; Florida Department of Health and Rehabilitative Services; Jacksonville, FL	1971 – 1973

V. ACADEMIC EXPERIENCE

Instructor, Division of Infectious Diseases; University of Maryland School of Medicine; Baltimore, MD	1970 – 1971

VI. ADDITIONAL TRAINING

Source	Date	Type	Certification
American Management Association	1980	3 week course	Yes
Oak Ridge Nuclear Facility: Response to Nuclear Disaster	1992	1 week course	Yes

VII. SOCIETY MEMBERSHIPS and OTHER PROFESSIONAL EXPERIENCES

Member, Armed Forces Epidemiology Board, US Department of Defense; 1998 to present
Georgian Academy of Sciences of Preventive Medicine and Human Ecology; 1996
Fellow, American College of Preventive Medicine; 1979
Diplomate, American Board of Preventive Medicine; 1978
Fellow, Royal Society of Hygiene and Tropical Medicine; 1975
Chairman, Scientific Advisory Committee; 1989-1991
Member, Scientific Advisory Committee, Caribbean Epidemiology Center (PAHO),
Port of Spain, Trinidad and Tobago; 1988-1991
Consultant, Assessment of Health Needs, USAID Assessment Team, Sultanate of Oman, 1980
WHO Epidemiological Services Consultancies:
Indonesia, 1979; Indonesia, Burma, Bangladesh, 1978; Republic of Korea, 1977
Post-liberation Nutrition Survey, CDC Assessment Team, Bangladesh; 1972
Research Physician, Infectious Diseases Hospital, University of Chile, Santiago, Chile; 1970
Attending Physician, Cholera Hospital, Pakistan-SEATO Cholera Research Laboratory; Dacca, East Pakistan; 1967-1968

VIII. HONORS

US Public Health Service Meritorious Service Medal - 1997
US Public Health Service Outstanding Service Medal - 1985
US Public Health Service Commendation Medal - 1979

IX. PUBLICATIONS

1. Music, S. I., Wenzel, R. P., Libonati, J. P., Snyder, M. J., Hornick, R. B., Woodward, T. E; Induced Human Cholera (abstract), Journal of Clinical Investigation, 49:69-70a, June 1970
2. Hornick, R. B., DuPont, H. L., Music, S. I., Snyder, M. J., Libonati, J. P.; Investigations into the Pathogenesis of Diarrheal Diseases, Trans Am Clin Climatol Assoc, Oct 26;82:141-7 1970.
3. Clyde, D. F., Miller, R. M., Music, S. I., McCarthy, V. C.; Prophylactic and Sporontocidal Treatment of Chloroquine-Resistant Plasmodium Falciparum from Viet Nam, American Journal of Tropical Medicine and Hygiene, 20:1-5, January, 1971.
4. Music, S. I., Fine, E.M., Togo, Y; Zoster-Like Disease in the Newborn due to Herpes Simplex virus, New England Journal of Medicine, 284:24-26, January 7, 1971.
5. Hornick, R. B., Dupont, H. L., Music, S. I., Snyder, M. J., Libonati, J. P.; Investigations into the Pathogenesis of Diarrheal Diseases, Trans AM Clin Climatol Assoc, 82: 26 October 1970.
6. Hornick, R. B., Music, S. I., Wenzel, R. P., Cash, R., Libonati, J. P., Snyder, M. J.; Woodward, TE; The Broad Street Pump Revisited: Response of Volunteers to Ingested Cholera Vibrios, Bull NY Acad Med, 47 (10): October, 1971.
7. Tamini, B. A., Music, S. I.; The Natural History of Syphilis: A Review, South Med J., 65 (2): February, 1972.
8. Snyder, M. J., et al; Trimethoprim-sulfamethoxazole in the Treatment of Typhoid and Paratyphoid Fevers, J Infect Dis 128:Suppl:734-7: November, 1973.
9. Music, S. I., Howell, J. T., Brumback, C. L.; Red Tide, its Public Health Implications, JFMA 60(11): November, 1973.
10. Cash, R. A., Music, S. I., Libonati, J. P., Snyder, M. J., Wenzel, R. P., Hornick, R. B.; Response of Man to Infection with *Vibrio cholerae*. I. Clinical, Serologic, and Bacteriologic Responses to a Known Inoculum, J. Infect Dis 129 (1): January, 1974.
11. Hattwick, M. A. W., Rubin, R. H., Music, S. I., Sikes, R. K., Smith, J. S., Gregg, M. B.; Postexposure Rabies Prophylaxis with Human Rabies Immune Globin, JAMA, Vol 227: 407-410: Jan. 28, 1974.
12. Cash, R. A., Music, S. I., Libonati, J. P., Craig, J. P., Pierce, N. F., Hornick, R. B.; Response of Man to Infection with *Vibrio cholerae*. II. Protection from Illness Afforded by Previous Disease and Vaccine, J. Infect Dis 130 (4): October, 1974.
13. Cash, R. A., Music, S. I., Libonati, J. P., Schwartz, A. R., Hornick, R. B.; Live Oral Cholera Vaccine: Evaluation of the Clinical Effectiveness of Two Strains in Humans, Infect Immun 19(4): Oct., 1974
14. Snyder, M. J., Gonzalez, O., Palomino, C., Music, S. I., et al: Comparative Efficacy of Chloramphenicol, Ampicillin, and Co-Trimoxazole in the treatment of Typhoid Fever. The Lancet, 2 (7966): 1155-7, Nov 27, 1976.
15. Music, S. I.: Surveillance, chapter in Guidelines for Analysis of Communicable Disease Control Planning in Developing Countries, International Health Planning Methods Series, Office of International Planning Methods Series, Office of International Health, USPHS, 1979 DHEW Publication No. (PHS) 79-50080.
16. Thacker, S. B., Music, S. I., Pollard, R. A., Berggren, G., Boulos, C., Nagy, T., Brutus, M., Pamphile, M., Ferdinand, R. O., Joseph, V. R.; Acute Water Shortage and Health Problems in Haiti, Lancet, 1:471-473, March 1, 1980.
17. Music, S. I.: The Role of Epidemiology in Helping CDC Improve Public Health. Annales Istituto Superiore di Sanità, 21(4): 431-4, 1985.
18. Schwartz, B., Al-Tobaiqi, A., Al-Ruwais, A., Fontaine, R. E., A'ashi, J., Hightower, A. W., Broome, C. V., Music, S. I.; Comparative Efficacy of Cephtriaxone and Rifampicin in Eradicating Pharyngeal Carriage of Group A *Neisseria meningitidis*, Lancet, 1:1239-42, June 4, 1988.
19. Music, S. I.: Schultz, M. G.: Field Epidemiology Training Programs, New International Health Resources, JAMA, Vol 263, No 24:3309-3311, June 27, 1990.
20. Simonsen, L., Khan, A. S., Gary, H. E. Jr., Hanson, C., Pallansch, M. A., Music, S., Holman, R. C., Stewart, J. A., Erdman, D. D. Arden, N. H., Arenberg, I. K., Schonberger, L. B.; Outbreak of Vertigo in Wyoming: Possible Role of an Enterovirus Infection. Epidemiol Infect 117(1):149-57, August, 1996.
21. Music, S. I., Khetsuriani, N.: Epidemiology Bulletin, Ministry of Health, Republic of Georgia. Vol 1, Nos. 1-6:1-120, January – June 1996. (Though listed officially as *CDC Advisor* my actual role was to first do and then train others in how to do every step from conception and writing through publication and distribution of the first six monthly issues of this official publication of the Georgian government. These are available in English via Internet and the CDC homepage on SANet: http://www.sanet.ge/cdc/index.html.

22. Music, S. I., Georgia's public-health problems. Ltr to the Editor in Lancet, 348 (9043), Dec 21, 1996.
23. Smith, C. G., Music, S. I.: Pfiesteria in North Carolina: The Medical Inquiry Continues. NC Medical Journal, 59(4), Jul-Aug 1998.
24. Furney, W., Music, S. I., Wiley, J.: North Carolina Childhood Asthma Management Initiative: A Summary of the Summary Report. NC Medical Journal, 60(4), Jul-Aug 1999.
25. Music, S.I.: The Elimination of Preventable Asthma: Lessons from Smallpox. NC Medical Journal, 60(4), Jul-Aug 1999.
26. Khetsuriani, N., Music, S., Deforest, A., Sutter, R.W.: Evaluation of a Single Dose of Diphtheria Toxoid Among Adults in the Republic of Georgia, 1995: Immunogenicity and Adverse Reactions. Journal of Infectious Diseases 181 (Suppl 1):S208-S212, February 2000.

CURRICULUM VITAE

NAME:	**BARRETT-CONNOR, Elizabeth Louise**
WORK ADDRESS:	**University of California, San Diego School of Medicine Department of Family and Preventive Medicine, 0607 La Jolla, California 92093-0607**
HOME ADDRESS:	(b)(6)
BIRTHPLACE: & DATE:	
MARITAL STATUS:	
COLLEGE:	**Mount Holyoke College, South Hadley, Massachusetts, 1952-1956 - Zoology**
MEDICAL SCHOOL:	**Cornell University Medical College, New York City, 1956-1960 - Medicine**
INTERNSHIP:	**University of Texas, Southwestern Medical School, Dallas, Parkland Memorial Hospital, 1960-1961**
RESIDENCY:	**University of Texas, Southwestern Medical School, Dallas, Parkland Memorial Hospital, 1961-1963** **University of Miami, School of Medicine, Jackson Memorial Hospital, Infectious Diseases, 1963-1964**
POST-DOCTORAL:	**London School of Hygiene & Tropical Medicine 1964-1965 – D.C.M.T., Diploma in Clinical Medicine of the Tropics** **University of Minnesota, Minneapolis, 1967 (3-week course) Advanced Epidemiology - Certificate** **Johns Hopkins University, Bar Harbor, Maine, 1968 (2-week course) Genetics - Certificate**

FELLOWSHIPS:

Medical Student Fellowship in Public Health and Preventive Medicine, Cornell University Medical College, 1958
Louisiana State University Interamerican Program in Central America, Summer 1962
National Institutes of Health Post-Doctoral Fellowship, London School of Hygiene and Tropical Medicine, 1964-5
Fulbright Award (declined), 1964

DEGREES:

B.A., Mount Holyoke College, 1956
M.D., Cornell University, 1960
D.C.M.T., London School of Hygiene and Tropical Medicine, 1965

FACULTY APPOINTMENTS:

University of Miami, School of Medicine
Instructor of Medicine, 1965-1968
Assistant Professor of Medicine, 1968-1970

University of California, San Diego School of Medicine
Assistant Professor of Community Medicine and Medicine, 1970-1974
Associate Professor of Community and Family Medicine and Medicine, 1974-1981
Chief, Division of Epidemiology 1974-present
Professor of Family and Preventive Medicine and Medicine, 1981-present
Acting Chair, Department of Community and Family Medicine, 1981-1982
Chair, Department of Family and Preventive Medicine, 1982-1997

HONORS, NAMED LECTURESHIPS, AND VISITING PROFESSORSHIPS:

Frederick Murgatroyd Prize, London, 1965
Invited Participant, Bicentennial Colloquium of the New York Hospital, 1971
Invited Participant, Meeting Commemorating the 25th Anniversary of Dr. Donald W. Seldin's Chairmanship of the Department of Internal Medicine, The University of Texas, Dallas, 1977
Invited Participant, Symposium on the Advances in Diabetes Epidemiology, Colloquium Inserm, NIH, OMS. Abbaye de Fontevraud, France, May 3-7, 1982
Kaiser Award for Excellence in Teaching, University of California San Diego, School of Medicine, 1982

Living Legacy Award, Women's International Center, San Diego, California, March 6, 1984
Alexander D. Langmuir Lecture, Centers for Disease Control, Atlanta, April , 1985
Honorary Doctor of Science Degree, Mount Holyoke College, South Hadley, Massachusetts, May 26, 1985
Doctor of the Year Award, San Diego Health Care Association, San Diego, November 18, 1985
Katharine Boucot Sturgis Lecture, American College of Preventive Medicine, Atlanta, April 5, 1986
Kelly West Memorial Lecture/Award, American Diabetes Association, Indianapolis, June 6, 1987
Merit Award, National Institute of Aging, July, 1987 –1996
Visiting Professor, Royal Society of Medicine, London, May 1989.
John Rankin Lecture, Madison, Wisconsin, October 20, 1989
Don McLeod Memorial Lecture, Halifax Nova Scotia, February 9, 1990.
Member, Institute of Medicine, 1991
Elizabeth Blackwell Lecture, Rochester, Minnesota, September 18, 1991
The Lila Wallace Visiting Professorship, The New York Hospital/Cornell Medical Center, March 4-5, 1992
The Donald P. Shiley Visiting Lectureship, Scripps Clinic and Research Foundation, San Diego, March 13, 1992
Outstanding Educator Award, Association of Teachers of Preventive Medicine, March 22, 1992
Leonard M. Schuman Lecture, University of Michigan, Ann Arbor, July 28, 1993
Wade Hampton Frost Lecture, American Public Health Association, San Francisco, October 25, 1993
Joe Stokes Lecture Research Seminar, Grand Rounds, Boston, November 11, 1993
University of California, San Diego, Faculty Research Lecturer Award, March 10, 1994
James D. Bruce Memorial Award, American College of Physicians, April 21, 1994
Soroptimist International of La Jolla Award, Making a Difference for Women, Health, June 7, 1995
Ancel Keys Lectureship, American Heart Association Scientific Sessions, November 13, 1995
American Heart Association, Elizabeth Barrett-Connor Research Award in Epidemiology and Prevention for Investigators In Training, November 14, 1995
UCSD Chancellor's Associates Faculty Excellence Award in Research, January 31, 1996
Honorary Doctor of Medicine Degree, University of Utrecht, The Netherlands, March 26, 1996
Honorary Doctor of Medicine Degree, University of Bergen (Norway), August 3, 1996
The Florence Mahoney Lecture on Aging, National Institutes of Health, September 25, 1996
Arthur Gordon Visiting Professor, University of California, Los Angeles, October, 1996
American Heart Association Council on Epidemiology and Prevention, Distinguished Service Award, November 12, 1996

The Donald P. Shiley Visiting Lectureship, Scripps Clinic and Research Foundation, March, 1997
The Cleveland Clinic Foundation Department of Cardiology Visiting Professor, June, 1997
John Cassell Memorial Lecture, Society for Epidemiologic Research, 30th Annual Meeting, June 12, 1997
Clinical Service Award, Society for the Advancement of Women's Health Research, June 24, 1997.
Raine Distinguished Visitor's Award, The University of Western Australia, October 26 - November 5, 1997
Distinguished Lecturer in Geriatrics, Duke University Medical Center, J January 29-30, 1998
13th Annual Harry S. Feldman Lecture, American Epidemiologic Society (AES) Meeting, Harvard Medical School, March 26, 1998
Award of Meritorious Achievement of the American Heart Association, Dallas, Texas, June 26, 1998
Women's Health Hero Award – American Health for Women, New York, September, 1998
Woman in Science Award – American Medical Women's Association, New Orleans, November, 1998
Nathan J. Kiven Oration and Brownwide Grand Rounds, The Miriam Hospital and Brown University,Rhode Island, April 9, 1998
Alvin L. Schultz Visiting Professor of Internal Medicine, Minneapolis, October 20, 1998
Visiting Professor, Brigham and Women's Hospital, Boston, Massachusetts, November, 1998
National Institutes of Health Award for Outstanding Work in Gender Differences in Osteoporosis, March, 1999
Heath Clark Lectureship, London School of Hygiene and Tropical Medicine, London, England, March, 1999
Invited Participant, Controversies and Dilemmas in Endocrinology, Royal College of Physicians of Edinburgh, Scotland, March, 1999

GRANTS:

National Institutes of Health, Lipid Research Clinic, Veterans Administration Hospital, La Jolla, California, 1970-1989 .
Janssen Drug Study Fund, 1976-1978.
National Institutes of Health, Peripheral Arterial Disease Grant #HL22255-01, April 1, 1978, - November 30, 1980.
American Heart Association, California Affiliate, Grant-in-Aid, #80-S114, July 1, 1980 - June 30, 1981.
National Institute of Arthritis, Diabetes, Digestive & Kidney Diseases, Epidemiology of Diabetes in an Adult Community #1 RO1 AM31801, July 1, 1983 - June 30, 1988.

UCSD/SDSU Teaching Nursing Home Project. #NIA AG03990-01A1, May 1, 1984 - April 30, 1989.

National Institutes of Health, National Heart, Lung and Blood Institute, PHS HL34591, Endogenous Sex Hormones & Cardiovascular Disease Risk in Men, April 1, 1986 - March 31, 1987.

American Heart Association California Affiliate, Orange County Chapter Grant-in-aid-Dietary Factors, Blood Pressure and Cardiovascular Disease. #85-S116, July 1, 1986 - December 31, 1988.

Weight Watchers - Analyzing in Detail Extensive Database with Regard to Obesity and Heart Disease, January 1,1987 - December 31, 1989.

National Institute of Health - National Institute of Aging- Study of Risk Factors for Osteoporosis in the Elderly. #NIH/NIA 1 R37 AG07181-01, UCSD #90-6518, August 1, 1987 - July 31, 1992 (Merit Award).

National Institute of Health - Postmenopausal Estrogen/ Progestin Interventions (PEPI). #NIH 1001- HL40207-01, UCSD #90-6500. September 3, 1987 - August 31, 1992.

University of California Academic Geriatric Resource Program-Interdisciplinary Geriatrics Fellowship Program. #87SD-C2D-2-01, July 1, 1987 - June 30, 1988.

National Institute of Diabetes and Digestive and Kidney Diseases - Epidemiology of NIDDM and IGT in an Adult Community. UCSD #88-5256, July 15, 1988 - June 30, 1990.

American Association of Retired Persons.- The Effects of Husbands' Retirement on Their Wives. UCSD #87-6259, January 1, 1988 - December 31, 1988.

National Institute of Health, NHLBI - LRC Follow-up Study--CPPT and Prevalence. UCSD #6947, June 29, 1971 - September 30, 1991.

National Institute of Health, NIA - Alzheimers Disease Research Center Competitive Supplement. UCSD #89-6638, August 17, 1990 - March 31, 1994.

National Institute of Health - Predictors of Cardiovascular Disease in the Elderly. UCSD #90-6070, January 1, 1991 - December 31, 1991.

National Institute of Health, NIDDK - Epidemiology of NIDDM and IGT in an Adult Community. UCSD #91-6083, December 1, 1991 - November 30, 1996.

National Institute of Health - Epidemiology of NIDDM and IGT Supplement. UCSD #92-6591, June 1, 1992 - February 28, 1993.

National Institute of Health, NIA - Study of Risk Factors for Osteoporosis

in the Elderly (Osteo II). UCSD #91-6122. August 1, 1992 - July 31, 1997. (Merit Award)

Merck, Sharp and Dohme, Fracture Intervention Trial (FIT). UCSD #92-5548, October 1, 1991 - March 31, 1997.

National Coffee Association, "Coffee/Caffeine/Bone Mineral Density". UCSD #92-6164, February 1, 1992 - January 31, 1993 (no cost extension August 31, 1993).

Solvay Pharmaceuticals - A Double-Blind, Parallel Group Study of the Effects of Estratest H.S. vs. Premarin in Surgically Menopausal Women. UCSD #92-6838. June 1, 1992 - May 31, 1995.

Wyeth-Ayerst, Heart & Estrogen/Progestin Replacement Study (HERS). UCSD #91-5180. October 8, 1992 - December 31, 1998.

National Institute of Health, NHLBI - Postmenopausal Estrogen/Progestin Interventions (PEPI). UCSD #92-5242. August 1, 1992 – July 31, 1994.

Weight Watchers. Sex hormones, obesity and diabetes in older women. UCSD #93-7168. November 1, 1993 - October 31, 1994.

National Institutes of Health, NIDDK. NIDDM Primary Prevention Trial. UCSD #94-5368, July 1, 1994 to June 30, 2001. (Co-PI)

National Institute of Health, NHLBI, Postmenopausal Estrogen-Progestin Intervention (PEPI) Safety Followup Study, N01-HV-48136, June 15, 1994 to December 14, 1997.

National Institute of Health, NHLBI, Postmenopausal Estrogen-Progestin Intervention (PEPI) Safety Followup Analysis Study, N01-HV-48136, August 1, 1994 to July 31, 1997.

Lilly Research Laboratory. Comparison of Raloxifene HCL and Placebo in the Treatment of Postmenopausal Women with Osteoporosis. UCSD #95-5368, November 1, 1994 to October 31, 1999.

Wyeth-Ayerst Laboratories. A Randomized, Double-Blind Placebo & Active Controlled, Parallel, Multicenter Study to Assess the Safety & Efficacy of 3 1/2 Day Combinations of 17B-Estradiol Norethindrone Acetate Transderma Delivery Systems for Relief of Menopausal Vasomotor Symptoms & Reduction of Endometrial Hyperplasia. UCSD#97-9150. May 27, 1997 to April 30, 1999.

Osteometer Meditech A/S. Bone Mineral Content & Density in the Forearm, Speed of Sound, & Boradband Ultrasound Attenuation in the Calcancus: Normal Range in US Caucasian Females & Males, 20-80 years of age. UCSD #98-9010. June 15, 1997 to December 31, 1997.

Osteometer Meditech A/S. Forearm Mineral Density in the Normal Caucasian Female Population in the Calcancus: Normal Range in US Caucasian Females & Males, 20-80 Years of Age. UCSD 97-9099. December 15, 1997 to January 31, 1997.

Merck & Co. A 5-Year, Double-Blind, Randomized, Placebo-Controlled Extension Study to Examine the Long-Term Safety & Efficacy of Oral Alendronate In Postmenopausal Women Who Previously Received Alendronate in Conjunction with the Fracture Intervention Trial (FLEX) UCSD #98-9051. January 3, 1998 to October 30, 2003.

National Institutes of Health, Soy Health Effects (SHE). 1RO1 HL57790-01, April 1, 1997 to March 31, 2000.

National Institutes of Health/NIDDK, Diabetes Primary Prevention Program (DPP). 5UO1 DK48339-04, September 10, 1994 to June 30, 2001.

National Institutes of Health, Comparison of Medical and Surgical Treatment for Abnormal Uterine Bleeding Post-Menopausal Women (Ms?). September 30, 1996 to September 29, 2001.

Eli Lilly & Co. Raloxifene Hydrochloride or Placebo in Postmenopausal Women At Risk for Major Cardiovascular Events. UCSD #98-9146. September 4, 1998 – September 30, 2005.

National Institutes of Health, NIA. Gender Differences in Osteoporosis (OSTEO III) UCSD #98-6285. December 1, 1998 to November 30, 2002.

National Institutes of Health, Osteoporotic Fractures in Men (MR.OS). UCSD #98-6088. December 10, 1998 to November 30, 2003.

MEDICAL QUALIFICATIONS:

Licensure, Florida, 1965
Licensure, California, 1970 (#C-32076)
Diplomate, American Board of Internal Medicine, 1968
Diplomate, National Board of Medical Examiners

PROFESSIONAL SOCIETY MEMBERSHIPS:

Fellow, American College of Physicians (Publications Committee, 1988-90)
Fellow, Council on Cardiovascular Epidemiology, America Heart Association (Chair, 1989)
Fellow, Royal Society of Health
Fellow, American College of Preventive Medicine
Fellow, American College of Nutrition
Fellow, The Royal Society of Medicine
Member, American Venereal Disease Association (Vice-President, 1977-1978)
Member, American Federation for Clinical Research
Member, Association of Teachers of Preventive Medicine (Board of Directors, 1987-90)
Member, Infectious Disease Society of America

Member, International Epidemiological Association
Emeritus Member, American Society of Tropical Medicine and Hygiene
Member, Society for Epidemiologic Research (President, 1983)
Member, Association for Practitioners in Infection Control
Member, California Academy of Preventive Medicine
Member, Western Association of Physicians
Member, American Epidemiological Society (President, 1993-94)
Member, American Diabetes Association
Consultant, Veterans Administration Hospital, Miami, 1969
Consultant/Lecturer in Internal Medicine (Infectious Diseases), U.S. Naval Hospital, San Diego, 1970-85
Consultant, Mercy Hospital, San Diego, 1970-85
Consultant, American Medical Association Department of Drugs, Chicago, 1976
Member, Hospital Infection Control Committee, University Hospital, San Diego, 1970-1972 (Chairman 1975-1977)
Member, Hospital Infection Control Committee, Veterans Administration Hospital, La Jolla, 1971-85
Member, Research Committee, Zoological Society of San Diego, 1978-86
Member-at-Large, Research Peer Review Sub-Committee, American Heart Association, California Affiliate, 1977-1981
Member, Advisory Committee for Genetic Disorders, California Department of Health, 1974-1975
Ad hoc member, Study Section, Center for Disease Control, Atlanta, 1971-1972
Member, Expert Advisory Committee, Food & Drug Administration, Rockville, 1972-1977
Member, Advisory Council on Immunization Practices, Center for Disease Control, Atlanta, 1973-1977
Member, Preventive Medicine and Public Health Test Committee, National Board of Medical Examiners, Philadelphia, 1974-1980 (Chair, 1977-1980)
Member, Epidemiology Working Group, National Commission on Arthritis and Musculoskeletal Diseases, Boston, 1975-1976
Ad hoc Member, National Institute of Allergies and Infectious Diseases Committee, HEW/NIH, 1977
Member, Consultant Task Force for the Study of Health in Egypt and Future U.S. Development Assistance Alternatives, National Institute of Medicine, 1978
Member, National Institute of Allergies and Infectious Diseases

Committee, 1978-1982
Member, American Tropical Medicine Delegation to China, American Society of Tropical Medicine and Hygiene, 1978
Member, The American Geriatrics Society, 1987-present
Member, Medical Research and Development Advisory Panel, Review Group Concerned with Parasitic Diseases, Walter Reed Army Institute of Research, Department of the Army, 1979-1982
Member, Special Consultants to Department of Defense Overseas Medical Research Laboratories, US Department of Defense, 1980
Consultant, Task Force, Institute of Medicine, Division of International Health, Health in Egypt: Recommendations for U.S. Assistance, January, 1979
Member, Core Faculty, Annual Seminars on Epidemiology of Cardiovascular Disease, American Heart Association, 1978-present
Member, California Medical Association Scientific Advisory Panel; Preventive Medicine and Public Health, 1982-present
Member, American Epidemiological Society Membership Committee 1987-present
Member, Advisory Committee, Role of BCG Vaccinations in the United States, Research Foundation, 1983-1985
Member, (San Diego) Mayor's Task Force for Acquired Immunity Deficiency Syndrome (AIDS), 1983-1985
Member, Epidemiology Research Unit, University of Texas, 1983-1986
Member, National Advisory Committee on Vital and Health Statistics, May 30, 1984 - February 28, 1987
Member, American Public Health Association, Epidemiology Section, (Chair, 1989-91)
Member, European Diabetes Epidemiology Study Group, 1984- present
Member, NHANES III Advisory Committee (FACEB), 1985
Member, Preventive Medicine Residency Advisory Committee, San Diego (Chair, 1985)
Member, Epidemiology and Biometry Program Working Group, Subcommittee of the Clinical Applications and Prevention Advisory Committee (CAPAC), National Heart, Lung, and Blood Institute, Bethesda, Maryland, 1985-1987
Member, Burroughs-Wellcome Fund/American College of Preventive Medicine Pharmacoepidemiology Award Advisory Committee, 1986-1989
Member, San Diego Foundation for Medical Care, 1986-present
Member, Resource Advisory Committee on the Epidemiology of the

Chronic Diseases of Aging of the National Archives of Computerized Data on Aging, 1988-1994
Member, Technical Advisory Committee for Diabetes Translation and Community Control Programs, Centers for Disease Control, February 6, 1989 - June 30, 1991.
Member, International Epidemiological Association (North American Councillor, 1990-present)
Member, International Scientific Committee for the 3rd International Conference on Preventive Cardiology, 1989-1990
Member, U.S. Army Research and Development Advisory Committee, Ft. Detrick, Frederick, Maryland 1990-1993
Member, International Society and Federation of Cardiology, Section of Epidemiology, 1990-present
Member, National Heart, Lung, and Blood Institute Task Force on Hypertension 1990-93
Member, National Diabetes Advisory Board, National Institutes of Health, 1990-1994
Member, The Royal Society of Medicine, 1992-present
Member, Advisory Board of the HERITAGE Study, 1992-present
Member, Faculty, WHO Postgraduate Seminar on Diabetic Epidemiology (Krakow, Poland), 1992
Member, Data and Safety Monitoring Board, Women's Health Initiative, 1993-present
Member, Faculty of International Society & Federation of Cardiology Teaching Seminar 1993-present
Councilor, Western Association of Physicians, 1994-97
Member, Human Subjects Program Review Committee, UCSD, 1994-present
Member, The New York Academy of Sciences, 1995-present
Member, Scientific Advisory Board, Ostex International, Inc., 1995-present
Member, Raloxifene Advisory Board, Eli Lilly and Company, 1995-present
Member, American Federation for Aging Research, National Scientific Advisory Committee, 1996
Member, Membership Committee, Institute of Medicine, 1996-1999
Member, Armed Forces Epidemiology Board, 1996 -
Member, Advisory Council, National Institute of Aging-1996-
Member, Advisory Council, National Institute of Aging, 1997 –
Board of Directors, North American Menopause Society, 1997-
National Institutes of Health/Women's Health Initiative: Data and Safety Monitoring Board, 1997-

Member, Editorial Board, American Journal of Preventive Medicine, 1998-
Sigma Xi – The Scientific Research Society, 1998 –
Member, National Lipid Education Council, 1998-
Member, Science Advisory Board, County of San Diego, 1999-
Member, Medical Committee, Royal Netherlands Academy of Arts and Sciences, 1999-
Member, Endocrine Society, 1999-

REVIEWER:

Annals of Internal Medicine, 1974-present
Review of Respiratory Diseases, 1974-present
New England Journal of Medicine, 1974-present
Journal of American Medical Association, 1975-present
Public Health Reports, 1975-1985
Emergency Medicine, 1975-1980
Western Journal of Medicine, 1975-present
American Journal of Tropical Medicine and Hygiene, 1979-present
Arthritis and Rheumatism, 1981-present
American Journal of Epidemiology, 1981-present
Reviews of Infectious Diseases, 1982-present
Arteriosclerosis, 1984-present
Circulation, 1985-present
Journal of Chronic Disease, 1982-present
Preventive Medicine, 1988-present
International Journal of Gynecology & Obstetrics, 1994-present

EDITORIAL BOARDS:

American Journal of Epidemiology
American Journal of Infection Control, 1981-1986
American Journal of Preventive Medicine
Annals of Epidemiology
Annals of Internal Medicine, 1979-82
Cardiovascular Risk Factors, 1995-present (Member of Advisory Board)
Circulation
International Journal of Epidemiology
Journal of Clinical Investigation (Consulting Editor), 1995-1997
Reviews in Clinical Gerontology
Sexually Transmitted Diseases, 1977-81
The Women's Letter
Menopause

November 1999

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High School:	Boston Latin School, 1959
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Medical School:	Harvard - M.D., 1967
Internship:	Cleveland Metropolitan General Hospital, 1967-1968
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Positions Held:

Current:

Mount Sinai School of Medicine, Ethel H. Wise Professor of Community and Preventive Medicine and Chairman of the Department of Community and Preventive Medicine, 1990-Present.

Mount Sinai School of Medicine, Director, Division of Environmental and Occupational Medicine, Department of Community and Preventive Medicine, 1985-Present.

Mount Sinai School of Medicine, Professor of Pediatrics, 1985-Present.

Previous:

U.S. Environmental Protection Agency, Senior Advisor to the Administrator on Children's Health and the Environment, 1997-1998.

National Institute for Occupational Safety and Health, Director, Division of Surveillance, Hazard Evaluations and Field Studies, 1979-1985.

Centers for Disease Control, Chief, Environmental Hazards Activity, Cancer and Birth Defects Division, Bureau of Epidemiology, , 1974-1979.

Centers for Disease Control, Director, Research and Development, Bureau of Smallpox Eradication, 1973-1974.

Centers for Disease Control, Epidemic Intelligence Service (EIS) Officer, 1970-1973.

Adjunct Positions:

University of Washington School of Public Health and Community Medicine, Clinical Professor of Environmental Health, 1983 - Present.
Harvard Medical School, Visiting Lecturer on Preventive Medicine and Clinical Epidemiology, 1982 - Present.
Harvard School of Public Health, Visiting Lecturer on Occupational Health, 1981 - Present.
University of Cincinnati, Department of Environmental Health, College of Medicine, Assistant Clinical Professor of Environmental Health, 1981 - 1986.
London School of Hygiene and Tropical Medicine, Visiting Fellow, TUC Institute of Occupational Health, 1976 - 1977.
Harvard Medical School, Clinical Instructor in Pediatrics, 1969 - 1970.

Memberships:

American Academy of Pediatrics, Fellow
Society for Epidemiologic Research, Member
American Public Health Association, Member
Occupational Health Section, Chair, 1989-90
Royal Society of Medicine, Elected Fellow
International Commission on Occupational Health, Member
Scientific Committee on Epidemiology
American College of Epidemiology, Fellow
Board of Directors, 1990 - 1993.
American Epidemiological Society, Elected Member
Collegium Ramazzini, Fellow
President, 1997-present
Herman Biggs Society, Member
New York Academy of Sciences, Fellow
New York Occupational Medicine Association, Member
Board of Directors, 1988 - 1990.
American College of Occupational and Environmental Medicine, Fellow
New York Academy of Medicine, Elected Fellow
Physicians for Social Responsibility, Member
Board of Sponsors, 1994-95; Board of Directors 1996-1999

Specialty Certifications:

American Board of Pediatrics - 1973
American Board of Preventive Medicine:
General Preventive Medicine - 1979
Occupational Medicine - 1983

Awards and Honors:

Institute of Medicine, National Academy of Sciences, Elected to membership, 1987
U.S. Department of Health, Education and Welfare, Volunteer Award, 1973
U.S. Public Health Service, Career Development Award, 1976
Centers for Disease Control, Group Citation as Member of Beryllium Review Panel, 1978
U.S. Public Health Service, Meritorious Service Medal, 1985
New York Committee for Occupational Safety and Health, Annual Honoree, 1985
New England College of Occupational and Environmental Medicine, Harriet Hardy Award, 1993
United Brotherhood of Carpenters, William Sidell Presidential Award, 1995
American Public Health Association, Herbert L. Needleman Medal and Award for Scientific Contributions and Advocacy on Behalf of Children, 1995.
International Association of Fire Fighters, Occupational Health and Safety Award, 1995
Physicians for Social Responsibility, Broad Street Pump Award in Environmental Health, 1996
Mayo Clinic, Department of Pediatrics, Amberg-Heimholtz Lecturer in Pediatrics, 1998
International Society for Occupational and Environmental Health, Vernon Houk Award, 1998
Centers for Disease Control and Prevention, Langmuir Memorial Lecturer, 1999
American College of Preventive Medicine, Katherine Boucot Sturgis Award, 1999
Mothers & Others for a Livable Planet, Award for Advocacy on Behalf of the Health of Children, 1999
Earth Day New York, Award for Excellence in Environmental Medicine, 1999

Visiting Professorships:

University of Tokyo, Visiting Professor of the Faculty of Medicine, September 1989
University of Tokyo, Visiting Professor of the University, July 1990
University of Cape Town Medical School, Visiting Professor, Department of Community Health, March 1992
Medical College of Pennsylvania, Catherine Boucot Sturgis Visiting Professor in Community and Preventive Medicine, March 1992
National University of Singapore, Visiting External Examiner in Occupational Medicine, 1994
Duke University Medical School, Visiting Professor, NIEHS Clinical Training Program in Environmental Medicine, 1995

Committees:

The White House
Presidential Advisory Committee on Gulf War Veterans' Illnesses, 1995-1996.

American Academy of Pediatrics
Committee on Environmental Hazards, 1976 - Present. Chairman, 1983-1987.

National Research Council

National Academy of Sciences, Assembly of Life Sciences. Board on Toxicology and Environmental Health Hazards, 1978-1987; Vice-Chairman, 1981-1984.

National Academy of Sciences, Assembly of Life Sciences, 1981-1982; Commission on Life Sciences, 1982-1984.

Institute of Medicine, Committee for a Planning Study for an Ongoing Study of Costs of Environment-Related Health Effects, 1979-1980.

National Academy of Sciences, Panel on the Proposed Air Force Study of Herbicide Agent Orange, 1979-1980.

National Academy of Sciences, Committee on the Epidemiology of Air Pollutants, Vice-Chairman, 1984-1985.

National Academy of Sciences, Committee on Neurotoxicology in Risk Assessment, 1987-1989.

National Academy of Sciences, Committee on the Scientific Issues Surrounding the Regulation of Pesticides in the Diets of Infants and Children, Chairman, 1988-1992.

National Academy of Sciences, Board on Sustainable Development, 1995-1998.

National Institutes of Health/U.S. Public Health Service

National Institutes of Health, Study Section on Epidemiology and Disease Control, 1986-1990.

National Institute of Environmental Health Sciences, Third Task Force for Research Planning in the Environmental Health Sciences; Chairman, Subtask Force on Research Strategies for Prevention of and Intervention in Environmentally Produced Disease, 1983-1984.

National Institute for Occupational Safety and Health, Board of Scientific Counselors, 1995-1997.

State and Local Government

State of New York, Governor's Blue Ribbon Committee on the Love Canal, 1978-1979.

State of New Jersey, Meadowlands Cancer Advisory Board, Chair, 1987-1989.

State of New York, Asbestos Advisory Board, Chair, 1987 - Present..

State of New York, New York State Advisory Council on Lead Poisoning Prevention, Chairman, 1993 - Present.

City of New York, Mayor's Lead Paint Poisoning Advisory Committee, 1991-1993.

State of New York, Public Health Priorities Committee, 1996.

State of New York, Health Research Science Board, 1997 - Present.

Academic

Harvard School of Public Health, Occupational Health Program, Residency Review Committee, 1981-1983; Chairman, 1981.

New York Academy of Medicine, Working Group on Housing and Health, 1987-1989; Chairman, 1989.

Association of University Programs in Occupational Health and Safety, 1985 – Present; President, 1986-1988.

New York Lung Association, Research and Scientific Advisory Committee, 1986-1989. Board of Directors, 1987-1990.

Milbank Memorial Foundation, Technical Board, 1986-1988.

Mickey Leland National Urban Air Toxics Research Center, National Advisory Committee, 1994-1995.

Cornell University, Dean's Advisory Council in Veterinary Medicine, 1996-1997.

International Organizations

World Health Organization. Contributor to the WHO Publication: "Guidelines on Studies in Environmental Epidemiology" (Environmental Health Criteria, No. 27), 1984.
International Agency for Research on Cancer, Working Groups on Cancer Assessment, October 1981 and June 1986. (IARC Monographs No. 29 and No. 42).

Environmental Organizations

INFORM, Board of Directors, 1991 - Present.
Environmental Health Foundation, Board of Directors, 1993 - Present.
Colette Chuda Environmental Fund, Scientific Advisory Committee, 1994 - Present.
Children's Health Environment Coalition, Board of Directors, 1996 - Present.
Children's Environmental Health Network, Board of Directors, 1995 - Present.

Labor Unions

United Automobile Workers (UAW) - Chrysler Corporation, Joint Scientific Advisory Committee, Member, 1990 - Present.
United Brotherhood of Carpenters, National Health and Safety Fund, Medical Advisory Committee, 1990 - Present; Chairman, 1994 - Present.
International Association of Fire Fighters, John Redmond Foundation, Medical Advisory Committee, 1989 - Present.
International Brotherhood of Teamsters, National Health and Safety Advisory Committee, 1994 - Present.
George Meany Center for Labor Studies, Board of Trustees, 1994-1997.

Other Organizations

Health Insurance Plan (HIP) of Greater New York, Board of Directors, 1992-1994.
American Legion, Science Panel, Chairman, 1988 - Present.

Editorial Boards:

Editor-in-Chief: *American Journal of Industrial Medicine*, 1992 - Present; Consulting Editor, 1979-1992.
Editor-in-Chief: *Environmental Research*, 1987-1994.
Consulting Editor: *Archives of Environmental Health*, 1982 - Present.
Editorial Board: *Annual Review of Public Health*, 1984-1990.
Senior Editor: *Environmental Research*, 1985-1987.
Editorial Board: *American Journal of Public Health*, 1987 - Present.
Editorial Board: *New Solutions*: A Journal of Environmental and Occupational Health Policy, 1990 - Present.
Editorial Board: *The PSR Quarterly*: A Journal of Medicine and Global Survival, 1990-1994.
Editorial Board, *Journal of Public Health Management and Practice*, 1995-1996.

National Service:

United States Public Health Service, Commissioned Corps, 1970-1985. LCDR (04) to CAPT (06).
United States Naval Reserve, Medical Corps, 1996 - Present.
LCDR (0-4) 1996-98; CDR (0-5) 1 April, 1998 - Present.

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Antibodies to Squalene in Gulf War Syndrome

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Gulf War Syndrome (GWS) is a multisystemic illness afflicting many Gulf War-era veterans. The molecular pathological basis for GWS has not been established. We sought to determine whether the presence of antibodies to squalene correlates with the presence of signs and symptoms of GWS. Participants in this blinded cohort study were individuals immunized for service in Desert Shield/Desert Storm during 1990–1991. They included 144 Gulf War-era veterans or military employees (58 in the blinded study), 48 blood donors, 40 systemic lupus erythematosus patients, 34 silicone breast implant recipients, and 30 chronic fatigue syndrome patients. Serum antibodies to squalene were measured. In our small cohort, the substantial majority (95%) of overtly ill deployed GWS patients had antibodies to squalene. All (100%) GWS patients immunized for service in Desert Shield/Desert Storm who did not deploy, but had the same signs and symptoms as those who did deploy, had antibodies to squalene. In contrast, none (0%) of the deployed Persian Gulf veterans not showing signs and symptoms of GWS have antibodies to squalene. Neither patients with idiopathic autoimmune disease nor healthy controls had detectable serum antibodies to squalene. The majority of symptomatic GWS patients had serum antibodies to squalene. © 2000 Academic Press

INTRODUCTION

The illnesses afflicting men and women who served in the military conflict in the Persian Gulf during 1990–1991 remain ill-defined. A constellation of symptoms including fatigue, rashes, headaches, arthralgias, myalgias, lymphadenopathy, diarrhea, memory loss, autoimmune thyroid disease, increased allergies and sensitivities to environmental elements, and neurological abnormalities collectively referred to as Gulf War Syndrome (GWS) have been described in veterans from this conflict (Persian Gulf Veterans Coordinating Board, 1985; Grady *et al.*, 1998; Fukuda *et al.*, 1998; Unwin *et al.*, 1999; Coker *et al.*, 1999). A symptom-based case definition of GWS has recently been described (Fukuda *et al.*, 1998). While GWS patients in general do not suffer from classic rheumatic diseases, the signs and symptoms are reminiscent of entities, such as arthralgias, fibromyalgia, lymphadenopathy, autoimmune thyroid disease, chronic fatigue syndrome, malar rashes, and musculoskeletal signs and symptoms associated with various autoimmune conditions and exposure to silicone, an organic material developed, in part, to be used as an immunological adjuvant for vaccines (Ismail *et al.*, 1999; Straus, 1999; Hyams *et al.*, 1996). Many, if not most, of these signs and symptoms are caused, promoted, or modulated by cytokines (Dinarello, 1988; Akiro *et al.*, 1990), further details of which are beyond the scope of this paper. Serological abnormalities including hypergammaglobulinemia and abnormal serum proteins have been reported in 45% of GWS patients (Grady *et al.*, 1998). A variety of possible explanations for GWS have been proposed. The Persian Gulf Veterans Coordinating Board addressed the issues of possible chemical and biological

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weapons to account for these illnesses (Persian Gulf Veterans Coordinating Board, 1995). Haley *et al.* (1997) grouped various reported symptoms into six different syndromes based upon self-reported possible exposure to chemicals in the Persian Gulf. It has been suggested that a combination of chemical and biological weapons exposure may account for GWS illnesses. Abou-Donia *et al.* (1996) examined the acute effects of pyridostigmine bromide and organophosphate exposure in chickens and suggested that the toxicity observed may be similar to that suffered by Gulf War veterans. Another explanation for GWS is that it is posttraumatic stress syndrome (Hyams *et al.*, 1996).

It has also been suggested that GWS may be due to exposure to biological weapons, dysregulation of the immune system (Rook *et al.*, 1998), or imbalance in the TH1/TH2 ratio, either as an adverse reaction to the intense vaccination schedule or as a result of exposure to biological agents in the Persian Gulf (Rook *et al.*, 1998).

Gulf War veterans and attendant civilian personnel received a variety of immunizations in preparation for possible deployment to the Persian Gulf theater. A similar intensive vaccination regimen was also used in British troops (David *et al.*, 1997). Epidemiological studies indicate that multiple vaccinations or vaccination against biological warfare agents are the factors with the highest correlation with GWS symptomatology (Unwin *et al.*, 1999).

We have identified a group of GWS patients who served in American and British military forces or worked as civilian employees to the U.S. military or their contractors during Desert Shield/Desert Storm in the Persian Gulf, 1990–1991. These patients served in all branches of the military and received the required immunizations. They served throughout the Persian Gulf, including on ships of the U.S. Navy not in combat or exposed to environmental toxins at ground level. We have found antibodies to squalene, an experimental immunological adjuvant, in a high percentage of these GWS cases.

MATERIALS AND METHODS

Patients were admitted to the study based upon service in the United States or the United Kingdom military or as civilian employees of the U.S. military or their contractors in the Persian Gulf during 1990–1991. Patients became aware of the study via the Internet and word of mouth with other veterans and were enrolled consecutively on a voluntary basis. No fees were paid by the subjects or to the subjects who participated in this study. Included were individuals who fit the recently proposed case definition for GWS (Fukuda *et al.*, 1998) and others without GWS symptoms. Service occurred in Desert Shield/Desert Storm, Operation Provide Comfort (in northern Iraq where there were no chemical weapons), CENTCOM in Saudi Arabia, Kuwait, Camp 4 (front lines), and medical units in various locations in Saudi Arabia. Some were in theater for months. Others were evacuated due to illness after as little as 48 h after arrival and before the war commenced. We tested deployed personnel who served in various parts in theater during the war, but were and are not sick. We tested patients referred to as nondeployed veterans, those immunized for duty in the Persian Gulf, but who did not leave the United States or were deployed elsewhere. None participated in NIH experimental vaccination trials, although our positive control subjects had participated in such trials and were known to have received squalene-containing adjuvant injections. Further controls had idiopathic autoimmune disease or silicone breast implants or were healthy subjects with no stigmata of autoimmune disease.

Patient records and histories were obtained from the Gulf War-era participants. Board-certified rheumatologists, neurologists, and endocrinologists made all diagnoses. Compilation of data, including commercial lab results, was done by chart review by one investigator (P.B.A.) and was reviewed by board-certified rheumatologists.[2] Serum samples from study participants were collected by laboratory personnel via standard phlebotomy procedures using vacutainer tubes and butterfly needles and were stored at −20°C until they were shipped to Tulane University School of Medicine in New Orleans. Samples from Gulf War-era veterans were blinded. The identities or exact number of samples from each category was not made available to the Tulane laboratory until after completion of the diagnostic testing. All samples were tested twice under the same conditions. Results from all samples in both tests were consistent. At the end of the study, patient data were matched with the outcome of the anti-squalene antibody (ASA) assay and results were tabulated.

Anti-squalene Antibody Assay

The ASA assay measures the binding of serum immunoglobulin (IgG) to squalene immobilized on nitrocellulose. It is similar in format to the antipolymer antibody (APA) assay

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for partially polymerized acrylamide (Tenenbaum *et al.*, 1997). Seropositivity on the APA assay has been shown to correlate with severe musculoskeletal signs and symptoms present in a subset of silicone breast implant recipients (Tenenbaum *et al.*, 1997). For the blinded study, squalene (>99% purity) was diluted 10-, 100-, 1000-, and 10,000-fold in distilled water, applied to nitrocellulose membranes, and allowed to air-dry. The nitrocellulose membranes were then cut into 4-mm-wide strips, placed in 20-well trays, and rinsed in wash buffer (Tris-buffered saline containing 0.3% polyoxyethylene sorbitan monolaurate and 0.005% thimerosal, pH 7.4). The strips were incubated in 2 ml blocking buffer (Tris-buffered saline containing 5% powdered instant milk, 4% goat serum, and 0.008% thimerosal, pH 7.4) for 45 min prior to the addition of 5 μl of patient sera (1:400 dilution) followed by a further 90-min incubation. This dilution factor was chosen based upon the very strong antibody responses found in GWS patients. All incubations and washes were carried out at room temperature on a rocking platform. The blocking buffer was then removed and the strips were washed with washing buffer (three times for 5 min each). After the strips were washed, 2 ml of blocking buffer containing biotin conjugated to goat anti-human IgG (Kirkengaard & Perry Laboratories, Gaithersburg, MD), diluted 1:1000, was added. After a 60-min incubation, the strips were again washed as above, and 2 μl of blocking buffer containing avidin-conjugated horseradish peroxidase (Jackson ImmunoResearch, West Grove, PA), diluted 1:500, was added. Following another 60-min incubation, the strips were washed, as above, and 2 ml of detection-buffered saline containing 30% methanol, 0.6 mg/ml 4-chloro-1-napthol, 0.03% hydrogen peroxide; pH 7.4) was added. The reaction was allowed to proceed for 15 min and was stopped by rinsing the strips in distilled water. The strips were allowed to air-dry for visual scoring on a scale of 0 to +4.

Statistical Analysis

The strength of binary relationships was tested using χ^2 tests of independence. This protocol was a feasibility study. Accordingly, no power studies were performed.

RESULTS

Primary Studies

To ascertain that our assay could detect antibodies to squalene, we had positive controls who were two subjects who had volunteered to participate in a vaccine trial at the NIH involving the use of a squalene-containing adjuvant (Table 1). Subsequent to vaccination, they developed a multisystem disorder similar to that of Persian Gulf veterans. Their symptoms are listed in Table 2.

TABLE 1
Squalene Reactivity of NIH Vaccine Trial Participants

Patient	Doses of squalene	ASA reactivity
A	1	+1
B	3	+3

Patient A received a single injection and became ill within 3 weeks, with signs and symptoms including arthritis, fibromyalgia, lymphadenopathy, photosensitive rashes, fatigue, headaches, and fasciculations. This patient had lower than normal acetylcholinesterase and histological evidence of IgG-mediated demyelinization. The NIH vaccine study code was broken; only adjuvant containing squalene had been administered as a placebo. This patient was weakly positive for ASA. Patient B went through the complete experimental vaccination protocol before manifesting a similar set of signs and symptoms and was +3 for ASA.

Fukuda and co-workers (1998) have reported that individuals deployed to the Persian Gulf who became sick have a chronic multisystem disease. The cohort of GWS patients in our study have many signs and symptoms of autoimmune connective tissue and neurological disease with arthritis (94%), fibromyalgia (94%), lymphadenopathy (94%), rashes (94%), weakness (86%), fatigue (81%), chronic headaches (78%), and memory loss (72%) as the most frequent symptoms (Table 3).

It should be noted, however, that most patients did not have

TABLE 2
Symptoms Which Appeared after a Single Adjuvant Injection

Arthritis
Fibromyalgia
Lymphadenopathy
Rashes
Photosensitive rashes
Malar rashes
Chronic fatigue
Chronic headaches
Fasciculations
Lymphocytic infiltrates around vascular tissue
IgG-mediated demyelinization
Lower than normal levels of acetylcholinesterase

TABLE 3
Symptoms and Diagnostic Lab in GWS Patient Groups

	D-S (%)	D-W (%)	ND-S (%)	UK-D (%)
Arthritis	94	0	100	100
Fibromyalgia	94	8	100	100
Lymphadenopathy	94	0	100	100
Rashes	94	0	100	100
Photosensitive rashes	25	0	75	100
Malar rashes	17	0	63	100
Chronic fatigue	81	33	100	100
Chronic headaches	78	0	100	100
Abnormal body hair loss	19	0	38	33
Nonhealing skin lesions	42	0	63	66
Aphthous ulcers	36	0	63	66
Dizziness	47	8	100	66
Weakness	86	17	100	66
Memory loss	72	25	100	66
Seizures	14	0	50	66
Mood changes	72	0	63	100
Neuropsychiatric problems	44	0	88	66
+FANA	20	0	50	Unknown
Anti-dsDNA	14	0	Unknown	Unknown
Low C3 and C4	14	0	Unknown	Unknown
Anti-thyroid	14	0	Unknown	Unknown
Anemia	14	0	50	Unknown
Elevated ESR &/or CRP	25	0	75	Unknown
SLE	17	0	50	Unknown
MS	3	0	Unknown	Unknown
ALS	8	0	0	0
Raynaud's phenomenon	42	0	75	66
Sjogren's syndrome	8	0	Unknown	33
Chronic diarrhea	36	0	63	66
Night sweats	36	0	88	66
Low grade fever	39	0	88	66

Note. D-S, deployed, sick (N = 36); D-W, deployed, well (N = 12); ND-S, nondeployed, sick (N = 8); UK-D, deployed, sick, UK (N = 3).

an optimal workup for connective tissue and neurological autoimmune diseases because of the limited resources in the Veterans' Administration hospitals or military hospitals. Nevertheless, all patients reported here meet the case definition recently established (Fukuda *et al.*, 1998). In agreement with a prior study (Grady *et al.*, 1998), some of these GWS patients also had abnormal laboratory values, including positive antinuclear antibodies (ANA;17%), anti-daDNA (14%), low C3 and C4 (14%), anemia (14%), anti-thyroid microsomal antibodies (14%), and elevated ESR and/or CRP (22%). A minority of symptomatic patients met diagnostic criteria for classical autoimmune diseases, including Sjogren's syndrome (8%), multiple sclerosis (3%), ALS (8%), and systemic lupus erythematosus (17%).

Likewise, military personnel from the United Kingdom have shown the same array of signs and symptoms as those from the United States. Their signs and symptoms included arthritis (100%), fibromyalgia (100%), lymphadenopathy (100%), rashes (100%), chronic fatigue (100%), chronic headaches (100%), and memory loss (66%). Laboratory data are not unavailable for this group. They also had malar rashes, Raynaud phenomenon, and sicca syndromes. Thus, our cohort represents a subset of veterans that displays manifestations of GWS. The severity of symptoms in our cohort can be explained by a self-selection bias in that the patients volunteered for our study.

Persons activated to deploy who were vaccinated, but did not deploy for a variety of reasons, had an array of signs and symptoms with even higher frequencies of arthritis (100%), fibromyalgia (100%), lymphadenopathy (100%), rashes (100%), weakness (100%), fatigue (100%), chronic headaches (100%), and memory loss (100%) (Table 3). The nondeployed individuals had higher rates of dizziness (100%), seizures (50%), and neuropsychiatric abnormalities (88%). The number in this group was small, and these differences were not statistically significant. Laboratory values for the nondeployed individuals with GWS were abnormal, with positive ANA (50%), anemia (50%), and elevated ESR and/or CRP (75%).

In contrast, abnormal signs, symptoms, and laboratory values were rare in the cohort of Gulf War-era veterans who considered themselves well and upon examination did not have debilitating health problems. They reported some signs and symptoms, but their illnesses were not multisystemic (Table 3). The signs and symptoms reported included fibromyalgia (8%), chronic fatigue (33%), weakness (17%), memory loss (25%), and thyroid disease (8%). None reported positive laboratory values for autoimmune processes or were so diagnosed.

Musculoskeletal signs and symptoms are more common in females than males, and autoimmune diseases are predominantly found in females in ratios ranging from 8:1 to 14:1 (Michet *et al.*, 1985; Geirsson *et al.*, 1994). We wished to determine why predominantly male military personnel, both deployed and nondeployed, initially found fit for duty during the war, would develop signs and symptoms common to autoimmune diseases. Many studies have shown that adjuvants used to enhance vaccine efficacy can induce autoimmune disease (Zamma, 1983; Lorentzen *et al.*, 1995; Madzhidov *et al.*, 1986; Kleinau *et al.*, 1995). Thus, we sought whether GWS patients who received immunizations had antibodies to an immunological adjuvant. Squalene was chosen as it has been used in many experimental vaccine adjuvant formulations since 1987. A variation of a previously

described assay, one which measures the binding of serum antibodies to low-molecular-weight polymers (Tenenbaum *et al.*, 1997), was used in the current study. This immunological assay, similar in format to Western immunoblotting, quantitates the binding of antibodies to squalene immobilized on nitrocellulose (Fig. 1). Serum samples were tested blindly. We found that GWS patients who deployed had ASA responses ranging in intensity from +1 to +4. Most of the sick Gulf War veterans had +2 and +3 reactivity to squalene at a serum dilution of 1:400. One individual had an especially strong reaction rated as +4. A high majority (95%) of symptomatic deployed individuals with GWS were positive on the ASA assay (Fig. 2A).

Interestingly, all sick veterans who did not deploy but had received immunizations as preparation for deployment also had antibody reactivity to squalene. In contrast, none of the persons deployed to the Gulf who thought of themselves as well were ASA positive.

Other Studies

Squalene is an organic polymer, with some antigenic epitopes which might be shared with other organic polymers, acting as immunostimulants. Antibodies to silicone and partially polymerized acrylamide (the antigen in the antipolymer assay) were weakly positive in fewer than 10% of the symptomatic Gulf War-era veterans. Four patients with musculoskeletal signs and symptoms and exposure to silicone breast devices were tested to see if antibodies to squalene were present; none were reactive (see below). To determine if antibodies to squalene occurred in idiopathic autoimmune diseases, samples were taken from patients who had defined autoimmune diseases, both rheumatic and neurologic, but none were reactive. To determine if healthy individuals from the general public might have antibodies to squalene, we tested members of the general public. Again, none showed antibody reactivity (Table 4).

In a broader unblinded antibody-screening study, antibodies to squalene were studied in larger groups of individuals (Fig. 2B). Blood samples of Gulf War veterans from different medical centers were tested for ASA. This group contained a high percentage of ASA-positive individuals (69%). The samples included were not segregated according to their clinical status and included healthy controls. Squalene is in some cosmetic products, so we tested to determine if antibodies were present in the general population. Samples of blood from blood banks indicated only 5% antibody reactivity to squalene and the reactions were much less intense (Fig. 1). To determine if antibody to squalene was a marker for autoimmune disease processes, tests were conducted on blood samples from patients with systemic lupus erythematosus. This group had 10% ASA weakly positive reactivity (Fig. 2B). Patients suffering from chronic fatigue syndrome have some of the signs and symptoms of GWS patients, but showed only 15% weak reactivity. Prior studies have shown that most individuals exposed to silicone breast devices with

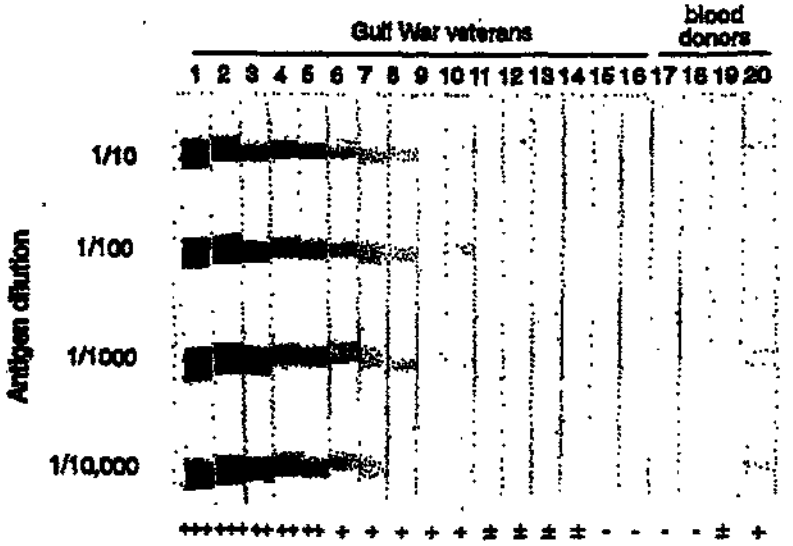

FIG. 1. Antisqualene antibody responses in representative Gulf War Syndrome patients and blood donors.

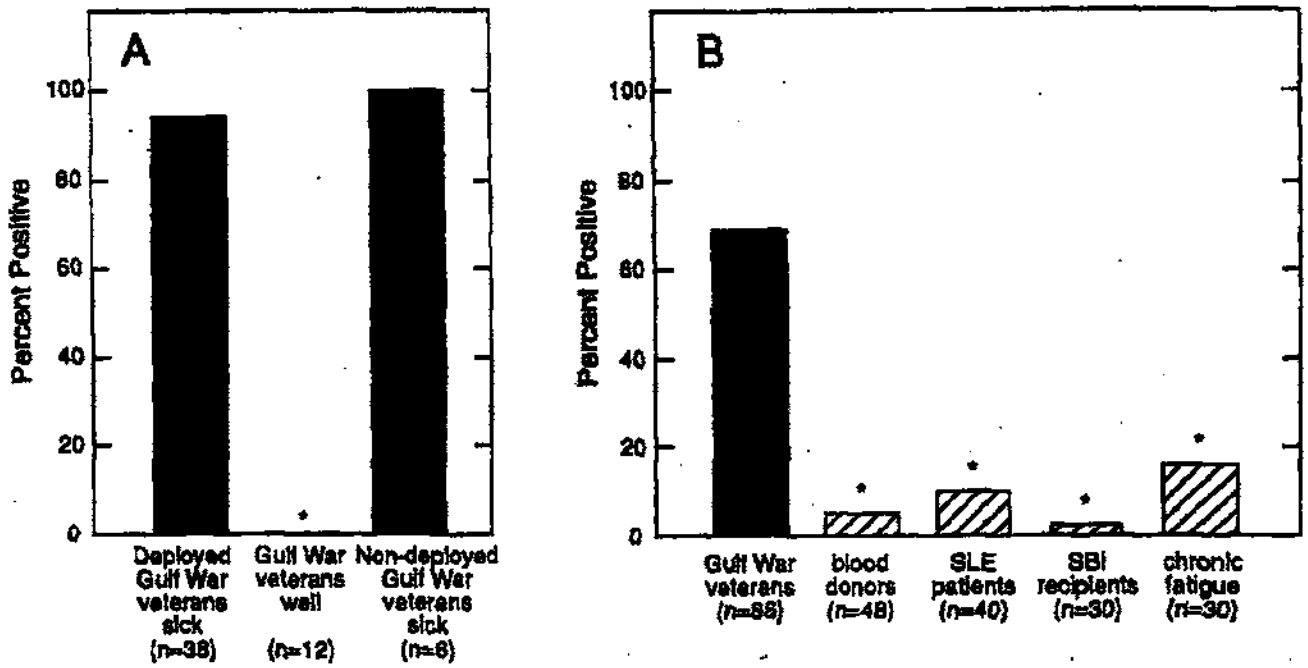

FIG. 2. Antisqualene antibody responses in Gulf War Syndrome patients, blood donors, systemic lupus erythematosus (SLE) patients, chronic fatigue syndrome patients, and symptomatic silicone breast implant (SBI) recipients. (A) Blinded samples. *, $P < 0.001$ compared to percentage positive in well Gulf War veterans by χ^2 test. (B) Unblinded samples. *, $P < 0.001$ compared to percentage positive in Gulf War Syndrome patients.

severe musculoskeletal signs and symptoms have serum antibodies reactive to a synthetic polymer (polyacrylamide) (Tenenbaum *et al.*, 1997). Both silicone and acrylamide, like squalene, are potent immunological adjuvants (Naim *et al.*, 1997; Nicholson *et al.*, 1996; Yoshida *et al.*, 1994; Sergott *et al.*, 1986). Therefore, we tested for cross-reactive antibodies to squalene in serum from patients exposed to SBI. Only 10% of this group were weakly positive for antibodies to squalene (Fig. 2B), confirming the results with the smaller sample in the blinded portion of the study.

TABLE 4

Squalene Antibodies—Blinded Study Patient Groups

Patient group	ASA reactivity (%)
D-S	95
D-W	0
ND-S	100
UK-D	100
Breastimplants	0
NIH vaccine participants	100
Idiopathic autoimmune disease	0
Healthy general public	0

Note. D-S, deployed, sick ($N = 38$); D-W, deployed, well ($N = 12$); ND-S, nondeployed, sick ($N = 6$); UK-D, UK deployed, sick ($N = 3$); NIH vaccine trial patients ($N = 2$).

DISCUSSION

The illnesses afflicting military veterans and civilians who served in the Persian Gulf in 1990–1991 have remained clouded in confusion and controversy. Several recent studies have indicated that the Gulf War-era patients are suffering from a chronic multisystemic illness, but with a continuum of signs and symptoms not within the definitions of "classic" rheumatic diseases or other specific disorders (Fukuda *et al.*, 1998; Ismail *et al.*, 1999; Straus, 1999). In some, onset of illness occurred within a few weeks after receiving immunizations. This includes personnel never deployed due to illness. It also included some who did deploy, but were in theater for as little as 48 h before being sent home before the war began because of severe joint and muscle pain and neurological problems. Other Gulf War veterans became ill

years after the war, but showed illnesses similar to those who became ill soon after vaccination. The variability of expression of symptoms and severity may be due to individual immune responses genetically regulated by the histocompatibility complex (Lorentzen *et al.*, 1995; Madzhidov *et al.*, 1986).

Our results suggest that ASA reactivity is a marker for the signs and symptoms of GWS. Finding serum antibodies to squalene in Gulf War patients is unexpected, and the basis for the presense of these antibodies remains unclear. ASA are not a general marker for autoimmune disease due to their absence in idiopathic autoimmune patients and rarity in patients with other, presumed environmentally induced, autoimmune diseases. The signs and symptoms of our Gulf War patients are similar to those of a subset of female patients following exposure to silicone. Some individuals with silicone exposure suffer from many of the multisystem symptoms, viz, arthralgias, myalgias, lymphadenopathy, and neurological disorders prevalent in GWS patients in the current study (Bridges *et al.*, 1993; Brautbar *et al.*, 1995; Wolford, 1997). Symptomatic silicone breast implant recipients also have high levels of antibodies to synthetic polymers (Teneinbaum *et al.*, 1997) and to silicone,[3] but did not have high prevalence of ASA.

It has been suggested that abnormal immune responses may be involved in GWS (Rook *et al.*, 1997). Immunological adjuvants have the generally desirable property of eliciting cell-mediated immunity and antibodies when administered with an antigen. They may also cause a more generalized and indiscriminate stimulation of the immune system and disrupt the balance of immune self-regulatory mechanisms, which may lead to autoimmune disease (Zamma, 1983; Lorentzen *et al.*, 1995; Madzhidov *et al.*, 1986; Kleinau *et al.*, 1995). Squalene has been used extensively as an adjuvant in animal models to induce autoimmune diseases (Lorentzen, 1999; Beck *et al.*, 1976; Kohashi *et al.*, 1977; Garrett *et al.*, 1985; Whitehouse *et al.*, 1974; Yoshino *et al.*, 1994). Cytokines are mediators of immunological regulation and inflammatory responses (Van der Meide *et al.*, 1996), and increased cytokine levels are associated with the development of autoimmune disease in established rodent models of autoimmunity (Fitzpatrick *et al.*, 1996). Squalene has been shown to induce increased levels of interleukin-5 (IL-5), IL-6, and interferon-γ (Valensi *et al.*, 1994). Several different adjuvants have been demonstrated to produce or exacerbate autoimmune diseases in experimental models. Adjuvant-induced arthritis is a well-characterized autoimmune disease induced in rats and other species (Zamma, 1983; Lorentzen *et al.*, 1995; Madzhidov *et al.*, 1986; Kleinau *et al.*, 1995). The disease process in adjuvant-induced arthritis is complex, affecting multiple organ systems. For example, a cachetic syndrome (Rofe *et al.*, 1994) and testicular dysfunction (Clemons *et al.*, 1989) have been associated with adjuvant-induced arthritis. Uveitis, a T-cell mediated intraocular inflammatory disease, can also be induced by adjuvants (Petty *et al.*, 1996). Neurological diseases can be the result of immunological mechanisms, including autoimmunity (Rogers *et al.*, 1996; Tebin *et al.*, 1996; Honnorat *et al.*, 1995; Wucherpfennig *et al.*, 1990; Cross *et al.*, 1991; Bansal *et al.*, 1994), and neurological symptoms are commonly seen in autoimmune diseases (McNichollet *et al.*, 1994; Zanone *et al.*, 1993; Moll *et al.*, 1993).

All pharmacology is controlled toxicology. Although not approved by the Food and Drug Administration for human use, squalene has been used as an adjuvant in experimental vaccines against a variety of pathogens, including *Bacillus anthracis* (Ivins *et al.*, 1994), *Plasmodium falciparum* (Hoffman *et al.*, 1994), and herpes simplex virus (Burke *et al.*, 1994). Effectiveness of adjuvants has been shown to parallel toxicity defined as the initiation of autoimmune disease processes (Zamma, 1983; Koga *et al.*, 1986). Adjuvants should not produce reactions at injection sites, be pyrogenic, or induce anterior uveitis, arthritis, or other protean autoimmune processes (Allison *et al.*, 1991). A study using squalene as an adjuvant in influenza vaccine reported moderate to severe local and systemic reactions in humans (Keitel *et al.*, 1993). The participants suffered induration, erythema, lymphadenopathy, fever, chills, nausea, and dizziness, symptoms which lasted for several days. Another squalene-containing adjuvant was used with gp120 in a human immunodeficiency virus vaccine, where it induced severe systemic and local reactions in 15 of 30 vaccinees (Keefer *et al.*, 1996). Similarly, in a study of simian immunodeficiency vaccine in macaques, squalene was used as an adjuvant, and the animals developed anti-human-cell antibodies and autoimmune-like symptoms (Vaslin *et al.*, 1992). Future studies should determine whether or not ASA have a role in these pathological processes.

Squalene is a naturally occurring molecule absorbed from food and synthesized as a precursor for cholesterol, myelin, and hormones. This synthesis occurs within the hepatocytes and is further processed into cholesterol in the endoplasmic reticulum (Stamellos *et al.*, 1993). Fecal analysis indicates that about 60% of dietary squalene is absorbed (Strandberg *et al.*, 1990). Dietary squalene is absorbed through lymphatic vessels after being cyclized to sterols during transit through

[3]Cao, Yan *et al.*, unpublished observations.

the intestinal wall (Tilvis *et al.*, 1983). It is processed into chylomicrons by the epithelial cells of the small intestines. It becomes a lipid droplet covered by β-lipoprotein containing triglyceride and cholesterol ester. This increases serum levels of free and esterified methyl sterol contents. About 90% of absorbed squalene is in lipoproteins, appearing in chylomicrons and VLDL, suggesting that removal of dietary squalene may indicate metabolism of intestinal lipoproteins (Gylling *et al.*, 1994).

Squalene is a nonsteroid precursor of cholesterol. Reports have indicated that high titers of autoantibodies to cholesterol, once considered to be a poorly immunogenic molecule, could be generated by immunization with liposomes containing cholesterol and lipid A as adjuvant (Swartz *et al.*, 1988; Alving *et al.*, 1991; Dijkstra *et al.*, 1996). Injection of either silicone gel or silicone oil intraperitoneally also resulted in high titers of autoantibodies to cholesterol (Alving *et al.*, 1996). The silicone component serves as an adjuvant as well as initiating the autoimmune process. The high titers were IgM with relatively low titers of IgG to cholesterol (Dijkstra *et al.*, 1996; Alving *et al.*, 1996). The specificity of these antibodies was to cholesterol and structurally similar sterols containing a 3β-hydroxyl group. Anticholesterol binding activity was significantly diminished if the 3β-hydroxyl domain was altered by oxidation, substitution, epimerization, or esterification (Dijkstra *et al.*, 1996). It has been reported that naturally occurring autoantibodies have been detected in humans (Alving *et al.*, 1989), but these were much lower in titer than those produced with either lipid A or silicone.

Several facts argue against our assay detecting cross-reactive antibodies to cholesterol instead of antibodies specific for squalene. First, squalene is neither a sterol nor does it have a 3β-hydroxyl group. The respective molecular structures, internal molecular bonding, charge distribution, and antigenic epitopes are different. Second, if high-titer autoantibodies to cholesterol that are cross-reactive with squalene are normal, we should see no difference between our various patient groups. The GWS patients and NIH positive control patients are very distinct in their strong IgG antibody reactivity to squalene. Third, if silicone alone can generate antibodies to cholesterol and these are cross-reactive to squalene, we should see high antibody reactivity to squalene in patients exposed to silicone in addition to the GWS and NIH patients. This did not occur.

In the course of these studies, we examined two volunteers for a vaccine trial at the NIH involving squalene as adjuvant. They developed a multisystem disease similar to that seen in Persian Gulf veterans subsequent to their participation in the trial. One received a single injection and became ill within a few weeks with signs and symptoms including arthritis, fibromyalgia, lymphadenopathy, photosensitive rashes, fatigue, headaches, and fasciculations. This individual had lower than normal acetylcholinesterase, histological evidence of lymphocytic infiltrates around vascular tissue, and IgG-mediated demyelinization. After this NIH vaccine study code was broken, it was found that only adjuvant squalene had been administered as placebo. This patient was weakly positive for ASA. Another patient who went through the whole experimental protocol before manifesting a similar set of signs and symptoms was 3+ positive for ASA.

Multiple vaccinations and vaccination against biological warfare agents are the factors with the highest correlation with GWS symptomatology (Unwin *et al.*, 1994). It is important to note that our laboratory-based investigations do not establish that squalene was added as adjuvant to any vaccine used in military or other personnel who served in the Persian Gulf War era. Several investigators have speculated that GWS is the result of either exposure to chemicals, chemical weapons, or to biological agents encountered in the Persian Gulf (Persian Gulf Veterans Coordinating Board, 1995; Abou-Donia *et al.*, 1996; David *et al.*, 1997; Haley,1997). However, such exposure would likely have immediate effects and many Gulf War veterans were well until months or years after the military conflict. Many of these GWS patients have improved on treatment regimens prescribed by their personal physicians, rheumatologists, and neurologists, namely the immunosuppressives used for classical rheumatological conditions.[4] These treatments have included steroids, methotrexate, hydroxychloroquine, and cytoxan. Such treatments would have no effect on subjects exposed to chemical weapons. If GWS was due to an exogenous infectious agent, the immunosuppressive regimens used would likely result in an exacerbation of the symptoms. This did not occur. The molecular pathology of GWS must be defined before its etiology can be assigned. We present here evidence of an immune factor based upon the adjuvancy of squalene. Further studies are required to define the role of ASA, if any, in the pathogenesis of GWS.

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[4]Asa, P.B. *et al.*, unpublished observations.

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March 3, 2000

The Honorable William S. Cohen
Secretary of Defense
The Pentagon
Washington, DC 20301-1010

Dear Secretary Cohen:

Please intervene to halt the obfuscation campaign Department of Defense officials seem intent on conducting concerning the issues surrounding antibodies to squalene research. Monday, February 28, 2000, I received a response to the letter I had sent to you. Nine of my colleagues in the House of Representatives joined me to request that DOD do an objective analysis of "Antibodies to Squalene in Gulf War Syndrome" -- an article recently published in the February 2000 issue of *Experimental and Molecular Pathology*.

DOD's letter, authored by Dr. Sue Bailey, avoids providing Congress a clear and direct answer to our request. The following excerpts illustrate my concerns with DOD's official reply.

1. In paragraph one, Dr. Bailey states that she has enclosed the Research Working Group (RWG) review. She does not mention that the RWG reviewed an early draft of the study, provided to them as a professional courtesy. The text of the final peer-reviewed article contains some significant changes. Members of Congress asked for an objective analysis of the peer-reviewed article. It is difficult to understand why Dr. Bailey chose to include a review not based on the published scientific article, unless her goal was confusion rather than clarity.

2. Also provided as an attachment, and referenced in paragraph one, is a review of the published article. I was dismayed that Dr. Bailey would provide this brief summary with no indication of the author's name or professional credentials to conduct and provide such a review. My colleagues and I stated clearly, "An internal review by the same individuals within the DOD who were unwilling to cooperate for months does not constitute the kind of science that those who sacrificed for this nation deserve." A half-page critical analysis, anonymously written, is not an appropriate response to the congressional request.

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3. Dr. Bailey continues in paragraph two by making a reference to an early theory that is completely irrelevant to our request. Dr. Asa's early and *confidential* correspondence with DOD regarding potential cause was motivated by concern for those suffering from Gulf War Illnesses. DOD must encourage researchers to explore hypotheses rather than setting them up for public criticism, if we are going to solve the mystery of Gulf War Illnesses. The congressional inquiry's focus is the peer-reviewed study and the assay used to detect the antibodies. Dr. Bailey's reference is an unnecessary distraction from the facts.

4. Dr. Bailey's third paragraph attempts to portray DOD as proactive in developing and validating an assay to test for the presence of squalene antibodies prior to the GAO recommendations. Nothing could be further from the truth:

A. DOD's response to the GAO accused them of being "scientifically and fiscally irresponsible" for suggesting that DOD conduct research to dispute or validate the independent research findings. DOD's position was clear: until the peer-review and publication process by the private scientists was completed, it would not consider action that could provide answers to those suffering from Gulf War Illnesses. (GAO/NSIAD-99-5)

B. When DOD was interviewed by GAO during the investigation, its spokespersons acknowledged DOD had the know-how to develop such an assay and could have tested for squalene antibodies but did not.

C. When Dr. Bailey provided DOD's final comments to the GAO report, she stated, "Our position and the concerns expressed in our comments to the draft report have not changed." (DOD letter to the GAO dated May 28, 1999)

D. It was only after the U.S. House of Representatives took action and instructed DOD to cooperate with the GAO recommendations that Congress received notice from DOD of its funding of related research. This confirmatory research is being conducted by a DOD researcher. *(House of Representatives Report 106-244, Department of Defense Appropriations Bill, 2000)*

In light of these facts, it is disturbing that Dr. Bailey would construct paragraph four in such a way as to revise the sequence of events, and in doing so, misrepresent DOD's consistent position prior to legislative action.

In closing, Dr. Bailey states; "We are committed to responsible and aggressive pursuit of research that will further our understanding of illnesses among Gulf War veterans and prevent similar illnesses following future deployments." Unfortunately, something vital is missing from her statement: treatment and answers for those who are suffering. It is not acceptable to ask sick Gulf War-era veterans and their families to wait decades for endless research projects which do not generate help and treatment for those suffering. The consequences of this failed policy approach are all too clear to Congress, the American public, and especially the veterans exposed to and sickened by Agent Orange during the Vietnam War.

Our request to you on January 31, 2000 was straightforward and simple: determine if the assay used in the peer-reviewed, published study could be utilized as a diagnostic tool to help sick Gulf War era veterans. I would greatly appreciate your personal assistance to insure that DOD provide the objective analysis initially requested, including identification of those who are providing the analysis and their

professional credentials.

Thank you.

Jack Metcalf

Jack Metcalf
House of Representatives

cc: Representative Norm Dicks
Representative Walter Jones
Representative Bob Filner
Representative Janice Schakowsky
Representative Lane Evans
Representative Ron Paul
Representative Joe Scarborough
Representative Bernard Sanders
Representative Dan Burton

THE ASSISTANT SECRETARY OF DEFENSE

1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

Honorable Jack Metcalf
United States House of Representatives
Washington, DC 20515-4702

MAR 2 [illegible]

Dear Congressman Metcalf:

Thank you for your recent letters on the Anthrax Vaccine Immunization Program's website and on the information I provided to you as requested in your inquiry of January 31, 2000. To address your request for additional objective analysis of this article, I have asked the Armed Forces Epidemiological Board to convene a subcommittee of experts to review and critique this work. I will provide you with this critique and, as requested, the curricula vitae of the reviewers. In addition, the National Academy of Sciences, Institute of Medicine (IOM), is assessing the role squalene may play as a cause of illnesses among Gulf War veterans and reviewing the work of Dr. Asa and her colleagues. The IOM expects to publish a report in August of this year.

The Department has considered your comments and suggestions regarding the Anthrax Vaccine Immunization Program's website. On March 10, 2000, the portion of the website describing the antibody test developed by Dr. Asa and colleagues was modified to read as follows: "Whether or not this test has any clinical meaning will be settled by medical experts over time. For now, it is sufficient to recognize the conclusions of the authors: "It is important to note that our laboratory-based investigations do not establish that squalene was added as adjuvant to any vaccine used in military or other personnel who served in the Persian Gulf War era.""

Our commitment to Gulf War veterans is unwavering. All known, testable hypotheses concerning illnesses among Gulf War veterans have been or are being pursued through our program of basic science research. All decisions on research funding are based on a process of rigorous, competitive, and independent peer review. We are committed to responsible and aggressive pursuit of research that will further our understanding of illnesses among Gulf War veterans and prevent similar illnesses following future deployments.

Sincerely,

Dr. Sue Bailey

Dr. Sue Bailey

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

Honorable Jack Metcalf
House of Representatives
Washington, DC 20515

FEB 24 2000

Dear Representative Metcalf:

Thank you for your letter asking for an objective analysis of Antibodies to Squalene in Gulf War Syndrome – an article published in the February 2000 issue of *Experimental and Molecular Pathology*. Prior to publication of the article, the Research Working Group (RWG) of the interagency Persian Gulf Veterans' Coordinating Board had objectively reviewed the work of Dr. Asa and her colleagues. We look forward to the scientific dialog and additional research that will now go forward as a result of long awaited publication of this data. I have enclosed the RWG review, our Report to Congress in response to the Fiscal Year 2000 Defense Appropriations Bill report language, and a review of the published article.

As you know, we have encouraged and awaited publication by these scientists ever since Dr. Asa first presented her theory on "human adjuvant disease" and its possible link to Persian Gulf War (PGW) veterans' illnesses. Prior to speculation about squalene, Dr. Asa theorized that silicone adjuvant (an agent added to a vaccine to increase antigenic response) was responsible for PGW veterans developing "human adjuvant disease."

The Department published in the February 10, 1999 Commerce Business Daily a specific request for research proposals on "Interactions Of Drugs, Biologics And Chemicals In Service Members In Deployment Environments," supporting our research on illnesses among Gulf War veterans. This preceded the recommendation of the General Accounting Office to pursue research in this area. In response to this solicitation, a research proposal was submitted to develop and validate an assay to test for the presence of squalene antibodies. This proposal received a high independent scientific review merit score, was funded, and the research is ongoing.

We wholeheartedly agree that the integrity of the assay is the first step in finding answers. Our commitment to Gulf War veterans is to support and fund quality research. This is best assured when all decisions on research funding are based on a process of rigorous, competitive, and independent peer review of all research proposals. We are committed to responsible and aggressive pursuit of research that will further our understanding of illnesses among Gulf War veterans and prevent similar illnesses following future deployments.

Sincerely,

Dr. Sue Bailey

Enclosures:
As stated

Scientific Manuscript: "Antibodies to Squalene in Gulf War Syndrome"

The study, by Drs. P. B. Asa, Y. Cao and R. F. Garry, appeared in the February 2000 issue of Experimental and Molecular Pathology. The paper by Asa and colleagues presents data obtained by using an immunological assay that reportedly can detect previously unknown antibodies against squalene, a relatively simple, linear hydrocarbon that is a naturally occurring molecule in humans, animals and plants. Squalene is normally found in cell membranes in humans and is one of the building blocks for producing cholesterol.

Summary: Using this novel assay, the authors' report finding anti-squalene antibodies in a high percentage of "Gulf War Syndrome" patients. The antibody test developed at Tulane University Medical Center is called the Anti-Squalene Antibody Assay, or ASA Assay. Tulane has a patent pending on the ASA Assay, and Autoimmune Technologies LLC, a New Orleans biomedical company, has licensed the rights to the ASA Assay from Tulane.

The published research reportedly included both blinded and unblinded studies. In the blinded study, the ASA Assay was reportedly used to test blood samples from 56 individuals who were in active military service or who were civilian employees of the U.S. armed forces or their contractors during 1990-1991. Most, but not all, of the members of this group were reportedly deployed to the Persian Gulf theater of operations. The group comprised 38 deployed individuals who were ill, 12 deployed individuals who were healthy, and 6 non-deployed individuals who were ill. The results of the blinded study showed that 95% of the deployed sick individuals tested positive, none of the deployed healthy individuals tested positive, and 100% of the non-deployed sick individuals tested positive for anti-squalene antibodies.

In the unblinded study, the ASA Assay was used as a screening tool to gather further data. Blood samples from 86 additional individuals who were in active military service or who were civilian employees of the U.S. armed forces or their contractors during 1990-1991, including healthy individuals, were tested, and 69% of them tested positive. Because squalene is used as an ingredient in some cosmetics, 48 samples from blood banks were tested to see if the antibodies were present in a larger segment of the general population. Of these, 5% tested positive. To see if the antibodies were a marker for other autoimmune disease processes, 40 samples from patients with systemic lupus erythematosus were tested. Of these, 10% tested positive. Because patients with chronic fatigue syndrome have many symptoms similar to those of "Gulf War Syndrome" patients, 30 chronic fatigue patients were tested. Of these, 15% were positive.

The research also included a small adjunct study in which two individuals who had previously volunteered to participate in a vaccine trial in which squalene was an adjuvant in the vaccine were tested for the presence of anti-squalene antibodies. Both subjects tested positive. These two were the only patients in the research group who had a known exposure to squalene from vaccines.
The conclusion reached as a result of this research study is that most patients in the study groups who are ill with "Gulf War Syndrome" have serum antibodies to squalene while most other people do not. The clinical significance of the presence of the antibodies, however, is still not known, and while it is possible that the antibodies play a role in the disease process itself, the study does not explore the mechanisms involved in developing the antibodies.

Critical analysis: It is unknown if informed consent was obtained from individuals submitting samples for testing or if an Institutional Review Board (IRB) reviewed and approved the research protocol.

The authors claim to create a novel assay that detects antibodies to squalene. The authors however, do not use valid positive or negative controls. There are no positive controls (i.e., sera previously proven to contain antibodies to squalene) to validate the argument that the assay can detect antibodies to squalene. For positive controls, the authors cite only results obtained using this novel assay on two individuals reportedly vaccinated once and thrice with a squalene-containing adjuvant in a clinical trial sponsored by the National Institutes of Health. The authors provide no preimmunization results to demonstrate that the presumptive anti-squalene activity in the so-called positive controls was not present before immunization with the squalene adjuvant.

Fundamental to interpretation of novel assay data are negative controls. Such negative controls are critical to prove that the assay is not detecting artifacts (extraneous, cross-reacting substances). The authors have no negative control in which the human serum containing the presumed antibodies is omitted; there is no negative control in which the avidin-conjugated horse radish peroxidase is omitted; there is no negative specificity control for nonspecific binding of IgG, i.e. for normal IgG molecules sticking nonspecifically to squalene.

A further criticism of the paper is the authors use of only a single dilution of serum, rather than a series of dilutions. Without using this technique, there is a no way to obtain a titer, i.e., a quantitative measure of the degree of activity in the sample. The test results were scored at +++, ++, +, +/-, and -, raising the possibility that at high concentrations most normal sera might give a positive result; and the total absence of antibodies in a "normal" population must be regarded with some suspicion. If "squalene antibodies" or derivatives are associated with "Gulf War syndrome," one may expect titers to parallel severity of symptoms. The paper gives no evidence of this.

The assay by Asa and colleagues remains an unvalidated and unproven assay.

~~INVESTIGATOR INITIATED~~ ~~PRIVILEGED COMMUNICATION~~

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RESEARCH WORKING GROUP (RWG)

of the

PERSIAN GULF VETERANS COORDINATING BOARD

WHITE PAPER

SQUALENE

Human Adjuvant Disease among Gulf War Veterans
Approved by the RWG on 31 Jan 00

Executive Summary

A draft article, hypothesis that illnesses afflicting veterans of the Gulf War are an atypical connective tissue disease (an autoimmune disease) resulting from use of the vaccine adjuvant squalene, was provided to the Research Working Group for review by Robert F. Garry, Ph.D. The paper's authors are Pamela B. Asa, Ph.D., an unaffiliated molecular biologist from Memphis, Tennessee, Yan Cao, M.D. and Robert F. Garry, Ph.D., both from Tulane University, New Orleans, Louisiana. These investigators report development of an immunoassay for detecting anti-squalene antibodies and used the assay to test blood serum samples from various patient and control groups.

Two studies involved Gulf War veterans. In an unblinded study, samples from 86 Gulf War veterans, both healthy and ill individuals, were tested with 69% testing positive; in 48 samples from blood donors tested, 5% tested positive; in 40 samples from patients with lupus, 10% tested positive; in 30 chronic fatigue patients tested, 15% were positive; in 30 "silicone breast implant" patients tested, 10% tested positive. In a blinded study of 38 Gulf War deployed individuals who were ill, 12 Gulf War deployed individuals who were healthy, and 6 non-deployed individuals who were ill (all of the non-deployed individuals had reportedly received the full compliment of immunizations given to those who were deployed to the Gulf theater) 95% of the deployed ill tested positive for anti-squalene antibodies, none of the deployed healthy individuals tested positive, and 100% of the non-deployed ill individuals tested positive.

The study protocol and manuscript attributes the hypothesis to findings in two patients from National Institutes of Health (NIH)-sponsored vaccine trial(s) using squalene as an adjuvant. The samples and the clinical and demographic data of the current unpublished work apparently originate from a protocol posted on the Internet calling for submission of blood samples and questionnaire data to Dr. Pam Asa. The protocol informs participants that their "serum will be tested against various adjuvants known to be used by the U.S. Department of Defense, in an antibody assay system developed by Dr. Bob Garry, Tulane Medical School, New Orleans, LA, as published in the Lancet Journal 1997." It is not explicit that informed consent was obtained from individuals submitting samples for testing or if an Institutional Review Board reviewed and approved the research protocol.

Review of the draft manuscript indicates the basic hypothesis and supporting evidence presented are flawed or inaccurate. According to the Department of Defense (DoD), no military member or civilian has received any squalene-containing vaccines other than with the person's informed consent in approved small-scale vaccine studies that followed Food and Drug Administration (FDA) regulations. There are no data that indicate squalene was used as an adjuvant in any vaccines administered to U.S. forces deploying to the Gulf War.

In their investigations of illnesses among Gulf War veterans, the Senate Special Investigations Unit (SIU) found no credible information indicating that vaccines used during the Gulf War contained squalene. In their report, the SIU states that according to the FDA, squalene can be contained in a vaccine due to two different processes: 1) as an adjuvant, which is an agent to enhance the immune response; or 2) in minute quantities in vaccines manufactured using eggs, since eggs are rich in squalene and cholesterol. The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant.

It is not possible to determine, based on current reports, if the paper's authors actually detected antibodies to squalene or a synthetic squalene adjuvant in the veterans they tested. They reportedly

used a variation of a previously described assay. This assay technique was used to claim findings of the first evidence from a blinded study of the existence of a laboratory marker that correlates with the severity of local and systemic complications in silicone breast implant recipients. The assay in question reportedly detected antibodies, not to silicone, but to a synthetic polymer whose characteristics have not been fully described. Dr. Garry and Tulane University reportedly received a U.S. patent in 1997 for an assay that could detect antibodies to polymers.

The clinical significance of the presence of anti-squalene antibodies, if they exist, is unknown. Any relationship with squalene and squalene antibodies to illnesses among Gulf War veterans is unknown. Squalene is normally present in humans as part of the body's production of cholesterol and skin oils. Current available scientific work focuses on squalene's beneficial role in human health and safety and efficacy as an adjuvant component. There may be alternative explanations for the reported laboratory findings, including: detection of naturally occurring squalene or squalene antibodies; cross-reaction with compounds similar to squalene; elevated levels of squalene due to known or unknown disease processes causing or associated with illnesses in veterans and potentially many other people; or laboratory error or contaminant.

The Research Working Group (RWG) of the Persian Gulf Veterans Coordinating Board has asked the Tulane investigators to submit for research funding to validate their testing, which to date they have not. The RWG's commitment to non-Government and Federal researchers and to Gulf War veterans is to support and fund research on potential causes of illnesses in Gulf War veterans. The RWG is interested in evaluating whether illnesses in service members may be associated with a specific antigenic marker, such as antibodies to squalene. The RWG, however, found no indication that squalene was ever used as an adjuvant in the anthrax vaccine and concurs with the DoD and FDA finding that no vaccines with squalene-containing adjuvants were given to U.S. troops deploying to the Gulf War. To investigate the squalene hypothesis, a scientifically proven test for squalene antibodies is needed to assess whether Gulf War veterans have antibodies to squalene.

In response to a DoD solicitation for research on illnesses among Gulf War veterans, a DoD investigator and nationally recognized expert in antibodies to cholesterol and other lipids submitted a research proposal to determine the feasibility of developing a test for antibodies to squalene. The RWG recommended DoD fund this proposal. The recommended funding level was $582,756. The RWG will follow closely the results of this work. This study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and can be detected in human serum. Based on this knowledge, further studies can be pursued to look at the existence of these antibodies in Gulf War veterans and any correlation to disease.

In recommending the portfolio of Gulf War veterans' illnesses research, the RWG has incorporated the use of peer review as a first guiding principle. Research directions, as articulated in solicitations for research, have been based on emergent peer reviewed research results published in the open literature, and upon ongoing assessments of the existing knowledge conducted by independent scientific panels.

Background

Squalene is a relatively simple, linear hydrocarbon. It is a naturally occurring molecule in the human metabolic process that synthesizes cholesterol.[1] Squalene is present in human sebum and cell wall structures. Squalene is also a component of shark liver oil, some vegetable oils, and plant and animal cell membranes.[2] Squalene is an approved dietary supplement in the United States, and is listed in the *Physicians' Desk Reference*. Squalene is used commercially in the cosmetic industry and in sunscreen products.[3]

Epidemiological studies of breast and pancreatic cancer in several Mediterranean populations have demonstrated that increased dietary intake of olive oil, naturally high in squalene, is associated with a small decreased risk or no increased risk of cancer, despite a higher proportion of overall lipid intake. Experimental animal model studies of high dietary fat and cancer also indicate that olive oil has either no effect or a protective effect on the prevention of a variety of chemically induced tumors. As a working hypothesis, it is proposed that the high squalene content of olive oil, as compared to other human foods, is a major factor in the cancer risk-reducing effect of olive oil. Experiments in vitro and in animal models suggest a tumor-inhibiting role for squalene.[4] In addition, studies using squalene in combination with low-dose pravastatin have demonstrated combination therapy significantly reduces total cholesterol and LDL cholesterol and increases HDL cholesterol to a greater extent than either drug alone.[5]

Squalene is one of several components of adjuvant formulations in a variety of vaccines.[6] One common formulation is MF59. MF59 is a safe, practical, and potent adjuvant for use with human vaccines.[7] Toxicology studies in animal models and Phase I-III studies in humans have demonstrated the safety of MF59 with HSV, HIV, and influenza vaccines.[7-17] Hilhers, et al, concluded that reactogenicity and stability but not adjuvanticity of synthetic sulfolipo-polysaccharide/squalane/water formulations depended on the molecular weight of synthetic sulfolipo-polysaccharide and that synthetic sulfolipo-cyclodextrin/squalane/water is a promising non-mineral oil adjuvant as it combines strong adjuvanticity (i.e., better than the mineral oil-based adjuvant presently applied) with low reactogenicity and good stability.[18]

However, Lorentzen has reported that the cholesterol precursor squalene (C30H50), through nonspecific activation of the immune system, can precipitate arthritis in rats. Using arthritis-prone rat strains to search for disease-triggering factors among molecules which initially induce innate defense reactions rather than specific immune responses, Lorentzen reported on the potential for endogenous lipids to precipitate arthritis.[19] In addition, there is evidence that in some instances squalene has a negative effect on the nervous system.[20-21]

Pamela B. Asa, Ph.D., an unaffiliated molecular biologist from Memphis, Tennessee and Yan Cao, M.D. and Robert F. Garry, Ph.D., from Tulane University, New Orleans, Louisiana have theorized that illnesses afflicting veterans of the Gulf War are an atypical connective tissue disease (an autoimmune disease) resulting from use of the vaccine adjuvant, squalene.[22] These investigators have reportedly developed an immunoassay for detecting anti-squalene antibodies and used the assay to test blood serum samples from various patient and control groups.

Two studies reportedly involved Gulf War veterans. In an unblinded study, samples from 86 Gulf War veterans, both healthy and ill individuals, were tested with 69% tested positive; in 48 samples from blood donors tested, 5% tested positive; in 40 samples from patients with lupus, 10% tested positive; in

30 chronic fatigue patients tested, 15% tested positive; in 30 silicone breast implant patients tested, 10% tested positive. In a blinded study of 38 deployed individuals who were ill, 12 deployed individuals who were healthy, and 6 non-deployed individuals who were ill (all of the non-deployed individuals had reportedly received the full compliment of immunizations given to those who were deployed to the Gulf theater) 95% of the deployed ill tested positive for anti-squalene antibodies, none of the deployed healthy individuals tested positive, and 100% of the non-deployed ill individuals tested positive. They reportedly have found antibodies to squalene in 95% of overtly ill "Gulf War Syndrome" patients and 100% of "Gulf War Syndrome" patients fully immunized for service in Desert Storm/Desert Shield who did not deploy.[23]

Discussion

Pamela B. Asa, who has worked in the area of rheumatology and silicone-gel breast implants, presented a theory of "human adjuvant disease" and its possible link to Persian Gulf War (PGW) veterans' illnesses in 1995. She theorized that silicone adjuvant (an agent added to a vaccine to increase antigenic response) was responsible for PGW veterans developing "human adjuvant disease".[24] An independent scientific review of Dr. Asa's September 13, 1995 "Report on Gulf War Syndrome" found the basic hypothesis and supporting evidence presented was based on a series of erroneous assumptions and unsupported conjectures.[25] A similar review by the Medical, Chemical and Biological Defense Research Program found the basic hypothesis and supporting evidence presented by Dr. Asa were flawed or inaccurate.[26] Available information strongly argues against Dr. Asa's hypothesis:

> All vaccines used during the Gulf War have a long history of safety and all, except BotTox that was used under an IND, were licensed by the FDA at the time of the Gulf War.
>
> Since the standard immunization series is given to individuals in basic and advanced training, only a relatively small number of additional vaccines were given prior to or during deployment to the Persian Gulf, and the previous use of these vaccines has not resulted in problems similar to those reported by GW veterans.
>
> All vaccine lots are individually licensed for safety and efficacy. The vaccines used, therefore, are unlikely to be contaminated or of low quality.
>
> The only adjuvant used in the vaccines given to Gulf War personnel was alum.
>
> Several recent studies have failed to show any association between silicone-gel implants and increased incidence of connective tissue disease. There is little supporting evidence, other than anecdotal reports, that silicone-gel implants cause an increase in connective tissue diseases or human adjuvant disease.

Dr. Asa's current work focuses on the presence of antibodies to squalene in a cohort of 142 Gulf War era veterans or military employees. She theorizes that "Gulf War Syndrome" manifests a spectrum of signs and symptoms similar to that of other atypical connective tissue diseases and that most "Gulf War Syndrome" patients have serum antibodies to squalene, an immunological adjuvant. The study protocol attributes the hypotheses to findings in one (1) patient from a NIH-sponsored trial using squalene as an adjuvant.[22] The findings of the current unpublished work apparently originate from samples collected under this protocol. It is unknown if informed consent was obtained from individuals submitting samples for testing or if an Institutional Review Board (IRB) reviewed and approved the research protocol. The findings from the study must be interpreted with caution as flawed methodology including biased sample selection and potential confounders weaken any potential association. The following information also strongly argues against the current hypothesis:

> If, in fact, antibodies to squalene are present in Gulf War veterans, the clinical significance of finding these antibodies in humans is unknown. Squalene is normally present in humans as part of the body's production of cholesterol. In addition, it is found in human sebum (skin oils) and plant and animal cell membranes. Antibodies to cholesterol in humans are common.[41]
>
> There may be alternative explanations for the reported laboratory findings including: detection of naturally occurring squalene; cross-reaction with compounds similar to squalene; elevated levels of squalene due to a known or unknown disease process causing or associated with human illnesses; or laboratory error or contaminant.

If in fact anti-squalene antibodies are present in the blood of Gulf War-era veterans, this is not sufficient to establish an association of squalene or squalene antibodies with any illness(es) among Gulf War veterans.

The assay for anti-squalene antibodies, which independent researchers at Tulane University developed, has not been validated at other laboratories nor have their findings been subjected to minimal peer review through publication in the scientific literature.

No experimental adjuvants were used by the military in vaccines administered to deploying military personnel.

The anthrax vaccine administered to service members during the Gulf War and given to them now did not and does not contain squalene.

The Army Surgeon General has verified that the anthrax vaccine was never produced at any alternate production facilities in the U.S. during the Gulf War, and anthrax vaccine production at the Michigan Biologic Products Institute (MBPI, now BioPort) never contained squalene. Stanford Research Institute, International has recently completed verification testing for squalene on 6 lots of anthrax vaccine and confirmed that no squalene was detectable in any of the vials.

There are no data demonstrating increased rates of autoantibodies in ill Gulf War veterans.

Unfortunately, we cannot be sure that antibodies to a synthetic squalene adjuvant were actually detected. The authors reportedly used a variation of a previously described assay.[27] This technique was used to claim findings of the first evidence from a blinded study of the existence of a laboratory marker that correlates with the severity of local and systemic complications in silicone breast implant recipients. The assay in question detects antibodies, not to silicone, but to a synthetic polymer whose characteristics have not been fully described. In subsequent letters to the editor, many noted the methodological flaws in the study, argued that since the antibody is not against silicone, there was no reason to suppose the implants had anything to do with the symptoms or antipolymer antibody assay test results, and noted that the investigators had reported similar high seroactivity in fibromyalgia patients.[28] A Committee named by the Institute of Medicine (IOM) recently reported that a careful study of all the evidence indicates that women with silicone breast implants are no more likely to develop chronic disease than women without the implants. The IOM Committee did not address antipolymer antibodies; however, they stated that "The clinical significance of a recently described antipolymer antibody test is unclear, although the polymer in question is not silicone or silicon containing, and it is extremely unlikely that it measures an antisilicone antibody."[29] Dr. Garry and Tulane University reportedly received a U.S. patent in 1997 for a antipolymer antibody (APA) assay for partially polymerized acrylamide[27].

In a letter from Dr. Gerry to DoD, Re: Anti-Squalene Antibodies, dated May 7, 1999, Dr. Gerry informed DoD that Tulane University Medical Center had applied for a patent on the use of anti-squalene antibodies in assessing Gulf War Syndrome. Dr. Gerry also informed DoD that Tulane was the sole owner of the intellectual property provided in the letter of May 7, and that DoD should share the data only with those who have a specific need to know. In this letter, Dr. Gerry reviewed the specifics of the anti-squalene antibody assay, or ASA Assay, that measures the binding of serum immunoglobulins to squalene.

Dr. Garry provided the manuscript outlining the details of his proposed assay to the Office of the Surgeon General (OTSG) U.S. Army, for review. It was the opinion of the reviewers, COL Alving and Dr. Matyas, that there were "dozens of important technical and theoretical flaws" in the assay -- many described by COL Alving as "fatal flaws." Dr. Garry had informed COL Alving and Dr. Matyas that, "even in the absence of peer-reviewed scientific validation, the patent rights to the technology for

measuring antibodies to squalene had been exclusively licensed by Tulane University for commercial development by a company called, Autoimmune Technologies, L.L.C." According to COL Alving, Dr. Gerry was also unaware of the scientific literature that exists on antibodies to cholesterol.

Excerpts of the General Accounting Office (GAO) report entitled, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" stated that independent researchers had developed a test based on a Western blot assay and had detected antibodies to squalene in the blood of sick Gulf War veterans. If the description of the test described in the GAO report is accurate, there are some technical points that would seem to invalidate such a test:

> Squalene is a non-charged long chain hydrocarbon that would not be expected to migrate on a gel such as required in a Western blot assay.
>
> Because squalene lacks charge, it would not be expected to transfer to nitrocellulose as is done in a Western blot assay.

A recently released *Vanity Fair* article, "The Pentagon's Toxic Secret," alleges that the Department of Defense possibly used "an illicit and secret anthrax vaccine" on its own soldiers.[31] According to a Vanity Fair news release, "the licensed formula for...anthrax vaccine may have been altered, without formal FDA approval, to contain an experimental, and potentially dangerous, additive. The additive—squalene—improves vaccine effectiveness but causes incurable diseases in lab animals and may be the cause of some cases of Gulf War syndrome." The author refers to declassified DoD documents from the Gulf War era that report on plans to expand the availability of a variety of vaccines. Some of the documents have been available for over two years on the Department's GulfLINK website. The *Vanity Fair* article also suggests that the modified anthrax vaccine "may be part of the stockpile now being administered in the wake of the DoD's December 1997 decision to immunize 2.4 million people in the armed services against anthrax."

The speculations, allegations and reported "clinical evidence" are not new. A *Washington Times* article, "Anti-HIV mix found in Gulf veterans," alleged that there was evidence of squalene, an experimental vaccine adjuvant, in the blood of ill Gulf War veterans.[32] Subsequent *Insight on the News* articles included "Sickness and Secrecy," "The Gulf War Mystery," "Gulf War Mystery and HIV," "Breakthrough on Gulf War Illness," and "GAO Calls for Squalene Tests."[33-37] A NewsWatch Associate editor presented a review of the press allegations entitled "Vanity Scare" in May 1999.[38]

On March 29, 1999, Congressman Jack Metcalf (Washington) announced the release of a GAO report, which he had requested, regarding squalene antibodies in veterans suffering from Gulf War illnesses. The GAO Report, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" (GAO/NSIAD-99-5) recommended that DoD "conduct research designed to replicate or dispute the independent research results that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans."[39] The GAO did a limited literature review for their investigation. The GAO incorrectly stated in the final report that DoD had not responded to the findings of Dr. Asa. The GAO also stated that DoD could "develop such an assay inexpensively and test it on a sample of sick Gulf War-era veterans." The GAO took for fact that antibodies to squalene are present in the blood of ill Gulf War veterans and failed to cite previous reviews of the issue, including the reviews by the FDA and the Senate Special Investigations Unit. The GAO did not comment on the ethical conduct of the research including informed consent and IRB review of the protocol. The GAO did note that Chiron and Ribi ImmunoChem reported that their squalene adjuvant formulation had been tested on over 9,000 and 1,000 human subjects, respectively.

The presence of anti-squalene antibodies in the blood of Gulf War era veterans would not establish an association of squalene or squalene antibodies with illnesses among Gulf War veterans. The clinical significance of finding antibodies to squalene in humans, if antibodies to squalene do in fact exist, is unknown. Squalene is normally present in humans as part of the body's production of cholesterol. It is found in human sebum (skin oils) and plant and animal cell membranes. The scientific work that has been done on squalene's role in human health and disease notes the positive effects of dietary squalene on cancer prevention and cholesterol regulation and the safety and efficacy of squalene as a vaccine adjuvant. There may be alternative explanations for the reported laboratory findings including: detection of antibodies to cholesterol;[40-43] detection of antibodies to naturally occurring squalene; cross-reaction with compounds similar to squalene; elevated levels of squalene due to a known or unknown disease process causing or associated with human illnesses; or laboratory error or contaminant.

The assay for anti-squalene antibodies developed by independent researchers at Tulane University has not been minimally validated through publication in the scientific literature. The investigators have reportedly submitted a manuscript to a peer-reviewed medical journal; to date, however, this effort apparently has not been successful. Until their findings are published in the scientific literature, reviewed by other scientists, and replicated by independent research, we cannot make a reasonable judgment on whether antibodies to squalene exist and if so, why antibodies to squalene are found in the blood of Gulf War veterans.

There is no basis for believing that Gulf War era veterans were exposed to squalene-containing vaccines. Military members did not receive any vaccines containing squalene during the Gulf War. There is absolutely no evidence that Gulf War veterans or other U.S. service members received "modified anthrax vaccine" or "experimental" AIDS vaccines. Approximately 8,000 service members deployed to the Gulf did receive botulinum toxoid vaccine as an investigational new drug. The MBPI, producer of vaccines against the biological warfare agents anthrax and botulinum toxoid, verified that they have never used adjuvant formulations containing squalene in their vaccines.

In their investigations of illnesses among Gulf War veterans, the Senate Special Investigations Unit (SIU) assessed the theory that vaccines used during the Gulf War contained squalene.[44] In their report, the SIU states that according to the Food and Drug Administration (FDA), squalene can be contained in a vaccine due to two different processes: 1) as an adjuvant, which is an agent to enhance the immune response; 2) in minute quantities in vaccines manufactured using eggs, since eggs are rich in squalene and cholesterol. The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant. The SIU found no credible information to the contrary. A recent assessment by the Canadian military verified that no squalene was present in any vaccines used by their forces.[45]

Since the Gulf War, squalene has been a component of vaccines undergoing limited testing by the Walter Reed Army Institute of Research (WRAIR). Volunteers received the vaccines in well-controlled studies that followed Food and Drug Administration (FDA) regulations. Squalene is one of several components of the adjuvants found in each of two vaccine products undergoing testing by WRAIR. Pharmaceutical grade squalene is used to produce the oil emulsion used in these vaccine products. The exact compositions of the adjuvant in these vaccines are proprietary and belong to DoD Cooperative Research and Development Agreement (CRDA) partners. Development, evaluation, and FDA approval for the use of these adjuvant systems has been conducted by DoD CRDA partners and WRAIR. The two vaccines are investigational products for the prevention of malaria and human

immunodeficiency virus (HIV) infection. Information on the study on the HIV vaccine has not yet been published and is considered proprietary information. Information on the study involving malaria vaccine has been published in the scientific literature.[46]

Prior to its use in humans, the vaccines containing the emulsion underwent extensive FDA-mandated Good Laboratory Practices repeat dose toxicology studies involving rodents, rabbits, guinea pigs and nonhuman primates. The details of these studies (four volumes) were filed with the FDA as part of the Investigational New Drug (IND) application. The studies revealed anticipated inflammatory responses surrounding the site of injection. No gross changes were observed. No laboratory abnormalities were found.

The Office of the Army Surgeon General (OTSG) requested an update in early May 1999 on investigations, tests, and projects to investigate allegations regarding squalene in the anthrax vaccine and plans for developing an assay for squalene antibodies.[30] In the update, the Army stated that all lots of the anthrax vaccine released by DoD would be tested and that current testing to date by Stanford Research Institute International, confirmed that no squalene was detectable in any of the vials. FDA is doing additional testing.

The RWG is confronted with the prospect of antibodies to squalene in the blood of Gulf war veterans as addressed in the GAO report and also in the articles that appeared in the journal *Insight*, *Vanity Fair*, and various other media. These articles suggest that antibodies to squalene may be linked to "Gulf War Syndrome." However, the more important question is whether or not antibodies to squalene actually exist. Since squalene is being used as an adjuvant in some of the newer vaccines, this question becomes of interest not only to the military but also to the general public. Squalene is also being examined as a dietary supplement that reduces the risk of cancer formation.

Squalene may not be immunogenetic by itself, but under some circumstances antibodies to the compound may arise. Although antibodies to cholesterol and possibly squalene occur naturally, this does not necessarily mean they do not have an adverse effect. The dynamics of the system and the threshold at which an autoimmune-like situation may arise are not known.

The RWG commitment to Gulf War veterans and civilian and Federal researchers is to support and fund research on potential causes of illnesses in Gulf War veterans. The RWG is interested in looking at whether illnesses in service members may be associated with a specific antigenic marker, such as antibodies to squalene. However, the RWG found no indication that squalene was ever used as an adjuvant in the anthrax vaccine and concurs with the DoD and FDA finding that no vaccines with squalene-containing adjuvants were given to U.S. troops deploying to the Gulf War. To investigate the squalene hypothesis, a scientifically proven test for squalene antibodies is needed. In response to a DoD solicitation for research on illnesses among Gulf War veterans, a DoD investigator and nationally recognized expert in antibodies to cholesterol and other lipids submitted a research proposal to determine the feasibility of developing a test for antibodies to squalene. The RWG recommended DoD fund this proposal. However, in accordance with the scientific peer review evaluation, the study was recommended for funding only for the purpose of determining whether antibodies for squalene are actually present. The recommended funding level was $582,756. The RWG will follow closely the results of this work. If other scientist submits for funding a research proposal for further studies of the alleged findings of antibodies to squalene, the RWG should ensure that the proposal receives scientific and programmatic evaluation.

In recommending the portfolio of Gulf War veterans' illnesses research, the RWG has incorporated the use of peer review as a first guiding principle. Research directions, as articulated in solicitations for research, have been based on emergent peer reviewed research results published in the open literature, and ongoing assessments of the existing knowledge conducted by independent scientific panels. There is no evidence to support the allegations that squalene was used as a vaccine component in vaccines administered to Gulf War veterans. Based on current knowledge, the presence or absence of squalene antibodies does not appear to be important in the evaluation, diagnosis, and treatment of Gulf War veterans for autoimmune disease, rheumatic symptoms, or other illnesses.

The misrepresentation of this work and allegations of an ongoing conspiracy by the media and others is troubling. These allegations may in fact be contributing to Gulf War veterans' illnesses through exacerbation of the somatic distress of patients by heightening their fears and pessimistic expectations and prolonging their disability. The currently funded study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and can be detected in human serum. Based on this knowledge, further studies can be pursued to look at the existence of these antibodies in Gulf War veterans and their correlation to disease.

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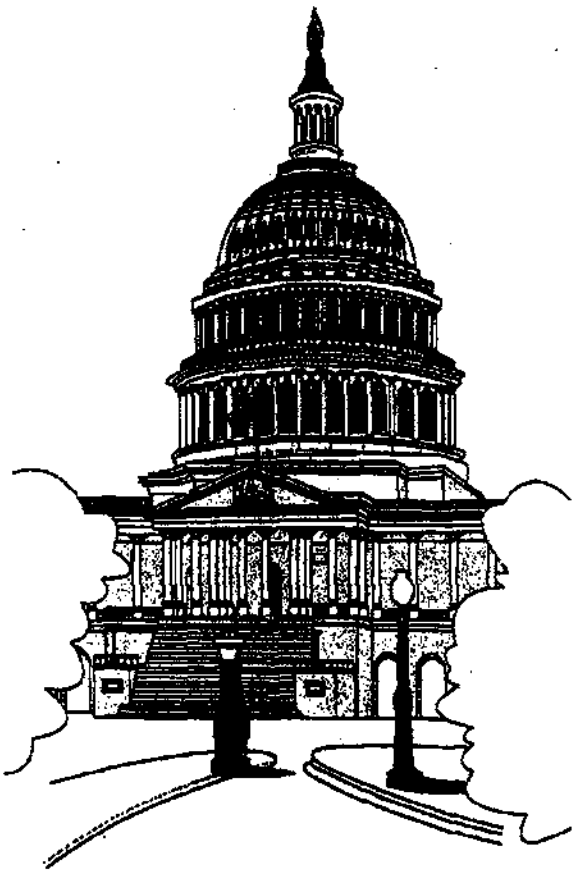
REPORT TO CONGRESS

GULF WAR ILLNESS



Development and Validation of an Assay to Test for the Presence of Squalene Antibodies

Executive Summary

This Report has been prepared in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill:

> The Committee concurs with the findings of a recent GAO report on squalene antibodies and is concerned by the Department's reluctance to test for squalene antibodies since squalene is a potential contributing factor in illnesses of veterans of the Persian Gulf War. The Secretary of Defense is directed to develop and/or validate the assay to test for the presence of squalene antibodies. A report detailing the proposals to carry out this requirement shall be submitted to the Committee by January 1, 2000.

A May 1999 *Vanity Fair* article, "The Pentagon's Toxic Secret," alleged that the Department of Defense possibly used "an illicit and secret anthrax vaccine" on its own soldiers.[31] According to a Vanity Fair news release, "the licensed formula for...anthrax vaccine may have been altered, without formal FDA approval, to contain an experimental, and potentially dangerous, additive," squalene, that reportedly "causes incurable diseases in lab animals and may be the cause of some cases of Gulf War syndrome." The *Vanity Fair* article went on to suggest that the modified anthrax vaccine "may be part of the stockpile now being administered in the wake of the DoD's December 1997 decision to immunize 2.4 million people in the armed services against anthrax." A NewsWatch Associate editor presented an opposing review of the allegations entitled "Vanity Scare" in May 1999.[32]

On March 29, 1999, Congressman Jack Metcalf announced the release of a General Accounting Office (GAO) report, which he had requested, regarding squalene antibodies in veterans suffering from Gulf War illnesses. The GAO Report, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" (GAO/NSIAD-99-5) recommended that DoD "conduct research designed to replicate or dispute the unpublished independent research results that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans."[33]

In its investigations of illnesses among Gulf War veterans, the Senate Special Investigations Unit (SIU) found no credible information indicating that vaccines used during the Gulf War contained squalene.[38] In its report, the SIU stated that according to the Food and Drug Administration (FDA), squalene can be contained in a vaccine due to two different processes: 1) as an adjuvant, which is an agent to enhance the immune response; or 2) in minute quantities in vaccines manufactured using eggs, since eggs are rich in squalene and cholesterol. The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant.

To investigate the squalene hypothesis, a scientifically proven test for squalene antibodies is needed to assess whether Gulf War veterans have antibodies to squalene. In response to a DoD solicitation for research on illnesses among Gulf War veterans, a DoD investigator and nationally recognized expert on antibodies to cholesterol and other lipids submitted a research proposal to determine the feasibility of developing a test for antibodies to squalene.

The funded research project to determine whether antibodies to squalene exist has five main objectives:

1) Development and validation of an ELISA assay for antibodies to squalene.
2) Evaluation and potential development of other assays for antibodies to squalene.

3) Development of a positive control antibody to squalene.
4) Production of the positive control antibody to squalene for use in the assays.
5) Testing of normal human serum for antibodies to squalene by ELISA and other methods.

The DoD funded study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and can be detected in human serum.

Background

Squalene is a relatively simple, linear hydrocarbon. It is a naturally occurring molecule in the human metabolic process that synthesizes cholesterol.[1] Squalene is present in human sebum and cell wall structures. Squalene is also a component of shark liver oil, some vegetable oils, and plant and animal cell membranes.[2] It is licensed by the FDA as a dietary supplement in the United States and is listed in the *Physicians' Desk Reference*. Squalene is used commercially in the cosmetic industry and in sunscreen products.[3]

Epidemiological studies of breast and pancreatic cancer in several Mediterranean populations have demonstrated that increased dietary intake of olive oil is associated with a small decreased risk or no increased risk of cancer, despite a higher proportion of overall lipid intake. Experimental animal model studies of high dietary fat and cancer also indicate that olive oil has either no effect or a protective effect on the prevention of a variety of chemically induced tumors. As a working hypothesis, it is proposed that the high squalene content of olive oil, as compared to other human foods, is a major factor in the cancer risk-reducing effect of olive oil. Experiments in vitro and in animal models suggest a tumor-inhibiting role for squalene.[4] In addition, studies using squalene in combination with low-dose pravastatin have demonstrated combination therapy significantly reduces total cholesterol and LDL cholesterol and increases HDL cholesterol to a greater extent than either drug alone.[5]

Squalene is one of several components of adjuvant formulations in a variety of vaccines.[6] One common formulation is MF59. MF59 is a safe, practical, and potent adjuvant for use with human vaccines.[7] Toxicology studies in animal models and Phase I-III studies in humans have demonstrated the safety of MF59 with HSV, HIV, and influenza vaccines.[7-17] Hilhers, et al, concluded that reactogenicity and stability but not adjuvanticity of synthetic sulfolipo-polysaccharide/squalane/water formulations depended on the molecular weight of synthetic sulfolipo-polysaccharide and that synthetic sulfolipo-cyclodextrin/squalane/water is a promising non-mineral oil adjuvant as it combines strong adjuvanticity (i.e. better than the mineral oil-based adjuvant presently applied) with low reactogenicity and good stability.[18]

However, Lorentzen has reported that the cholesterol precursor squalene (C30H50), through nonspecific activation of the immune system, can precipitate arthritis in rats. Using arthritis-prone rat strains to search for disease-triggering factors among molecules which initially induce innate defense reactions rather than specific immune responses, Lorentzen reported on the potential for endogenous lipids to precipitate arthritis.[19] In addition, there is evidence that in some instances squalene has a negative effect on the nervous system.[20-21]

Pamela B. Asa, Ph.D., an unaffiliated molecular biologist from Memphis, Tennessee and Yan Cao, M.D. and Robert F. Garry, Ph.D., from Tulane University, New Orleans, Louisiana have theorized that illnesses afflicting veterans of the Gulf War are an atypical connective tissue disease (an autoimmune disease) resulting from use of the vaccine adjuvant, squalene.[22-23] These investigators have reportedly developed an immunoassay for detecting anti-squalene antibodies and used the assay to test blood serum samples from various patient and control groups.

To investigate this hypothesis, DoD has funded a scientific program which will answer several major questions. Initially, the research staff will determine if antibodies to squalene exist and if an assay can be developed to detect and quantify these antibodies. In addition, an animal model will be used to induce anti-squalene antibodies to use as positive controls to characterize anti-squalene antibodies in

humans. If a positive antibody response to squalene can be induced in mice, then normal human serum can be tested for possible antibodies to squalene. Next, the research program will focus on qualitative detection of squalene and development of a chemical assay. Finally, the research program will examine the biological implications of antibodies to squalene.

Discussion

Pamela B. Asa, who has worked in the area of rheumatology and silicone-gel breast implants, presented a theory in 1995 of "human adjuvant disease" and its possible link to Persian Gulf War (PGW) Veterans' Illnesses. She theorized that silicone adjuvant (an agent added to a vaccine to increase antigenic response) was responsible for PGW veterans developing "human adjuvant disease."[24] A scientific review prepared by an independent non-governmental medical expert on September 13, 1995 of Dr. Asa's "Report on Gulf War Syndrome" found the basic hypothesis and supporting evidence presented was based on a series of erroneous assumptions and unsupported conjectures.[25] A similar review by the Medical, Chemical and Biological Defense Research Program found the basic hypothesis and supporting evidence presented by Dr. Asa were flawed or inaccurate.[26] Available information also strongly argues against Dr. Asa's hypothesis:

- All vaccines used during the Gulf War have a long history of safety and all, except BotTox that was used under an Investigational New Drug (IND), were licensed by the FDA at the time of the Gulf War.
- Since the standard immunization series is given to individuals in basic and advanced training, only a relatively small number of additional vaccines were given during deployment to the Persian Gulf, and the previous use of these vaccines has not resulted in problems similar to those reported by GW veterans.
- All vaccine lots are individually licensed for safety and efficacy. The vaccines used, therefore, are unlikely to be contaminated or of low quality.
- The only adjuvant used in the vaccines given to Gulf War personnel was alum. Alum is an FDA-approved adjuvant with a long history of safety. It has been given to millions of people worldwide without significant problems. No experimental adjuvants were used by the military.
- There are no reports of alum causing human adjuvant disease or any other chronic disease.
- There are no reports of chronic inflammatory responses at the sites of immunization with vaccines containing alum as would be expected if human adjuvant disease were to occur.
- Several recent studies have failed to show any association between silicone-gel implants and increased incidence of connective tissue disease. There is little supporting evidence, other than anecdotal reports, that silicone-gel implants cause an increase in connective tissue diseases or human adjuvant disease.

Dr. Asa's current work focuses on the presence of antibodies to squalene in a cohort of 142 Gulf War-era veterans or military employees. She theorizes that "Gulf War Syndrome" manifests a spectrum of signs and symptoms similar to that of other atypical connective tissue diseases and that most "Gulf War Syndrome" patients have serum antibodies to squalene, an immunological adjuvant. The study protocol attributes the hypotheses to findings in one (1) patient from a NIH-sponsored trial using squalene as an adjuvant.[22] The findings of the current unpublished work apparently originate from samples collected under this protocol. It is unknown if informed consent was obtained from individuals submitting samples for testing or if an Institutional Review Board (IRB) reviewed and approved the research protocol. Review of the draft manuscript indicates the basic hypothesis and supporting evidence presented as flawed or inaccurate. The findings from the study must be interpreted with caution as flawed methodology including biased sample selection and potential cofounders weaken any potential association. The following information also strongly argues against the current hypothesis:

- If in fact antibodies to squalene are present in Gulf War veterans, the clinical significance of finding these antibodies in humans is unknown. Squalene is normally present in humans as part of the body's production of

cholesterol. In addition, it is found in human sebum (skin oils) and plant and animal cell membranes. Antibodies to cholesterol in humans are common.

There may be alternative explanations for the reported laboratory findings, including: detection of naturally occurring squalene; cross-reaction with compounds similar to squalene; elevated levels of squalene due to a known or unknown disease process causing human illnesses, or; laboratory error or contaminant.

If in fact anti-squalene antibodies are present in the blood of Gulf War-era veterans, this is not sufficient to establish an association of squalene or squalene antibodies with any illness(es) among Gulf War veterans.

The assay for anti-squalene antibodies, which independent researchers at Tulane University developed, has not been validated at other laboratories nor have their findings been subjected to minimal peer review through publication in the scientific literature.

The only adjuvant used in the vaccines given to Gulf War personnel was alum. Alum is an FDA-approved adjuvant with a long history of safety. It has been given to millions of people worldwide without significant problems. No experimental adjuvants were used by the military.

The anthrax vaccine given to service members during the Gulf War and subsequently did not and does not contain squalene.

The Army Surgeon General has verified that the anthrax vaccine was never produced at any alternate production facilities in the U.S. during the Gulf War, and anthrax vaccine production at the Michigan Biologic Products Institute (MBPI, now BioPort) never contained squalene. Stanford Research Institute, International has recently completed verification testing for squalene on 6 lots of anthrax vaccine and verified that no squalene was detectable in any of the vials.

There are no data demonstrating increased rates of autoantibodies in ill Gulf War veterans.

Unfortunately, we cannot be sure that the theorists actually detected antibodies to a synthetic squalene adjuvant in the veterans they tested. They reportedly used a variation of a previously described assay.[27] This technique was used to claim findings of the first evidence from a blinded study of the existence of a laboratory marker that correlates with the severity of local and systemic complications in silicone breast implant recipients. The assay in question detects antibodies, not to silicone, but to a synthetic polymer whose characteristics have not been fully described. In subsequent letters to the editor, many noted the methodological flaws in the study, argued that since the antibody is not against silicone, there was no reason to suppose the implants had anything to do with the symptoms or antipolymer antibody assay test results, and noted that the investigators had reported similar high seroactivity in fibromyalgia patients.[28] A Committee named by the Institute of Medicine (IOM) recently reported that a careful study of all the evidence indicates that women with silicone breast implants are no more likely to develop chronic disease than women without the implants. The IOM Committee did not address antipolymer antibodies; however, they stated that "The clinical significance of a recently described antipolymer antibody test is unclear, although the polymer in question is not silicone or silicon containing, and it is extremely unlikely that it measures an antisilicone antibody."[29]

Dr. Garry and Tulane University reportedly received a U.S. patent in 1997 for an assay that could detect antibodies to polymers, of which squalene is one. In a letter from Dr. Garry to DoD, Re: Anti-Squalene Antibodies, dated May 7, 1999, Dr. Garry informed DoD that Tulane University Medical Center had applied for a patent on the use of anti-squalene antibodies in assessing Gulf War Syndrome. Dr. Garry also informed DoD that Tulane was the sole owner of the intellectual property provided in the letter of May 7, and that DoD should share the data only with those who have a specific need to know. In this letter, Dr. Garry reviewed the specifics of the anti-squalene antibody assay, or ASA Assay, that measures the binding of serum immunoglobulins to squalene.

The Office of the Army Surgeon General (OTSG) requested an update in early May 1999 on investigations, tests, and projects to investigate allegations regarding squalene in the anthrax vaccine and plans for developing an assay for squalene antibodies.[30] In the update, the Army stated that all lots of the anthrax vaccine released by DoD would be tested and that current testing to date by Stanford Research Institute, International confirmed that no squalene was detectable in any of the vials. The FDA is doing additional testing. Dr. Garry provided the manuscript outlining the details of his proposed assay to OTSG for review. It was the opinion of COL Alving and Dr. Matyas that there were "dozens of important technical and theoretical flaws" in the assay-many described by COL Alving as "fatal flaws." Dr. Garry had informed COL Alving and Dr. Matyas that, "even in the absence of peer-reviewed scientific validation, the patent rights to the technology for measuring antibodies to squalene had been exclusively licensed by Tulane University for commercial development by a company called, Autoimmune Technologies, L.L.C." Dr. Garry was unaware of the scientific literature that exists on antibodies to cholesterol. When informed of the antibodies to cholesterol by COL Alving, Dr. Garry "agreed that the purported antibodies that he observed might well represent antibodies that react with cholesterol."

Excerpts of the GAO report entitled, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" stated that independent researchers had developed a test based on a Western blot assay and had detected antibodies to squalene in the blood of sick Gulf War veterans. If the description of the test described in the GAO report is accurate, there are some technical points that would seem to invalidate such a test:

> Squalene is a non-charged long chain hydrocarbon that would not be expected to migrate on a gel such as required in a Western blot assay.
>
> Because squalene lacks charge, it would not be expected to transfer to nitrocellulose as is done in a Western blot assay.

On March 29, 1999, Congressman Jack Metcalf (Washington) announced the release of a GAO report, which he had requested, regarding squalene antibodies in veterans suffering from Gulf War illnesses. The GAO Report, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" (GAO/NSIAD-99-5) recommended that DoD "conduct research designed to replicate or dispute the independent research results that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans."[33] The GAO did not comment on the ethical conduct of the research including a requirement for informed consent and IRB review of the protocol. The GAO did note that Chiron and Ribi ImmunoChem reported that their squalene adjuvant formulation had been tested on over 9,000 and 1,000 human subjects, respectively.

The clinical significance of finding antibodies to squalene is unknown. Squalene is normally present in humans as part of the body's production of cholesterol. It is found in human sebum (skin oils) and plant and animal cell membranes. The scientific work that has been done on squalene's role in human health and disease notes the positive effects of dietary squalene on cancer prevention and cholesterol regulation and the safety and efficacy of squalene as a vaccine adjuvant. There may be alternative explanations for the reported laboratory findings, including: detection of antibodies to cholesterol;[34-37] detection of antibodies to naturally occurring squalene; cross-reaction with compounds similar to squalene; elevated levels of squalene due to a known or unknown disease process causing human illnesses, or; laboratory error or contaminant.

The assay for anti-squalene antibodies developed by independent researchers at Tulane University has not been minimally validated through publication in the scientific literature. The investigators have

reportedly submitted a manuscript to a peer-reviewed medical journal; to date, however, this effort apparently has not been successful.

Since the Gulf War, squalene has been a component of vaccines undergoing testing by the Walter Reed Army Institute of Research (WRAIR). Volunteers received the vaccines in well-controlled studies that followed FDA regulations. Squalene is one of several components of the adjuvants found in each of two vaccine products undergoing testing by WRAIR. Pharmaceutical grade squalene is used to produce the oil emulsion used in these vaccine products. The exact compositions of the adjuvant in these vaccines are proprietary and belong to DoD Cooperative Research and Development Agreement (CRDA) partners. Development, evaluation, and FDA approval for the use of these adjuvant systems has been conducted by DoD CRDA partners and WRAIR. The two vaccines are investigational products for the prevention of malaria and human immunodeficiency virus (HIV) infection. Information on the study on the HIV vaccine has not yet been published and is considered proprietary information. Information on the study involving the malaria vaccine has been published in the scientific literature.[39]

Prior to its use in humans, the vaccines containing the emulsion underwent extensive FDA-mandated Good Laboratory Practices repeat dose toxicology studies involving rodents, rabbits, guinea pigs and nonhuman primates. The details of these studies (four volumes) were filed with the FDA as part of the IND application. The studies revealed anticipated inflammatory responses surrounding the site of injection. No gross changes were observed. No laboratory abnormalities were found.

Conclusion

Allegations of an ongoing conspiracy by the media and others is troubling. Squalene is not a foreign substance. It is normally present in the human body in large quantities because it is a precursor to the biosynthesis of cholesterol in the liver. The DoD funded study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and if they can be detected in human serum. Since squalene is being used as an adjuvant in some newer generation vaccines, this question becomes of interest not only to the military but also to the general public. Previously, these investigators were able to demonstrate antibodies to cholesterol. Squalene may not be immunogenic by itself, but under certain circumstances antibodies to the compound may arise. Although antibodies to cholesterol and possibly squalene occur naturally, this does not necessarily mean they have an adverse effect.

This research proposal was submitted in response to a competitive solicitation for proposals. The proposal was peer reviewed independent of the Department, by the American Institute of Biological Sciences, and received a high scientific merit score. Programmatic review was accomplished by the Department and the Research Working Group of the Persian Gulf Veterans Coordinating Board. Based on the results of this research, further studies can be pursued, if appropriate, to look at the existence of these antibodies in Gulf War veterans and their correlation to disease.

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CONGRESSIONAL or SPECIAL CORRESPONDENCE

CMAT: 0202

Date: 7/21

Office of Special Assistant fo[redacted]r I[redacted]
Internal Routing/Tas[redacted]eet

Coord/ Routing	Position/Organization		Action	Info	Comments
	Special Assistant	(SA)			
3	Deputy Special Assistant	(DSA)	✓ 7-21		For Signat
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	Executive Assistant to DSA	(EADSA)			
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Prepare reply for signature of:
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☐ Congress ☐ Oversight ☐ FOIA ☐ OSD ☐ WBM ☐ VSO/MSO ☐ Outgoing
☐ Ltr to SA ☐ IR ☐ E-Mail ☐ OGA ☐ Other ☐ Veteran

KEYWORDS:

05/11/00 Issuance

SPECIAL ASSISTANT
FOR
GULF WAR ILLNESSES

OFFICE OF THE SECRETARY OF DEFENSE
1000 DEFENSE PENTAGON
WASHINGTON, DC 20301-1000

JUL 21 2000

✓ 7-21

MEMORANDUM FOR DEPUTY SPECIAL ASSISTANT FOR GULF WAR ILLNESSES

THROUGH: Project Manager, Gulf War Illnesses

FROM: Medical Outreach and Issues
Dr. Michael E. Kilpatrick MEK

SUBJECT: Health Affairs response to Congressman Jack Metcalf on the AFEB review of the Antibodies to Squalene in Gulf War Syndrome article by Dr. Pam Asa (Tab C)

PURPOSE: To provide coordination on the response (Tab B)

DISCUSSION: The proposed response forwards to MOC Metcalf a copy of the AFEB review of Dr. Asa's work with squalene. Background information on this issue is provided at Tab D.

The review of the Antibodies to Squalene paper by the subcommittee of the AFEB is a brutally scientific assessment. The flaws of the study design, laboratory procedures and analysis of data precluded the researchers from validating their conclusions.

The interesting part of the assessment by the AFEB subcommittee is that they suggested the authors participate in a replication of their study using a study design that eliminates the flaws in their published work. This would include an appropriate selection (and defining) of the study participants, an appropriate blinding of the samples with chain of custody, and a comparison of laboratory results by Dr Garry with those from other lipid laboratories using more standard antibody techniques.

RECOMMENDATION: Concur and sign the coordination memo at Tab A

July 14, 2000

MEMORANDUM FOR ACTING ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: John F. Mazzuchi, Ph.D., DASD (Clinical & Program Policy)
Prepared by LtCol Riddle, Program Director, Public Health

SUBJECT: Response to Member of Congress request for further objective analysis of an article recently published in the February 2000 issue of *Experimental and Molecular Pathology* – ACTION MEMORANDUM

BACKGROUND: Tab A is a 3 Mar, 2000 letter from Congressman Jack Metcalf (R-Washington) regarding an article published in the February 2000 issue of *Experimental and Molecular Pathology* (TAB B). Congressman Metcalf is asking for further objective analysis of the article, "Antibodies to Squalene in Gulf War Syndrome," by Dr. Parn Asa and colleagues.

The response to the 3 Mar, 2000 letter (Tab C) informs Congressman Metcalf that DoD has requested on his behalf the Armed Forces Epidemiological Board (AFEB) to convene a subcommittee of experts to review and critique this work.

DISCUSSION: The AFEB found that:

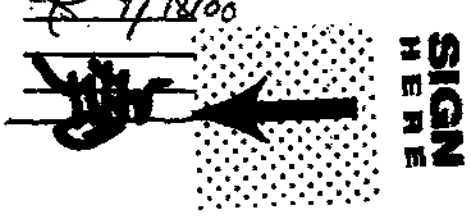
- The research reported in the paper does not support the claim that the test for squalene may identify individuals ill with "Gulf War Syndrome."
- The paper contains numerous shortcomings, several of them serious, that combine to invalidate the authors' findings.
- It remains unclear if the assay actually measures antibodies to squalene, as the authors assert; the assay may measure something else or their findings may be a non-specific chemical reaction.

The AFEB analysis supports the previous assessment of Dr. Asa's work provided to Congressman Metcalf on 24 Feb 2000 (TAB D).

RECOMMENDATION: ASD(HA) sign memorandum and forward response to Congressman Metcalf.

COORDINATION:
LA
PD(HOP)
DUSD(S&T)BIOSystems
COS
OSA6W1

7/18/00



THE ASSISTANT SECRETARY OF DEFENSE

1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

Honorable Jack Metcalf
United States House of Representatives
Washington, DC 20515-4702

Dear Representative Metcalf:

I am pleased to provide for you the additional objective analysis requested of the article "Antibodies to Squalene in Gulf War Syndrome" published in the February 2000 issue of *Experimental and Molecular Pathology*. The Armed Forces Epidemiological Board convened a subcommittee of experts to review and critique this article and the attached response was unanimously endorsed and approved by the Board.

I hope we have answered the questions raised in your letter. Thank you for your interest in the health of Gulf War veterans.

Sincerely,

J. Jarrett Clinton, MD, MPH
Acting Assistant Secretary

Attachment:
As stated

cc:
Special Assistant for Gulf War Illnesses

(56)

OFFICE OF THE SECRETARY OF DEFENSE
WASHINGTON, DC 20301

22 AUG 2000

MEMORANDUM FOR DEPUTY ASSISTANT TO THE SECRETARY OF DEFENSE
(CHEMICAL AND BIOLOGICAL DEFENSE)
DEPUTY DIRECTOR FOR MEDICAL READINESS, OFFICE OF THE JOINT CHIEFS OF STAFF
COMMANDER, U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
ASSISTANT CHIEF, OPERATIONAL MEDICINE AND FLEET SUPPORT, U.S. NAVY BUREAU OF MEDICINE AND SURGERY
COMMANDER, 311th HUMAN SYSTEMS WING, AIR FORCE MATERIEL COMMAND

SUBJECT: Minutes of the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee Meeting

The minutes of the ASBREM Committee meeting, July 11, 2000, are provided for your information. The briefing material distributed at the meeting has been integrated into the meeting minutes that were subsequently coordinated through the ASBREM Secretariat.

A summary of action items can be found on page 13 of the minutes. If you have any questions concerning the meeting or resultant actions, please contact Mr. (b)(6), ASBREM Executive Secretary, at (voice) (b)(6), (fax) (b)(6), or (e-mail) (b)(6)@acq.osd.mil.

J. Jarrett Clinton, MD, MPH
Acting Assistant Secretary of Defense
(Health Affairs)

Robert Foster, Ph.D.
Director, BioSystems
Office of the Deputy Under Secretary
of Defense (Science and Technology)

Attachments

cc: Dr. Cirone
Col Cropper
COL Glenn
CAPT Frank
LTC Ross
LTC Unger
Dr. Sheridan

Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee

Meeting Agenda
Tuesday, July 11, 2000, 1300-1500
Room 3, Conference Center, 15th Floor, 1777 N. Kent Street, Rosslyn, Virginia

Item	Topic	Presenter
1.	Welcome and introductions	Dr. Foster
2.	Lightweight chemical biological protection for future soldier systems	Dr. Wilusz
3.	Joint Vaccine Acquisition Program	Mr. Paul, JVAP PM
4.	Partition of biological threats between JTCG-2 and JTCG-4, and common bio and emerging infectious disease threats	COL Glenn
5.	Status Report: Modification of Title 10, Sec. 980	Dr. Cirone
6.	Observation from Human Systems TARA: Reliance Panel Partnering	Dr. Foster
7.	Vaccine Development Seminar	Dr. Foster
8.	Joint Medical S&T Assessment	CAPT Lane
9.	New business • NGIC assessment/thermobarics • Panel members for the next TARA	General Discussion
10.	Next meeting date	General Discussion
11.	Summary and adjournment	Dr. Foster

Minutes of the ASBREM Committee Meeting
Tuesday, July 11, 2000, 1300-1500
Room 3, Conference Center, 15th Floor, 1777 N. Kent Street, Rosslyn, Virginia

1. Welcome and Introductions

Dr. Robert Foster, Director, Bio Systems, Office of the Deputy Under Secretary of Defense (Science and Technology) [ODUSD (S&T)], called the meeting to order and welcomed the attendees, asking them to introduce themselves.

The following ASBREM Committee and ASBREM Secretariat (ASEC) members or representatives were present:

Dr. Robert Foster, Director Bio Systems, ODUSD(S&T) [Representing Dr. Hans Mark, Director of Defense Research and Engineering], Chair
Dr. Salvatore Cirone, ASD(HA), ASEC [Representing RADM J. Jarrett Clinton, M.D., M.P.H., USPHS, DASD(HA)(HOP)], co-Chair
Dr. Anna Johnson-Winegar, DATSD(CBD)
RADM Richard Mayo, MC, USN, J-4 (Medical Readiness Division)
Brig Gen Lloyd Dodd, MC, USAF, 311th HSW/CC
COL J. Frazier Glenn, MS, USA, ASEC [Representing MG John Parker, MC, USA, USAMRMC]
CAPT Steve Hart, MC, USN, Assistant Chief, Operational Medicine and Fleet Support, Navy Bureau of Medicine and Surgery
LTC Jeff Unger, USA, J-4, (Medical Readiness Division), ASEC
Lt Col Tom Berg, BSC, USAF, [Representing Col Thomas Cropper, BSC, USAF, ASEC]
CAPT Larry Frank, MSC, USN, BUMED, ASEC
Mr. Bart Kuhn, ODUSD(S&T), EXSEC

The following additional individuals also attended:

Ms. Winifrede Fanelli, Deputy PM, JPO BD
Mr. Richard Paul, Acting PM, JVAP
Dr. Eugene Wilusz, USASBCCOM
Mr. Chrisopher Shaffer, USASBCCOM
COL Robert Eng, MS, USA, AFRRI
COL Charles Hoke, MC, USA JTCG-2 Chair, USAMRMC
COL Edwin Armitage, MS, USA, USAMRMC, JTCG-3/4
COL Dave Danley, MS, USA, USAMRMC
CAPT Ed Lane, MSC, USN, Navy Bureau of Medicine and Surgery
LTC Michelle Ross, VC, USA, ODATSD(CBD)
LTC John Skvorak, VC, USA, USAMRMC
Dr. Garrett Polhamus, Litton/TASC
Dr. (b)(6), Science Applications International Corporation, Recorder

2. Introduction of the ASBREM Committee meeting topics by Dr. Foster.

Topic # 1: Lightweight Chemical Biological Protection for Future Soldier Systems

A. Presentation:

Dr. Foster introduced this topic by stating that during the recent off-year Technology Area Review and Assessment (TARA) Activity and ASBREM Review of RDA, Brig Gen Dodd asked about the status of the Army's development of new-generation chemical/biological (CB) protective suits. As a result, Dr. Foster invited Dr. Eugene Wilusz, U.S. Army Soldier Biological Chemical Command (USASBCCOM), to brief developments in the Lightweight CB Protection Program for Future Soldier Systems to the ASBREM Committee. Dr. Foster also indicated that Dr. Wilusz would be available immediately following the meeting to answer questions.

Dr. Wilusz introduced his presentation (TAB A) by saying he would brief the program and then Mr. Shaffer would demonstrate several of the prototype items. He said the program's objective was to develop lightweight, selectively permeable fabrics for application as overgarments, closure systems, and duty uniforms that provide effective CB protection. The major thrust is in the area of selectively permeable materials (SPM) that allow greater loss of body moisture (i.e., trying to facilitate evaporate cooling to reduce the heat-load burden associated with conventional CB protective garments).

Dr. Wilusz said they were moving away from charcoal and noted that their preliminary studies, comparing the newer SPMs with the materials (e.g., USA Battle Dress Overgarment (BDU) and USMC Saratoga Overgarment) being used by the different Services, indicate they are achieving greater CB protection and improved evaporative cooling with the newer SPMs. The new closure systems include zippers, molded cuffs, and charcoal-tight cuffs. Dr. Wilusz indicated there had been some durability problems identified during recent field trials with prototype SPM systems; however, these problems are being addressed.

In summary, Dr. Wilusz said that noncarbon-based CB protective clothing, incorporating novel closure systems, have been developed using SPMs that are approximately 50% lighter than conventional ensembles and provide greater CB protection and improved evaporative cooling. He said the SPMs have clear dual-use application in such areas as environmental clean-up, emergency hazardous spill responders, and for hazardous material handlers.

B. Discussion:

- Dr. Foster

Dr. Foster asked if the physical characteristics of the SPMs were selected for use with dismounted troops only.

- Dr. Cirone

  Dr. Cirone asked if the prototype ensembles had been subjected to post-field testing to determine if they retained the desired characteristics.

- Brig Gen Dodd

  Brig Gen Dodd asked if the prototype SPM ensembles had been subjected to flammability testing.

- COL Danley

  COL Danley asked if any studies had been done looking at possible CO_2 accumulation within the prototype SPM ensembles, noting that gas exchange across materials could be problematic.

- COL Glenn

  COL Glenn asked if an affordability analysis had been done comparing the prototype SPM ensembles to the BDU.

- Dr. Wilusz

  In response to Dr. Foster's question regarding selection of SPM physical characteristics, Dr. Wilusz said the selection criteria were based, in part, on dismounted troop requirements but were applicable to crew and USAF requirements as well.

  Dr. Wilusz replied to Dr. Cirone's question about the physical characteristics of prototype ensembles following field tests by saying we are assessing them.

  Dr. Wilusz responded to Brig Gen Dodd's question about flammability testing of the prototype SPM ensembles by saying he recognized this as an issue but thought it could be addressed by using a nonflammable outergarment material.

  With regard to COL Danley's question about possible CO_2 accumulation within the prototype SPM ensembles, Dr. Wilusz said this needs to be addressed.

  Dr. Wilusz said, in response to COL Glenn's affordability question, that the current SPM material was expensive; however, he said that industry indicates that with scale-up the cost would be about the same as that for the current BDU. Dr. Wilusz said he thought it would be for use as a standard CB protective garment not for issue as a standard duty uniform.

C. Action/Decision:

- None required.

Topic # 2: Joint Vaccine Acquisition Program: Analysis of Alternatives (AoA) for DoD Vaccine Production Capabilities

A. Presentation:

Dr. Foster introduced Mr. Richard Paul, saying he was the Acting Project Manager (PM), Joint Vaccine Acquisition Program (JVAP), and would provide an update on JVAP activities.

Mr. Paul began his presentation (TAB B) by stating that his presentation would be limited to an update on the AoA for DoD vaccine production capabilities. He said the AoA was based on a Deputy Assistant to the Secretary of Defense (Chemical and Biological Defense (DATSD(CBD)) memorandum on Program Objective Memorandum (POM) guidance and involves multiple shareholders addressing the issues through a process involving a Blue Ribbon Panel, Overarching Integrated Product Team (OIPT), Working Integrated Product Team (WIPT), and a support contractor. Mr. Paul said the WIPT meeting is scheduled for Monday, July 17, 2000, and both COL Takafuji and Dr. Cirone will attend for Health Affairs (HA). The Blue Ribbon Panel includes the Food and Drug Administration (FDA). He said they would leverage information available from previous biological defense (BD) production analyses. Mr. Paul said they were looking at four alternatives (i.e., PSC, GOCO, COCO) and would brief out their recommendations to the DATSD(CBD) by November 20, 2000.

B. Discussion:

- Dr. Johnson-Winegar

Dr. Johnson-Winegar commented that the DoD is looking for a long-term capability and that the AoA will be taken to the Program Review Group as overguidance.

With regard to the OIPT, Dr. Johnson-Winegar said Dr. Raub from the Department of Health and Human Services (DHHS) may attend the meetings.

Dr. Johnson-Winegar responded to COL Glenn's comment on the ongoing infectious disease study being sponsored by COL Hoke by saying it would be good to see the results but she had to press ahead in order to meet priority requirements in the biological defense program.

- COL Glenn

COL Glenn said that COL Hoke, the Research Area Director for the Military Infectious Diseases Research Program (MIDRP), has already initiated a study that involves production capabilities for infectious disease vaccines of military importance, and felt there may be value added in considering the results of that study.

- Dr. Foster

Dr. Foster asked if the AoA would be considering scalability issues.

- Mr. Paul

  Mr. Paul responded to Dr. Foster's question about scalability affirmatively, stating that additional capability for add-on production suites will be considered.

C. Decision/Action:

- None required.

Topic # 3: Partition of biological threats between JTCG-2 and JTCG-4, and common bio and emerging infectious disease threats

A. Presentation:

COL Glenn introduced his presentation (TAB C) by saying that by congressional intent, there is minimal overlap between the Medical Biological Defense Research Program (MBDRP) and the MIDRP, with deliberate separation regarding threats—that is, biological warfare (BW) threats posed by forces hostile to U.S. interests as compared to endemic disease threats. He said there were both similarities (e.g., core capability needs, technological approaches, and scientific staff) and differences (e.g., research prioritization, oversight and management, and clinical trials). COL Glenn also noted that emerging infectious disease threats could become future BW threats, and that by Public Law 80% of the BD research must focus on validated threats for the near to mid-term, and 20% on long-term considerations.

B. Discussion:

- Dr. Foster

  With regard to the MIDRP organizational environment (p. 4, TAB C), Dr. Foster asked about the Navy equivalent of Deputy Chief of Staff for Operations-Force Development (DAMO-FD) for MIDRP requirements proponency.

  Dr. Foster asked if the ASBREM's Needs Integration Subcommittee (NIS) should look at the threat priorities for the MIDRP. He also asked if the ASBREM Committee Chair and Co-chair should send a memorandum to the Army Medical Department Center and School (AMEDD C&S) on the issue of updating the list of infectious diseases of operational importance to the military.

- COL Glenn

  COL Glenn replied to Dr. Foster's query about proponency for Navy MIDRP requirements by stating that the AMEDD C&S serves as the proponent for all MIDRP requirements as part of the Army's lead agent responsibilities. The Navy's input is through the AMEDD C&S, with the AMEDD C&S providing requirements through the Training and Doctrine Command (TRADOC) to DAMO-FD.

COL Glenn, in response to Dr. Foster's question about having the NIS look at the threat priorities for the MIDRP, said that COL Hoke has initiated a study with the Institute of Medicine (IOM) to look at aspects of the MIDRP, including review of the AMEDD priorities. He noted that the AMEDD C&S list of priorities does not necessarily translate to MIDRP execution priorities. He explained that factors such as technological maturity and affordability also have a role in setting execution priorities. Further, he said the Joint Staff was also working on development of a list of infectious disease threat requirements.

- CAPT Hart

CAPT Hart added to COL Glenn's response to Dr. Foster's question about proponency for the Navy's MIDRP requirements by saying that his office was reviewing how the Navy validates medical requirements (MIDRP) before they are put forward.

CAPT Hart, in commenting on remarks about priorities, stated that it was important that all the Services should have a say in how priorities are set.

- Brig Gen Dodd

Brig Gen Dodd responded to Dr. Foster's question about having the NIS look at the threat priorities for the MIDRP by saying that the Army system is good at setting priorities; however, his concern was with the apparent observation that priorities change with changing personalities. He stated that the issue of Service input and establishment of MIDRP priorities needed resolution.

- COL Hoke

COL Hoke remarked that the IOM would be examining the list of infectious diseases having military importance and will be recommending a set of criteria (e.g., disrupt deployment) for sorting when and how to address established requirements. He also indicated that it has been several years since the AMEDD C&S issued a list of prioritized infectious diseases posing an operational threat; however, they are working on an updated version of the list.

C. Decision/Action:

- ACTION 85 (071100-). The Executive Secretary (EXSEC) will convene a meeting of the ASECs to discuss the issue of MIDRP priorities and will provide the ASBREM Steering Group or the ASBREM Chair with a recommended course of action (e.g., review by NIS). This action is to be completed NLT September 15, 2000.

Topic # 4: Status Report: Modification of Title 10, Section 980

A. Presentation:

Dr. Cirone began his presentation by saying the issue–that DoD, unlike NIH, is precluded from performing experimental procedures in emergency rooms without direct informed consent–had been discussed at the off-year activity this past March. He briefly outlined the background for the request to modify Title 10, Section 980, as presented to DoD by Dr. Howard Champion. He then said that at the off-year review, MG Parker indicated that the timing was not right for introducing the proposed legislative change. He suggested postponing action until after the elections. Dr. Champion sent a message that stated "Communications with appropriate majority and ranking minority staff on this issue confirm the fact that General Parker's concerns are well-founded regarding the pursuit of this issue this year." He also stated "Any changes in Title 10, Section 980, irrespective of their merit and irrespective of the broad-base of support by those knowledgeable, should be put on hold probably until the next administration."

B. Discussion:

- COL Glenn

COL Glenn said that MG Parker checked with congressional staffers and although they supported the proposed change to Title 10, Section 980, they did not believe it would be a good idea to introduce it right now, particularly since there had been so much controversy regarding immunizing military forces with the current anthrax vaccine. He then expressed the view that the issue wrapped up in the proposed change to Title 10 was one of the most important issues in the DoD biomedical RDA program. COL Glenn said that unless we can provide efficacious intervention in the first 10 minutes following major body trauma there is little chance of reducing the killed in action numbers. Further, he said that there are candidate products that have been languishing since the 1980s as a direct result of PL that precludes their testing.

- CAPT Frank

CAPT Frank added to COL Glenn's comments on the importance of resolving the issue by saying critical research that needs to be done now could not be resourced unless Title 10, Section 980, is modified.

- Dr. Foster

Dr. Foster suggested that this might well be an official ASBREM Committee issue for the DoD to address.

C. Decision/Action:

- ACTION 86 (071100-). The ASECs will develop a proposed legislative initiative and strategy, and present it for validation by ASBREM Committee principals at the next scheduled meeting. The EXSEC is to place the topic of the proposed modification to Title 10, Section 980, on the agenda for that meeting.

Topic # 5: Observation from Human Systems TARA: Reliance Panel Partnering

A. Presentation:

Dr. Foster said that he felt there were many opportunities for partnering between the Human Systems Panel and the Biomedical Panel (e.g., Military Operational Medicine), especially between the Navy and Air Force that could lead to establishment of a new Defense Technology Objective.

B. Discussion:

- Brig Gen Dodd

Brig Gen Dodd said he is working with his counterpart in the Human Systems Research Program, Dr. Hal Guard, ONR, to prepare something for a future ASBREM Committee meeting.

B. Decision/Action:

- None required.

Topic # 6: Vaccine Development Seminar

A. Presentation:

Dr. Foster said that the Deputy Under Secretary of Defense for Science and Technology and the Deputy Assistant Secretary of the Army for Research and Technology are co-sponsoring the first medical Defense Science and Technology Seminar. He said the topic for the seminar is "Vaccines to Protect the Warfighter." The seminar will be held on Friday, 11 August 2000, at the Crystal City Marriott (Crystal Forum), 1999 Jefferson Davis Highway, Arlington, Virginia. Dr. Foster asked that everyone consider taking the opportunity to attend this important and timely seminar.

B. Discussion:

None.

C. Decision/Action:

- ACTION 87 (071100-072000). The EXSEC is to e-mail the details of the Defense Science and Technology Seminar, "Vaccines to Protect the Warfighter," to the members of the ASBREM. This action is to be completed NLT July 21, 2000. [ACTION COMPLETE]

Topic # 7: Joint Medical S&T Assessment

A. Presentation:

Dr. Foster introduced CAPT Ed Lane and indicated that he (Dr. Foster) had previously resourced ($250K) Navy (POC: CAPT Lillenthal) to conduct the Joint Assessment; however, CAPT Lillenthal has since been reassigned and CAPT Lane now has the lead. Dr. Foster also noted that the AMEDD C&S had already completed a Joint medical operations wargame.

CAPT Lane introduced his presentation (TAB D) by saying he was now fully engaged in the process of setting up the Joint Medical S&T Assessment, which had been tasked to the Navy by the Office of the Director, Research and Engineering (ODDR&E). The scope of the tasking was to identify future military medical capabilities needed to provide next-generation medical support across the spectrum of military conflict and assist in planning and programming medical S&T.

CAPT Lane said that the USA, USN, USAF, and Joint Staff have all conducted multiple games; however, the results have not been integrated in a way that really allows one to assess interoperability, as well as determining what is missing. He said the Joint Medical S&T Assessment would review what has been done, assess the validity of the results, and determine if there are critical gaps in information to meet the DDR&E tasking.

CAPT Lane said the timeline for conducting and completing the assessment is tight and potentially problematic. Further, he said there was a significant shortfall in resources to conduct the seminar. He said he was looking for a facility to house the meetings and needed help with scoping and resourcing.

B. Discussion:

- Dr. Foster

Dr. Foster said he was looking to the Services and J-4 Medical to put resources on the table to conduct this assessment. He said it was extremely important to have the results by the end of the first quarter FY01 in order to influence the POM if major issues arise.

Dr. Foster said he understood and agreed with Brig Gen Dodd's comment that the Service operators may not support the outcome; however, he felt it was important to assess the results from previous exercises in a systematic and integrated manner to determine if there are critical holes in our knowledge base.

- COL Glenn

  COL Glenn said that MG Parker has questions about the need to do another exercise when so many have already been done. COL Glenn then asked if there were some specific issues that needed to be addressed.

- CAPT Lane

  CAPT Lane responded affirmatively to COL Glenn's question about whether or not there were specific issues to be addressed, saying we want to look at the holes in our knowledge base.

  CAPT Lane responded to CAPT Frank's question about who would be the active players by saying he was working the issue and was looking for decision makers.

- Brig Gen Dodd

  Brig Gen Dodd questioned the practical utility of any outcome of the assessment and said he thought this might be more appropriate for the J-4 to handle. He said the outcome might be a list of priorities for research; however, from a practical perspective, if they do not match USAF priorities they will not have the support of the USAF operators.

- CAPT Hart

  CAPT Hart said this was the first time he had heard this briefing and does not believe it will generate a new list of requirements; rather, he feels this will identify data gaps and possible solutions.

- CAPT Frank

  CAPT Frank asked who would be the active players in the assessment.

C. Decision/Action:

- DECISION. Dr. Foster said he would consider sending a memorandum to the Services and Joint Staff asking for resources, both personnel and funding, for the Joint Medical S&T Assessment.

- ACTION 88 (071100-). Navy ASEC, with CAPT Lane, to provide a recommendation NLT August 15, 2000, as to the need for NIS engagement in the Joint Medical S&T Assessment.

Topic # 8: New Business

A. Presentation:

Dr. Foster said he had two new business matters to discuss. First, he said there are concerns about threats to Soldier Systems, indicating that both AFMIC and the British have raised questions about potential bioeffects from thermobaric devices to military personnel, even when wearing body armor. Dr. Foster asked that the JTCG-5 and -6 look into this matter. Second, Dr. Foster said he needed nominations for Biomedical TARA Panel members. He said RADM Clinton, RADM Mayo, Dr. Johnson-Winegar, and he (Dr. Foster) will be members. Seven additional members are needed.

B. Discussion:

- Brig Gen Dodd

Brig Gen Dodd said the Biomedical TARA is scheduled for February 26 – March 2, 2001. He said that the Holiday Inn Riverwalk Hotel will be the site for the meeting. Brig Gen Dodd said that Col Cropper is getting information together on this issue.

- CAPT Frank indicated that the Chief of Naval Operations (CNO) is very interested in the issue of blunt trauma.

C. Decision/Action:

- ACTION 89 (071100-). EXSEC will task JTCG-5 (Military Operational Medicine) and -6 (Combat Casualty Care) to review the issue of bioeffects from thermobaric devices. This action is to be completed NLT August 18, 2000.
- ACTION 90 (071100-). The Chairs of JTCG-5 (Military Operational Medicine) and -6 (Combat Casualty Care) will brief the ASBREM Committee on their assessment and recommendations regarding potential bioeffects from thermobaric devices to military personnel wearing body armor. A status report will be briefed at the next regularly scheduled (late October 2000) ASBREM Committee meeting.

Topic # 9: Next ASBREM Committee Meeting Date

A. Presentation:

Dr. Foster said he would like to schedule the next meeting of the ASBREM Committee during the third week of October 2000. He asked that the ASECs check the calendar of their ASBREM principal for that time period and report that to the EXSEC.

B. Discussion:

- COL Glenn thanked the Service ASBREM Committee principals for allowing members of their staff to participate in the Medical R&D Management Workshop hosted by USAMRMC. He said that their participation was a key factor in the success of the workshop, noting that the perspectives provided by the participants from the other Services were extremely helpful.

C. Action/Decision:

- ACTION 91 (071100-). The ASECs are to advise the EXSEC about their ASBREM Committee principal's availability for a meeting of the ASBREM Committee during the third week of October 2000. This action is to be completed NLT July 31, 2000.

3. Summary of Action Items.

- ACTION 85 (071100-). The Executive Secretary (EXSEC) will convene a meeting of the ASECs to discuss the issue of MIDRP priorities and will provide the ASBREM Steering Group or the ASBREM Chair with a recommended course of action (e.g., review by NIS). This action is to be completed NLT September 15, 2000.
- ACTION 86 (071100-). The ASECs will develop a proposed legislative initiative and strategy, and present it for validation by ASBREM Committee principals at the next scheduled meeting. The EXSEC is to place the topic of the proposed modification to Title 10, Section 980, on the agenda for that meeting.
- ACTION 87 (071100-072000). The EXSEC is to e-mail the details of the Defense Science and Technology Seminar, "Vaccines to Protect the Warfighter," to the members of the ASBREM. This action is to be completed NLT July 21, 2000. [ACTION COMPLETE]
- ACTION 88 (071100-). Navy ASEC, with CAPT Lane, to provide a recommendation NLT August 15, 2000, as to the need for NIS engagement in the Joint Medical S&T Assessment.
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- ACTION 91 (071100-). The ASECs are to let the EXSEC know about their ASBREM Committee principal's availability for a meeting of the ASBREM Committee during the third week of October 2000. This action is to be completed NLT July 31, 2000.

4. Summary and Adjournment.

Dr. Foster thanked everyone for participating and adjourned the meeting.

Lightweight Chemical Biological Protection for Future Soldier Systems

Eugene Wilusz and Quoc Truong
U.S. Army Soldier and Biological Chemical Command
Soldier Systems Center, ATTN: AMSSB-RIP-C(N)
Natick, Massachusetts 01760-5019

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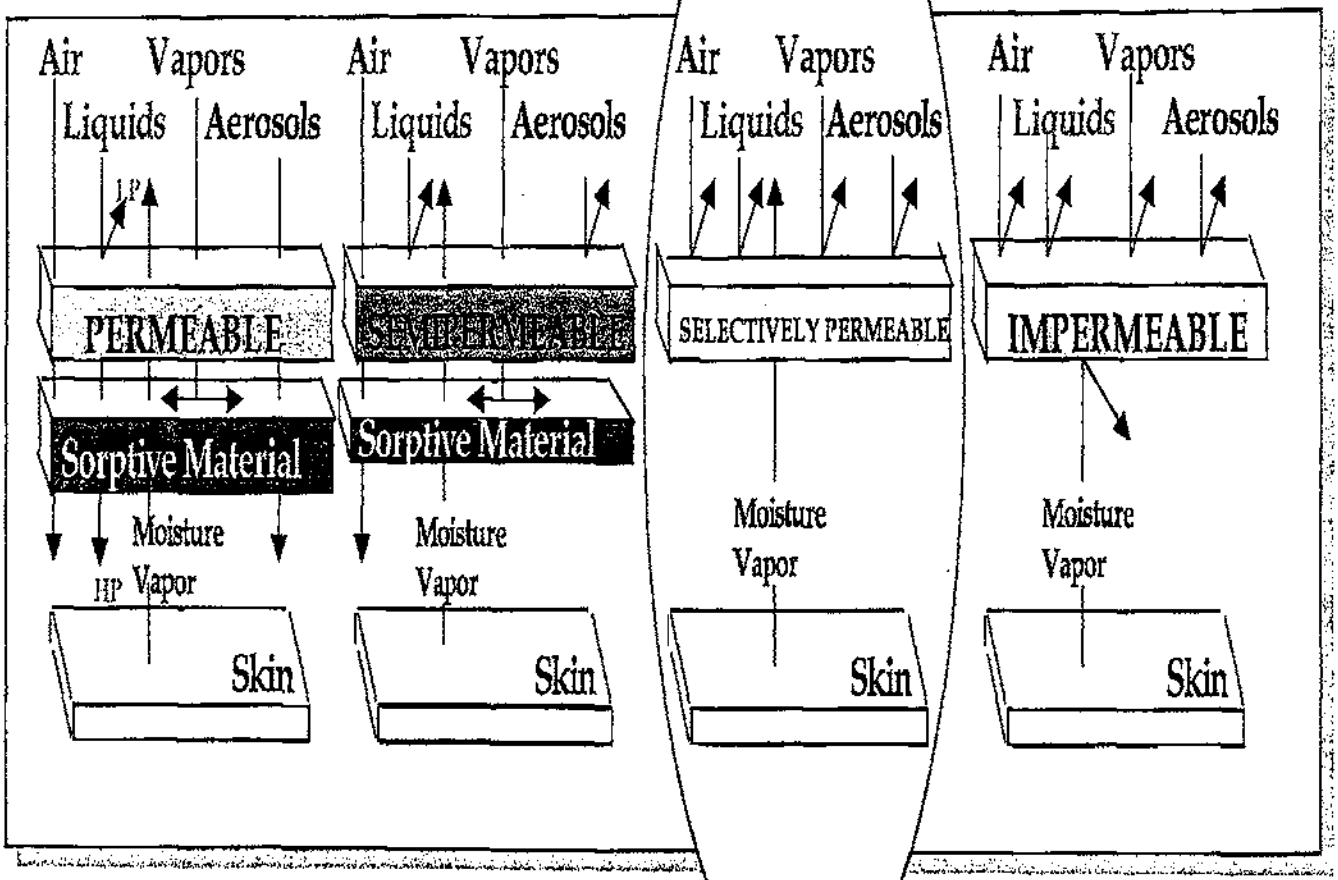
Objectives

- Develop selectively permeable fabric systems and effective garment and closures designs that provide chemical biological (CB) agent vapor, aerosol, and liquid protection.

Technical Approaches

- Develop material systems that meet performance goals.
- Fabricate CB overgarments and conduct limited field evaluations.
- Develop and identify effective CB protective closure systems.
- Integrate selectively permeable fabric systems with novel CB protective closures.
- Demonstrate effectiveness and acceptability of a CB protective duty uniform.

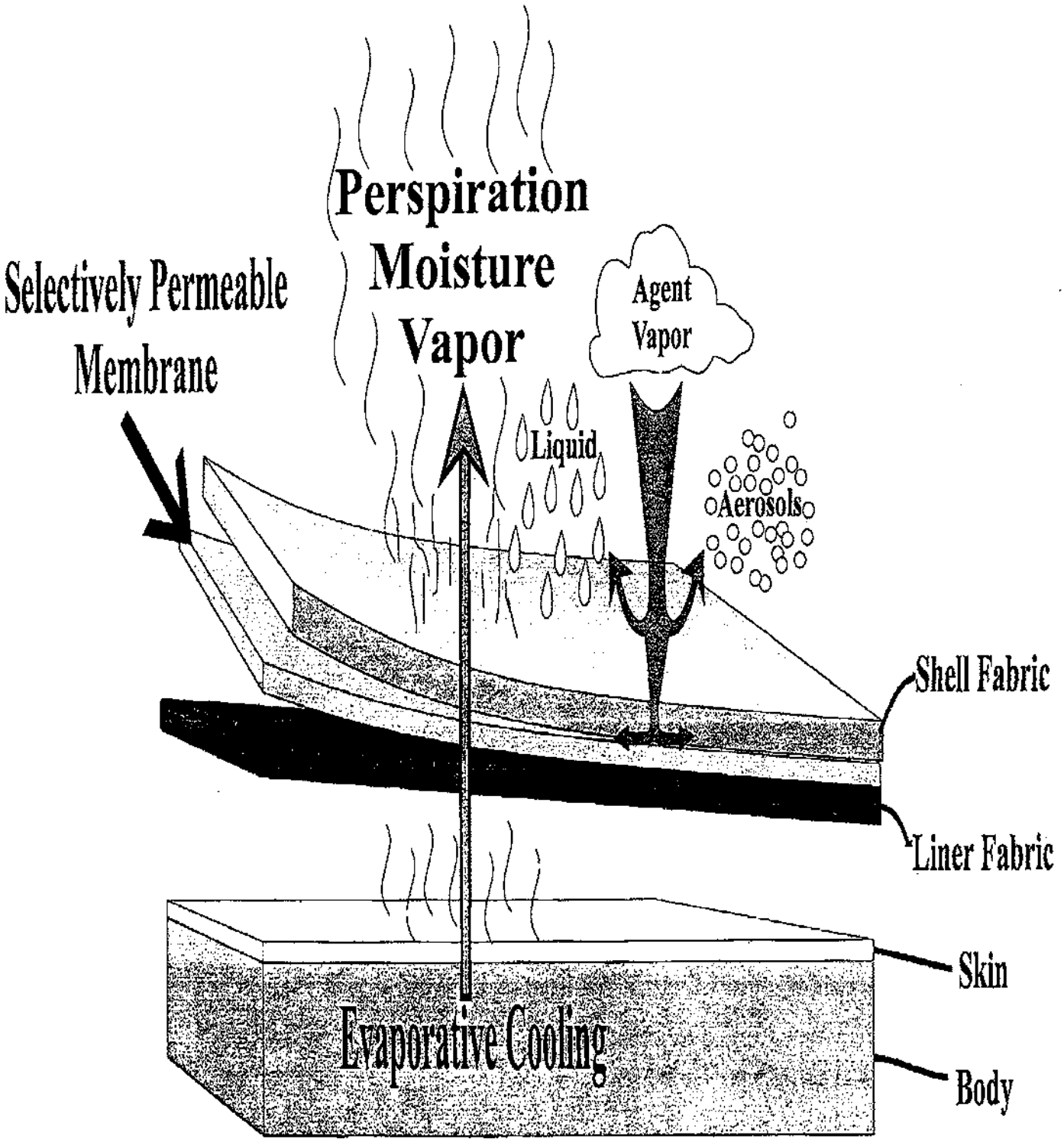
Types of Materials



This is the major thrust of our program.

LP: Low Hydrostatic Pressure

HP: High Hydrostatic Pressure



Material Concept

Performance Goals

Chemical Protection: Blister (HD), Nerve (GD, VX) Agents
Biological Protection: Microorganisms (10 to 0.001 μm)

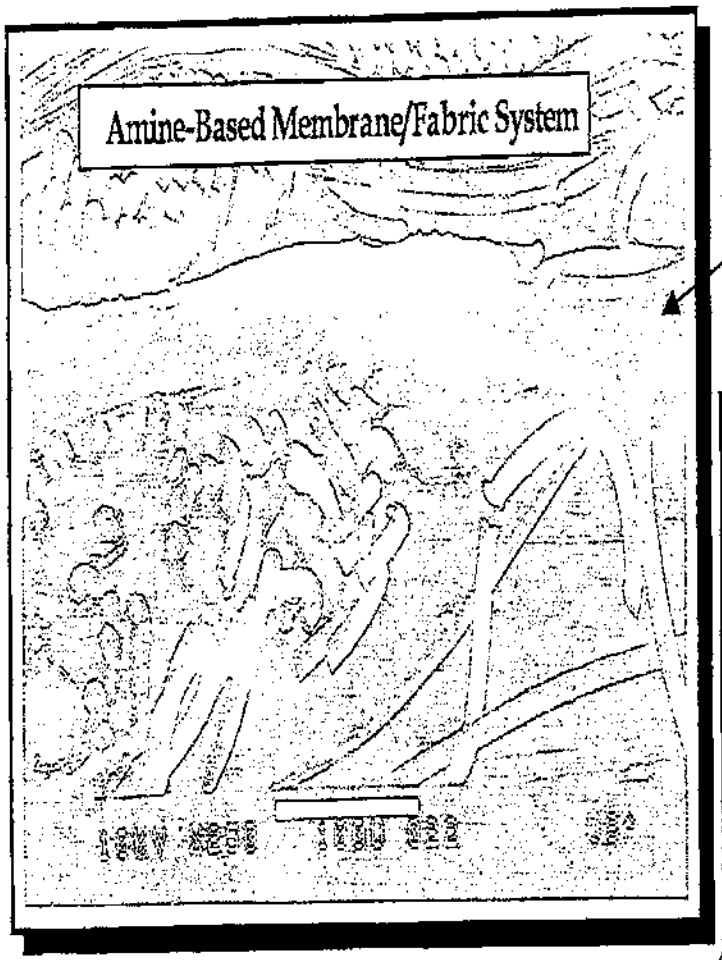
Water Vapor Flux @ 32°C $\geq$ 1800 $g.m^{-2}/24\ h$*
Hydrostatic Resistance $\geq$ 35 lb/in^2

Bonding Strength $\geq$ 10 lb/in^2
Weight $\leq$ 7 oz/yd^2
Stiffness $\leq$ 0.01 lb
Thickness $\leq$ 18 mils

Torsional Flexibility: Pass
Water Permeability after Flexing at 70 °F and -25 °F: Pass

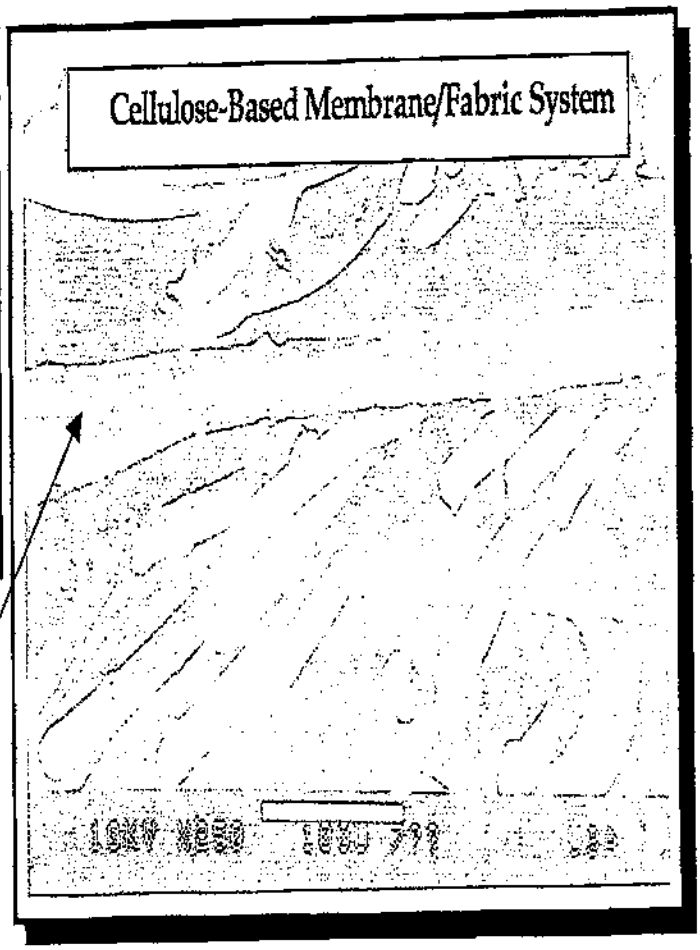
*SSC Dynamic Moisture Vapor Permeation Cell

Perm-selective Membrane/Fabric Structures



Membrane

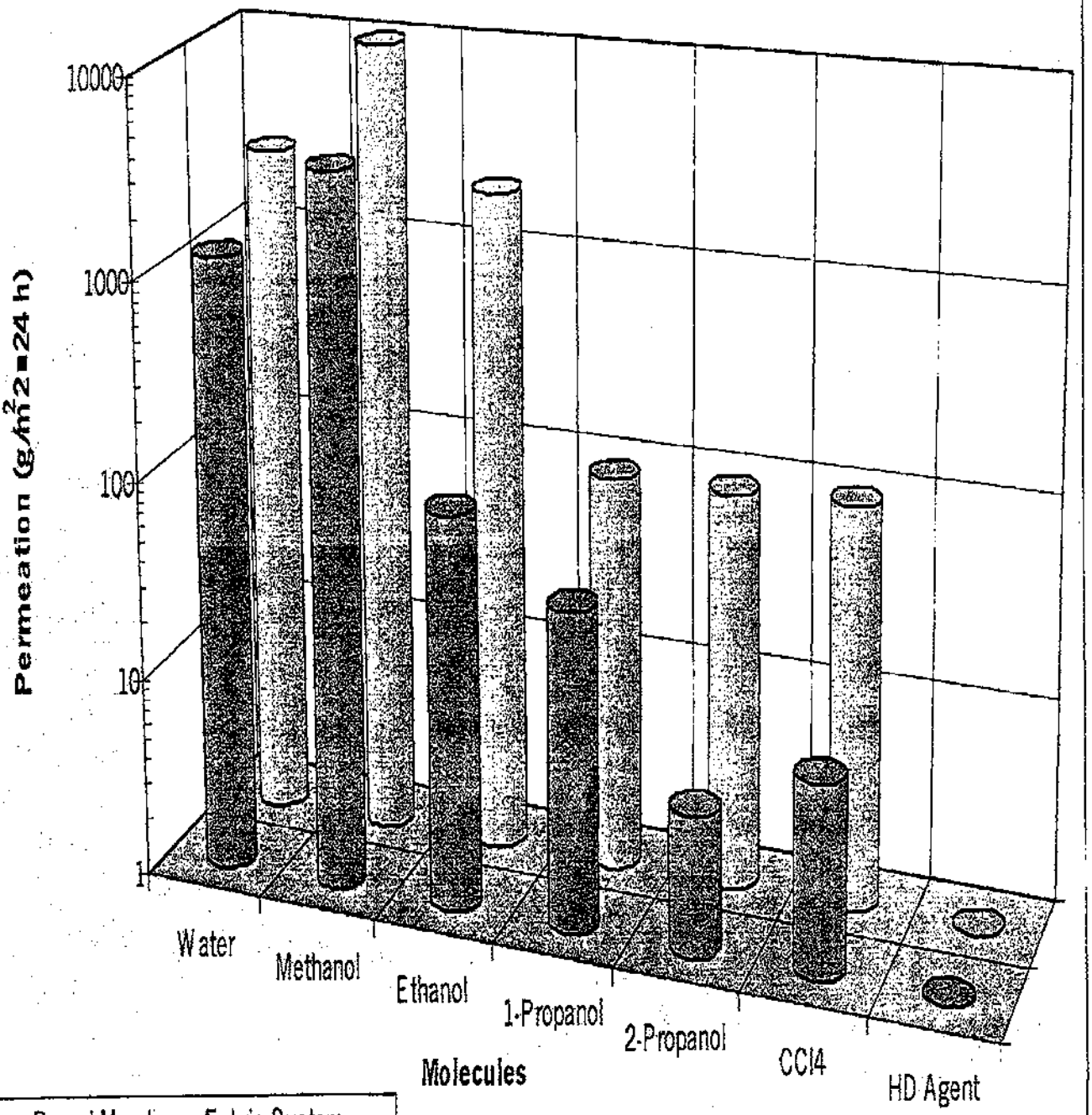
Cross-Sectional View (x250)



Membrane

Cross-Sectional View (x250)

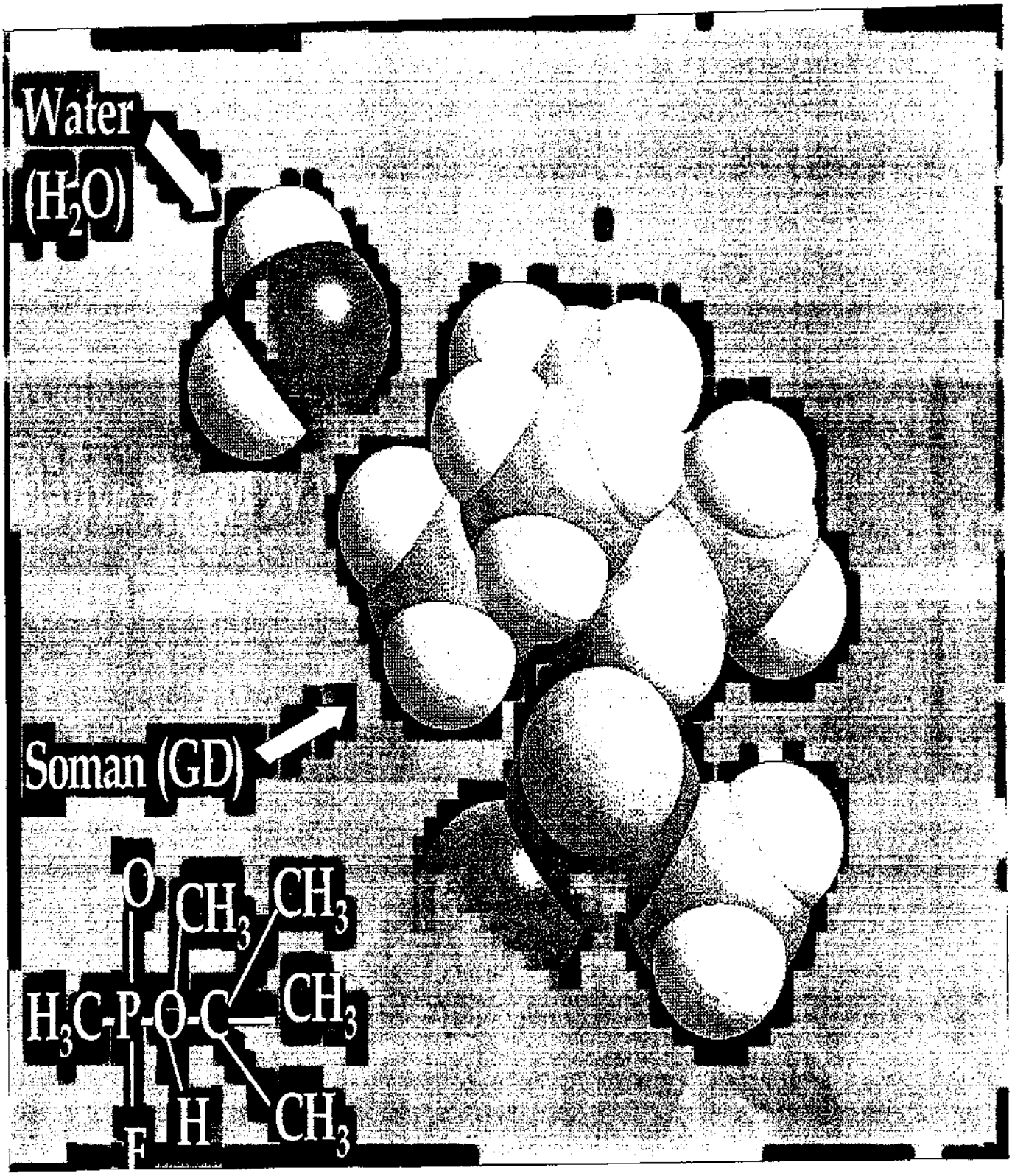
Permeation of Water and Organic Vapors Through Selectively Permeable Materials



HD Agent: Dichloroethyl Sulfide (Blister Agent)

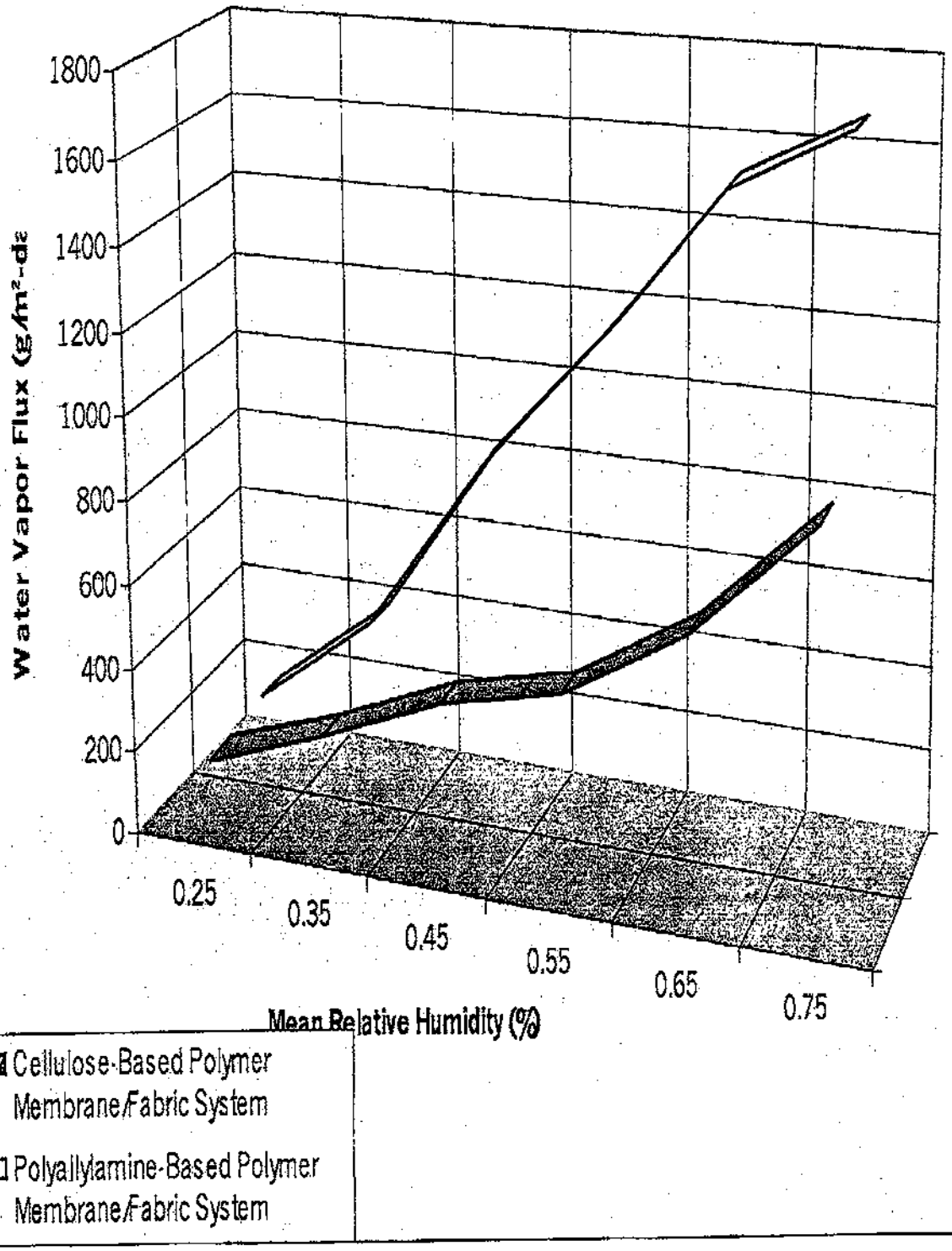
CCL_4: Carbon Tetrachloride

Relative Size of Water and Soman Molecules



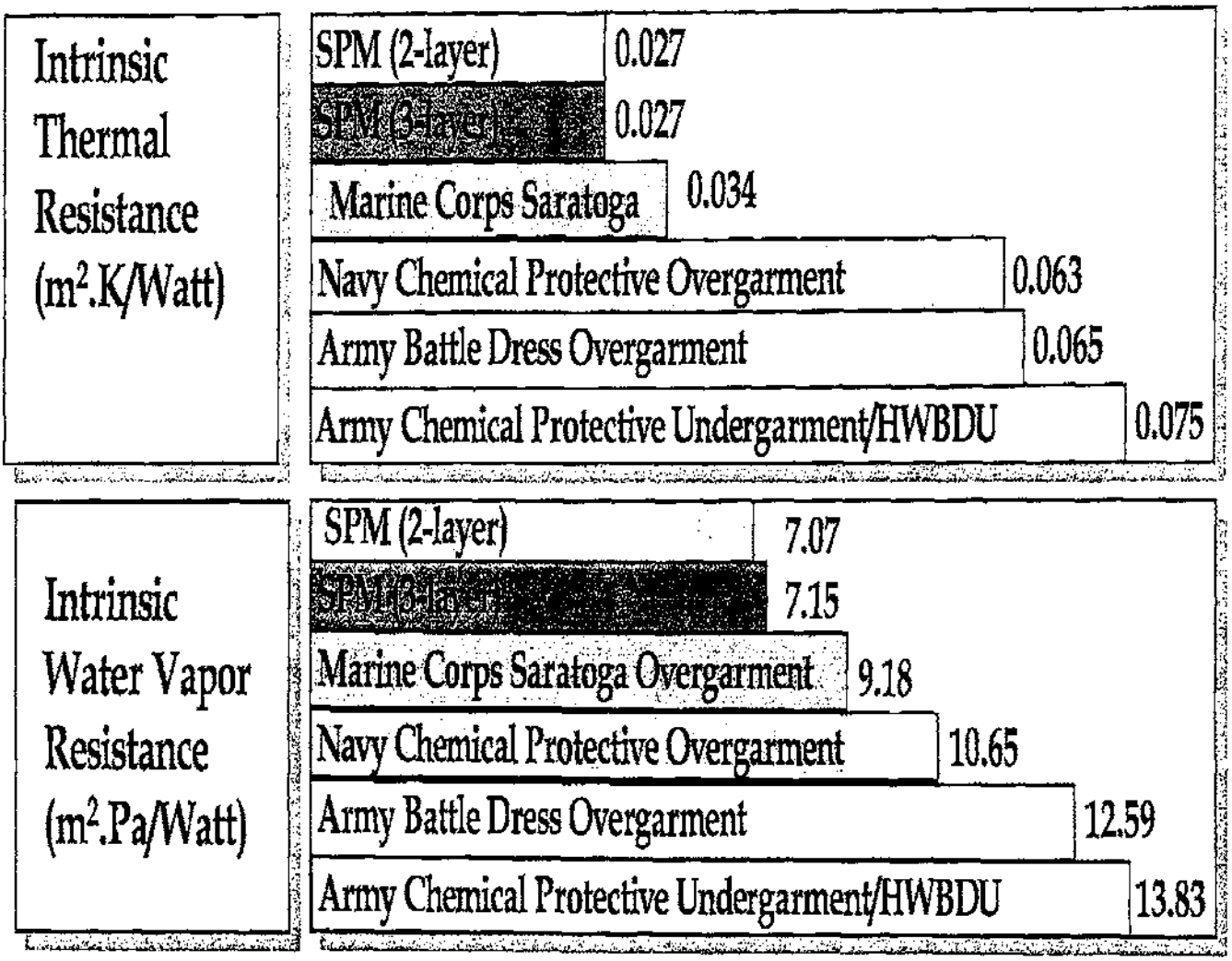
Moisture Vapor Transmission Rate

(Dynamic Moisture Vapor Permeation Cell)



Evaporative Cooling Potentials

(Guarded Hot Plate)

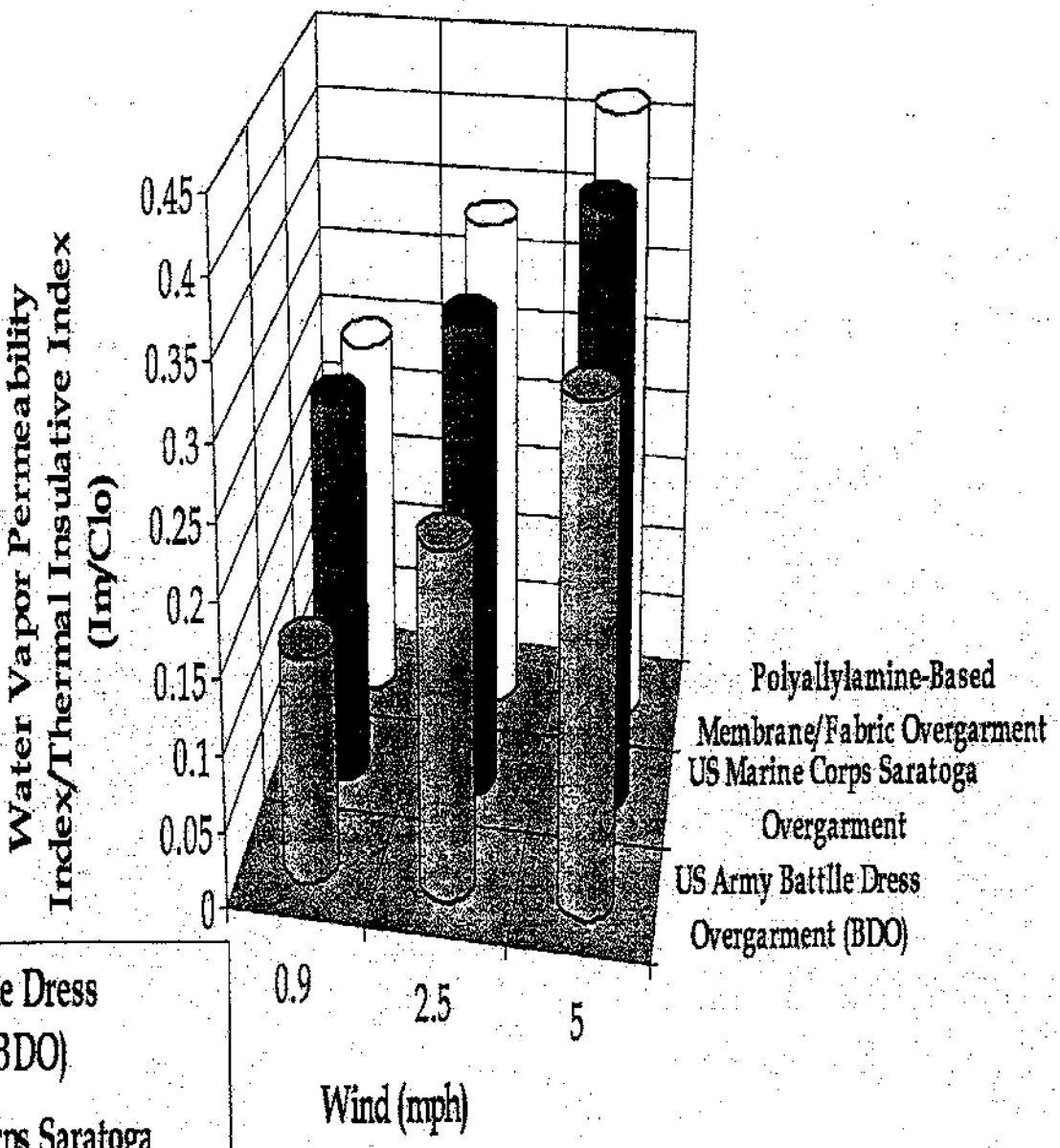


SPM (2-layer): Polyallylamine-Based Membrane Laminated to Shell Fabric

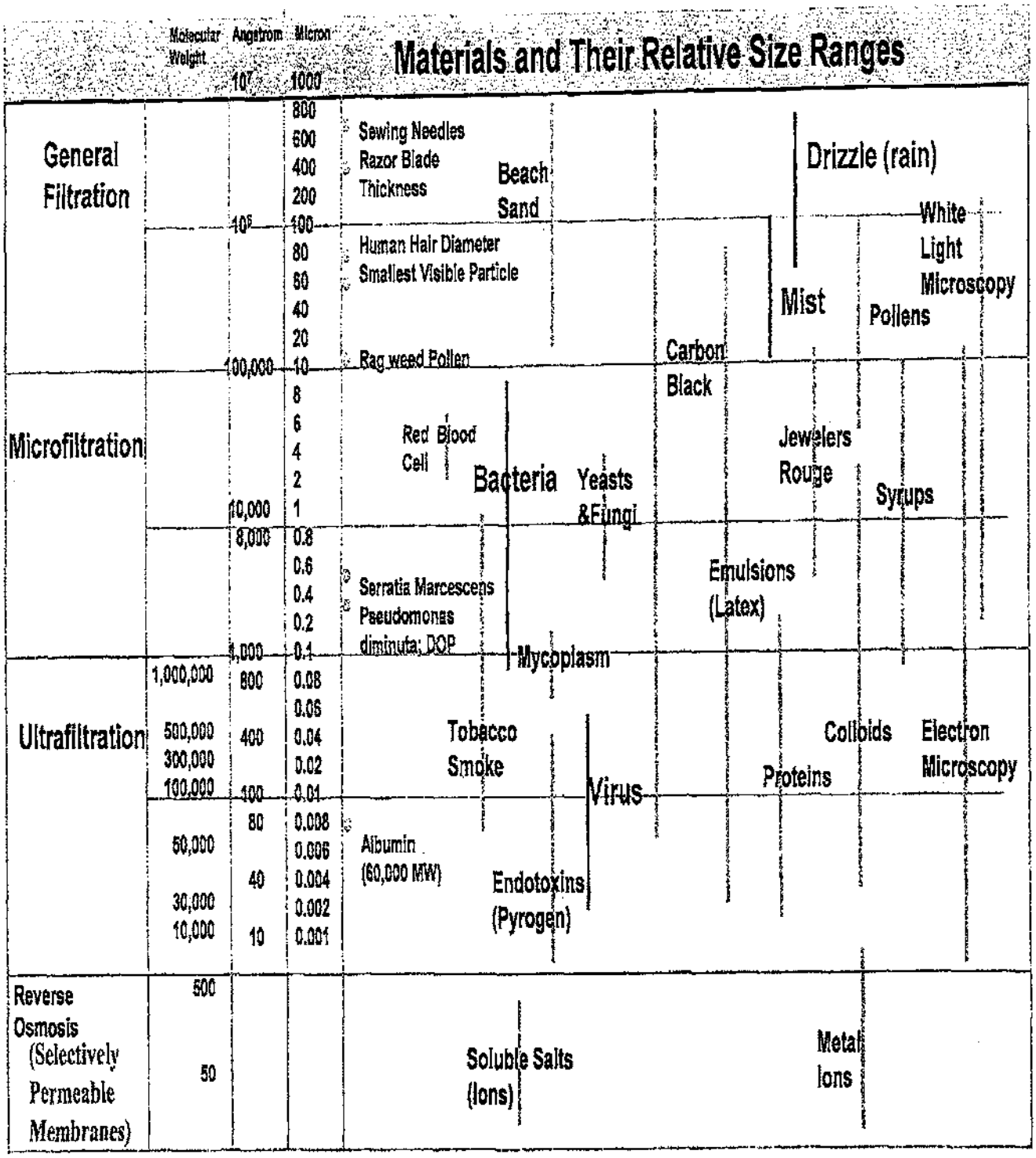
SPM (3-layer): Polyallylamine-Based Membrane Laminated to Liner & Shell Fabric

HWBDU: Hot Weather Battle Dress Uniform

Evaporative Cooling Potentials (Thermal Manikin)



Resistance to Microorganisms and Small Particles



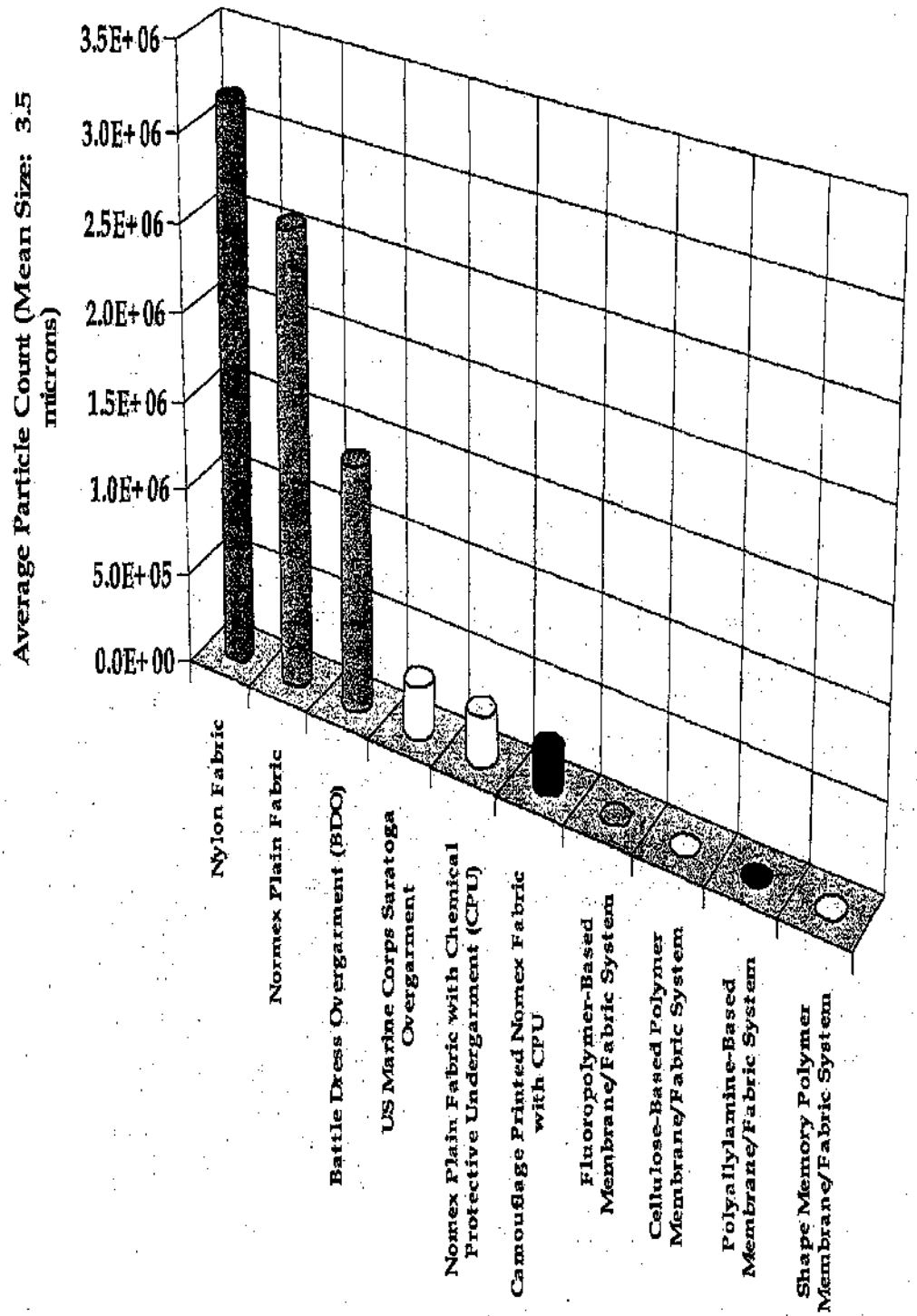
1 Angstrom = 10^{-8} cm

1 μm = 10^4 A

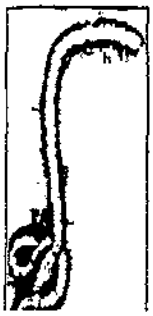
1 mil = 0.001 in. = 25.4 μm

Source: Gelman Sciences
(Membrane & Device Division)

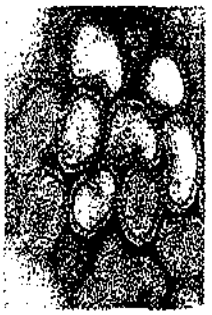
Aerosol Penetration Through Various Fabrics



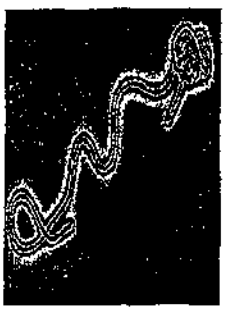
Smallpox virus
(Variola)



Ebola Virus

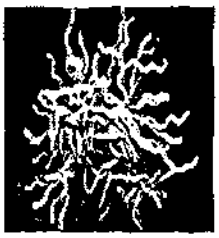


Influenza Virus

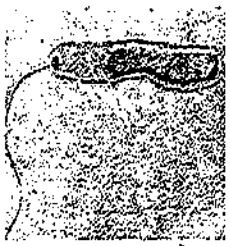


Ebola Virus

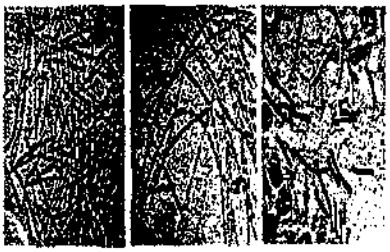
AIDS/HIV Virus



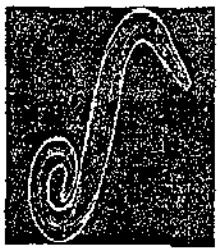
Lyme Disease
Bacterium



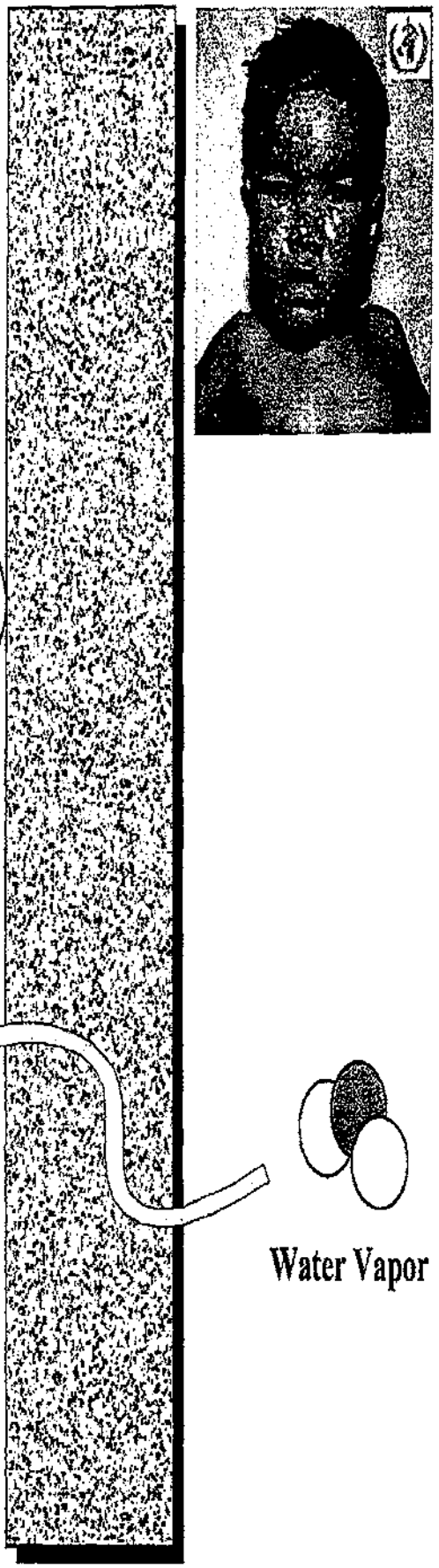
Cholera Bacterium



Anthrax Bacteria
(Anthracis Bacillus)

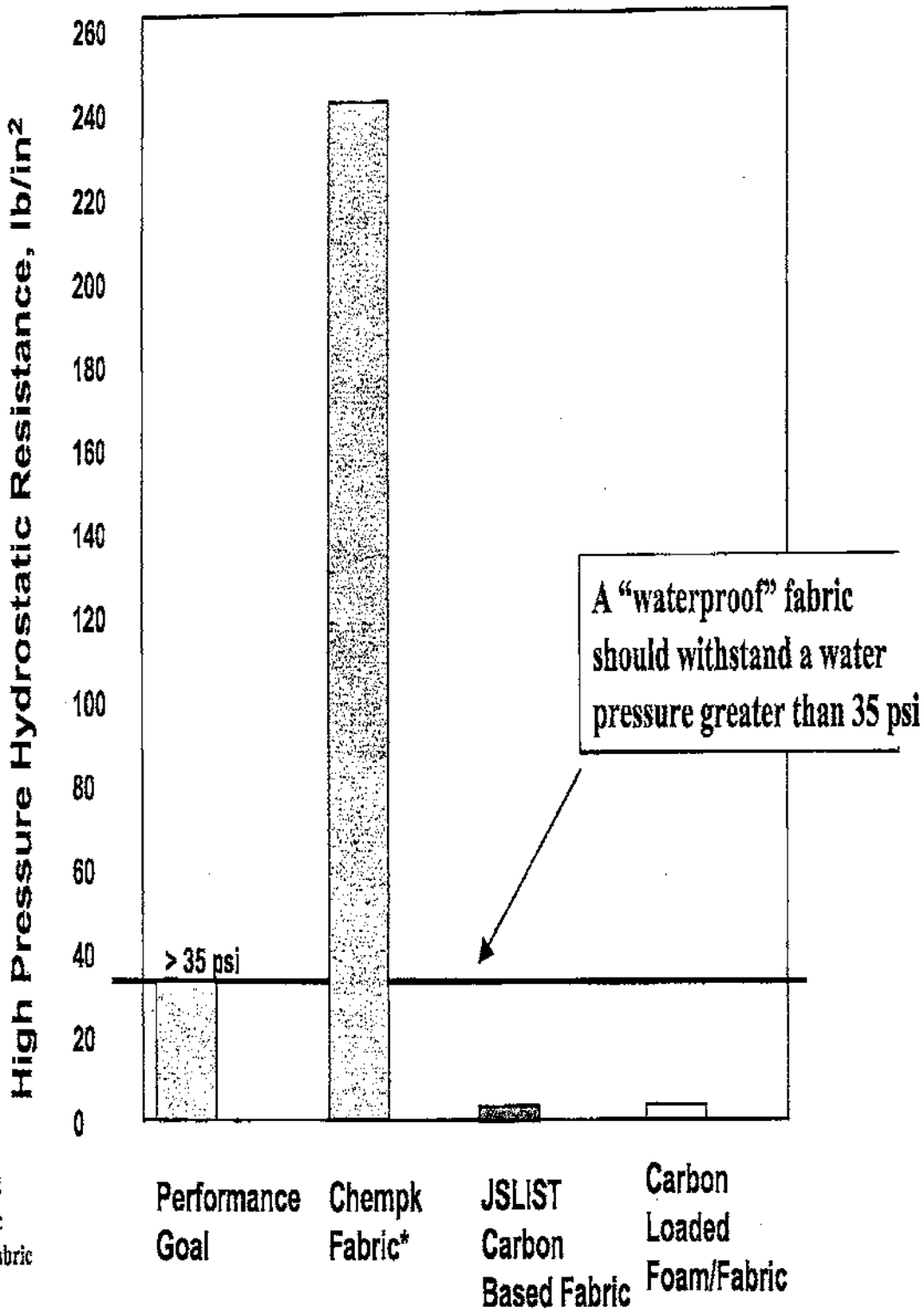


Malaria Parasite



Water Vapor

High Pressure Hydrostatic Resistance of Gore's Chempk Selectively Permeable Fabric vs. Other Fabrics



*Laminated to 4.3 oz/yd2 nomex/kelvar shell fabric and aramid jersey knit fabric

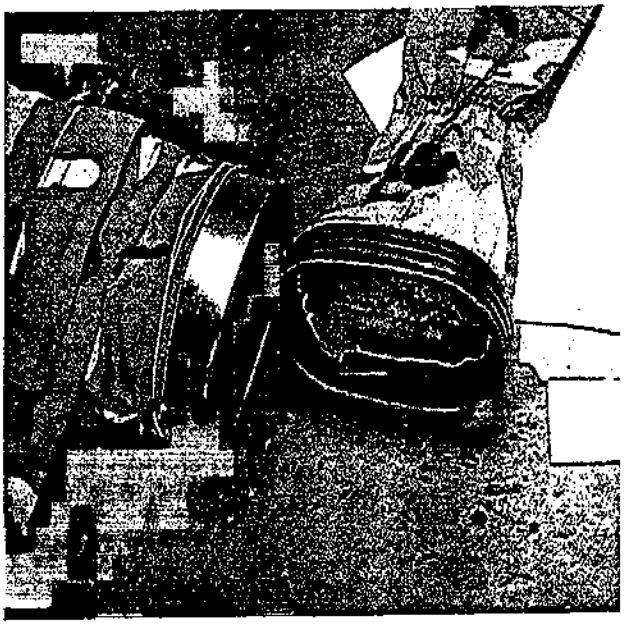
Weight Comparison

Fabric (oz/yd^2)	ChemPk Overgarment	JSLIST Overgarment
	7.3	17.3

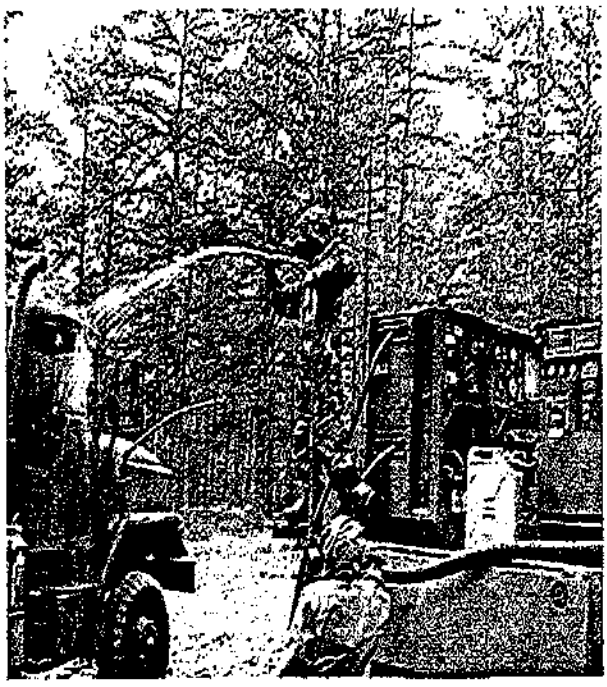
Garment (lb/suit)	CBDU	JSLIST Overgarment & BDU
	10.4*	18.5

ChemPk: W.L. Gore's selectively permeable CB Agent Protective Overgarment
JSLIST: Joint Service Lightweight Integrated Suit Technology Overgarment

*Based on Akzo Nobel Membrane with same NYCO shell and liner fabrics as of the JSLIST overgarment. Chempk and Akzo Membranes have similar weight.



Vapor, Aerosol, Liquid, (VAL) Chemical, and Biological Agent Protective Closure Systems



Recent Accomplishments ✓

- Produced 26 prototype selectively permeable membrane (SPM) garments for limited field evaluations and systems tests
- Conducted a 2-week quick response demonstration of SPM garments (@ the US Army Maneuver Support Battle Lab, Ft. Leonard Wood, Missouri)
- Conducted a 2-week limited field evaluation to assess user acceptance and durability of SPM garments (@ the US Army Research Laboratory (ARL), Aberdeen Proving Ground, Maryland)
- Conducted a 2-week Battle Lab Warfighting Experiment to determine user acceptance and durability of SPM garments (@ Ft. Lewis, Tacoma, Washington)
- Developed and integrated novel closure systems into prototype garments.
- Performed two Man-In-Simulant Vapor Systems Tests (MIST) on SPM garments (@ the US Army Edgewood CB Center, Edgewood, Maryland and @ the US Army Dugway Proving Ground, Dugway, Utah)

Recent Accomplishments ✓

- Soldiers at Ft. Leonard Wood found SPM garments to be durable and comfortable.
- Soldiers at ARL and Ft. Lewis liked SPM garments because they are lightweight, flexible, and comfortable.
- Soldiers at ARL preferred SPM garments over the control JSLIST Overgarments in all three limited field tests.
- W.L. Gore garments (SPM1) with novel closure systems performed well in Man-in-Simulant Tests (MIST) at both ERDEC and DPG test facilities.
- Akzo Nobel garments (SPM2) performed well in the ERDEC MIST test, but poorly at the DPG MIST test. Poor seam-seal and closure/interface donning were the suspected causes.

Summary

Non-carbon based lightweight CB protective clothing has been developed using perm-selective membranes.

These perm-selective membrane/fabric systems have excellent dual use for emergency responders, pesticide and industrial chemical handlers, medical personnel, and environmental clean-up personnel.

Novel closure systems have been developed and integrated into prototype ensembles.

Acknowledgements

Test fabrics were developed/provided by W.L. Gore & Associates, Inc. and Akzo Nobel Central Research (now known as Acordis Research.)
Durability/comfort field relevance tests were performed by the Human Research and Engineering Directorate, US Army Research Laboratory.
Live agent tests were performed by the Design Evaluation Directorate, Edgewood CB Center, US Army SBCCOM and Veridian, Calspan Operations.
Thermal manikin tests were performed by the Bio-Physics Division, US Army Research Institute of Environmental Medicine.

Joint Vaccine Acquisition Program

JOINT VACCINE ACQUISITION PROGRAM PROJECT MANAGEMENT OFFICE

Analysis of Alternatives for DoD Vaccine Production Capabilities

Presented To:

Armed Services Biomedical Research Evaluation and Management Committee

Presented By:

Richard B. Paul
Acting Project Manager

11 July 2000

Purpose/Background

- Purpose
  - Update ASBREM on the Analysis of Alternatives (AoA) for Department of Defense Vaccine Production Capabilities

- Background
  - DATSD(CBD) 1 Feb 2000 Memo on POM guidance directs analysis on vaccine production alternatives

Share Holders

- Working Integrated Product Team (WIPT)

  (JVAP-PMO, JPO-BD, DTRA, ACEAC, ASA(ALT), JTCG-4, USACOE, USAHFPA, JSIG, OTSG, OSD(HA), Joint Staff)

- Overarching Integrated Product Team (OIPT)

  (DATDS(CBD), JSIG, OTSG, JPO-BD, PA&E, OSD(Policy), OSD(Legislative Affairs, OSD(Public Affairs), OSD(FM), DDR&E, DTRA, Joint Staff, OSD(HA), OSD(AG)

- Blue Ribbon Panel

  (Health Technology Networks, Department of Health and Human Services, National Defense University, University of Maryland, Center for Vaccine Development and FDA)

Vaccine Production Alternatives

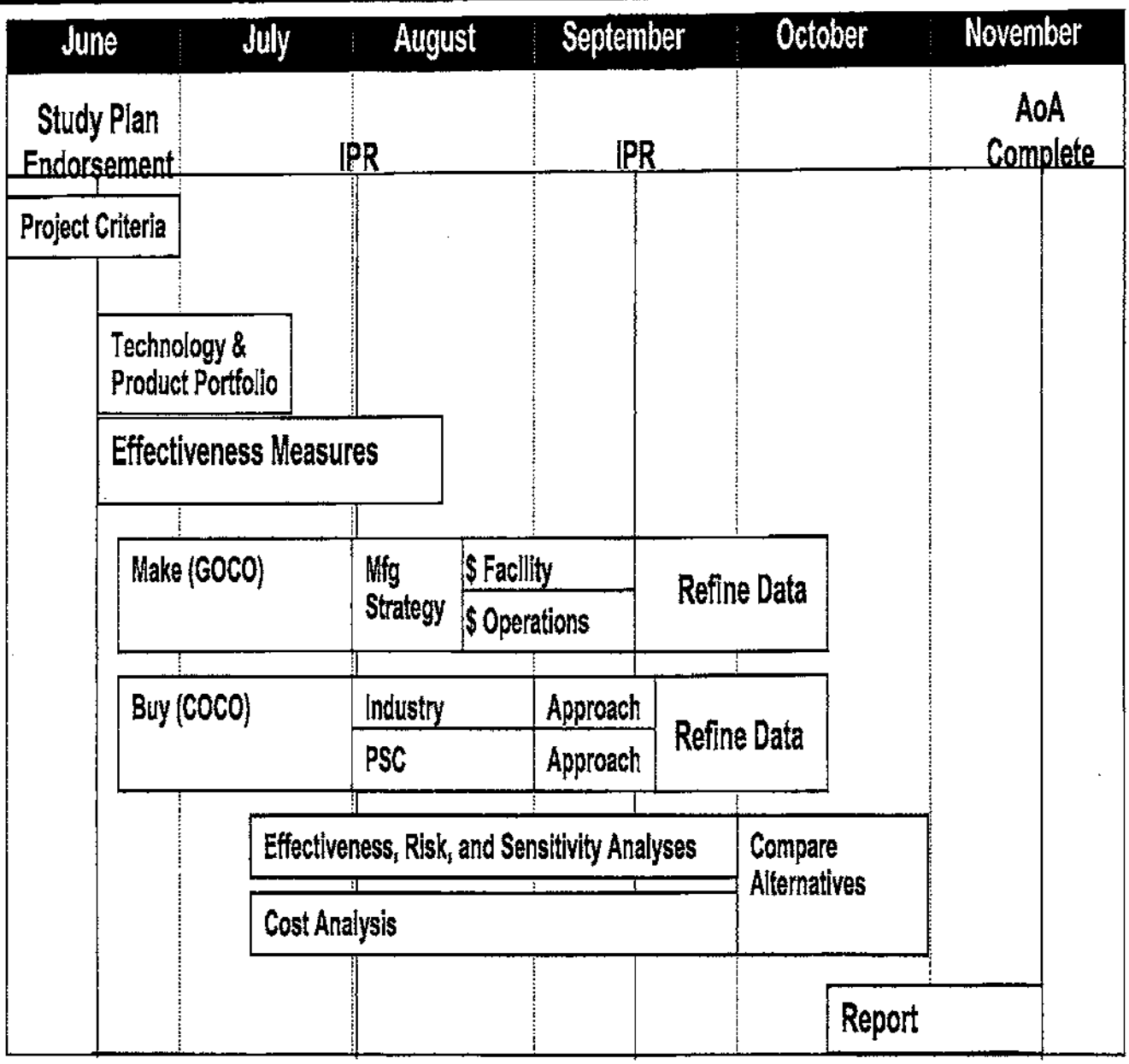
- Alt 1 - Existing industrial base through Prime System Contractor (PSC) approach with BioPort for AVA
- Alt 2 - Government Owned, Contractor Operated (GOCO) facility
- Alt 3 - Contractor Owned, Contractor Operated (COCO) facility
- Alt 4 - Vaccine industry example (similar to Millennium Initiative)

Guiding Principles

- Regulatory requirements (FDA, NEPA, BioSaftey)
- Update security assumptions
- Optimize transition of developed products
- Apply lessons learned from BD development and production programs
- Leverage information available from previous BD production analyses

Analysis Schedule

JOINT VACCINE ACQUISITION PROGRAM PROJECT MANAGEMENT OFFICE



Summary

- Analysis of Alternatives process initiated
- WIPT and Support Contract established
- OIPT and Blue Ribbon Panel being established
- Analysis Recommendations due to DATSD(CBD) on 20 Nov 00

Medical Biological Defense Research and Military Infectious Disease Research Programs

Similarities and Differences

Presentation to the ASBREM Committee

COL J. F. Glenn

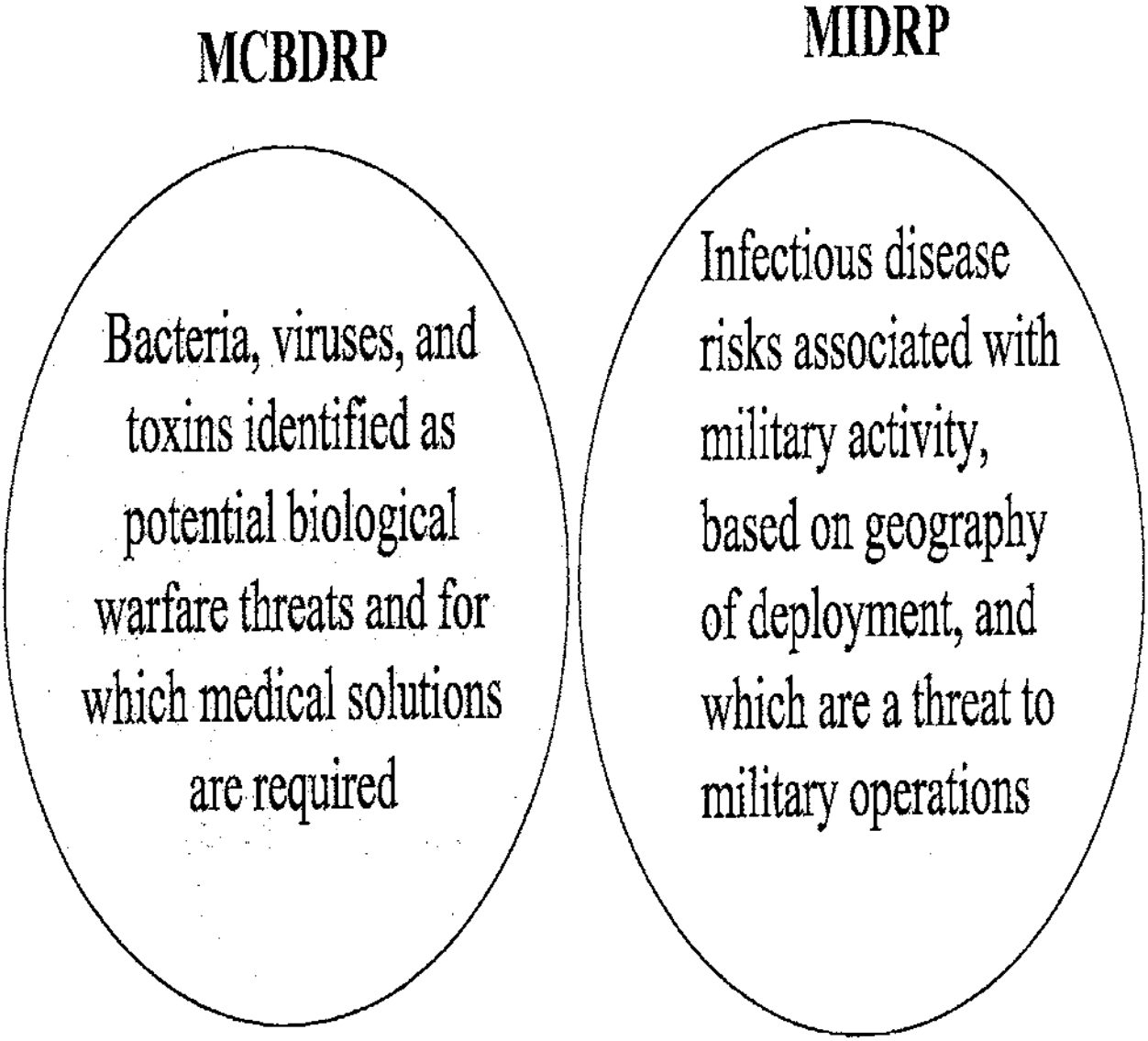
11 July 2000

MBDRP/MIDRP
Program Similarities

- Similar types of medical solutions (vaccines, therapeutics and diagnostics) are sought by both programs.

- Researchers use similar scientific methodologies and approaches to technology development: genetic engineering, DNA and novel vaccine platforms, drug screening, common diagnostic technologies, and genomics.

Divergent Program Focus with Minimal Overlap



Each program staffed with appropriate scientific expertise & capabilities.

Programmatic Contrasts

MBDRP

- OSD funding, Army Executive Agent, Joint coordination of Service requirements & program including ASBREM oversight
- S&T execution
  - USAMRMC Labs
  - Navy
- Clinical trials for efficacy are not possible (surrogate markers & animal models required for FDA licensure)
- JPO-BD - ACAT II Acquisition Program (under DAB oversight), has MDA role, JVAP is Advanced Developer

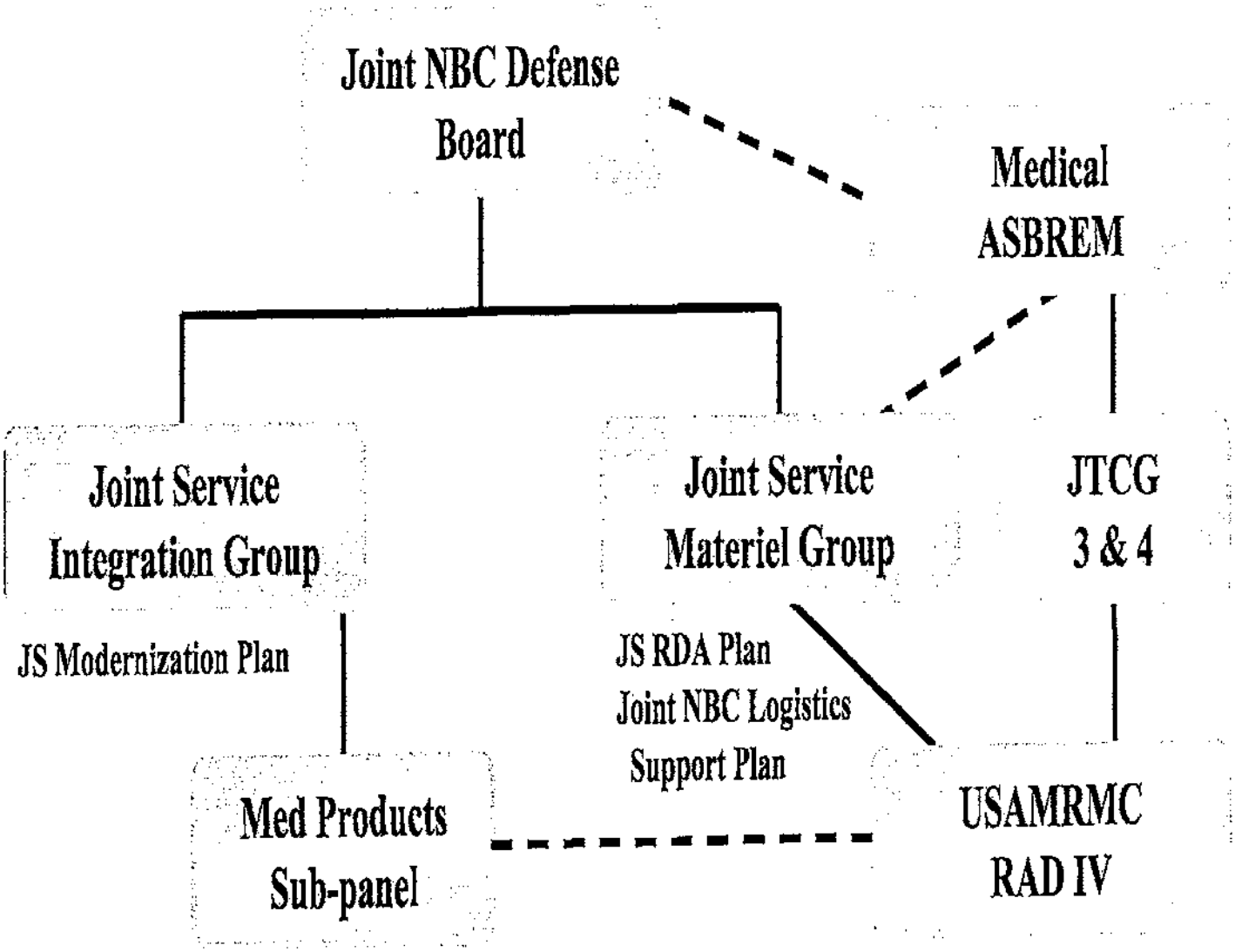
MIDRP

- Army funding, Army Lead Agent, ASBREM Committee coordination
- Funding
  - 6.1-6.3 from ASA-ALT
  - 6.4-6.5 from DCSOPS
- S&T AND Advanced Development execution (6.1-6.5)
  - WRAIR
    - 2 OCONUS Labs for field efficacy tests
    - Pilot Bioproduction Facility
    - Clinical trials facility
  - NMRC
    - 3 OCONUS Labs for field efficacy tests
  - USAMRIID
- ACAT III/IV Acquisition Program, CG USAMRMC is MDA, USAMMDA is Advanced Developer

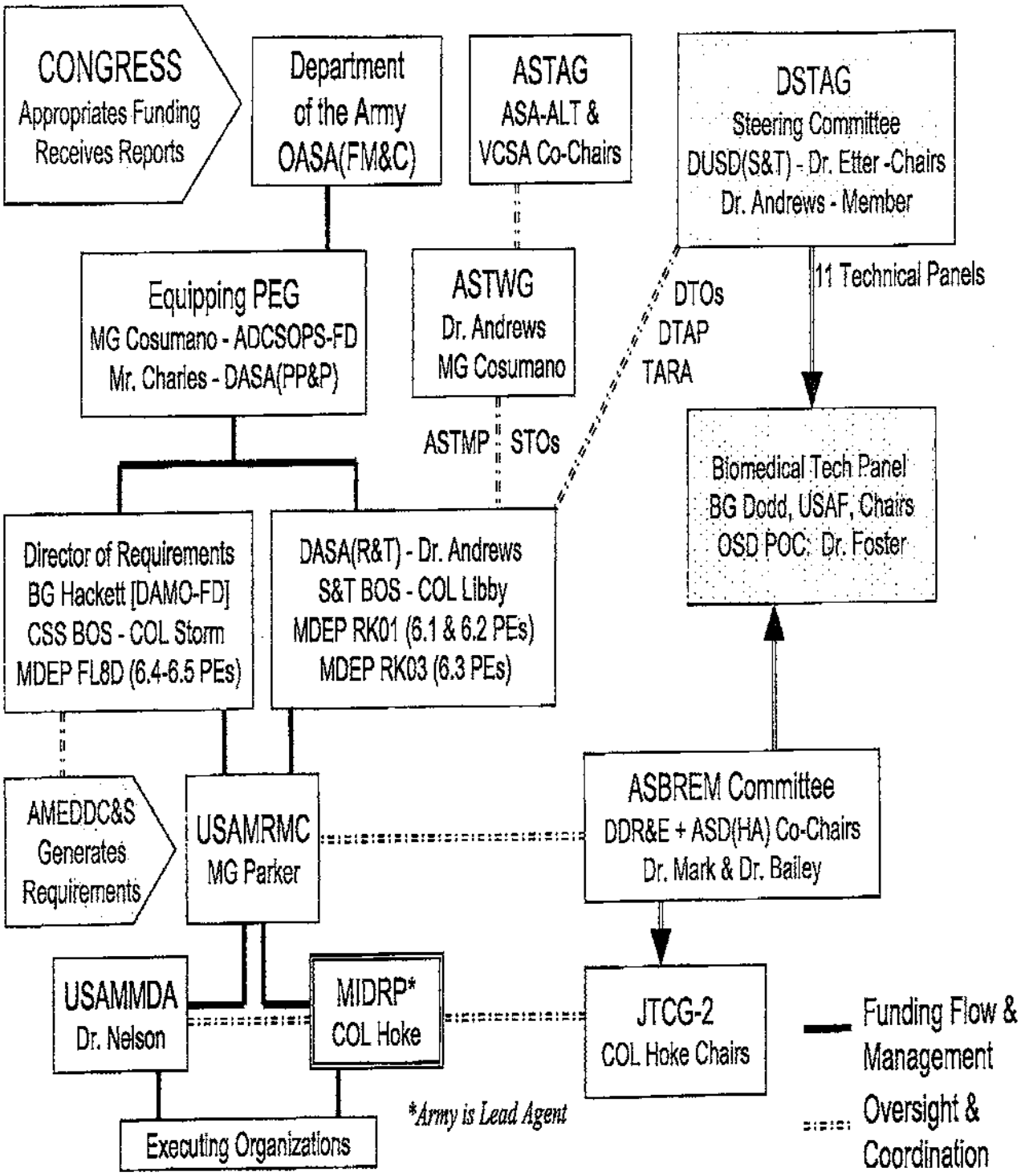
Research Prioritization

MBDRP	MIDRP
• Threat-based/Requirements driven - classified Threat List • Requirements generated and prioritized by the Joint Service Integration Group (JSIG) – CinC surgeons have a role – JTCG 4 - ASBREM – Medical Program Sub-Panel (JSIG) addresses joint medical requirements and capabilities (JORDs, JFOCs) • AMEDD C&S • DSTAG recommendations from CBD TARA on DTOs • Limited input from AFEB	• FOCs • Professional input from ongoing epidemiological analysis from multiple sources • List prepared in Aug by MIDRP for FY beginning 14 months later • JTCG 2 of ASBREM reviews • AMEDD C&S assigns scores to workpackages – Periodic briefings of Medical Force Protection ICT • STOs and DTOs; ASTAG & JWSTP • Limited input from AFEB

Medical BD Program
Organizational Environment



Military Infectious Disease Research Program
Organizational Environment



Comparisons in Oversight

MBDRP	MIDRP
• Multi-level Oversight – RAD IV oversees program for the CG (staff office) – RAD is JSMG Medical CAM (total lifecycle oversight) and JTCG 3 and 4 Chair – Annual CBD TARA (DTOs) (and Biomedical TARA) – Annual JSMG Program Review (6.1 - 6.5 funded programs) – R-forms (JCBIS)	• Multi-level Oversight – RAD 1 manages program for CG (staff office) – Biannual Biomedical TARA (DTOs) – RAD chairs JTCG-2 – STOs reviewed annually for Army – R-forms (ASTMIS)

Conclusions

- Scientific methodology and technical approaches are essentially the same
- Each program is targeted to different military problems (BW threats vs. endemic ID threats)
- Requirements generation, prioritization, and definition is different for each program
- Program oversight is different for each program

BACKUP SLIDES

Medical Biological Defense Program – Historical Highlights

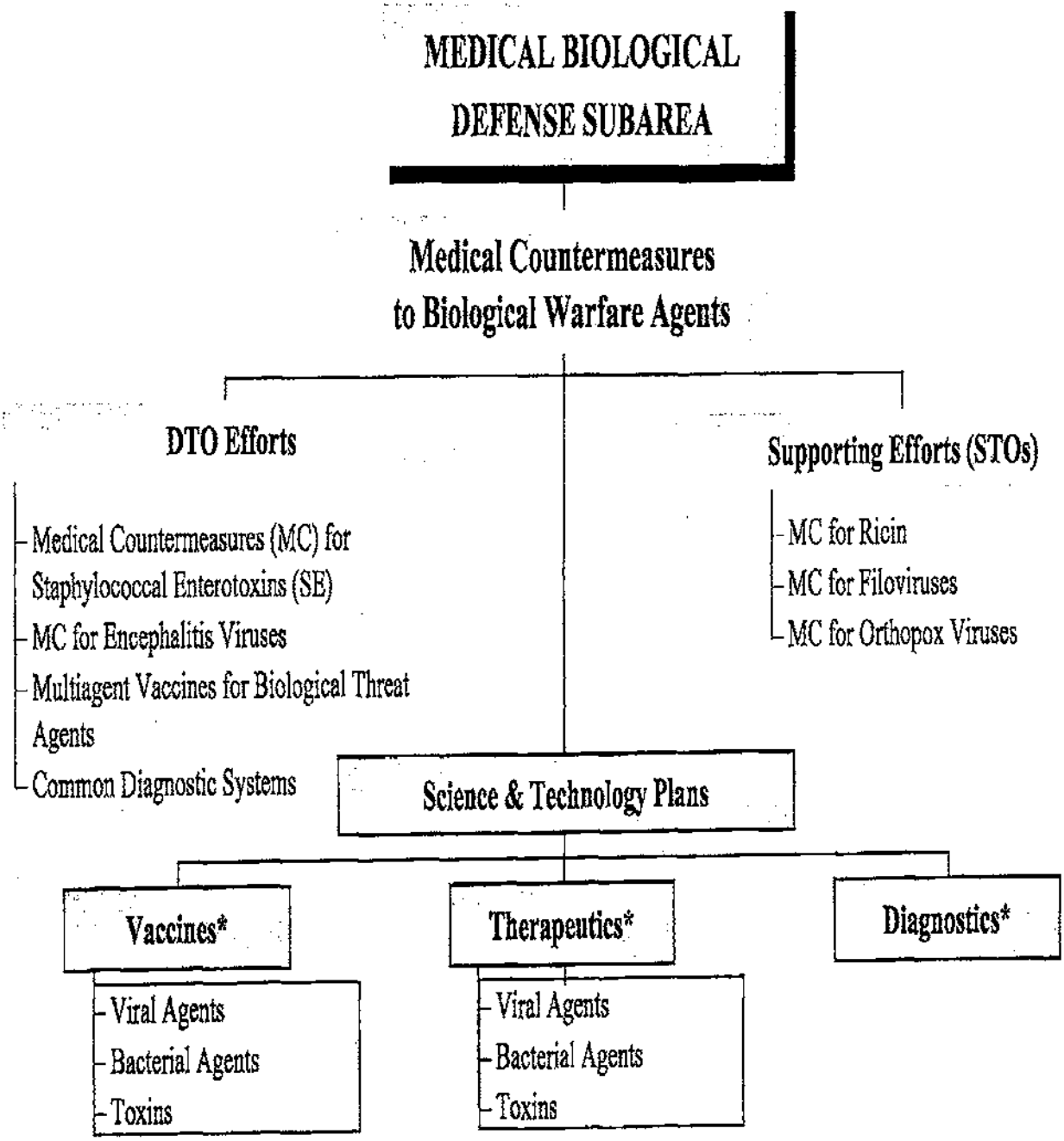
- Biological & Toxin Weapons Convention (ratified by U.S in 1975)
  - Provides rationale for differentiating biodefense (BD) from endemic infectious disease (ID)
  - Review conferences added Confidence Building Measures (declares biodefense program information)
- High national visibility in mid- to late 80s (National Environmental Policy Act litigation, Congressional and GAO investigations)
- Gulf War and follow-on GWI issues (1991)
- USAMRMC splits management of medical BD program from MIDRP (1991)
- Budget authorizations contain threat-related restriction on medical BD investment (1992/1993)

Medical Biological defense Program - Major Milestones

- Codification (10 USC 2370a) of medical BD RDT&E budget allocations by near-term and other threats (1994)
- Public Law 103-160 (1994)
  - Assign single office of responsibility for Chem/Bio Defense within DoD
  - Consolidation of chemical & biological defense programs under DATSD (CBD) (1994)
- Joint Program Office for Biological Defense established (1994)
- Joint Vaccine Acquisition Program Prime Systems Contract for development, licensure, procurement, storage, and distribution of vaccines awarded (1997)

Medical Biological Defense

Organizational Taxonomy



*Include initiatives in emerging threats & genetically engineered microbes

Summary of Enabling Documents for Infectious Diseases Research Program

Infectious Diseases Program: Enabling Documents

Tab	Authority	Document	Comments
1	Congress	DoD Appropriation Bill - 1982	• ASBREM committee authorized as interim measure to eventual consolidation • Authorized inter-service assignment of officers • Army directed as "Lead Agent" for DOD ID research • Lead Agent = responsible for planning, programming and budgeting of all DOD and service unique resource requirements • Consolidation of ID research to be complete by 1984
2	DoD	USDRE Memorandum – 2 Aug 1982, SUBJ: Medical Research and Development Consolidation: Infectious Disease and Combat Dentistry	• Lead agent authorized to ask for and receive detailed information [from both Army and Navy laboratories] required to accomplish planning, programming, and budgeting responsibility...including progress reports, research reports and funding requirements. • Lead agent responsible for programming 6.1-6.4 RDT&E funds.
3	DoD	USDRE Memorandum - 26 Jul 1984 - SUBJ: Medical Research and Development Consolidation: Infectious Disease and Combat Dentistry, Amended Operational Procedures	• "Consolidation" of ID research programs formalized • Instituted JTCG-2 • Prescribed periodic program review of all program components • Prescribed timetable for formulation of infectious research plan • Outlined joint POM planning responsibilities • Prescribed annual "OCONUS Commanders' Laboratory Strategy Planning Conferences" to address coordination of ID research efforts in OCONUS labs with major program efforts in CONUS labs • Prescribed "Project Coordinators and assistant project coordinators" [from opposite service] for major thrust areas • Prescribed Product Managers for identified products in development
4	DA	USAMRDC Memorandum, o/a 25 Oct 1990, SUBJ: Explanation of USAMRDC Congressional lead agency/DOD Executive Agent Roles	• Document of a phone conversation clarifying Congressional Lead Agency and DoD Executive Agent roles

Infectious Diseases Program: Enabling Documents

Tab	Authority	Document	Comments
5	DA/DoN/ DAF	Memorandum of Agreement, 4 March 1991 ***This document has been determined to be outdated. A new MOA is being staffed.	• MOA for Infectious Disease Research Between the US Army Medical Research and Development Command, the Naval Medical Research and Development Command and the Air Force Human Systems Division

6	DoD	Charter of the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee - 23 Sep 1994	• Established the ASBREM Committee to provide management oversight, direction and coordination of Defense medical research, development, test and evaluation (RDT&E) programs
			• ASBREM Objectives (selected)
			  • Continue and enhance cost effective resource utilization by improving the responsiveness of Tri-Service coordination and cooperation...
			  • Obviate unnecessary duplication in the Military Departments and other Agencies' medical science, technology, and development programs
			  • Provide the mechanism to address medical RDT&E organizational roles, conduct research management studies, resolve organizational and functional alignment issues regarding biomedical research among the Medical Departments and Agencies.

7	N/A	DRAFT Memorandum of Agreement to replace 4 March 1991 document.	• Distributed to service ASECs 3 May 2000.
8	DA, MRMC	Memorandum, Assignment of Naval Officer to the Staff of the Military Infectious Diseases Research Program, 27 May 1999	• Memorandum requests Asst. Chief for Operational Medicine and Fleet Support, BUMED consideration of assigning a Naval Officer full time to MIDRP staff.

FY01 JTCG-2 Prioritized Structure

STEP F - Malaria Vaccine Research

STO A1 - Multi-Antigen, Multi-Stage *Plasmodium vivax* Malaria Vaccine

STO AF - Multi-Stage, Multi-Antigen Recombinant *Plasmodium falciparum* Malaria vaccine

STEP Q - Malaria Drug Discovery and Development

STO AQ - Drug for Prevention of Multi-Drug Resistant Malaria and Severe & Complicated Malaria

STEP D - Prevention of Diarrheal Diseases

STO AD - Prevention of Diarrheal Diseases

STEP S - Flavivirus Vaccine Research (includes TBE)

STO AS - Nucleic Acid (DNA-based) Vaccines to Prevent Dengue

STEP L - Diagnostic Systems for Infectious Diseases

STO AL - Common Diagnostic Systems for Biological Threats & Endemic Infectious Diseases

STEP C - Malaria Genome Project

STEP U - Identification & Control of Insect Vectors of Infectious Diseases

STO AU - Development of a New Standard Military Insect Repellent

STEP N - Hepatitis Virus Vaccines

STEP M - Meningococcal Vaccine Research

STEP T - Research on Hemorrhagic Fever & Other Highly Lethal Viruses (includes Hantavirus)

STEP J - Rickettsial Diseases Research

STEP P - Leishmania Research (Gulf War Funding, Not Ranked)

STEP H - Prevention of Military HIV Infections (Separate Funding Lines, Not Ranked)

ACRONYM DEFINITIONS

AMEDDC&S - Army Medical Department Center & School, Ft Sam Houston, TX
ASA-ALT - Assistant Secretary of the Army for Acquisition, Logistics & Technology
ASA(FM&C) - Assistant Secretary of the Army for Financial Management and Comptroller
ASBREM - Armed Services Biomedical Research & Evaluation Management Committee
ASD(HA) - Assistant Secretary of Defense (Health Affairs)
ASTAG - Army S&T Advisory Group
ASTBMP - Army Science & Technology Master Plan
ASTWG - Army Science & Technology Working Group
BOS - Budget Operating System
CSS - Combat Service Support
DASA(PP&P) - Deputy Assistant Secretary of the Army for Plans, Programs, and Policy (OASA-ALT)
DASA(R&T) - Deputy Assistant Secretary of the Army for Research & Technology (OASA-ALT)
DCSOPS - Deputy Chief of Staff for Operations & Plans (Army)
DDR&E - Director, Defense Research & Engineering (Works for USDA&T)
DSTAG - Defense Science & Technology Advisory Group Steering Committee
DUSD(S&T) - Deputy Undersecretary of Defense for Science & Technology [Works for DDR&E]
DTAP - Defense Technology Area Plan
DTO - Defense Technology Objective
JTCG - Joint Technology Coordinating Group
MDEP - Management Decision Package
MIDRP - Military Infectious Diseases Research Program
STO - Science & Technology Objective
PE - Program Element
PEG - Program Evaluation Group
TARA - Technology Area Review & Assessment
USAMRMC - U.S. Army Medical Research & Materiel Command
USAMMDA - U.S. Army Medical Materiel Development Activity
USDA&T - Undersecretary of Defense for Acquisition & Technology
VCSA - Vice Chief of Staff of the Army

A JOINT MEDICAL SCIENCE AND TECHNOLGY ASSESSMENT

DDR&E Tasking

"Identify future military medical capabilities needed to provide next-generation medical support across the spectrum of military conflict and assist in planning and programming medical S&T."

Terms of Reference

- Provide a forum for Service and Federal Agency communication, cooperation, and coordination to review common problems and shared visions through a dialog of requirements.
- Identify common Service and Federal Agency S&T future capabilities.
- Develop recommendations for research leading to enhanced Joint medical support capabilities. (For medical personnel and the Warfighter)
- Identify biomedical S&T capabilities that reduce medical manning, training, and the logistics footprint.
- Develop and promote a combined biomedical vision for future medical care across the spectrum of military conflict.

Tasks

- Review and Assess Medical S&T Capabilities and Requirements to support a Joint Operational Concept for future warfare.
- Identify new Joint Medical S&T Capabilities that fill gaps in identified Service Capabilities and Requirements, or emerging Biomedical Technologies that will provide new or enhanced capabilities to a Joint Force, especially Special Operations.
- Project identified requirements in a Joint environment and determine their value as an enhanced capability in Joint Operations.
- Explore concepts for Biomedical Support that enable enhanced medical mobility which supports a smaller, more flexible Joint Force.

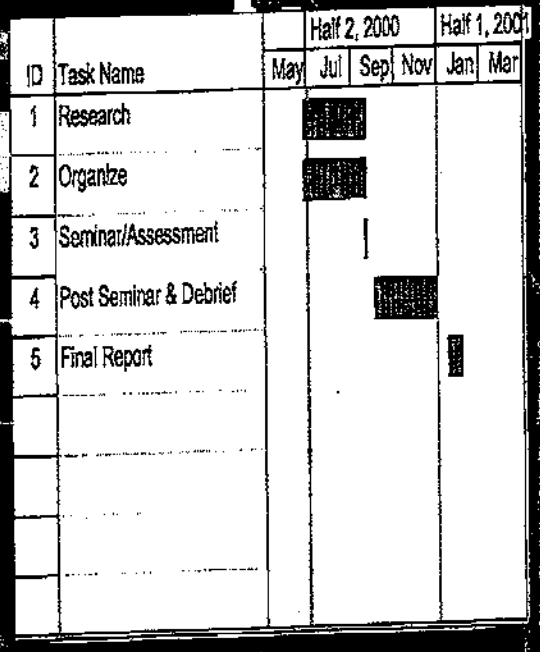
Tasks (con't)

- Recommend technologies that will reduce redundant biomedical capabilities in future Joint Operations.
- Determine and recommend technologies to be integrated into Service medical departments.
- Identify opportunities for experimentation or field testing Joint Biomedical Initiatives that have the potential to enhance Joint Operations

Note: Tasks are optimal; Proper Scoping or Doable Tasks within ongoing timeframe.

A JOINT MEDICAL SCIENCE AND TECHNOLGY ASSESSMENT

Game Assessment Timeline



Assessment Schedule

	MON	TUES	WED	THURS	FRI
AM	Register Background Scope Task Backdrop	Cell Work Plenary Session	Plenary Session Cell Work	Plenary Session Cell Work	SEMINAR BREF OUT
PM	Plenary Session Cell Work	Cell Work	Cell Work	Capabilities Requirements Tech ID Prioritization	SEMOR LEADER SEMINAR

* Looking for facilities to move this event into the late October and November timeframe.

CMAT Control # 57
2002227-0000036

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

APR 30 2001

HEALTH AFFAIRS

MEMORANDUM FOR DIRECTOR, JOINT STAFF

SUBJECT: Review of the Draft Contingency Protocol for Vaccination of Volunteers with Anthrax Vaccine Absorbed (AVA) after Possible Exposure to Bacillus Anthracis Spores

This is in response to your memorandum of April 4, 2001, regarding the subject document review. Your memorandum notes that, "As such, this protocol is not executable during combat operations."

The Joint Staff and CINCs should be advised that, absent a Food and Drug Administration (FDA) approved protocol, any request for use of an Investigational New Drug (IND) during combat operations will most likely be disapproved. There is precedence regarding such protocols. In a memorandum dated February 24, 1998, USCENTCOM requested USCINCCENT be formally identified "as the sole issue authority for the use of PB (pyridostigmine bromide) as a nerve agent pretreatment within the Central Region," and also requested a DoD waiver from the requirement to follow the FDA's required IND protocol. In reply, Mr. Christopherson, Acting Assistant Secretary of Defense for Health Affairs, noted that until such time as an acceptable treatment use protocol has been filed with the FDA, DoD policy, based on federal regulations, prohibits DoD from issuing or using PB. Based on that memorandum, the Joint Staff responded to CINCCENT by disapproving the request and advising that "PB is not, repeat not, to be issued to individual service members or directed for use in this or any military operation unless specifically approved by OSD. If acceptable protocols are approved, the Joint Staff will identify USCINCCENT as the sole authority for how, when, and to whom PB is to be issued."

The problem identified by USCENTCOM in 1998 is relevant today. Unless we can resolve the problems identified in the Joint Staff memorandum of April 4, 2001, it is likely that any request for use of an IND will be disapproved. Your memorandum notes that the Joint Staff and Office of the Army Surgeon General will co-sponsor the Joint Medical Nuclear, Biological and Chemical Readiness Conference from April 30 through May 4, 2001, which will convene an IND working group to address implementation of this type of protocol. A member of my staff, Salvatore M. Cirone, Program Director, Health Science Policy, will be a member of this IND working group. It is imperative that we resolve all concerns and develop a protocol that will be acceptable to the Joint Staff and CINCs. If we cannot reach concurrence on the subject protocol before the conclusion of the conference, I intend to forward the issue to the Under Secretary for his consideration.

J. Jarrett Clinton, MD, MPH
Acting Assistant Secretary

HA Control No.:
Document No.:
Due Date:

April 16, 2001

MEMORANDUM FOR ACTING ASSISTANT SECRETARY OF DEFENSE (HA)

THROUGH: Robert S. Driscoll, COL, MS, USA, Acting DASD(HA)HOP 4/16/01

FROM: Salvatore M. Cirone, Program Director, Health Science Policy

SUBJECT: Review of the Draft Contingency Protocol for Vaccination of Volunteers with Anthrax Vaccine Absorbed (AVA) after Possible Exposure to Bacillus Anthracis Spores - ACTION MEMORANDUM

DISCUSSION: This is a reply to the Director, Joint Staff, regarding the JS memorandum dated April 4, 2001 (TAB A), same subject. The JS notes in the memorandum that the subject protocol is not executable during combat operations. He states that the JS and Army OTSG are sponsoring Joint Medical Nuclear Biological and Chemical Readiness Conference from April 30-May 4, 2001. He states that the work of the conference IND work group should be considered in producing the final version of this protocol.

The reply states that it is imperative that we resolve JS concerns and develop a protocol that will be acceptable to the Joint Staff and CINCs. It is critical that the Joint Staff and CINC participants come to the conference with a determination to make this protocol workable so we can get concurrence to forward this protocol to the Food and Drug Administration. The Joint Staff and CINCs need to be cognizant that without an FDA approved protocol, any request for use of an IND during combat operations will most likely be disapproved. The memo notes that if we cannot develop concurrence on the subject protocol following the conference, the ASD(HA) anticipates notifying the Secretary of the situation. The reply references a memo from the CINCCENT in February 1998 (TAB B) and the ASD(HA) reply (TAB C). The DRAFT JS reply to CINCCENT is at TAB D. It is my understanding that the JS did send out the reply as noted in the draft, but I do not have a copy.

RECOMMENDATION: Sign the memorandum.

COORDINATION:
OGC: 4/16/01

THE JOINT STAFF
WASHINGTON, DC

Reply ZIP Code:
20318-0300

DJSM-0256-01
04 April 2001

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

Subject: Review of the Draft Contingency Protocol for Vaccination of Volunteers with Anthrax Vaccine Absorbed (AVA) after Possible Exposure to Bacillus Anthracis Spores

1. Thank you for the opportunity to review[1] the subject document. We have reviewed the protocol and request incorporation of the enclosed comments and resubmission of the protocol to the Joint Staff for final staffing.

2. While Service members must receive the vaccine in order to survive, operational commanders will not be able to complete all the training and documentation requirements for this protocol in theater during combat operations. The Services do not have an executable plan to train the unit level Associate Investigators and the Principal Investigators. As such, this protocol is not executable during combat operations.

3. The Joint Staff and Army Office of the Surgeon General are co-sponsoring the Joint Medical Nuclear Biological, and Chemical Readiness Conference from 30 April through 4 May. The conference includes an Investigational New Drug working group that will address how to implement this type of protocol. Their work should be considered in producing the final version of this protocol.

4. The Joint Staff point of contact is (b)(6) (b)(6).

S. A. FRY
Vice Admiral, U.S. Navy
Director, Joint Staff

Enclosure

Reference:

1 OASD(HA) e-mail, 18 December 2000, "DRAFT Contingency Protocol for Volunteers with Anthrax Vaccine Absorbed (AVA) after Possible Exposure to Bacillus anthracis Spores – ACTION MEMORANDUM"

ENCLOSURE

JOINT STAFF COMMENTS ON THE CONTINGENCY PROTOCOL FOR VACCINATION OF VOLUNTEERS WITH ANTHRAX VACCINE ADSORBED (AVA) AFTER POSSIBLE EXPOSURE TO *BACILLUS ANTHRACIS* SPORES.

1. Section 2.0

a. Page 3, first paragraph, last sentence. Change as follows: "Anthrax Vaccine Adsorbed (AVA) . . . ."

REASON: Completeness. This is the first time the abbreviation is used within the document.

b. Page 3, third paragraph, first sentence. Change as follows: ". . . the CDC and ACIP (13, 16) . . . ."

REASON: Completeness

c. Page 3, fifth paragraph, fourth sentence. Delete and substitute the following:

"The intent of this protocol is for contingency use of anthrax vaccine in a post-exposure setting, not to support a labeling change for the licensed anthrax vaccine."

REASON: Allows the use of information collected while stating the proper intent of the protocol.

d. Page 4, first paragraph. Comment: Define the timeframe and when data collection will cease, so that analysis and reporting to FDA can begin and end.

REASON: Clarity of the research design.

2. Section 2.2.2.2

a. Page 8, first paragraph. Add to the end of paragraph the following statement: "Some of the most robust evidence of the safety of anthrax vaccine comes from the Defense Medical Surveillance System (DMSS), which shows that anthrax-vaccinated and –unvaccinated are hospitalized at the same rates."

b. Page 9, fourth paragraph, last sentence. Change as follows: "No deaths have been causally linked to the ~~resulted from~~ anthrax vaccine."

c. Page 12, first paragraph, last sentence. Change as follows: "Anthrax Vaccine Expert Committee (AVEC) found no . . . ."

REASON: Accuracy. The DMSS constitutes a capability more robust than VAERS for post-marketing surveillance of health events potentially associated with the anthrax vaccine. The ACIP recommendations note two deaths were reported through VAERS as of publication date, but were not "causally associated".

3. Section 2.3.4

a. Page 14, first paragraph, third line. Change as follows: ". . . .The ~~AVIP~~ ACIP recommends . . . ."

REASON: The ACIP is a more authoritative reference than the AVIP and adds credibility to the statements as a civilian advisory group.

b. Page 14, second paragraph. Change as follows: "~~Protective clothing and gas masks can~~ Individual protective masks (gas masks) and collective protection systems (NBC MOPP suit) provide excellent . . . ."

REASON: Protective clothing provides minimal protection against anthrax spores. However individual protective masks and collective protection systems provide inhalation protection against anthrax spores. The correct terminology should be used, however the document should also be written in lay language.

4. Page 16, Table 5, Anthrax Vaccine Administration Guideline for Post-Exposure Prophylaxis

a. Page 16, doses 4 through 6, second and third columns. Change as follows: "~~14 days~~6 month" and "~~2 weeks~~6 months."

b. Page 16, dose 7, second and third columns. Change as follows: "~~14 days~~ 12 months" and "~~2 weeks~~ 12 months."

REASON: Consistency with the current anthrax program. The current dosage schedule for doses 4 through 6 are given at a 6 month interval with subsequent doses being required annually.

c. Page 16, Notes section. Add the following:

"In a "vaccine tight" environment, triage emphasis should be given to those who have not received doses 1, 2, and 3 before considering boosting of those who have received four or more doses of the vaccine."

REASON: Large amounts of vaccine might be squandered by boosting of those who have nearly completed the full vaccine schedule.

5. Page 17, section 2.7, References, item 13. Change as follows: "United States, 2000 (~~draft~~December 15, 2000)~~.~~"

REASON: Accuracy

6. Section 4.0

a. Page 20, first paragraph, third sentence. Change as follows: "The Secretary of Defense ordered the implementation of a plan ~~(contingency protocol under an IND)~~ to protect service . . . ."

b. Page 20, first paragraph, fifth sentence. Change as follows: ". . . The Surgeon General of the Army and the absence . . ."

c. Page 24, Figure 5, Responsibilities Associated with Anthrax Vaccine Contingency Protocol

(1) Responsibilities of the Combatant CINC section: Add the following:

"3. Request approval from SECDEF to implement the anthrax contingency protocol.

4. Inform SECDEF of decisions related to the execution of the protocol."

REASON: IAW DODD 6200.2 the implementation authority rests with SECDEF, not the CINC. The CINC is responsible for informing the SECDEF of any decision made after the SECDEF gives approval to execute the protocol.

(2) Page 24, Responsibilities of Site Investigator, item 11. Change as follows: ". . . AEs to ~~RCQ, USAMRIID Human Use Committee, and~~ Clinical Project Manager."

(3) Page 24, Responsibilities of Clinical Project Manager section. Add the following: "8. Forward copies of serious and unexpected AEs to the RCQ, HSRRB and USAMRIID's Human Use Committee."

REASON: The Clinical Project Manager should be responsible for forwarding the information to the RCQ and USAMRIID Human Use Committee. This will reduce the reporting requirements for the Site Investigator and require him/her to only have one primary office to report all information/reports. By centralizing the reporting, this will

help to ensure the information is forward to the proper agencies/committees.

(4) Page 24, end of figure. Add the following:

"Responsibilities of the Secretary of Defense:

1. To approve/disapprove CINC request to implement the protocol. The Secretary of Defense has the authority under DODD 6200.2 Section 4.2 to approve protocols for use on volunteers who give informed consent.
2. Request a waiver of informed consent from the President of the United States when necessary IAW DODD 6200.2 Section 4.3."

d. Page 25, end of paragraph 2. Add the following:

"To reduce bias, a comparable control group of personnel who did not participate in the protocol will be surveyed six months after receiving the influenza vaccine, for comparison."

REASON: Clarity, completeness and consistency. Avoids confusion with other Service Surgeons General. This portion of the protocol should show all of the key responsibilities. Under DODD 6200.2, the SECDEF does have the ability to request the President waive the requirement for informed consent. The SECDEF must personally request the waiver. The protocol should recognize this option and address the steps when necessary. Improves study design by adding a bias control measure for the survey.

7. Section 4.9

a. Page 27, 4.9 Source Data section, first paragraph. Delete and substitute the following:

"The following data fields will be completed via Service automated immunization tracking systems (AITS) and will serve as the Case Report Form for subjects enrolled in the contingency protocol: (The Service's AITS are MEDPROS (Army), SAMS (Navy & Marine Corp), and MITS (Air Force).)"

b. Page 27, Immunization Table, subparagraph 1. Add the following:

"Series Number, Route of administration (e.g., SC, ID, IM, etc.)."

c. Page 27, Temporary Personnel Table, subparagraph 2. Add the following:

"National Identity Number or other ID number."

d. Page 27, subparagraph 3, first bullet. Change as follows: ". . . used in ~~MODS~~Service AITS."

e. Page 28, subparagraph 4, first bullet. Change as follows: "used in ~~MODS~~Service AITS."

REASON: Accuracy, completeness and clarity. The protocol can be given to non-US service volunteers. Thus the protocol must comply with the requirements of DODI 6205.4, Section 5.5.4.1 Immunization of Other Than US Forces for Category 2 through 4 personnel.

8. Page 29, section 5.3. Comment: Clearly define the withdrawal (voluntary and involuntary) criteria for the protocol. Identify the documentation requirements when an individual is withdrawn from the protocol. Individuals who do not desire to take non-FDA-released AVA will be allowed (indeed, encouraged) to take the antibiotic regimen.

9. Page 30, section 6.1, third paragraph, first sentence. Change as follows: ". . . further exposure to *B. anthracis* spores ~~should~~ will be advised to complete the FDA . . . ."

REASON: Clarity

10. Page 33, section 6.5, end of paragraph. Add the following:

"Monitoring/ensuring that subjects complete the requisite number of vaccinations must be a partnership among the subjects, themselves, their commanders or other unit leaders, and the medical community, especially considering the stress of implementing this protocol within military operations."

REASON: Accuracy

11. Page 34, section 8.0. Comment: Describe plans that establish accountability for documentation of protocol treatments in individual medical records of vaccine recipients. Address the documentation of adverse events during a military operation in the health record. The protocol must establish accountability for tasks. As written, this section loosely requires AE outcome documentation (paragraph 3).

12. Page 34, section 8.1, end of first paragraph. Add the following:

"Loss of duty greater than 24 hours is a mandatory VAERS reporting criteria."

REASON: Accuracy

13. Page 35,section 8.3. Add the following:

"Volunteered and observed AEs will be recorded in the volunteer health records in addition to any protocol specific records."

REASON: Clarity

14. Section 8.5

a. Page 38, Clinical Project Manager. Change as follows: Move the Clinical Project Manager at USAMRIID to the top of the addressee list for serious and unexpected AEs.

b. Page 38, after the Clinical Project Manager. Add the following statement: "The USAMRIID Clinical Project Manager will forward AE information to:"

c. Page 38, Clinical Project Manager. Add the telephone #, fax #, and email address information to the Clinical Project Manager after the position has been filled.

REASON: The Clinical Project Manager works within the same organization as the US Army Medical Research and Materiel Command (USAMRMC) Office of Regulatory Compliance and Quality and the US. Army Medical Research Institute of Infectious Diseases (USAMRIID) Chairman, USAMRIID Human Use Committee. He/she can forward this information to these committees. This will reduce administrative burden on deployed operational units and help to ensure each committee receives the necessary information. Deployed operational units will not be able to forward AE information for central collection without it.

15. Page 39, section 8.7, first sentence. Change as follows: "review." Replace with "investigate." Delete "Human Subjects Research Review Board (HSRRB)." Replace with "Clinical Project Manager at the USAMRIID."

REASON: Accuracy. The medical officer will likely be called on to examine and possibly treat the affected individual. This is not a technical review. To help ensure compliance with the protocol, the deployed operational units should deal with only one office. The Clinical Project Manager at USAMRIID will need to have this information anyway and can forward the report to the HSRRB. This change will simplify the flow of information from the deployed unit to the central collection point.

16. Page 40, section 12.1, first sentence. Change as follows: ". . . by the Code of Federal Regulations (in particular parts 21, 56, 314, and 601 of CFR 312) and ICH . . . ."

REASON: The protocol should clearly identify applicable CFRs.

17. Page 41, section 12.2, paragraph 1, second sentence. Add the following:

"DoD's quad-fold brochure and the CDC's Vaccine Information Statement (VIS) on anthrax vaccination may be used as training aids to provide additional information."

REASON: Uniformity and consistency of information by utilizing existing resources.

18. Sections 12.4 and 12.5

a. Page 42. Comment: Ensure compliance with the Privacy Act (5 U.S.C § 552a) if establishing any database of service members with data retrievable by their social security numbers. See AR 340-21, The Army Privacy Program, 5 July 1985, paragraph 4-6.

b. Page 42. Comment: Ensure that the listing in sections 12.4 and 12.5 of those individuals who will have access to these records is the same as that on the Informed Consent Form.

c. Page 42. Comment: Explicitly state on the informed consent form all of the parties who will have access to the data (consistent with sections 12.4 and 12.5).

d. Page 42. Comment: The Privacy Act also requires that a Privacy Act statement be furnished to individuals whenever personal information is requested from them that will become part of a system of records retrievable by their names or personal identifiers. See AR 340-21, paragraph 4-2 for a list of required data. See also AR 15-6, Appendix B for additional guidance on drafting a systems notice.

e. Page 42. Add the following:

"Your signature below constitutes consent to disclosing this data to these individuals."

REASON: Accuracy, consistency and to ensure compliance with the Privacy Act. Per AR 340-21, Chapter 3, the Army is prohibited from disclosing a record from a system of records without obtaining the prior written consent of the data subject, except, for example, when disclosure is made to officers

and employees of DOD who have a need for the record in the performance of their duties (the so-called "need-to-know" exception to the Privacy Act), or permitted by a routine use that has been published in the Federal Register. Any invocation of the "need-to-know" exception must be documented by the official responsible for invoking it.

19. Page 42, section 14.0 and section K of the Informed Consent Form. Comment: Consult with US Army Medical Research and Materiel Command (USAMRMC) legal counsel to determine whether the passage "Should a subject be injured as a direct result of participating in this protocol, he/she will be entitled to medical care at no cost for that injury. The subject will not receive any injury compensation, only medical care" should be changed to "The subject will not receive any injury compensation beyond that provided by law." Further, request USAMRMC counsel coordinate with the Office of Workers Compensation to determine if they have any provisions affecting civilians who are exposed to anthrax and to develop plans to accommodate medical care for civilian and contractor personnel who are injured as a direct result of participating in the protocol. It is likely that questions about such care will arise during the briefing for the informed consent and unit support personnel will need to know how to care for members who need to exercise this component of the protocol.

20. Appendix Section. Comment: Add a copy of the FDA Form 1572, instructions on how to fill this form out, and how to obtain a copy of the form through the internet and/or mail. The protocol should be inclusive and provide the Principal Investigators a copy of each form they must complete.

21. Appendix A, Logistic Annex

a. Page A-2, second paragraph, first line. Change as follows: ". . . Vaccine to be used under this protocol may not have ~~not~~ been released . . . ."

REASON: Accuracy. If vaccine which has been released is available, then this vaccine will be used. If FDA released vaccine is not available, then non-FDA released vaccine will be use.

b. Pages A-3 and A-4. Comment: Provide an agency email account when possible.

(1) Add the following: "Navy and Marine Corps".

(2) Change as follows: ". . . (b)(6)
(b)(6)

REASON: Accuracy. The vaccine may or may not have been released. Avoids any unnecessary limitations on the protocol. Providing agency email accounts will allow field units to forward the necessary information once individuals PCS.

c. Page A-3, subparagraph e. Comment: Ensure a mechanism is in place to keep the POC listing current and accurate. Recommend referencing the USAMMA website (http://www.armymedicine.army.mil/USAMMA/anthrax/poc.stm) in the protocol. USAMMA must ensure changes and updates are posted on the website in a timely manner as necessary.

d. Page A-13, paragraph 2. Comment: The first sentence states: "The antibiotics Ciprofloxacin, Doxycycline and Penicillin are all approved by the FDA for either the prevention or treatment of disease caused by *B. Anthracis*. As such, they are not considered investigational agents under this protocol." This statement is contradictory to the statement on page 33 (6.4.2.3.), "Penicillin is approved by the FDA for the treatment of anthrax disease but not for post-exposure prophylaxis." Clarify which statement is correct and then make necessary changes to ensure consistency throughout the protocol.

REASON: Accuracy and clarity

22. Appendix B

a. Page B-3, after "Number of anthrax vaccinations received:" Change the blank line with check boxes, indicating the number of potential doses. "__1 __2 __3 __4 __5 __6 __7 or more."

b. Page B-3, "Experience with antibiotic" section. Delete "Yes No". Replace with check boxes listing "__ <5 __ 5-10 __ 11-20 __ 21-40 __ 41-60 __ 61-80 __ 81-100 __ 101-120."

REASON: Check boxes give more easily analyzed information than free text entries. An estimate of the total number of antibiotic doses taken is more informative assessment of compliance than a simple yes or no answer.

23. Appendix C

a. Page C-2, after the line "Do you smoke?" Add the following: "Do you drink alcohol? How many drinks per week?" Then list in check box format several options.

b. Page C-2, after last question, "How many doses have you taken? Add the following check boxes "<5, 5-10, 11-20, 21-40, 41-60, 61-80, 81-100, and 101-120."

REASON: Alcohol use is an important contributor to the overall health status along with tobacco use. Check boxes give more easily analyzed information than free text entries.

24. Appendix G

a. Page G-6, Precaution paragraph. Comment: Include information about avoiding excessive sunlight/photosensitivity while taking Doxycycline.

b. Page G-6, Drug Interactions paragraph. Add the following: "Doxycycline can increase sensitivity to sunlight."

c. Page G-6. Comment: Include a summary paragraph to summarize the important points at the end of the consent form (e.g. how to avoid excessive sunlight, be aware of dizziness, decreased effectiveness of birth control pills, how and when to take the medications).

d. Page G-7, Drug Interactions paragraph. Add the following: "Penicillin can increase sensitivity to sunlight."

e. Informed Consent Form

(1) Comment: Create three separate Informed Consent Forms. Version 1 is for use of FDA released vaccine, version 2 is for use with non-FDA released vaccine, and version 3 is for when either FDA released or non-FDA released vaccine will be available. In each case the third paragraph under sub-paragraph A must be adjusted to correctly identify which vaccine (FDA released or non released) is being used. The third version could use a check box style question such as: "You will be given a dose of vaccine from (check the one that describes the vaccine) __ FDA released AVA vaccine or __ non-FDA released AVA vaccine but which the FDA agrees may be used in this protocol." For version 2 and 3, add a paragraph that describes why the protocol is using non-FDA release AVA vaccine.

(2) Paragraph G, subparagraph 3. Delete "or triceps."

(3) Comment: Add the risks of no treatment.

(4) Second page (page unnumbered), paragraph 2. Comment: The protocol addresses taking all the antibiotics together. This part of the form suggests that volunteers may take any one antibiotic only. The protocol and consent form must be consistent.

(5) Third page (page unnumbered). Comment: Ensure information on the antibiotics is consistent with the previous antibiotic information. Each drug that imposes effects from excessive sunlight and affects the effectiveness

of oral contraceptives needs to so state at every point these drug factors are mentioned. Include tips on managing oneself when taking these drugs (e.g. use of sunscreen, coincident use of supplemental contraceptives, etc.).

(6) Fifth page (page unnumbered). Comment: Add information about how the volunteer may get the information about his/her participation.

(7) Section N, fifth page (page unnumbered). Comment: List the organization and address for the Regulatory Compliance and Quality Office.

(8) Comment: Add to the protocol a discussion of the status of participants while they are under treatment (e.g., need for isolation of those exposed, hazardous material management).

REASON: Completeness and accuracy. The precautions for use of Doxycycline are not correct. As per the Physician Desk Reference 2001, sun exposure (photo-sensitivity) is a possible side effect from the use of quinolones however it is a warning in Doxcycline use and should be included in all antibiotic precautions. The injection should be into the deltoid area to avoid possible ulnar neuropathy. The protocol can be used with either FDA release or non-FDA release vaccine. Recipients need to be aware of which category of vaccine they are receiving and why they are receiving non-FDA released vaccine.

THE JOINT STAFF
WASHINGTON, DC

Reply ZIP Code:
20318-0300

DJSM-346-98
30 March 1998

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

Subject: Investigational New Drug Protocol for Military Use of Pyridostigmine Bromide

1. The Deputy, USCINCCENT, requested[1] Joint Staff assistance related to pyridostigmine bromide (PB) availability. He asked that USCINCCENT be identified as the sole issue authority for PB within his area of responsibility (AOR) and requested a waiver from the requirement to follow US Food and Drug Administration (FDA) protocols for using this investigational new drug (IND) product.

2. The Joint Staff response to USCENTCOM (enclosure) reiterates your position that the Department of Defense does not have the authority to grant a waiver from the requirement to follow federal investigational new drug (IND) regulations for PB use. It further states that the Joint Staff would forward its request for waiver of existing IND protocols to OSD.

3. USCENTCOM's intent is to establish control over issue and use of PB in their AOR within the framework of treatment protocols acceptable to USCINCCENT, Department of Defense, and the FDA. The Joint Staff believes that the operational exigency would preclude compliance with some existing IND requirements, and further agrees that, once acceptable resolution is obtained, USCINCCENT should be the sole authority for how, when, and to whom PB is to be issued.

4. The Joint Staff point of contact is (b)(6)
(b)(6)

DC Blair
Dennis C. Blair
Vice Admiral, U. S. Navy
Director, Joint Staff

Enclosure
Reference:
1 USCENTCOM memorandum, 24 February 1998, "Investigational New Drug (IND) Protocol for Military Use of Pyriodostygmine Bromide (PB)"

UNITED STATES CENTRAL COMMAND
OFFICE OF THE COMMANDER IN CHIEF
7115 SOUTH BOUNDARY BOULEVARD
MACDILL AIR FORCE BASE, FLORIDA 33621-5101

CCSG

24 Feb 98

MEMORANDUM FOR DIRECTOR OF THE JOINT STAFF, 300 JOINT STAFF
PENTAGON, WASHINGTON, DC 20318-0300

SUBJECT: Investigational New Drug (IND) Protocol for Military Use of Pyridostygmine Bromide (PB)

1. USCENTCOM requests your help to formally identify USCINCCENT as the sole issue authority for use of PB as a nerve agent pretreatment within the Central Region. We also request a DOD waiver from the requirement to follow the U.S. Food and Drug Administration (FDA) required IND protocol. Although we would only authorize issuance of the tablets in the event of an actual nerve agent attack, the operational exigency in that situation precludes the ability to adhere to a peacetime protocol.

2. As background, the FDA has restricted use of PB for nerve agent pretreatment under an IND protocol. Observance of the protocol is operationally unsupportable due to the time and resources required to medically screen, follow, and evaluate service members as study participants before, during and after taking PB. The requirement for obtaining informed consent from each individual service member is also of concern. Tactical use of PB would be contingent upon unambiguous warning of impending use of chemical weapons against U.S. troops or the actual use of chemical weapons. This is obviously incompatible with gaining the formally documented voluntary permission of every at risk individual service member to participate in a medical study.

3. Although we are cognizant of the concerns over a possible linkage between PB use in Operation DESERT STORM and the development of Gulf War Illness, the CINC must have all protective measures available to him if chemical weapons are used against our troops. I would appreciate any assistance you could provide to establish USCINCCENT as the single authority to allow individual issue in the event of a confirmed nerve agent attack and obtain an FDA waiver for use of PB by military personnel without observing the IND protocol.

Thomas R. Case

THOMAS R. CASE
Lieutenant General, USAF
Deputy Commander in Chief
and Chief of Staff

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

25 MAR 1998

MEMORANDUM FOR DIRECTOR OF THE JOINT STAFF

SUBJECT: USCINCCENT Request for Military Use of Pyridostigmine Bromide (PB) Within the USCENTCOM Area of Responsibility (AOR)

The Department of Defense does not have the authority to grant a waiver from the requirement to follow federal Investigational New Drug (IND) regulations for PB use and formally recognize USCINCCENT as the sole issue authority for PB in the USCENTCOM AOR. Only the Food and Drug Administration (FDA) has the authority to waive any of the IND restrictions imposed by federal law.

When used as a nerve agent pretreatment, PB has been designated by the FDA as an IND. Federal law requires the distribution and use of an IND in accordance with approved treatment use protocols. During Operation Desert Storm, the FDA waived informed consent and many other federal IND restrictions imposed on PB use as a nerve agent pretreatment. The treatment use protocol as well as these waivers expired at the conclusion of Operation Desert Storm and no standing treatment use protocol with or without waivers for PB exists today. Furthermore, based on many of the issues raised after Operation Desert Storm regarding the military use of medical countermeasures and illnesses among Gulf War veterans, it is clear that DoD will need to do a much better job complying with applicable record keeping and other IND requirements.

FDA has clearly indicated an unwillingness to grant a waiver of informed consent. Formal recognition of USCINCCENT as the sole issue authority for the use of PB as a nerve agent pretreatment within the USCENTCOM AOR cannot be granted until a treatment protocol acceptable to USCINCCENT, the DoD leadership and the FDA is developed and approved. Health Affairs is prepared to work with the Joint Staff in taking this issue to the senior leadership of the Department for a decision on whether or not to pursue filing an IND treatment use protocol with the FDA for use of PB in USCENTCOM AOR.

Until such time as an acceptable treatment use protocol has been filed with the FDA, DoD policy, based on federal regulations, prohibits DoD from issuing or using PB.

Gary A. Christopherson
Acting Assistant Secretary of Defense

UNCLASSIFIED

Facsimile Cover Sheet

The Joint Staff, J-4
Medical Readiness Division
(b)(6)

TO: (b)(6)

OFFICE: OSD/HA

FAX: (b)(6)

VOICE (b)(6)

SUBJ: Draft message on PB

Date: 26 Mar 98 **# PAGES WITH COVER SHEET: 4**

Terry: Need OSD/HA review and concurrence by 1200 today. Thanks.

(b)(6)

UNCLASSIFIED

DRAFT

1 03 RR UUUU

JOINT STAFF WASHINGTON DC//DJS//
USCINCCENT MACDILL AFB FL//CCDC//
INFO CINCUSACOM NORFOLK VA//J01//
USCINCEUR VAIHINGEN GE//ECDC//
USCINCPAC HONOLULU HI//J01//
USCINCSO MIAMI FL//SCDC//
USCINCSPACE PETERSON AFB CO//UD//
USCINCSOC MACDILL AFB FL//SODC//
USCINCSTRAT OFFUTT AFB NE//J001//
USCINCTRANS SCOTT AFB IL//TCDC//
COMUSKOREA SEOUL KOR//FKDC//
DA WASHINGTON DC//DAMO-ZA//
CNO WASHINGTON DC//N3/N5//
CSAF WASHINGTON DC//AF/XO//
CMC WASHINGTON DC//PP&O//

UNCLAS

MSGID/GENADMIN/JOINT STAFF DJS//

SUBJ/ISSUE AUTHORITY FOR PYRIDOSTIGMINE BROMIDE//

REF/A/DOC/USCINCCENT/CCDC/24FEB98/-/NOTAL//

(b)(6) TOPS: SOA 0059-98

RELEASER

JSISC ALTERNATE MESSAGEFORM

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02 03 RR

AMPN/REQUEST BY USCENTCOM/CCDC TO IDENTIFY USCINCCENT AS SOLE AUTHORITY FOR USE OF PB IN CENTRAL REGION//

(b)(6) (b)(6)

RMKS/1. IN RESPONSE TO REF A, DOD DOES NOT HAVE THE AUTHORITY TO GRANT A WAIVER FROM THE REQUIREMENT TO FOLLOW FEDERAL INVESTIGATIONAL NEW DRUG (IND) REGULATIONS FOR PB USE NOR FORMALLY RECOGNIZE USCINCCENT AS THE SOLE AUTHRITY FOR ISSUE AND USE OF PB IN THE USCENTCOM AOR. NO STANDING TREATMENT USE PROTOCOL WITH OR WITHOUT WAIVERS FOR PB EXISTS TODAY. UNTIL A TREATMENT PROTOCOL ACCEPTABLE TO USCINCCENT, DOD AND THE FOOD AND DRUG ADMINISTRATION (FDA) IS DEVELOPED AND APPROVED, SOLE ISSUE AUTHORITY CANNOT BE GRANTED.
2. CURRENTLY DOD POLICY, BASED ON FEDERAL REGULATION, PROHIBITS DOD FROM ISSUING OR USING PB. FOR ALL ADDRESSEES, NOTE THAT PB IS NOT, REPEAT NOT, TO BE ISSUED TO INDIVIDUAL SERVICE MEMBERS OR DIRECTED FOR USE IN THIS OR ANY MILITARY OPERATION UNLESS SPECIFICALLY APPROVED BY OSD. IF ACCEPTABLE PROTOCOLS ARE APPROVED, THE JOINT STAFF WILL IDENTIFY USCINCCENT AS THE SOLE AUTHORITY FOR HOW, WHEN, AND TO WHOM PYRIDOSTIGMINE BROMIDE (PB) IS TO BE ISSUED.
3. THE JOINT STAFF IS REQUESTING OSD ASSISTANCE IN OBTAINING PROTOCOLS THAT ARE MUTUALLY ACCEPTABLE TO THE FDA AND DOD. THE JOINT

DRAFT

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DRAFT

03 03 RR ALW

STAFF POINT OF CONTACT IS (b)(6) (b)(6)
(b)(6) .//

DRAFT

RELEASER

JSISC ALTERNATE MESSAGEFORM

UNCLASSIFIED

CMAT Control # 2002197-0000005 (58)

HA/TMA Document Profile

38724

Subject:	Anti-Squalene Antibodies Link Gulf War Syndrome and the Anthrax Vaccine
Author:	Charbonnet, Michael D.
Date of Document:	7/12/2002
OSD # :	U 11202-02
PR # :	
Organization:	Autoimmune Technologies, LLC
Department:	
Assigned To:	FHP&R
Prepared For:	DASD
Suspense Date:	7/26/2002
Coord Office(s):	
Congressional Name:	
Input By:	(b)(6)
Profiler's Directorate:	HA
Response Signed By:	
Dt Response Signed:	
Doc Type:	LETTER
Application:	DOCSIMAGE
Previous Documents:	
Related Documents:	
Notes:	

Beneficiary Info

Beneficiary Name:	
Address 1:	
Apartment #	
Phone #	
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City:	
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Question: when at Lem for 4 days

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Action Required: **REPLY DIRECT (Forward copy of reply to CCD, Room 3A948)**
Coordinate With:

Remarks:

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Suspense Date: **July/26/2002**	Routing Date: **July/15/2002**	OSD CONTROL #: **U11202-02**

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COVER MEMO:
ORIG RCY(S) PG(S) CY NO THRU . OF CYS, ENCL(S)

REPLY TO: INTERIM REPLY TO:

DESTRUCTION:

Signature: PAR: FILE NUMBER:

ACTION: UPR FOR: RD SUSPENSE DATE: 7/26/2002 COORD:

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ACTION MEMO

July 26, 2002, 11:45 AM

FOR: Ellen P. Embrey, DASD, Force Health Protection and Readiness

FROM: Michael E. Kilpatrick, Deputy Director, Deployment Health Support **//s// 7/26/02**

SUBJECT: Response to Letter to Secretary of Defense About Anti-Squalene Antibodies

- The attached letter responds to a July 12, 2002, letter to the Secretary of Defense from Michael D. Charbonnet, CEO of Autoimmune Technologies, LLC in New Orleans, the licensee for a 2001 patent for a laboratory test that claims to detect the presence of squalene antibodies in humans. This claim was first made in an article published in February 2000 (Asa et al.) that asserted there was a correlation between the presence of such antibodies and Gulf War Syndrome. Mr. Charbonnet included a copy of an upcoming article (August 2002), which again reports a link between squalene antibody and illness in both Gulf War veterans and more recent recipients of the military anthrax vaccine. He asks that DoD review the new article and sponsor a study to validate the patented testing method's results.

- DHSD provided Mr. Charbonnet's letter to Dr. Carl Alving of the Walter Reed Army Institute of Research for comment. He is internationally known for his studies of antibodies to cholesterol and was funded to study the feasibility of detecting antibodies to squalene after the February 2000 report was published. Dr. Alving drafted the enclosed response to Mr. Charbonnet. The main points are summarized below:

  - The Institute of Medicine (IOM) examined the literature for health effects of squalene. IOM concluded the Asa study failed to provide evidence that the investigators detected antibodies to squalene. The IOM also faulted the selection and classification of the patients studied.
  - The Alving group's published study (Matyas et al. 2000) showed that it was difficult but possible to provoke mice to produce antibodies to squalene.
  - Mr. Charbonnet is incorrect in stating that Matyas' work confirmed the Asa study. Matyas could not reproduce Asa's results, even when using Asa's methods or those in the U.S. patent.
  - Ongoing Army studies will address the question of whether sick Gulf War veterans have a greater prevalence of antibodies to squalene and the results will be published.

RECOMMENDATION: Sign memo at TAB A. cc House Subcommittee on National Security, Veterans Affairs and International Relations and GAO, Applied Research and Methods Group.

COORDINATION: None

Attachment:
As Stated

Prepared by: CDR (b)(6), DHSD, (b)(6)
PCDOCS: 38724/R 39097

Mr. Michael D. Charbonnet
CEO, Autoimmune Technologies, LLC.
144 Elks Place, Suite 1402
New Orleans, Louisiana 70112

Dear Mr. Charbonnet:

Thank you for your letter of July 12, 2002, and for the attached recent publication by Asa et al. 2000 regarding the anthrax vaccine and antibodies to squalene. As you correctly mentioned in your letter, DoD has taken steps to investigate the potential role of antibodies to squalene as a risk factor for the health of DoD personnel, and for Gulf War veterans in particular.

As part of this process, the Institute of Medicine (IOM) was asked to examine the literature, including the publication by Asa et al. 2000, on potential health effects of squalene. The conclusions of the IOM Committee on Health Effects Associated with Exposures During the Gulf War were published in 2000 [Fulco, C.E., Liverman, C.T., Sox, H.C. 2000. Gulf war and health: depleted uranium, pyridostigmine bromide, sarin, and vaccines. Vol. 1. National Academy Press, Washington, DC, pp. 307-312, Chapter 7]. The conclusion of the Committee regarding the Asa publication is noteworthy, as quoted below:

> "This study has several shortcomings. The subjects were self-selected, rather than being chosen at random from a larger sample, which can introduce substantial selection bias and does not allow inferences to the broader population of Gulf War veterans. Sample sizes were small, and the study may suffer from misclassification errors since the group of Gulf War veterans categorized as healthy (n = 12) was not devoid of individuals with serious symptoms (1 had fibromyalgia, 1 had thyroid disease, 3 had memory loss, and 4 had chronic fatigue). Further, the report provides inadequate evidence that the assay is able to accurately detect antibodies to squalene. Many of the methods used in the study are not described; as a result it is not possible to fully assess the study's methodology or to reproduce the assay. The study did not attempt to demonstrate that the substance giving the positive response in the assay was found in the immunoglobulin G (IgG) fraction of serum where antibodies are found. Further the authors did not show that the assay was specific to squalene. To prove the specificity of the assay, the investigators would have had to show inhibition, in a dose-response manner, with squalene and no inhibition with other substances, as is seen in most reports of new enzyme-linked immunosorbent assays (ELISAs). The committee does not regard this study as providing evidence that the investigators have successfully measured antibodies to squalene."

From the Institute of Medicine report, it appears that there is substantial doubt among

scientific experts that the patients that were reported by Asa et al. 2000 represented a scientifically valid selection. In addition, the Asa study, which purports to measure antibodies to squalene, has not actually been described in such a way "as providing evidence that [it] successfully measured antibodies to squalene."

In view of the doubts about the scientific validity of the published assay for antibodies to squalene, DOD funded research to be performed by U.S. Army scientists at the Walter Reed Army Institute of Research, who are well-known as pioneers and international leaders in this field of immunology. The first installment of their research was published in the peer-reviewed scientific literature in 2000 [Matyas, G.R., Wassef, N.M., Rao, M., Alving, C.R., 2000. Induction and detection of antibodies to squalene. Journal of Immunological Methods, Vol 245, pp. 1-14]. The purpose of this initial publication was to determine whether an assay could be created that would pass rigorous scientific scrutiny in which positive and negative controls help to validate the technical findings of the study. The Asa 2000 study was greatly criticized for the absence of such controls. Since no validated antibodies to squalene existed that could serve as positive controls, Matyas endeavored to produce such antibodies by injecting numerous formulations containing squalene into mice. In the course of this work, the scientists failed to find that squalene alone could successfully induce antibodies to squalene. However, with very high concentrations of squalene incorporated into liposomes containing a bacterial component, Matyas did succeed in creating monoclonal antibodies in mice that could recognize squalene alone, but not a related molecule known as squalene.

Although the work of Matyas et al. 2000 did demonstrate that by using their method it was possible to produce antibodies in mice that could recognize squalene, it would be incorrect to conclude that their work validated the work of Asa et al. 2000. The Matyas group has indicated that by using either the assay published by Asa or the assay published in the U.S. patent that was licensed by Autoimmune Technologies, LLC, they have failed to reproduce the assay results of Asa et al. 2000 with Army monoclonal antibodies to squalene as positive controls. Thus, the Asa study, which fails to detect monoclonal antibodies to squalene, still lacks the necessary scientific validation that it can perform in the described manner when tested with a positive control antibody that is known to be able to bind squalane.

I am pleased to say that the work of the Army scientists is still ongoing and studies that will address the question of whether sick Gulf War veterans have a greater prevalence of antibodies to squalene are currently in progress. These studies should appear soon in peer-reviewed scientific literature. In the meantime, if you wish to receive further information regarding the research from the Army scientists, I urge you to contact them directly.

Sincerely,

Ellen P. Embrey
Deputy Assistant Secretary of Defense
(Force Health Protection & Readiness)

We maintain a waiting list of GWS patients and their physicians who may be interested in having the anti-squalene antibody test run for investigational use. We believe that the test is a very valuable tool for use in diagnosing GWS and that the antibodies may also provide important clues to treating the illness. However, we have also felt that making the test generally available for investigative use before the DoD acknowledges the possible utility of the test would cause unwarranted confusion. We hope that this waiting period will soon be over.

I am taking the liberty of sending a copy of this letter, the August 2002 article and the news release to the House Subcommittee on National Security, Veterans Affairs and International Relations and to the U.S. General Accounting Office. We would very much like to receive a positive response from the DoD concerning the confirmatory study, and we look forward to making arrangements with the DoD to use the test.

Sincerely,

Michael D. Charbonnet
CEO

Enclosures:

"Antibodies to Squalene in Recipients of Anthrax Vaccine," *Experimental and Molecular Pathology*, 73, 19-27 (2002)

News Release, Autoimmune Technologies LLC, July 15, 2002

Copies, with enclosures, to:

House Subcommittee on National Security, Veterans Affairs and International Relations

U.S. General Accounting Office,
Applied Research and Methods Group

Experimental and Molecular Pathology 73, 19–27 (2002)
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Antibodies to Squalene in Recipients of Anthrax Vaccine

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We previously reported that antibodies to squalene, an experimental vaccine adjuvant, are present in persons with symptoms consistent with Gulf War Syndrome (GWS) (P. B. Asa *et al., Exp. Mol. Pathol* 68, 196–197, 2000). The United States Department of Defense initiated the Anthrax Vaccine Immunization Program (AVIP) in 1997 to immunize 2.4 million military personnel. Because adverse reactions in vaccinated personnel were similar to symptoms of GWS, we tested AVIP participants for anti-squalene antibodies (ASA). In a pilot study, 6 of 6 vaccine recipients with GWS-like symptoms were positive for ASA. In a larger blinded study, only 32% (8/25) of AVIP personnel compared to 15.7% (3/19) of controls were positive ($P > 0.05$). Further analysis revealed that ASA were associated with specific lots of vaccine. The incidence of ASA in personnel in the blinded study receiving these lots was 47% (8/17) compared to an incidence of 0% (0/8; $P < 0.025$) of the AVIP participants receiving other lots of vaccine. Analysis of additional personnel revealed that in all but one case (19/20; 95%), ASA were restricted to personnel immunized with lots of vaccine known to contain squalene. Except for one symptomatic individual, positive clinical findings in 17 ASA-negative personnel were restricted to 4 individuals receiving vaccine from lots containing squalene. ASA were not present prior to vaccination in preimmunization sera available from 4 AVIP personnel. Three of these individuals became ASA positive after vaccination. These results suggest that the production of ASA in GWS patients is linked to the presence of squalene in certain lots of anthrax vaccine.

Key Words: anthrax vaccines; adverse adjuvant effect; squalene toxicity; Gulf War Syndrome; multisystem disorders.

INTRODUCTION

Bioterrorism is an important domestic and international security concern (Friedlander, 2000; Henderson, 1999; Leggiadro, 2000; Mazzuchi *et al.*, 2000; Wiener, 1996; Zoon, 1999). Much of this concern has focused on *Bacillus anthracis*, the etiological agent of anthrax (Gordon, 1999; Ibrahim *et al.*, 1999; Inglesby *et al.*, 1999). The study of immunological responses to the anthrax bacillus and the development of vaccines to immunize populations against this organism have been and should continue to be pursued vigorously (Abalakin *et al.*, 1990; Baillie *et al.*, 1999; Coulson *et al.*, 1994; Ezzell *et al.*, 1988; Friedlander *et al.*, 1999; Habig, 1993; Ivins *et al.*, 1986; Ivins *et al.*, 1988; Ivins *et al.*, 1992; Ivins *et al.*, 1994; Ivins *et al.*, 1998; McBride *et al.*, 1998; Miller *et al.*, 1998; Pasechnia *et al.*, 1992; Pile *et al.*, 1998; Pittman *et al.*, 2000; Sharma *et al.*, 1996; Shlyakhov *et al.*, 1997; Singh *et al.*, 1998; Stepanov *et al.*, 1996; Turnbull *et al.*, 1986; Welkos *et al.*, 1988A; Welkos *et al.*, 1988B; Williamson *et al.*, 1999).

The United States Department of Defense (DOD) announced the Anthrax Vaccine Immunization Program (AVIP) on December 15, 1997 (Cohen, 1997), to immunize 2.4 million military personnel (Cohen, 1998a,b) at risk for exposure to the anthrax bacillus. Adverse reactions to the vaccine have been reported by Hayes and World (2000), Hotopf *et al.* (2000), and Swanson-Bierman and Krenzelok (2001). Hotopf *et al.* (2000) categorized reported signs and symptoms into four groups: (1) psychiatric morbidity, (2) fatigue, (3) health perception, and (4) physical functioning.

We here report medically more traditional, more specified signs and symptoms experienced by many of the individuals entered into our study. These included joint and muscle pain, rashes, chronic fatigue, dizziness, headaches, seizures, and possible autoimmune thyroid disease. This constellation of signs and symptoms is similar to those referred to collectively as Gulf War Syndrome (GWS) (Coker *et al.*, 1999; David *et al.*, 1997; Fukuda *et al.*, 1998; Grady *et al.*, 1998; Hotopf *et al.*, 2000; Ismail *et al.*, 1999; Persian Gulf Veterans Co-ordinating Board, 1995; Unwin *et al.*, 1999). While the illnesses reported by United States and British military personnel after the Persian Gulf War in 1991 remain ill defined, multisystemic (Hotopf *et al.*, 2000) and rheumatological (Asa *et al.*, 2000a)

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aspects constitute the core of the disorder, as these eight citations amply demonstrate. The Anthrax Vaccine Immunization Program has been the subject of vocal controversy (Alving and Grabenstein, 2000; Asa *et al.*, 2000b; Goldstein, 1999; Morris, 1999).

We previously reported the finding of antibodies to squalene, an experimental vaccine adjuvant, in persons with clinical signs and symptoms consistent with the case definition of Gulf War Syndrome (Asa *et al.*, 2000a). Antibodies were found in military personnel of the United States and United Kingdom, both deployed and nondeployed, and in civilian employees of these agencies during the Gulf War (Asa *et al.*, 2000a). This was an unexpected finding, and the basis for the antibodies was not identified by that study. Three key observations suggested the possibility of one or more autoimmune disorders in these individuals: (1) an association between vaccinations received just before and during the Gulf War and ill health (Hotopf *et al.*, 2000), (2) an unexpectedly high incidence of adverse reactions to anthrax vaccine per se (Hayes *et al.*, 2000), and (3) a similarity between the signs, symptoms, and laboratory findings we observed in AVIP personnel and those of Gulf War era veterans (Asa *et al.*, 2000a; this report). Accordingly, we have now tested for anti-squalene antibodies in several groups of AVIP personnel.

MATERIALS AND METHODS

The subjects admitted to the study were American military personnel vaccinated against anthrax through the Army program. Lot numbers of the anthrax vaccine were taken from patient immunization records issued by the DOD. The site location of each vaccination was recorded as well. Age- and sex-matched controls were 19 healthy individuals recruited by accepted institutional review board standards and practices. None had concurrent or recent military service or civilian employment by the United States military after 1988 or had been enrolled in any other vaccine trials by any agency of American government or any other health program. No fees were paid by or to participants in this study.

Patient medical records and data, including diagnostic laboratory results from commercial laboratories, were collected by one of us (P.B.A.). These were reviewed by a board certified rheumatologist.[4]

Serum samples were collected from study participants by laboratory personnel using standard phlebotomy methods with vacutainer tubes and butterfly needles and then stored at −20°C until shipped to the laboratory for assay for anti-squalene antibodies. This assay was blinded (RFG and RBW); viz., samples and controls were randomized and assigned numbers for identification during all subsequent processing. All samples were tested four times under identical conditions. At the conclusion of the assays, patient data were matched with the outcome of the anti-squalene antibody test (ASA) and the results were tabulated.

Anti-squalene Antibody Assay

The ASA method used was the same as that previously reported (Asa *et al.*, 2000a), except that a squalene dilution of 1:20,000 in water was used in test strips for this particular study. Briefly, the method involves drying progressive dilutions of squalene on nitrocellulose membranes, rinsing in wash buffer, and preincubating with a blocking buffer prior to adding a 1:400 dilution of serum from each subject. Incubation times, washing, and biotin–avidin-conjugated horseradish peroxidase marking steps were in accordance with commonly used procedures with detection by buffer containing methanol, 4-chloro-1-naphthol, and 0.03% hydrogen peroxide. The final reaction was ended after 15 min by rinsing in distilled water. Air-dried strips were scored visually on a scale of 0 to 4+. Further particulars are described in U.S. Patent 6,214,566 (2001).[5]

RESULTS

Pilot Study

After the initiation of the AVIP, verbal reports of adverse reactions came to us from some recipients of the anthrax vaccine. These reactions included extreme pain and swelling at the injection site and rashes. Then, weeks and months later, many recipients experienced joint and muscle pain, dizziness, chronic headaches, low-grade fevers, chronic fatigue, weakness, seizures, memory loss, and cognitive problems. The similarity of these clinical symptoms to the cluster of health problems reported by Gulf War era veterans (Asa *et al.*, 2000a; Coker *et al.*, 1999; David *et al.*, 1997;

[4] D. Kevin Asa, M.D., Memphis, TN.

[5] Tulane University holds U.S. Patent 6,214,566 for the anti-squalene antibody assay. Autoimmune Technologies LLC, a private New Orleans, LA, start-up company, has been granted exclusive rights by Tulane University for use of the assay. Drs. Asa and Garry will receive royalties from this agreement. Dr. Wilson is Chief Scientific Officer and President of Autoimmune Technologies LLC.

TABLE 1
AVIP Participants Initially Tested for ASA

Patient	ASA[a]	Vaccine lot (number of injections)	Clinical and laboratory findings
1. 23 years, male	+	FAV020 (2)	Fatigue, joint pain, GI dysmotility
2. 36 years, female	+	FAV020 (2)	Ataxia, seizures, chronic fatigue, chronic severe headaches, weakness; being evaluated now for possible multiple sclerosis
3. 42 years, male	+	FAV030 (4)	Ataxia, cognitive problems, chronic fatigue, severe headaches, muscle weakness, joint and muscle pain
4. 47 years, male	+	FAV030 (2)	Ataxia, chronic fatigue, rashes, frequent severe headaches, memory problems, cognitive disorders, polyneuropathy, antibodies to myelin basic protein
5. 34 years, female	++	FAV030 (2)	Fatigue, joint pains
6. 38 years, male	+++	FAV030 (2)	Joint and muscle pain

[a] Intensity of anti-squalene antibody reaction.

Fukuda *et al.*, 1998; Grady *et al.*, 1998; Hotopf *et al.*, 2000; Ismail *et al.*, 1999; Persian Gulf Veterans Co-ordinating Board, 1995; Unwin *et al.*, 1999) is obvious.

We tested serum samples from six anthrax vaccine recipients for ASA; all six were positive for the anti-squalene antibodies (Table 1). We then performed a larger, blinded study to confirm and further examine the association between ASA and anthrax vaccination.

Expanded Blinded Testing of AVIP Participants

Sera from AVIP participants ($n = 25$) and controls who did not receive the vaccine ($n = 19$) were blinded and submitted for ASA analysis. After completion of the assay we found 8 of the 25 vaccinated service personnel (32%) to be positive for ASA, while only 3 of 19 controls (15.8%) were positive.

This difference is not statistically significant in this size sample.[b] The 3 positive controls had neither symptoms nor other laboratory evidence for autoimmune disorders; however, they had remote histories of major surgery with no sequelae, a finding absent from the histories of the other controls. Age, sex, and the clinical findings for ASA-positive AVIP personnel are shown in Table 2; those for ASA-negative AVIP personnel are in Table 3. Inspection of the data in Tables 2 and 3 revealed a clustering of reported sequelae and ASA reactivity with certain vaccine lot numbers. These were FAV030, FAV038, FAV041, and FAV043. When the AVIP personnel were divided into groups according to which lots they received, those vaccinated from the five lots and those who were not, a significant effect is seen in the data (Table 4). The four lots, FAV020, FAV030, FAV038, FAV041, and FAV043, were given to 17 of the 25 vaccinated individuals; 8 of these (47.06%) tested positive for ASA while none receiving other lots was positive (Table 4). Although the number of samples tested was small, the difference between the two groups was statistically significant ($P < 0.025$).

Two individuals who tested positive after vaccination had been tested prior to receiving anthrax vaccine; both earlier samples were negative for ASA. Patient No. 4 was sampled 3 months after a third inoculation using lot FAV043. Patient No. 7 became symptomatic after his third shot from lot

[b] $n = 44$, $df = 1$, $\chi^2 = 1.513$, $P = 0.2187$. However, a sample of 112 subjects with the same ratios between positive and negative results would be statistically significant, with $\chi^2 = 3.841$, $P = 0.0500$; similarly, a sample of 132 would yield $\chi^2 = 4.5389$, $P = 0.0331$. More positives in an expanding sample would, of course, mean fewer individuals were needed to reach $P \leq 0.05$.

TABLE 2
AVIP Participants Positive for Anti-Squalene Antibodies

Patient	ASA[a]	Vaccine lot (number of injections)	Clinical and laboratory findings
1. 36 years, male	+	FAV030 (2)	Arthritis: +FANA
2. 39 years, male	+	FAV030 (2)	Joint, muscle pain
3. 40 years, male	+	FAV030 (2)	Joint, muscle pain, +FANA
4. 39 years, male	+	FAV043 (3)	Uticaria, chronic fatigue, headaches, joint and muscle pain, rashes[b]
5. 52 years, male	+	FAV043 (3)	Fatigue, joint pain
6. 23 years, male	+++	FAV038 (1) FAV043 (3)	Anterior uveitis
7. 30 years, male	+++	FAV041 (3)	Autoimmune thyroid disease, polymyositis, elevated liver enzymes[b]
8. 38 years, male	++++	FAV030 (2)	Arthritis, active synovitis, +FANA 1:160

Note. FANA, Fluorescent Anti-Nuclear Antibody

[a] Intensity of anti-squalene antibody reaction.

[b] These individuals had been tested before anthrax vaccination (both were negative for ASA) and twice afterward (see also Table 5).

TABLE 3
AVIP Participants Negative for Anti-Squalene Antibodies

Patient	ASA[a]	Vaccine lot (number of injections)	Clinical and laboratory findings
1. 34 years, female	0	FAV030	Arthritis, myalgias, chronic fatigue, chronic headaches; +FANA (titer not stated, >1:40 assumed)
2. 38 years, male	0	FAV030	EEG-confirmed seizures, fatigue
3. 31 years, male	0	FAV030	None
4. 37 years, male	0	FAV030	None
5. 34 years, male	0	FAV030	None
6. 33 years, male	0	FAV030	None
7. 42 years, male	0	FAV041	Joint pain, chronic fatigue, memory loss; +FANA (titer not stated, >1:40 assumed)
8. 39 years, male	0	FAV043	Blistering rash after second shot
9. 51 years, female	0	FAV043	Seropositive rheumatoid arthritis
10. 23 years, male	0	FAV017	None
11. 34 years, male	0	FAV017	None
12. 33 years, female	0	FAV031	None
13. 37 years, male	0	FAV031	None
14. 48 years, male	0	FAV031	None
15. 28 years, male	0	FAV034	None
16. 32 years, female	0	FAV035	None
17. 23 years, male	0	FAV037	None

Note. FANA, Fluorescent Anti-Nuclear Antibody; EEG, Electroencephalogram.
[a] Intensity of anti-squalene antibody reaction.

FAV041. Both had sought care for illness before the ASA results were known.

Individual reactions for those who tested negative for ASA are listed in Table 3. Five individuals who received lots FAV030, FAV038, FAV041, and FAV043 tested negative for ASA but had some of the clinical findings found in personnel positive for ASA. AVIP participants receiving lot numbers other than those seemingly associated with a positive finding of ASA reported no reactions to the shot at the time of administration, were not diagnosed with any related clinical disorders, and had no demonstrable antibodies to squalene.

TABLE 4
Anti-Squalene Antibody Reactions in AVIP Participants

Number (male:female)	ASA-positive	Vaccine lot numbers	Clinical disorders	P^a
17 (15:2)	47% (1+ to 4+)	FAV020, 030, 038, 041, 043	Yes	—
8 (6:2)	0%	All others with known lot numbers	No	<0.025
19 (16:3)	15.8% (1+)	None	No	<0.01

[a] Compared to those receiving vaccine lot numbers 020, 030, 038, 041, or 043, Student's *t* test.

TABLE 5
Time-Comparative Anti-Squalene Antibodies in AVIP Participants

Patient	Antibody reaction: Prevaccination	2000	2001	Lot number
1. 39 years, male[a]	0	+	+	FAV043
2. 42 years, male	0	ND	+++	FAV043
3. 41 years, male	0	ND	0	FAV043
4. 50 years, male[a]	0	+++	++	FAV041[b]
5. 52 years, male	ND	+	++	FAV043
6. 51 years, male	ND	0	0	FAV043

Note. ND, not done.
[a] These two individuals are also listed in Table 2
[b] Inoculated Dover AFB, Dover, DE. All other personnel were vaccinated at the 164th TN ANG, Memphis, TN

Time-Related Studies

Little is known about antibody responses to squalene over time. Several additional samples became available after the completion of the blinded portion of our study. These included anthrax vaccine recipients who had developed antibodies to squalene within a few months of immunization, including personnel sampled before immunization. Prevaccination serum samples, where available, were run simultaneously. The samples were blinded as noted earlier during the ASA assay. The results are shown in Table 5. There were six such individuals with a total of 14 independent antibody tests; four were tested twice and two were tested three times. There were 10 postvaccination tests with 7 positive results (70.0 percent).

Posttrial Observations

Three additional individuals were tested after the conclusion of the main blinded sequence of this study (Table 6). All received vaccine from Lot FAV043 and all three were positive for ASA.

TABLE 6
Postmal Observations

Patient	Antibody reaction			Lot number
	Prevaccination	2000	2001	
1. 37 years, female	ND	ND	+	FAV043
2. 27 years, male	ND	ND	++	FAV043
3. 37 years, male	ND	ND	++	FAV043

Note ND, not done.

DISCUSSION

We previously reported persons suffering with the symptom-based case definition of Gulf War Syndrome to have serum antibodies to squalene (Asa *et al.*, 2000a). The antigen(s) inducing these antibodies in Gulf War veterans is unknown at the time, but it is possible that predeployment immunizations against various biowarfare agents is associated with induction of ASA. Our testing for anti-squalene antibodies in persons receiving anthrax immunization as part of AVIP identified many antibody-positive individuals. This contrasts with a lack of antibodies in all of the preimmunization sera so far available. In addition, we found that all of the current cohort positive for antibodies to squalene had received anthrax vaccine from a specific subset of lot numbers as part of AVIP. In all but one case (19/20; 95%), ASA were restricted to personnel immunized with lots of vaccine known to contain squalene. This suggests fairly strongly that anti-squalene antibodies are related specifically with these lots of vaccine.[7]

Investigators at the U.S. Food and Drug Administration (FDA) assayed anthrax vaccine in June 1999 for squalene content by gas/liquid chromatography (GLC). Identified as positive were certain lot numbers: FAV020, FAV030, FAV038, FAV043, and FAV047 (Committee, 2000). Squalene can be isolated and quantitated using either high-performance liquid chromatography (HPLC) or GLC, the latter yielding a more precise quantitation (Sulpice *et al.*, 1984). Lots with small amounts of squalene identified by the FDA closely match the lots associated in this study with anti-squalene antibodies. There is one exception; we identified one ASA-positive individual who received vaccine from Lot FAV041.

The source of the squalene in certain lots of anthrax vaccine is unknown; however, squalene is not found in *Bacillus anthracis* (Kaneda, 1977). *Bacillus anthracis* lipid chains are no longer than 17 carbons and are exclusively monounsaturated (Kaneda, 1977), while squalene contains 30 carbons and is highly polyunsaturated with six double bonds and iodine numbers in the range of 380–400, depending on the formulation (Whitehouse *et al.*, 1974). In addition, squalene is not present in the growth medium used to prepare cultures of *B. anthracis* (Johnson *et al.*, 1981; Lynch *et al.*, 1963; Wright *et al.*, 1954, 1957).

The amount of squalene, in four of the five lots of anthrax vaccine for which we found antibodies, was determined by the FDA to be 10–83 parts per billion (Committee, 2000). These levels have been dismissed as too low to have an immunological effect (SqualeneFacts.HTM, 2000). It is true that the precise biological significance of low levels remains to be determined, and in what context, but we suggest that they cannot be dismissed summarily. The immune system is exquisitely sensitive to small quantities of antigen. This sensitivity results from cell-to-cell priming, clonal proliferation, upregulation of MHC II molecules, and elaboration of cytokines and prostaglandins, amplifying the effect of small amounts of an antigen (Baker *et al.*, 1985; Carnaud, 1994; Crabbe *et al.*, 1996; Hodgkin *et al.*, 1998; Mudde *et al.*, 1996; Nakashima *et al.*, 1975; Volpe, 1988). Moreover, before the molecular nature of antibodies was fully appreciated, it was accepted that as little as a single molecule of antigen could stimulate antibody production (Cannon, 1942). Booster shots received in the AVIP program would enhance these effects. There is no lower safety concentration limit as yet established for squalene in vaccines with it as a supplemental adjuvant. It is possible that the quantities of squalene determined by the FDA do not accurately represent the original concentration of squalene in these vaccines. First, squalene is a nonpolar lipid which readily separates into a distinct layer from the aqueous vaccine antigen solution.[8] Secondly, squalene is subject to oxidation and peroxidation (Whitehouse *et al.*, 1974). The oxidative and peroxidative changes in chemical structure and their effect on antigenicity of squalene have been described (Whitehouse *et al.*, 1974). These changes can be detected in squalene within 4 h of atmospheric exposure (Dennis *et al.*, 1990). The breakdown products or other chemicals of the anthrax vaccine by GLC analysis were not provided by the FDA, as reported in the Congressional Record (Metcalfe, 2000). Squalene is one of a few naturally occurring lipids which function as immunological adjuvants when injected (Lorentzen *et al.*, 1995; Lorentzen, 1999; Whitehouse *et al.*, 1974). Immunological adjuvants have been sought for the past century to enhance the efficacy of vaccines. Increased resistance of bacteria to antibiotics and the human immu-

[7] The lot number for the severely ill person reported by Swanson-Biermann and Krenzelok (2000) is unknown (personal communication to the Editors)

[8] RIBI Immunochemicals, Inc., Hamilton, MT (personal communication to the authors).

nodeficiency virus epidemic are just two of the many reasons for an increased desire to find such agents.

Adjuvants have not been generally acceptable for human use, however, due to a capacity to induce the loss of self-tolerance and, often, to induce autoimmune disease. This feature has been used to study pathogenesis and treatment of many autoimmune illnesses, including inflammatory cardiomyopathies, autoimmune hepatitis, autoimmune uveoretinitis and anterior uveitis, autoimmune labyrinthitis, myositis, and peripheral neuritis (Broekhuyse *et al.*, 1993; Clemons *et al.*, 1989; Howell *et al.*, 1994; Ikezono *et al.*, 2000; McAllister *et al.*, 1995; Petty *et al.*, 1989; Roberge *et al.*, 1992; Schultheiss *et al.*, 1998; Stucky *et al.*, 1993).

More specifically, squalene, and the saturated form, squalane, have been shown to initiate autoimmune rheumatologic and neurologic disease (Beck *et al.*, 1976; Carlson *et al.*, 2000; Gajkowska *et al.*, 1999; Garrett *et al.*, 1985; Kohashi *et al.*, 1977; Lorentzen, 1999; Smialek *et al.*, 1997; Tsujimoto *et al.*, 1986; Whitehouse *et al.*, 1969, 1974; Whitehouse, 1982). Indeed, it has been shown that a single injection of squalene induces T-cell-mediated arthritis (Carlson *et al.*, 2000). Other studies have shown that adjuvant arthritis, experimental allergic encephalomyelitis, and experimental autoimmune thyroid disease, initiated by adjuvants containing squalene, could be passively transferred to syngeneic animals by thoracic duct lymphocytes (Whitehouse *et al.*, 1969; Whitehouse *et al.*, 1974). When squalene was substituted for mineral oil in Freund adjuvant, the resistance of the Buffalo and Norway strains of rats against the development of autoimmune disease was overcome, compared to treatment with only standard Freund adjuvant (Kohashi *et al.*, 1977). The RIBI adjuvant formulation, which contains squalene, is known to induce pathological changes as severe as those induced by Freund adjuvant (Leenaars *et al.*, 1994, 1998a,b; Leenaars and Hendriksen, 1998). In another study, RIBI adjuvant induced significant granulomatous lesions, but less severely than Freund adjuvant per se (Lipman *et al.*, 1992). When serial inoculations of adjuvant formulations were studied, RIBI adjuvant produced significantly lower antibody levels, and booster inoculations produced greater intradermal reactions with chronic lesions detectable at necropsy (Johnston *et al.*, 1991). TiterMax, which contains squalene, has also been shown to induce swelling and encapsulation (Zwerger *et al.*, 1998). These studies clearly demonstrate that significant problems do exist if squalene is used as an adjuvant in humans.

When squalene is administered intravenously, it disappears from the circulation within 2 to 4 min and is rapidly cyclized to methyl sterols and cholesterol, as well as biliary and fecal sterols and bile acids (Tilvis and Miettinen, 1982). However, when squalene is administered intramuscularly, as part of an adjuvant formulation, it drains into lymph nodes, where it remains for at least 48 h (Dupuis *et al.*, 1998). Effective antigen presentation by macrophages requires 60 min, and B-cells require between 6 and 8 h (Singer and Linderman, 1990). Once in the lymph nodes, squalene comes into contact with antigen-presenting cells, including dendritic cells, and lymphocytes. Dendritic cells displaying markers DEC-205 and MHC class II molecules have been shown to internalize squalene (Dupuis *et al.*, 1998). Adjuvants not only stimulate the immune system nonspecifically but may also serve as immunogens themselves. By stimulating an immune reaction, an adjuvant also comes under the definition of an immunogen. The concept of looking at adjuvants as antigens was initially suggested with Calmette-Guerin bacillus and *Vibrio cholera* neuraminidase (Seiler, 1980). The possible antigenicity of squalene was first shown in the military serving in the Persian Gulf War (Asa *et al.*, 2000a). This finding was confirmed by the induction of antibodies to squalene in an animal model, although significant levels of anti-squalene antibodies require coadministration of an adjuvant formulation (Matyas *et al.*, 2000). Also, Matyas and co-workers (2000) could not detect antibodies to squalene prior to immunization. In this study, as well as in our previous report (Asa *et al.*, 2000a), we found mostly males with rheumatological and neurological signs and symptoms. Idiopathic autoimmune diseases have been mostly in women at ratios of 8:1 to 14:1 (Michet *et al.*, 1985; Giersson *et al.*, 1994), while autoimmune disease induced by adjuvants have shown no difference between the sexes with regard to incidence or severity (Taurog *et al.*, 1988). Thus, our results are consistent with the possibility that the illness observed in GWS patients and AVIP personnel is due to an adjuvant reaction. The limits of this study, small sample size and likely a self-selection bias, constrict efforts to definitively address this issue.

We also found some personnel receiving vaccinations from squalene-positive lots to be ASA-negative, and we found some vaccinated by lots with squalene who did not develop signs or symptoms. There are several possible explanations for these observations:

(1) Adjuvants can act as superantigens and have been shown to induce immunological anergy to themselves in humans (Lamoureux *et al.*, 1974).

(2) Our test detects only IgG antibodies to squalene. Anti-squalene IgM antibodies have already been identified in mice (Matyas *et al.*, 2000), and anti-squalene IgA, IgE antibodies may also be produced.

(3) The relationship between the development of autoimmunity, the production of antibodies to squalene, and their relationship to each other is yet to be defined.

(4) Adjuvant disease has been shown to have a latency of onset in humans ranging from 2 weeks to 18 years after exposure (Brawer, 1996).

(5) It cannot be assumed that inoculations from multiple dose vials (5-ml vials programmed for 10 injections) are fully uniform in volume or degree of chemical mixing.

(6) Finally, these patients may not be genetically predisposed to develop antibodies to squalene or to other, as yet unidentified, immunogens.

These results and those of others (Asa *et al.*, 2000a; Matyas *et al.*, 2000) strongly suggest that the production of anti-squalene antibodies is linked to symptoms of Gulf War Syndrome and to the presence of squalene in certain lots of anthrax vaccine in some individuals.

A large epidemiological and biochemical study incorporating the ASA assay and a precise vaccination history, medical record review, and complete medical and physical examination of a large cohort of Gulf War Syndrome patients and AVIP personnel is justified from this evidence. The common practice of using squalene in vaccine enhancement is challenged by these data and the supportive literature. Prudence in use and redesign of the process henceforth would seem to be an appropriate recommendation.

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FOR IMMEDIATE RELEASE

ANTIBODIES LINK GULF WAR SYNDROME TO ANTHRAX VACCINE

(New Orleans, July 15, 2002) There is new immunological evidence that a contaminant in certain lots of the Department of Defense's anthrax vaccine may be the cause of Gulf War Syndrome.

Gulf War Syndrome, or GWS, is an illness that was first described in veterans of the 1990-1991 Persian Gulf war. Symptoms include muscle aches and joint pain, chronic fatigue, headaches, anxiety, depression, dizziness, sleep disorders, rashes, and loss of concentration. Cases of a similar illness have been seen in personnel who were not deployed to the Persian Gulf theater of operations in 1990 or 1991 and also in personnel who joined the armed forces after 1991, though the illness in these patients has not been called GWS.

Data published in the August 2002 issue of *Experimental and Molecular Pathology* shows that serum anti-squalene antibodies were found in patients with the GWS-like illness who received anthrax vaccine known to be contaminated with squalene, a naturally-occurring lipid. These patients were all vaccinated after 1997, and the published data indicates that receipt of the contaminated vaccine was associated with the production of the antibodies.

In an earlier study, published in the same journal in February 2000, antibodies to squalene were found in GWS patients who were veterans of the 1990-1991 Persian Gulf war. The presence of these antibodies in both groups of patients strongly suggests that the GWS-like illness experienced by the post-1997 patients is actually GWS, and, further, that GWS is not related to any event which took place in the 1990-1991 Persian Gulf theater. Contaminated vaccine lots might therefore account for the 1990-1991 GWS cases as well as for the post-1997 cases.

Neither study suggests how the vaccine may have become contaminated with squalene. Squalene is found in humans, animals and plants, and squalene from shark oil and other sources has been used for many years as an ingredient in cosmetics and other personal care preparations. It is possible that the small amounts of squalene found in the contaminated post-1997 vaccine lots could have been accidentally introduced during the production process. Squalene has been used as an adjuvant in several experimental human vaccines, including HIV vaccines, in efforts to boost the immune response, but the DoD has stated in the past that squalene was never intentionally added to the anthrax vaccine.

To determine if a vaccine did cause an illness, epidemiologists would conduct a study of the exposures of the ill individuals to the vaccine and to all other possible causative agents. An epidemiological study of non-U.S. Gulf War soldiers published in *The British Medical Journal* in 2000 (Hotopf *et al*)

found a significant association between vaccinations and ill health. Incomplete U.S. medical records have made it impossible to adequately determine the vaccine exposures of many U.S. GWS patients, so an epidemiological study to examine whether certain lots of the anthrax vaccine cause GWS in U.S. troops cannot easily be conducted by the DoD. The presence of anti-squalene antibodies appears to be a useful laboratory marker for use in identifying and characterizing GWS patients, and, in the absence of epidemiological data, the anti-squalene antibody test may also prove to be useful in studying the origins of GWS.

The announcement of the August 2002 publication was made by Autoimmune Technologies LLC, a New Orleans biomedical company. The research described in both the August 2002 article and the February 2000 article makes use of the anti-squalene antibody test. The antibodies were discovered by Dr. Robert F. Garry, a professor of microbiology and immunology at Tulane University Medical School who developed the test. Tulane has licensed the anti-squalene antibody technology to Autoimmune Technologies. Dr. Garry is the senior author of the August 2002 article.

U.S. Army researchers confirmed the discovery of the antibodies with their own version of the anti-squalene antibody test and published their work in November 2000. U.S. Patent No. 6,214,566 covering the anti-squalene antibody test was awarded to Tulane several months later, in April 2001. Because the testing method used by the Army researchers is covered by the Tulane patent, Autoimmune has recently offered the test to the DoD so that the DoD can sponsor a confirmatory study of all of the published data.

The August 2002 study looked at individuals who had participated in the DoD's Anthrax Vaccine Immunization Program, or AVIP. The DoD initiated the AVIP in 1997 to immunize 2.4 million military personnel considered to be at risk for exposure to anthrax. The U.S. Food and Drug Administration (FDA) subsequently assayed the AVIP anthrax vaccine for squalene content and found that five lots of the vaccine tested positive for small amounts of squalene. Some individuals participating in AVIP reported adverse vaccine reactions with GWS-like symptoms, so, because of the symptom similarities, the researchers tested several groups of AVIP participants for the presence of anti-squalene antibodies.

The researchers initially tested serum samples from six AVIP vaccine recipients who exhibited GWS-like symptoms and found that all six were positive for anti-squalene antibodies. All of these individuals had received inoculations from lots of the vaccine shown by the FDA to contain squalene.

The researchers conducted further blinded tests with 25 AVIP vaccine recipients plus 19 control individuals who did not receive the vaccine and did not have GWS symptoms. Of the 25 vaccine recipients, 17 had received vaccine from the five squalene-containing lots. Eight of these 17 individuals tested positive for anti-squalene antibodies, while none of the individuals who had received vaccine from other lots tested positive, a statistically significant difference ($p<0.025$). In addition, of the total of 20 AVIP vaccine recipients who tested positive for the antibodies in the study, 19 received vaccine from the squalene-containing lots. These results suggest that vaccination with the squalene-containing vaccine lots is associated with the production of the antibodies.

Of the 19 controls in the blinded study, only three tested positive for anti-squalene antibodies. All three of these individuals had undergone major surgery in the past, and they were the only members of the control group to have done so. The study presented no data that might explain this phenomenon, though it is possible that cell damage associated with major surgery exposes the surgery patients to immunologically significant amounts of intracellular squalene.

The researchers also conducted time-related tests which included four AVIP-vaccinated individuals for whom both pre-vaccination and post-vaccination sera were available. The post-vaccination sera from

three of these four individuals tested positive for anti-squalene antibodies, while the pre-vaccination sera from all four individuals tested negative.

The article published in February 2000 looked at 1990-1991-era patients instead of AVIP participants. This article included a blinded study which showed that anti-squalene antibodies were found in 36 of 38 GWS patients who had been deployed to the Persian Gulf theater, in all 6 of the 6 GWS patients who had not been deployed to the Persian Gulf theater, and in none of the 12 control subjects who had been deployed but were not ill.

Data from two patients who had participated in a vaccine trial involving squalene was also discussed in the February 2000 article. After receiving a vaccine to which squalene had been added as an experimental adjuvant, both of these patients developed a multisymptom disorder similar to GWS. Both tested positive for anti-squalene antibodies, though this sample of two patients was too small to determine the statistical significance, if any, of this finding.

GWS is usually difficult to differentiate from other rheumatic disorders, many of which have similar symptoms. Before the anti-squalene antibody test was developed, there was no specific laboratory test for GWS. Both articles suggest that the antibodies can serve as an excellent laboratory marker for GWS, since none of the control subjects in either published study tested positive for the antibodies except the three surgery patients in the August 2002 study. Using the antibodies as a laboratory marker for GWS could be very useful in helping physicians diagnose the disorder and in differentiating it from other rheumatic illnesses.

Anti-squalene antibodies might also provide a key to more effectively treating GWS patients. The presence of the antibodies in GWS patients indicates that the immune system is involved in the development of GWS. Effective drugs which modulate the human immune system are already in wide use, but they have not been previously considered to be appropriate for GWS patients. The published data now suggests that the use of immune modulators in GWS patients should be studied.

Prior to the publication of the February 2000 article, representatives of the U. S. General Accounting Office (the GAO) visited with Dr. Garry, reviewed the laboratory methods used in the anti-squalene antibody test, and discussed the initial data obtained by testing GWS patients. The GAO representatives determined that the test methodology was sound and that the patient data appeared compelling. On March 29, 1999, the GAO issued Report No. GAO/NSIAD-99-5, entitled "Gulf War Illnesses - Questions About the Presence of Squalene Antibodies Can Be Resolved." This report is available on the Web at:

http://frwebgate.access.gpo.gov/cgi-bin/useftp.cgi?IPaddress=162.140.64.88
&filename=ns99005.pdf&directory=/diskb/wais/data/gao

The GAO report urged the DoD to conduct its own research into anti-squalene antibodies with two objectives in mind: (1) to confirm the existence of the newly-discovered antibodies, and (2) to acquire patient data, explore the apparent link between the antibodies and the illness in GWS patients, and attempt to confirm or disprove the existence of such a link.

To satisfy the first GAO objective, the Army researchers confirmed that anti-squalene antibodies do indeed exist and can reliably be detected. They published their findings in an article entitled "Induction and Detection of Antibodies to Squalene" which appeared in the November 2000 issue of the *Journal of Experimental Methods*. The Army researchers conducted their testing by applying squalene to the wells of ELISA plates, and Dr. Garry and his colleagues conducted their testing by applying squalene to nitrocellulose strips in a Western-blot-type assay. There is no material difference between the two test methods.

Although the Army researchers confirmed the validity of the test and thus added support to the February 2000 patient data, their November 2000 article included no patient data of its own and as a result did not specifically address the GAO's second objective. The Army researchers also failed to embrace the peer-reviewed February 2000 data itself, as is discussed in the statement Dr. Garry submitted to the House Subcommittee on National Security, Veterans Affairs and International Relations for the record of its hearing into Gulf War illnesses on January 24, 2002. This statement can be seen on the Subcommittee's Web site at:

http://www.house.gov/reform/ns/statements_witness/garry_jan_24.htm

Dr. Garry pointed out that neither the February 2000 study nor the August 2002 study included large numbers of patients, and he also noted that both studies made use of self-selected volunteers, which were the only subjects available to the researchers. "Large studies can sometimes reveal relationships not seen in smaller studies, and studies which use pre-defined inclusion and exclusion criteria to recruit participants are preferred because they are less likely to be subject to possible self-selection biases," Dr. Garry said. "But the published data is so compelling as to transcend these minor shortcomings."

"A large confirmatory study of subjects who are not self-selected appears to us to be the only appropriate step at hand, and we are urging the DoD to sponsor such a study," said Dr. Russell B. Wilson, president of Autoimmune and another author of the August 2002 article. "We believe that an investigation into the relationship between anti-squalene antibodies and GWS will lead to a better understanding of the illness and ultimately to more effective treatments for the patients who have it," he said.

Although it maintains a waiting list of GWS patients and their physicians who may be interested in having the anti-squalene antibody test run for investigational use, the company has not yet made the test generally available.

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CMAT Control #
2002232-0000002

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ployment Health Support Directorate

CMAT #: 2232-002

Date: Aug 20, 2002

Action Tasking // Internal Routing Sheet

		Action	Info	Comments
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5	Director DHSD (DIR)			sign
4	Deputy Director (DEP)	WJS		
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1	Editorial Review (ER)	BW		
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SUSPENSE: 22 Aug 02

Prepare reply for signature of: ☐ SA ☐ Director ☐ Dep. Director ☐ IAD / PA / MR / LLID / IT&SEC

Prepare response for Ms. Embrey

☐ Congress	☐ Oversight	☐ FOIA	☐ OSD	☐ WBM	☐ VSO/MSO	☐ Outgoing
☐ Ltr to Director	☐ IR	☐ E-Mail	☐ OGA	☐ Other		☐ Veteran

KEYWORDS: Anthrax Vaccine

06/05/02 Issuance

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PH: 1-888-411-3200 • e-mail: contact@anthraxvaccine.net
http://www.anthraxvaccine.net

July 20, 2002

→ DHS
Pls prep response for Mr E sig

Ms. Ellen P. Embrey
Deputy Assistant Secretary of Defense
OASD(HA)/FHP & R
1200 Defense Pentagon
Washington, DC 20301-1200

Dear Ms. Embrey:

Thank you for taking the time to respond to my letter. It is extremely unfortunate that your response contains the inaccuracies and mis-statements that it does.

I am going to take several of your statements and reply to them. If you can prove me wrong, I would greatly welcome a chance to look at the evidence, and so would many other people. I will start with your statements in quotes, followed by a response.

1. "The anthrax vaccine is licensed by the Food and Drug Administration..."
The truth: The anthrax vaccine is not licensed for use against aerosolized anthrax. In addition, the original license - for cutaneous anthrax only - was granted based on data from a different vaccine. The FDA and DOD both know this: the vaccine is now, and has been for years, on file with the FDA as an Investigational New Drug, which by law requires informed consent. No man or woman in uniform has ever received informed consent.

•1995 -- SAIC Corporation contracted to develop an Army plan to obtain FDA approval for a license amendment to include aerosolized anthrax exposure saying, *"This vaccine is not licensed for aerosol exposure expected in a biological warfare environment."*

(Ref.: SAIC Corporation plan, 29 Sep 1995, enclosure to memorandum from Dr. Anna Johnson-Winegar, US Army, to Dr. Robert Myers [MDPH], US Army Medical Research and Material Command, Fort Detrick, Frederick, MD, 5 Oct 1995.)

• 1996 IND (Investigational New Drug) Application submitted by MBPI, the anthrax vaccine manufacturer, to obtain inhalation anthrax approval. *This IND application is still pending with the FDA.*

2. "...and its manufacturer's recently renovated facility has received approval to produce vaccine which is safe and effective in protecting against inhalational anthrax infection."
The truth: There is no proof that the anthrax vaccine is either safe or effective. The Brachman study is often cited as such proof; however, the Brachman study dealt, again, with a different vaccine, one produced by Merck, Sharp and Dohme.

Other studies which BioPort likes to tout as proof of the vaccine's safety have not been peer-reviewed or published, casting substantial doubt on their integrity and credibility.

In addition, an IOM letter dated March 30, 2000, to the Department of Defense, stated: "There is a paucity of published peer-reviewed literature on the safety of the anthrax vaccine. The committee located only one randomized peer-reviewed study of the type of anthrax vaccine used in the United States (Brachman et al., 1962). However, the formulation of the vaccine used in that study differs from the vaccine currently in use."

(Ref.: An Assessment of the Safety of the Anthrax Vaccine -- March 30, 2000 http://www.nap.edu/html/anthrax_vaccine

Finally, it should be obvious to any thinking person that there is no way to determine the effectiveness of the anthrax vaccine unless a portion of the population which has been

vaccinated is deliberately sprayed with aerosolized anthrax - similar to the way the Pentagon has now admitting exposing troops with nerve gas.

In fact, the current IOM report - which we'll discuss more in a moment - flatly states that no human studies of inhalation anthrax exist. The animal study data presented in a recent JAMA article demonstrate that the anthrax vaccine, used alone, is marginally effective. Col. Friedlander's much-vaunted monkey studies of inhalation anthrax demonstrated 90% mortality without vaccination or antibiotics, but *80% mortality WITH vaccination and no antibiotics.*

If the vaccine is so safe, why is there an entire clinic at Walter Reed Army Hospital dedicated to treating illnesses that arise from the anthrax vaccine?

Why does the new label admit to an adverse reaction rate of up to 35%, as compared to the old label claiming 0.2%? Quite a jump, don't you think?

Why does the new label talk about the six deaths which have resulted from the vaccine? And specify the long-term illnesses which can and do result?

If the vaccine is so safe, does that mean you believe that independent studies of US, UK and Canadian Gulf War veterans associating anthrax vaccination with long-term adverse health effects - most recently the study from Kansas State University - are all fraudulent?

3. "The U.S. Government and the vast majority within the American medical community accept FDA's stringent approval and release process as a means to assure production of a safe and effective product. The recent report from the Institute of Medicine on the anthrax vaccine supports this."

The truth: The vast majority of people, both inside and outside the government and the medical community, have no idea what's really gone on with the anthrax vaccine; but many people are certainly aware that the FDA has released unsafe drugs more than once.

- The FDA didn't even inspect the Michigan Dept. of Public Health (MDPH) facilities for years. MDPH was the original manufacturer of the vaccine, and sold its biologic division in 1996. But from 1988 on, the FDA found numerous manufacturing problems with the vaccine, including the use contaminated lots, non-sterile lots, the switching of expiration dates on labels, the improper use of equipment, the fact that one lot was left out unrefrigerated, and more. *The vaccine was used on the troops anyway.*

- Here's the big one: In 1990, the filtering and fermenting equipment used to make the vaccine was changed, without notification to the FDA as required by law. This change resulted in a 100-fold (100 times, not 100%) increase in the potency of the vaccine. In 1991, Gulf War troops were suddenly being told they were getting a "super one-shot anthrax vaccine," and that they wouldn't need more doses. Ten years after the fact - after a private individual investigating the situation notified the FDA of the change - the changes were approved retroactively.

The simple fact is, the FDA has not upheld its own rules and regulations. Yet BioPort has been cleared to produce; and is once again granted immunity in its production, meaning that it does not have to pay to defend itself against the lawsuits which have started - the American taxpayer will.

I've already addressed the recent IOM report to some degree. But here are the other points to make about that report, as we have stated in our formal response:

1. Suddenly there is plenty of research to indicate the vaccine is safe - contrary to IOM's own opinion just two years ago. An IOM letter dated March 30, 2000, to the Department of Defense, stated: "There is a paucity of published peer-reviewed literature on the safety of the anthrax vaccine. The committee located only one randomized peer-reviewed study of the type of anthrax vaccine used in the

United States (Brachman et al., 1962). However, the formulation of the vaccine used in that study differs from the vaccine currently in use."

(Ref.: An Assessment of the Safety of the Anthrax Vaccine – March 30, 2000 http://www.nap.edu/html/anthrax_vaccine)

We submit to you that additional data has been supplied by the DOD to conform to anthrax vaccine policy, and that there is still a paucity of genuine scientific data.

II. The report leaves out all dissenting research, including that from the Dept. of Defense itself. We refer you to the Briefing Book at http://www.anthraxvaccine.net for a full report.

The report also solicited, and then left out, written testimony by Major Russell E. Dingle of the Connecticut Air National Guard which said, in part:

"The U.S. military is virtually the sole proprietor and source of any safety and efficacy data for AVA. As such, the current military opinion of AVA must be addressed in the following context: *Either the first forty years of data, observation, and opinion is wrong, or the last two years of data, observation and opinion is wrong...*"

III. The verbiage in the report doesn't speak to the problems listed on the label, even though the entire new label is included as an appendix. The FDA required a wide range of severe illnesses to be listed on the new label; and *the rate of reaction admitted on that new label is 175 times that on the old label.* But this is suddenly a safe vaccine? How is it that this change is not discussed?

IV. There is no acknowledgment in the report of under-reporting. IOM apparently didn't want to know that our troops live in fear of retaliation simply for talking about the vaccine, as well as for getting sick after being vaccinated. They do not want forced medical retirement; they do not want their careers to end. In addition, a self-selected audience - which is the basis of the VAERS reports - is not a valid basis for extrapolating statistics, as any qualified researcher could tell you.

V. The IOM committee fails to mention that BioPort's long and public history of regulatory problems were serious violations of law for which no one has been held accountable. We refer you to our web site for the full set of FDA reports on this vaccine; and for our Citizen Petition to the FDA, documenting BioPort's 1990 change in fermenting and filtering equipment which resulted in a 100-fold increase in the potency of the vaccine. Why was this change in equipment, and its resulting potency increase, left out of the report? Why has this never been related to the ongoing six-shot protocol, which IOM has at least admitted has no scientific rationale behind it?

VI. The IOM committee found that, despite limited data on long-term effects, reports of serious illnesses and reports of links to Gulf War Syndrome, no special follow-up efforts should be made. Even guinea pigs in the lab get follow-up efforts. In this experiment, our troops have to fight for what medical care they do get, and much of it is substandard and inadequate to meet their needs.

VII. The IOM report points out the double standard that exists between our troops and civilians, clearly stating that our troops are being used as experiments. Exactly where is the legal line drawn between civilians and service members in this regard - and who draws it?

"The anthrax vaccine is effective and safe enough to use to protect U.S. soldiers, says a panel of medical experts. But there are not enough studies to assure its safety for wide use by the public, and a better vaccine is needed, according to a report released Wednesday by the Institute of Medicine."

"Anthrax vaccine found safe for troops – More study needed before public use"
By Anita Manning, USA TODAY

4. "DOD will continue to used only FDA released vaccine to protect our dedicated men and women in uniform."

The truth: This vaccine is not licensed for its current use, is on file as an Investigational New Drug, uses a shot protocol with no scientific basis behind it, and is - by the Army's own admission - a vaccine with an extremely high rate of reactogenicity. If this is the DOD's idea of a safe, FDA-released drug, God help us.

5. "In your letter you suggest that the program be administered on a voluntary basis. However, it is important that all personnel who are at higher risk and whose duties are essential to certain mission capabilities be vaccinated for both their personal protection and the success of the military mission."

The truth: To date, only civilians have been subjected to an anthrax attack, and from what anyone can find out, those attacks were most likely perpetuated by someone working inside the U.S. defense industry. This doesn't exactly do much for the DOD's credibility.

In addition, it remains difficult from both a manufacturing and dissemination perspective to produce aerosolized anthrax. This vaccine does not even protect against all strains of anthrax, if it protects at all; and there's certainly nothing to prevent someone from bioengineering a strain completely resistant to this vaccine.

And the only reason we know that Iraq has anthrax is because we sold it to them.

The threat is hyped, and always has been. While the DOD has been paranoid about anthrax, the first World Trade Center attack occurred in 1993; Khobar Towers was bombed in 1996; the U.S. Embassies were bombed in 1998; the U.S.S. Cole was bombed in 2000; and of course there is no need to remind you of 9/11. :

But because anthrax spores last forever, and can be fatal, it's a great fear to spread. This is the first of many bioterrorism vaccines the DOD has admitted are in the pipeline; naturally, it needs to be tested, whether or not anyone is granted informed consent. Naturally, fear alone seems to be a reasonable justification given the new world in which we live.

6. "We fight and win as teams. If one or several team members in areas of higher risk are not vaccinated, and subsequently fall victim to the anthrax, they could jeopardize the lives of other team members, and ultimately, the mission and its success."

You do not mention what happens when the credibility of a team leader is lost, because people under his or her command can no longer believe they are being told the truth. You fail to note that in October of 2000, the GAO came out with a report that of the Air National Guard units required to take the anthrax vaccine, a full 25% of the pilots resigned rather than submit to the vaccine.

25%. What happens to your team now? What happens to your team when up to a third of them become extremely ill from the vaccine itself, as the label indicates is possible? Are you telling me it's preferable to risk having pilots now in the Gulf have seizures and blackouts while in the cockpit, all for the sake of teamwork? That it's preferable that our ground troops suffer debilitating bone and joint pain, and cannot perform their duties? That you'll risk up to one-third of all active duty troops for a vaccine that doesn't even protect against all strains of anthrax - if it protects much at all? Are you telling me that teams stay cohesive and gung-ho when they can no longer believe in their chain of command?

This past April, two vaccinated workers at Ft. Detrick were given antibiotics following anthrax exposure, even though they were not symptomatic. This says a lot about the lack of confidence the Army has in the efficacy of the current vaccine.

6. "Our ultimate loyalty is to the health and safety of our people."
Would that were true.

If it were true, military troops would never be used as medical guinea pigs. Nerve gas tests, LSD experiments, being forced to watch nuclear explosions, Agent Orange - all these are documented and public information. And the use of an Investigational New Drug without informed consent - a legal right the troops do NOT give up when entering the military - constitutes medical experimentation.

If it were true, DOD would not only acknowledge but seek out the truth about the extremely high adverse reaction rate to the vaccine, and not rely on VAERS reports alone.

If it were true, military doctors would be informed about adverse reactions to the vaccine.

If it were true, troops who become ill would receive immediate and adequate medical treatment.

If it were true, better protective equipment and detection devices would have been developed long ago.

If it were true, troops who were hailed outstanding, committed leaders before they took the vaccine would never be called malingers and liars because they had the nerve to get sick.

If it were true, you and each person involved in communicating anything about this policy, or in making decisions about this policy, would finally put the health and safety of the troops first, and, realizing the AVIP is a travesty, halt it or make it voluntary.

If it were true, you would not put your jobs and politics first - you would put the troops first.

You probably feel you cannot afford to look at the truth, because it would cost you your job or a promotion. You probably feel you must speak as you are directed to speak. I predict that there will come a day - maybe soon, maybe 20, 30, even 40 years from now - when at last one of you will look back and say, "We should never have done that. I can admit that now." But it will be too late for the troops whose lives and careers you have decimated.

7. Finally: "We have an obligation to provide them with the best protection available, and for now, the best around-the-clock protection from the very real threat of anthrax is the anthrax vaccine."

The truth: Anthrax can be cured. Even inhalation anthrax is not as fatal as people once thought, and can be cured.

But the illnesses arising from the anthrax vaccine cannot be cured.

The DOD knows this. The rush to use antibiotics in the wake of last year's anthrax attacks was a very revealing thing. The constant denial to treat troops ill from the vaccine is a very revealing thing. It is most interesting that troops overseas been taught, this year, how to take Cipro in event of anthrax exposure.

I've welcomed the opportunity to discuss this with you, as well. Again, I heartily welcome any proof you can provide me which counteracts the facts as I've stated them above. Meanwhile, should you care to find out what actually happens when someone gets sick from the vaccine, please visit the Heroes page on our web site. Try to keep in mind these are real human beings - the 1/3rd of our fighting force you would willingly sacrifice.

Sincerely,

Kathryn D. Hubbell
President

Office of the Assistant Secretary of Defense for Health Affairs
Force Health Protection & Readiness (FHP&R)

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Fax

To: DHS From: (b)(6)

Fax: Pages:

Phone: Date: 8/19/02

Re: Tasker CC:

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OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

MEMORANDUM FOR DEPUTY ASSISTANT SECRETARY OF DEFENSE (FORCE HEALTH PROTECTION AND READINESS)

FROM: Michael E. Kilpatrick, M.D., Deputy Director, Deployment Health Support Directorate 8-22-02

SUBJECT: Response to letter from Kathryn D. Hubbell, President, Anthrax Vaccine Network, Inc.

- Attached at TAB B is the letter from Ms. Kathryn Hubbell, President, Anthrax Vaccine Network, Inc., that attempts to refute the anthrax immunization program and the steps DoD is taking to protect service members.
- A draft response, coordinated with Mr. (b)(6) from the Anthrax Vaccine Immunization Program (AVIP), is provided at TAB A.

RECOMMENDATION: Sign letter at Tab A.

COORDINATION: As stated above.

Attachments:
As stated

Prepared by: CDR (b)(6) AVIP Liaison for ASD (HA), (b)(6)
Deployment Health Support Directorate

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

AUG 26 2002

Kathryn D. Hubbell
President
Anthrax Vaccine Network, Inc.
P.O. Box 844
Missoula, MT 59806

Dear Ms. Hubbell:

Thank you for your letter concerning the anthrax vaccine. The Department of Defense recognizes that there is a very real threat of anthrax exposure both on the battlefield and by terrorist action. In accordance with many independent studies by reputable medical panels and agencies, the DoD also realizes that there exists a safe and effective countermeasure to this threat in the anthrax vaccine. It is the best countermeasure we have at this time.

The safety and effectiveness of the anthrax vaccine has been assessed and reviewed by experts since it was fully licensed by the Food and Drug Administration (FDA) over 30 years ago. The DoD is required to make risk-benefit decisions regarding the protection of its service members, relying upon the FDA and other such agencies for their expertise, years of medical experience, and the care they exercise in guarding our nation's health. You may wish to contact them and share your concerns.

I remain committed to protecting the health of our dedicated men and women of the armed forces. If I may be of further assistance, please contact my office.

Ellen P. Embrey
Deputy Assistant Secretary of Defense
Force Health Protection and Readiness

CMAT Control #
2002226-0000014

(60)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

MAY 25 2000

(b)(6)

Dear (b)(6)

Thank you for your recent letter to President Clinton in which you requested that he revoke Executive Order 13139.

Executive Order 13139, Improving Health Protection of Military Personnel Participating in Particular Military Operations, September 30, 1999, implements section 1107 of title 10 of the United States Code, enacted by Congress in 1998. In accordance with 10 U.S.C. 1107, the President may waive the informed consent requirement for the administration of an investigational drug to a member of the Armed Forces in connection with the member's participation in a particular military operation, upon a written determination by the President that obtaining consent: (1) is not feasible; (2) is contrary to the best interests of the member; or (3) is not in the interests of national security.

Section 1107, reflects a Congressional recognition that when an investigational product is the only means available to protect against a lethal chemical or biological weapon, the lives of individual members, the safety of their comrades who rely on them, and the success of the military mission may require uniform use of the medical protection. Further, the nation would demand that military commanders do all in their power and authority to employ prudent medical countermeasures in the face of a biological and chemical threat. The consequences of an action which leads to foregoing availability of a needed investigational new drug will lead to an unacceptable military operational setting in which the lives of personnel and the accomplishment of missions are jeopardized. But section 1107 also strikes a careful balance. Cognizant that use of investigational products generally requires informed consent under FDA rules, section 1107 says two things: first, that the "informed" part of "informed consent" will always be done through specific notice requirements; and second, that the "consent" part may only be waived by the President. This careful balance is also incorporated into Executive Order 13139, which makes clear that: "Waivers of informed consent will be granted only when absolutely necessary."

Revocation of the Executive Order would not eliminate 10 U.S.C 1107. It would only eliminate the stringent requirements that the Presidents has set for the Secretary of Defense to achieve prior to requesting the waiver under 10 U.S.C. 1107.

Thank you for your interest in the Department of Defense.

Sincerely,

RADM J. Jarrett Clinton, MD, MPH., U.S.P.H.S.
Deputy Assistant Secretary of Defense
Health Operations Policy

HA Control No.: 12276/12361
Document No.: Constitutent13139-(b)(6)
(b)(6)
Due Date: 5/15/2000

May 23, 2000

MEMORANDUM FOR ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

THROUGH: Ron Richards, Principal Director, OASD(HA)HOP 5/23/00

FROM: Salvatore M. Cirone, Program Director, Health Science Policy

SUBJECT: Writer Requests that Executive Order 13139 be Rescinded Ref Administration of Experimental Vaccines to Service Members - ACTION MEMORANDUM

DISCUSSION: (b)(6) wrote to President Clinton objecting to Executive Order 13139 and requesting him to rescind the order and make use of experimental vaccines voluntary.

The reply explains 10 U.S.C. 1107 and Executive Order 13139. It notes that revocation of the Executive Order would not eliminate 10 U.S.C 1107. It would only eliminate the stringent requirements that the Presidents has set for the Secretary of Defense to achieve prior to requesting the waiver under 10 U.S.C. 1107.

RECOMMENDATION: Sign the letter to (b)(6).

COORDINATION:

GC:_Coordination attached.

(b)(6) **CIV, OASD/HA**

From: (b)(6), Mr, DoD OGC [(b)(6)@osdgc.osd.mil]
Sent: Tuesday, May 23, 2000 9:06 AM
To: Cirone, Salvatore, , ASD/HA
Subject: FW: Constituent Mail -13139

Sal -- See suggested edits. Concur as modified. -- JC

-----Original Message-----
From: (b)(6)
Sent: Tuesday, May 23, 2000 8:18 AM
To: (b)(6), Mr, DoD OGC
Subject: Constituent Mail -13139

(b)(6) Attached is a reply to constituent mail to white house requesting revocation of 13139. I think you reviewed the last one to (b)(6), but I can't find your e-mail concurrence. Can you review this reply and concur or must I send the package with the handwritten letter? I'm late because the first tasking did not have the address of the constituent. Can you expedite? Sal

(b)(6)
Program Director, Health Science Policy
Office of the Assistant Secretary of Defense
(Health Affairs)
Health Operations Policy
(b)(6) Fax (b)(6)

(b)(6)

Dear (b)(6):

Thank you for your recent letter to President Clinton in which you ~~concerning your~~ request that he revokes Executive Order #13139.

Executive Order #13139, Improving Health Protection of Military Personnel Participating in Particular Military Operations, September 30, 1999, implements ~~S~~section 1107 of ~~T~~title 10 of the United States Code, enacted by Congress in 1998. ~~10 U.S.C. 1107, Notice of use of an investigational new drug or a drug unapproved for its applied use, was passed by Congress with the Fiscal Year 1999 Defense Authorization Bill.~~ In accordance with 10 U.S.C. 1107, the President may waive the informed consent requirement for the administration of an investigational drug to a member of the Armed Forces in connection with the member's participation in a particular military operation, upon a written determination by the President that obtaining consent: (1) is not feasible; (2) is contrary to the best interests of the member; or (3) is not in the interests of national security.

Section 1107 reflects a Congressional recognition that when an investigational product is the only means available to protect against a lethal chemical or biological weapon, the lives of individual members, the safety of their comrades who rely on them, and the success of the military mission may require uniform use of the medical protection. Further, the nation would demand that military commanders do all in their power and authority to employ prudent medical countermeasures in the face of a biologic and chemical threat. The consequences of an action which leads to foregoing availability of a needed investigational new drug will lead to an unacceptable military operational setting in which the lives of personnel and the accomplishment of mission are jeopardized. But section 1107 also strikes a careful balance. Cognizant that use of investigational products generally requires informed consent under FDA rules, section 1107 says two things: first, that the "informed" part of "informed consent" will always be done through specific notice requirements; and second, that the "consent" part may only be waived by the President. This careful balance is also incorporated into Executive Order 13139, which makes clear that: "Waivers of informed consent will be granted only when absolutely necessary."

~~Executive Order #13139 provides the requirements and procedures that must be met before the President would consider approving a request for a waiver of informed consent. It notes that the President is required by law to apply the standards and criteria~~

~~set forth in the relevant Food and Drug Administration regulations. In the Executive Order, the President has set a very high bar for the Secretary of Defense to attain before the Secretary can request a waiver under 10 U.S.C. 1107.~~

Revocation of the Executive Order would not eliminate 10 U.S.C 1107. It would only eliminate the stringent requirements that the Presidents has set for the Secretary of Defense to achieve prior to requesting the waiver under 10 U.S.C. 1107.

Thank you for your interest in the Department of Defense.

Sincerely,

J. Jarrett Clinton, RADM, M.D., U.S.P.H.S.
Deputy Assistant Secretary of Defense
Health Operations Policy

Search Criteria: SEARCH_IN = '0', DOCNUM = '12276'

Edited	Name	Doc #	Application	Author
5/22/00	Writer Requests that Executive Order 13139 be Rescinded Ref: Administration of Experimental Vaccines to Service Members	12276	DOCSIMAGE	(b)(6)

Due 5/24

Dr Crone

CORRESPONDENCE TASKER

Classification: UNCLASSIFIED

Date: 05/02/2000

Control Number: 0087955

External Reference: WB 75976

Document Date: 02/25/2000

Document Originator: (b)(6)

Route To: ASD HA

Controlling Organization: ADMIN/CCO

Original Suspense Date: 05/15/2000

Current Suspense Date: 05/15/2000

Create Date: 05/02/2000

Signature Level:

Subject: ANTHRAX

Action: Reply Direct

ADDITIONAL INSTRUCTIONS:

COORDINATIONS

Signature: _____ **Date/Time:** _____

Printed Name: _____

** WHITE HOUSE BULK REFERRAL **

OSD CONTROL NUMBER: **WB75976** DATE OF RECEIPT: **3/27/00**

ACTION AGENCY: **UPR** SUSPENSE DATE: **5/15/00**

DOC: **2/25/00** ACD:

NAME: (b)(6)

SUBJECT: ANTHRAX VACCINE. TRANS FROM SA TO UPR 5/1/00

********** PROCESSING INSTRUCTIONS **********

THIS WHITE HOUSE PUBLIC MAIL REFERRAL IS ASSIGNED TO YOUR AGENCY FOR DIRECT REPLY TO THE WRITER. YOU ARE THE OFFICE OF RECORD. A COPY OF THE REPLY MUST BE PROVIDED TO CORRESPONDENCE AND DIRECTIVES. IF YOU HAVE ANY QUESTIONS, PLEASE CALL (b)(6) . THE OPENING SENTENCE OF THE REPLY SHOULD READ 'Thank you for your recent letter to President Clinton concerning .....'

SECRETARY OF DEFENSE CORRESPONDENCE ACTION REPORT

This form must be completed and delivered to the Correspondence Control Division (CCD), WHS Room 3A948, not later than (YYMMDD)

1. DATE (YYMMDD) 28 APR 2000

2. ACTION TAKEN (X one)

- [ ] a. ACTION HAS BEEN COMPLETED (Copy attached)
- [ ] b. REQUEST CANCELLATION / EXTENSION OF SUSPENSE DATE TO _____ *(Justify below)*
- [ ] c. INTERIM REPLY HAS BEEN SENT (Copy attached)

3. JUSTIFICATION

Ref: WB75976. Rtnd w/o action. Pls send to ASD(HA) for action.

WHITE HOUSE

4. REPORTING AGENCY

a. ACTION AGENCY	c. TELEPHONE NO.	e. APPROVING MILITARY / EXECUTIVE ASSISTANT *(Service Secretary / Under Secretary / ASD Level)*	
SA WHLO	77425	Signature CHARLES W. GRANT, WHLO	Date Signed 28 APR 2000
b. NAME OF ACTION OFFICER	d. DATE *(YYMMDD)*		

5. CCD CONTROL	6. ACTION TAKEN *(For Correspondence Control Division Use Only)*			
WB75976	a. EXTENSION / CANCELLATION		Approved	Disapproved
	b. OTHER (Specify)			

SD FORM 391, AUG 87 *Previous editions are obsolete.*

ELECTRONIC FORM EXCEPTION APPROVED BY WHS/DIOR, MAR 90

Feb 25, 2000.

DOD

SA

ANTHRAX VACCINE

Dear Pres. Clinton:

It has been brought to my attention that you signed order # 13139 into law on Sept 30, 1999. This requires U.S. military personnel to receive experimental vaccines or as referred to in your order "investigational new drugs", not approved by the F.D.A.

I strongly object to our young men and women in the service being forced to comply with this order. They are not "lab animals".

When experimental drugs are to be used on humans it is always for volunteers to do this. Our young men and women in the service deserve no less consideration, no less respect. 007597 6 M

I am praying you will be big enough a person to rescind this order and make it on a voluntary basis.

Sincerely,

(b)(6)

(b)(6)

President Wm. Clinton
White House
Washington, D.C
20500

(61)

STATEMENT BY

EDWARD D. MARTIN, M.D.

PRINCIPAL DEPUTY ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

BEFORE THE

PRESIDENTIAL ADVISORY COMMITTEE

ON GULF WAR VETERANS' ILLNESSES

MILITARY USE OF INVESTIGATIONAL NEW DRUGS (INDS) FOR THE PROTECTION OF U.S. FORCES IN THE GULF WAR

JANUARY 12, 1996

NOT FOR PUBLICATION
UNTIL RELEASED BY
PRESIDENTIAL ADVISORY COMMITTEE
ON GULF WAR VETERANS' ILLNESSES

Introduction

Mr. Chairman, distinguished Members of the Committee, I am Edward D. Martin, M.D., Principal Deputy Assistant Secretary of Defense for Health Affairs. It is a privilege for me to appear before this committee today to represent the Department of Defense (DoD). Today, I would like to discuss the use of investigational new drugs (INDs) in the Persian Gulf War and the procedures we have, both then and now, in place which protect the health and welfare of our military personnel when such INDs are used, both in peacetime and during military combat exigencies.

The Advisory Committee's charter includes a review of the "possible risks associated with service in the Persian Gulf Conflict," including "prophylactic drugs and vaccines." I commend the Committee for its efforts to date to review these "risk factors," and I especially want to commend the Committee staff for the day-long consultation which it convened December 12. This consultation involved a broad range of participants. We at DoD look forward to continuing this type of constructive review of the issues surrounding Gulf War Veterans' illnesses.

Let me first set the stage by reminding the committee that as we entered the Gulf War, we faced the awesome threat of a powerful adversary prepared to employ both biological and chemical warfare agents against the Coalition forces. Iraq had a well-documented track record of chemical warfare agent use against its enemies. Iraq had invested heavily in the resources necessary to wage very sophisticated biological and chemical warfare against our potentially vulnerable force. Indeed, a recent United Nations Special Commission report has documented the declaration of horrendous quantities of anthrax spores, botulinum toxin and chemical agents. We now know that the Al-

acutely aware of the possibility of tens of thousands of casualties. Respected Committee Members, our job was to protect our Service men and women and carry out the mission. We made the best medical defense decisions possible with the information available. Fortunately, we made the correct decisions.

When it first became apparent that U.S. forces might be endangered by Iraq's using biological or chemical weapons in the Persian Gulf, the DoD initiated a series of extensive ethical discussions regarding the medical defensive measures, if any, which should be used and how this question should best be decided. It was recognized that these ethical questions were unprecedented and critically important because the medical measures which would protect Service members from biological and chemical weapons had not been tested in humans for that purpose. Consequently, in addition to discussions involving the military and other governmental agencies, including the FDA and the Public Health Service, the DoD contacted civilians outside DoD with recognized expertise in medical and medical research ethics to participate with them in answering these questions. As a result of these discussions, the DoD concluded that ethically, the principal concern should be protection of the lives of U.S. Service members. The DoD also concluded that in this context, the medical measures which would be used to protect Service members would be employed solely as prophylaxis or treatment. Thus, the DoD finally concluded that since the biological and chemical agents would be highly lethal to our Service members if they were used by Iraq, certain IND products should be given to Service members without having obtained their prior consent.

During Operation Desert Shield/Desert Storm, the medical countermeasures employed by the DoD for Biological and Chemical Threats included Anthrax vaccine (which has been fully licensed by the Food and Drug Administration since 1972) as a prophylaxis

Pyridostigmine Bromide tablets, to enhance the effectiveness of antidotes against nerve agent effects.

I would like to make it very clear to this Committee that the intended use of INDs employed during the Persian Gulf War was as prophylactic treatments against biological and chemical warfare agents and represented the best and most current treatments available. This was not a research effort but rather the best available prevention and pretreatment to protect the health and safety of Service members against known biological and chemical threats.

Referring to these drugs and vaccines as "investigational" is in accordance with Food and Drug Administration (FDA) regulations and is not a definitive statement regarding the scientific information available about the INDs. Per the FDA, a drug or vaccine is an IND if it has not been approved by FDA for general commercial marketing for a particularly stated medical purpose. Drugs often remain in an IND status for an indefinite period for reasons that have a great deal more to do with commercial profit potential than scientific evidence of safety and efficacy. In addition, the use of INDs for treatment purposes is well established in FDA regulations.

Any objective review of this issue should take care to avoid the semantical trap of equating the term "investigational new drug" with the term "research." Equating them in all circumstances may be academically appealing, but it ignores real life health care challenges, including challenges with potentially real life and death consequences. This critical point was clearly understood by the courts in the litigation which challenged the actions of the FDA and DoD. In upholding the government's actions, the U.S. District Court for the District of Columbia rejected the plaintiff's contention "that any use of unapproved drugs is research *per se*, despite the fact

> responded to very real circumstances and chosen what it views as the best alternative given current knowledge. The primary purpose of administering the drugs is military, not scientific. The fact that the DoD will collect information on the efficacy of the drugs does not transform the strategic decision to use the unapproved drugs in combat into research. Furthermore, the FDA has interpreted the FDCA [Food, Drug and Cosmetic Act] to permit using unapproved drugs in a "treatment-investigational setting" in the past. . . . The FDA, therefore, does not view every use of unapproved drugs as research, and nothing in the DoD Act [10 U.S.C. 980, requiring informed consent in DoD "research"] suggests that Congress intended the term to have such a broad meaning.

Doe v. Sullivan, 756 F.Supp. 12, 15-16 (D.D.C. 1991). This decision was affirmed by the United States Court of Appeals for the District of Columbia Circuit. *Doe v. Sullivan*, 938 F.2d 1370 (D.C. Cir. 1991) (opinion by Judge Ruth Bader Ginsburg).

The fact that the use of the INDs in the Persian Gulf War was not research, however, did not mean that it was ordinary treatment either. On the contrary, DoD recognized that any treatment use of an IND presents a very special circumstance, one that requires very special limitations and controls. In this case, a very unique circumstance was presented: the infeasibility of allowing individual military members to refuse the treatment. It was the best judgment of the people responsible for the medical protection of the fighting force that any member who, for whatever reason, refused the treatment would jeopardize his or her own life or health, the safety of other personnel, and the success of the military mission.

Based on this reality, senior officials of DoD and the FDA

and among the two primary agencies involved, and many others with other interested agencies and groups, including the Office for the Protection of Research Risks of the National Institutes of Health, the National Security Council, the Department of Justice, the Office of Management and Budget, the Armed Forces Epidemiological Board (a group of outside experts that advises DoD), and others. The Secretaries of DoD and HHS were personally involved, as was the White House. The actions taken were not taken lightly.

The deliberateness and discipline of the decision making process is reflected in the output of that process. The interim final rule issued December 21, 1990, is extremely limited, as were the actions taken by DoD and FDA under the authority of that regulation. For informed consent to be waived, the Commissioner of Food and Drugs must find that "a military combat exigency exists" because of circumstances in which --

> in order to facilitate accomplishment of the military mission, preservation of the health of the individual and the safety of other personnel require that a particular treatment be provided to a specified group of military personnel, without regard to what might be any individual's personal preference for no treatment or for some alternative treatment.

A duly constituted institutional review board must have approved the use of the IND without informed consent. The factors that must be considered in connection with any waiver include "the extent and strength of the evidence of the safety and effectiveness of the investigational drug for the intended use," the nature of the condition for which the IND is intended, and, in recognition of ethical principles, "the nature of the information to be provided to the recipients of the drug concerning benefits and risks." Perhaps most importantly, the

to the best interests of military personnel and there is no available satisfactory alternative therapy.

The very limited use made during the Gulf War of the "military combat exigency" rule underscores the deliberate and disciplined character of the decision making process. In the Persian Gulf War, DoD used two INDs that, although not approved by FDA for general commercial marketing for the particular medical purposes involved, were specifically allowed by FDA for the special military uses proposed by DoD. FDA allowed these uses because there was evidence they would be effective; no recognized alternative existed; and because FDA determined through available data that their use would likely be safe. The FDA also specifically allowed the use of these drugs in the military combat circumstances involved without the usual informed consent requirements required for INDs. Withholding the use of these INDs would have been contrary to the best interests, and possibly the lives, of our military personnel.

Decisions to use such vaccines and drugs were made during the Gulf War, and continue to this day to be made as required when our Service men and women are placed in harm's way. However, these decisions are only made after weighing the potential risks associated with use, versus the threats to U.S. forces, and then only for those personnel deemed at risk. These decisions, however, are not possible unless there is evidence that the proposed medical solution is already proven to be safe according to the regulatory oversight of the FDA.

I now would like to discuss the procedures which protect the health and welfare of our military personnel when INDs are used, either in peacetime or during military combat exigencies.

The decision process for the use of INDs during Operation Desert Shield/Desert Storm (ODS) involved many steps, one of which was the requirement to have an Institutional Review Board

evaluation of the medical benefits versus the risks for use of drugs and vaccines labeled as IND and also, the evaluation of the risks of not using these INDs in a potential life and death situation.

The Department of Defense (DoD) IRB review for ODS was accomplished through The Army Surgeon General's Human Subjects Research Review Board (HSRRB). The HSRRB was established in 1975, replacing the review functions of three other committees which existed at that time: The Army Investigational Drug Review Board, the Contract Review Board, and the Clinical Investigations Committee. The HSRRB is administered by the Human Use Review and Regulatory Affairs Division (HURRAD) of the U.S. Army Medical Research and Materiel Command. The HURRAD was established in 1974 as the Human Use Review Office during the same time frame that the Office for Protection from Research Risks (OPRR) was established at the National Institutes of Health (NIH). The HURRAD performs similar functions for the Office of The Army Surgeon General (OTSG) as does the OPRR for NIH. The HSRRB acts for OTSG as an IRB, ethics advisory board and human research policy board. The HSRRB recommends protocols for approval by OTSG and may also recommend revisions to, or disapproval of, protocols. The HSRRB provides both a second level IRB review and acts as the sole IRB for selected protocols, especially those from institutions which do not have their own IRB, or for contingency or mobilization type protocols.

At the time of ODS, the HURRAD and the HSRRB were well experienced in the regulatory processes and the ethics of the human subject experience with INDs. The Acting Chairman of the HSRRB at that time was a physician with approximately ten years experience as Acting Chairman. The HSRRB acted as the sole IRB in this case to centralize the process for several different INDs coming from different sources. In the situation with ODS, the

decisions on each individual IND on a case-by-case basis. The medical risks versus the benefits of using the specific INDs were weighed against the risks of not using the INDs. The primary decision put before the HSRRB was whether or not the autonomy of an individual Service member to make his/her own decision outweighed the need to protect that Service member and/or fellow Service members in potentially life-threatening situations. Based on the long history of human use of the approved drug, Pyridostigmine Bromide (Mestinon®), and also that of the IND Botulinum Toxoid vaccine, and the human safety and animal efficacy, these INDs were determined to be the best medical protective measures available against the threat of potential exposure to certain nerve agents and botulinum toxins. The HSRRB recommended the approval of the use of these two products for medical pretreatment and prophylaxis without the requirement of obtaining informed consent. The FDA required the epidemiological follow-up for collecting adverse event data, where possible. These recommendations represented the best medical treatment decisions at the time for the protection of our Service men and women.

The Department of Defense conducts a highly respected research and development program to provide its personnel with the safest and most effective medical countermeasures for health threats anticipated during deployments anywhere in the world. One aspect of this medical defense posture is the protection of our Service members against the threat of biological and chemical warfare agents. Vaccines and pre-exposure chemoprophylaxis are developed and administered to provide the best possible protection of individuals before encountering a particular threat. Treatments such as antibiotics, antitoxins and nerve agent antidotes are administered after an exposure to these agents. In all instances where vaccines, drugs, and

highly developed INDs that are approved for use by the FDA under stringent guidelines.

The issues pertaining to the myriad of possible causalities of Gulf War Veterans' illnesses were reviewed by the National Academy of Sciences, Institute of Medicine (IOM) which convened a Committee to Review the Health Consequences of Service During the Persian Gulf War to examine these issues. As stated in its 1995 published report, the IOM found no evidence that BW-related vaccines nor Pyridostigmine administered to Service members during the Gulf War caused the complaints associated with Gulf War Illnesses. There are also no conclusive data on putative interactive effects of Pyridostigmine with other medical products issued to DoD for personal protection against insects and insect-borne diseases (repellents DEET and permethrin) with Gulf War Veterans' illnesses. Nonetheless, DoD is aggressively pursuing the possibility of any such correlations.

The overriding concerns for human use of any medical product in DoD are its safety and efficacy. As such, products must be approved for use by the FDA, either under licensure, or via the IND regulations. The ultimate goal for the DoD is for all of its medical products to be fully licensed for use in protecting Service members against the threats and anticipated exposure scenarios. Due to the nature of the potential route of exposure by high dose aerosol, and the extreme rarity of natural human contact via aerosol with many of these agents, data to support evidence of protective efficacy for the FDA must be obtained from non-human models. Anthrax vaccine has a good record of safety and efficacy in humans administered the vaccine for occupational exposure, with anecdotal demonstration of protection by virtue of lack of clinical illness. However, evidence of the vaccine's protective value against high doses of the agent administered in an aerosol can be derived only from non-human primate testing.

Pentavalent Toxoid vaccine and from animal protocols using Pyridostigmine Bromide.

Anthrax Vaccine

The Anthrax Vaccine is safe, effective, and has been fully licensed by the FDA since 1972. It is produced by the Michigan Department of Public Health and is currently administered in a series of six immunizations over 18 months. There are no known contraindications for its use and no known adverse long-term health effects. While there is no specific protocol for tracking long-term health effects (i.e. years to decades), should such adverse reactions be recognized, the incidents should be reported and entered into the Vaccine Adverse Events Reporting System (VAERS), which is maintained by the FDA and the Centers for Disease Control and Prevention. There are no indications of any long term safety risk associated with the use of anthrax vaccine. Agencies such as the Centers for Disease Control and Prevention continue to recommend its use. Additional studies are underway to fully evaluate efficacy in animal models and to identify correlates for immunity in vaccine recipients.

Botulinum Pentavalent Toxoid Vaccine

Toxins produced from the bacteria Clostridium botulinum are stable, easy to produce, and extremely lethal. They are in fact among the most poisonous toxins known to man. Botulinum Pentavalent Toxoid vaccine's intended use is to protect Service members from exposure to these toxins when used as biological warfare (BW) agents or in terrorist attacks. We believe this vaccine will protect our Service members from the effects of

Botulinum Pentavalent Toxoid vaccine has been shown to protect laboratory animals from the effects of botulinum toxins (types A through E). Its demonstrated effectiveness in animals gives us confidence that the product will also protect our soldiers, sailors and airmen from the effects of this terrible BW agent.

Botulinum Pentavalent Toxoid vaccine is a combination of five botulinal toxoids (ABCDE). It has an immunization schedule and reaction rate typical of toxoid vaccines and is currently distributed within DoD under the U.S. Army's IND and to the public under the Centers for Disease Control and Prevention's IND.

Prior to Operation Desert Storm/Desert Shield (ODS), Botulinum Toxoid vaccine had been shown to effectively protect laboratory animals against both intraperitoneal and aerosol challenge with botulinum toxin. Safety and immunogenicity had been demonstrated in over 3000 volunteers (mostly at-risk laboratory workers and food handlers in the canning industry) who were given over 13,000 immunizations. Ninety-two percent (92%) of these volunteers reported no side effects. Four to eight percent (4-8%) of volunteers reported only local effects such as pain, swelling, redness and/or itching at the site of injection, and less than one percent (1%) reported generalized side effects such as fever, tiredness, headache, and/or muscle pain. Of all the people immunized with Botulinum Toxoid vaccine less than 0.1%

to protect them against this very real and very lethal form of BW, which the Iraqi's were entirely capable of delivering. Of those immunized there is to date no research evidence linking use of this vaccine to Gulf War Veterans' illnesses.

Since ODS, a program has been undertaken to license Botulinum Pentavalent Toxoid vaccine and additional work also has been done to further refine the product and reduce both local and generalized side effects. The main obstacle to licensing this IND is overcoming the FDA's requirement to demonstrate effectiveness in humans. Because botulism caused by BW or terrorist attack is not a naturally occurring disease there is no ethical way to actually demonstrate its effectiveness in humans prior to its actual use as a BW agent. To overcome this obstacle we are conducting surrogate efficacy studies which we believe will satisfy the FDA's requirement for phase III clinical trials and allow licensure. Our intent is to have this product licensed within two years.

Pyridostigmine Bromide

During Operation Desert Storm/Desert Shield (ODS), U.S. Forces were given tablets of Pyridostigmine Bromide and directed to take them when instructed as a pretreatment against nerve agent poisoning. Since that time, various groups and committees have questioned whether or not Pyridostigmine may have had some bearing on Gulf War Veterans' illnesses. A lot of these comments have centered on the fact that Pyridostigmine is an "investigational" drug, and that it had not been fully tested before we gave it to Service members.

Pyridostigmine is arguably among the most tested drugs which the military has fielded. It is not a new drug. It was first synthesized in 1945 and, following a decade of studies by Hoffmann-LaRoche, approved for use in 1955 by the Food and Drug

Pyridostigmine was identified as a drug which potentially could be used to protect against the effects of nerve agents. During the 1970s, this drug was tested by other countries for this indication. These studies were done, both in animals for safety and effectiveness, and in humans for safety.

This information was encouraging enough that the U.S. military began an active program to investigate Pyridostigmine for this use. Over the next few years, and before ODS began, at least 25 toxicology studies were done in five different animal species. These studies were conducted to determine what side effects could be attributed to Pyridostigmine. Pyridostigmine was given in single doses and in multiple doses out to 34 weeks. The side effects were well established and consistent with the known mechanism of action of Pyridostigmine.

To evaluate the effectiveness of Pyridostigmine as a pretreatment, 26 different studies were conducted in five different animal species prior to ODS. These studies confirmed that Pyridostigmine enhanced the effectiveness of the treatment drugs atropine and oxime as much as 40 fold against the nerve agent soman.

In 1984, the U.S. Army filed an Investigational New Drug Application for Pyridostigmine in order to be able to test its safety in humans. Prior to its use in ODS, 17 studies in 150 subjects were conducted. These studies evaluated the safety in not only conventional ways but also specifically addressed safety in military operational environments such as heat, cold, altitude, flying helicopters, etc. In these studies, Pyridostigmine was given in single doses and in multiple doses for six days. Again, no significant side effects were observed.

During ODS hundreds of thousands of Service members took Pyridostigmine. A large number of Service members complained of side effects; however, less than one tenth of one percent had to

(nausea, vomiting, stomach cramps and gas), and headaches. It also was noted anecdotally that a large number of these events occurred in females. Subsequently, the Army conducted a large study to evaluate whether there were any gender differences that could be attributed to Pyridostigmine, or whether any of these side effects could be due to smaller individuals being given too much drug. The results of this recently completed study were that Pyridostigmine was found to be safe and well tolerated, and that any side effects such as headaches and gastrointestinal were found in both males and females and in light and heavier individuals.

With reference to the use of Pyridostigmine Bromide in ODS, I want to emphasize that the Department of Defense did act in a deliberate and responsible manner by providing Pyridostigmine to our Service members. There were data in dozens of animal studies attesting to its safety and effectiveness. There were data in over 700 volunteers (U.S. and other countries) attesting to its safety under multiple environmental conditions. Pyridostigmine had been used in thousands of people at much higher doses for the treatment of myasthenia gravis. The FDA reviewed all of this information and concurred with our estimates that the potential benefits of using Pyridostigmine far outweighed any risks.

Adequacy of Interim Final Rule for Future Use

DoD believes the Interim Final Rule worked well in the Persian Gulf War, and that it is essential that this authority remain available to deal with future military combat exigencies. Lessons learned from the Gulf War will, we believe, improve record keeping and other implementation actions in future uses, if they are necessary.

At the same time, we believe DoD and FDA should pursue aggressively the possibility of approving new drug applications or product license applications for certain drugs and vaccines

reliance on animal models or other surrogate data indicates the need for a special approval category, perhaps that could be accommodated through marketing restrictions such as "military use only." This type of approach would more clearly separate the reality of meeting life and death medical challenges in military combat exigencies from the research paradigm normally associated with the use of drugs and vaccines not approved by FDA for general commercial marketing. Such an approach might also have application to the important issue of contingencies for dealing with the threat of the use of chemical or biological weapons against Americans by international terrorists organizations.

DoD has filed a new drug application for Pyridostigmine Bromide and hopes to use that as a model to pursue this approach as an additional strategy to ensuring that we can carry out our obligation to protect the fighting force.

Conclusion

The threat was very real. The potential for a high mortality rate was substantial. After extensive, in-depth, and exhaustive consultation over a protracted period of time the correct decisions were made, decisions that put in place the best medical prophylaxis available to preserve our fighting force.

Anthrax vaccine, Botulinum Pentavalent Toxoid vaccine and Pyridostigmine Bromide tablets were not used for experimental purposes in Operation Desert Shield/Desert Storm (ODS) and the military personnel who received these products were not experimental subjects. These products were used only after careful review by a duly constituted human use review committee and the FDA. These products were used as prophylactic treatments against biological and chemical warfare agents and represented the best and most current treatments available. This was not a research effort but rather the best available prevention and pretreatment to protect the health and safety of Service members

peacetime and in combat. Regardless of the scenario, the application of medical products must remain responsive in the face of evolving military requirements and biomedical technologies.

I want to thank you, Mr. Chairman, and the Members of this Committee for your interest in these issues, but more importantly for your concern for the health of our Service members and Veterans.

(62)

OFFICE OF THE ARMY SURGEON (

CMAT Control #
1999169-0000001

EXECUTIVE OFFICER

HQDA (DASG)
5109 Leesburg Pike
Falls Church, VA
22041-3258

THIS HEADER IS PAGE 1 OF 2 PAGES

SUBJECT: Mycoplasma

TO: Col Huddleston
FAX: (b)(6)

FROM:
EXECUTIVE OFFICER: COL RICHARD URSONE
SECRETARY: Ms (b)(6)

Telephone Numbers:
(703) (b)(6)
DSN:
FAX
(703) (b)(6)
DSN:

COMMENTS:
Sue,
LTG Blanck asked that Dr. Rostker receive this EXSUM in regards to mycoplasma testing. Regards
Dick

EXECUTIVE SUMMARY

16 June 1999

(u) CURRENT STATUS OF MYCOPLASMA TESTING FOR ANTHRAX VACCINE, ADSORBED. (U) (USAMRIID) The efforts to evaluate the possibility of mycoplasma contamination in the licensed product Anthrax Vaccine, Adsorbed is nearing completion. Results for the first two phases of the effort have been previously reported. This included the demonstration that mycoplasma could not be cultured from existing vaccine in phase 1 studies, and that mycoplasma DNA could not be identified in vaccine samples based on a commercially available polymerase chain reaction (PCR) assay specific for mycoplasma DNA detection. In the third phase of study, vaccine has been spiked with live mycoplasma to determine the survivability of the organisms in the vaccine. The vaccine contains preservatives and stabilizers which are inimical to mycoplasma growth. Testing performed at the National Cancer Institute mycoplasma laboratory demonstrates that even very high doses (10^8 CFU/ml) of *M. fermentans* were not able to survive for a 24 hour period in a time-course study of survival. The final report for this work is expected by 22 June. All of this evidence strongly suggests that viable mycoplasma exposure is a very unlikely event for personnel receiving this vaccine. PROVIDE MEMO_____.

LTC George W. Korch/MCMR-UIZ-B/(b)(6)

APPROVED BY Gerald W Parker

(63)

CMAT Control #
1999085-0000009

ANTHRAX VACCINE IMMUNIZATION PROGRAM

Statement by

Dr. Sue Bailey
Assistant Secretary of Defense for Health Affairs

Submitted to

Subcommittee on National Security,
Veterans Affairs and International Relations
Committee on Government Reform
U.S. House of Representatives

March 24, 1999

Not for Publication
Until Released by
Committee on Government Reform
U.S. House of Representatives

Chairman Shays, Representative Blagojevich and Distinguished Committee Members, I very much appreciate this opportunity to appear before your Committee today on one of the Department's most important force health protection efforts – the Total Force Anthrax Vaccine Immunization Program (AVIP). Today I am accompanied by Army Surgeon General Ron Blanck, Air Force Surgeon General Chip Roadman and Navy Deputy Surgeon General Todd Fisher. We will be addressing the decision-making process that led to the implementation of the AVIP program. Although we will be focusing on the medical aspects of the program, I would like to emphasize that this is *not* primarily a medical program. It is a line commanders' program to keep our deployed military personnel safe and prevent combat casualties.

Building upon many lessons learned over the past several years and the Department's strong commitment to force health protection, the AVIP employs a very different and effective approach, incorporating a safe and efficacious vaccine, effective risk communication, extensive immunization tracking, strong command leadership with medical support. As we say often, "anthrax kills; vaccination protects". To date, I am pleased to tell you that 223,000 soldiers, sailors, airmen and marines have received Anthrax immunizations under this program.

As identified by the Chairman of the Joint Chiefs of Staff, anthrax is a major threat to our troops. Anthrax is the primary biological warfare threat faced by U.S. forces. More than 10 countries, including Iraq, have or are suspected of developing this biological warfare capability. Anthrax is the biological weapon most likely to be encountered because it is highly lethal, easy to produce in large quantities, and relatively easy to develop as a weapon.

Further, the nation expects military commanders to do all in their power and authority to employ prudent medical countermeasures in the face of biologic and chemical threats to preserve the safety and well-being of our service personnel as well as to assure a satisfactory completion of their military missions. The Total Force AVIP, a line-managed force health protection program, provides U.S. troops with a much needed measure of protection against a deadly threat.

The Total Force AVIP involved a detailed, deliberative process that culminated in Secretary of Defense Cohen's decision to approve implementation of the program on May 18, 1998.

The deliberative process began with development and implementation of Department of Defense Directive 6205.3, DoD Immunization Program for Biological Warfare Defense, dated November 26, 1993. This directive prescribes the process for addressing requirements for immunization against biological warfare threats against U.S. personnel. A series of discussions within the Department regarding a policy on immunizing US forces against anthrax took place between 1993-1995.

Subsequently, the Chairman, Joint Chiefs of Staff (CJCS) identified anthrax as the primary biological warfare threat to our deployed forces in his Threat Matrix. The CJCS Program Assessment also recommended immunizing the entire force against anthrax. In January 1997, the Deputy Secretary of Defense directed the Assistant Secretary of Defense (Health Affairs) and the Joint Staff to prepare planning guidance to implement anthrax immunizations for US forces.

While in the process of developing the planning guidance, questions arose about the manufacturer, Michigan Biologic Products Institute (MBPI). These questions primarily involved the proposed sale of MBPI by the State of Michigan and also a Food and Drug Administration (FDA) inspection of MBPI in November 1996. The inspection resulted in the FDA directing the manufacturer to take immediate actions to correct facility inspection deficiencies.

Subsequently, a DoD team visited MBPI and determined that the facility had made significant improvements and was moving forward in meeting objectives under its strategic plan for improving its manufacturing facility and processes. Additionally, the State of Michigan assured the Department that the future manufacture of anthrax vaccine would not be adversely affected by sale of the state-owned facility. As a result, the ASD(HA) and Joint Staff again addressed the planning guidance within the Department. After receiving concurrences, the ASD (HA) and Joint Staff incorporated the planning guidance into a Secretary of Defense decision package recommending anthrax immunizations for the total force.

On December 15, 1997, the Secretary of Defense approved the plan for immunization of the total force against anthrax contingent upon the successful completion of four conditions prior to implementation of the program.

(1) supplemental testing, consistent with Food and Drug Administration (FDA) standards, of anthrax vaccine lots in the stockpile to assure their potency, purity, sterility, and general safety

(2) approval of the Services' implementation plans that describe how they plan to administer their respective anthrax vaccine immunization program and communications plans that describe efforts to inform military personnel of the overall program

(3) implementation of a system for fully tracking anthrax vaccinations

(4) review of the health and medical aspects of the program by an independent expert.

On February 3, 1998 due to increasing tensions in his region, the Commander In Chief (CINC) Central Command (CENTCOM) requested acceleration of the total force AVIP for the CENTCOM region. Subsequently, the Deputy Secretary of Defense conditionally approved the CJCS recommendation supporting the CINC CENTCOM request and mandated a final medical review to ensure that the four conditions set by the Secretary of Defense were successfully completed before the program was implemented in the CENTCOM region.

A final medical review, conducted on March 2, 1998, determined that the four conditions specified by the Secretary of Defense had been successfully met for the CENTCOM region.

(1) supplemental testing had been completed on all lots of FDA-licensed anthrax vaccine that would be used in the CENTCOM region

(2)interim automated immunization tracking systems were in place for each service and operational in the CENTCOM region

(3) approved operational plans for administering the anthrax immunization and health risk communications information and briefings were in place in the region

(4) an independent review of the health and medical aspects of the overall program was completed by Dr. Gerard Burrow, Special Advisor for Health Affairs for the President of Yale University, on February 19, 1998.

The Secretary of Defense gave approval for CENTCOM to begin anthrax immunizations in the region on March 2, 1998, with forces assigned or deployed to Southwest Asia (SWA). Immunizations began on March 10, 1998.

On May 18, 1998, Secretary Cohen approved implementation of the Total Force AVIP. As with the Accelerated AVIP for SWA, all four conditions set by Secretary Cohen on December 15, 1997, were met before approval for program implementation was given.

The Total Force AVIP is being implemented in three phases over a seven to eight year period. Under the time-phased implementation plan, forces expected to deploy to high threat areas are the first to be immunized against anthrax. This phase, referred to as Phase I, includes service members and mission essential DoD civilians assigned or deployed to Joint Staff-designated high threat areas in SWA and Korea. Early deploying forces supporting SWA and NWA, to include Active and Reserve Component personnel, constitute Phase II. Phase III will include the remainder of the force, both Active and Reserve Component, and accessions.

Like other immunizations that are required to prepare military personnel for deployment, the anthrax immunization is mandatory. Personnel will be required to have the anthrax immunization unless medically deferred. The authority to direct usage of medical countermeasures constitutes a lawful military order. Why is it essential that the anthrax immunization be mandatory? Military commanders have the responsibility to ensure the health and safety of their troops and to carry out their mission responsibilities. Anthrax is a serious threat. We have a safe and efficacious vaccine. To not use the vaccine constitutes a failure to protect our troops and a risk to carrying out military missions.

Each Service has its own policy for how it will handle Service members who refuse a lawful military order to take the anthrax immunization.

The Department is confident, as is the Food and Drug Administration (FDA), that the FDA-licensed anthrax vaccine is safe and efficacious for its intended use of immunizing the total force against anthrax. The anthrax vaccine has been licensed by the FDA since 1970 and has been recommended for veterinarians, laboratory workers, and livestock handlers in the US for more than 25 years. There have been no long-term side effects reported with the FDA-licensed anthrax vaccine.

Since 1973, USAMRIID has monitored 10,451 injections, or 4605 primary series doses, and 5846 booster doses of FDA-licensed anthrax vaccine administered to USAMRIID laboratory personnel. Short-term reactions were reported to be about 4% for both primary and booster vaccinations (passive data collection). No long-term adverse effects have been reported. As of March 16, 1999, more than 634,000 anthrax immunizations have been given to over 223,000 Service members. To date, there have been 42 Vaccine Adverse Event Reporting System (VAERS) reports submitted to the FDA and CDC (an adverse reaction rate of 0.007 percent). Only 7 service members required hospitalization or experienced loss of duty for more than 24 hours. There was one case of Guillain-Barre Syndrome and that person has subsequently recovered. Compared to other vaccine reaction rates, the anthrax vaccine has a very good safety record. In addition to tracking adverse effects in the overall program, we are also conducting a population-based study at Tripler Army Medical Center, Hawaii, on over 600 military medical personnel (i.e., doctors, nurses, and medical technicians) who have received the anthrax immunization. The survey was specifically designed to derive all possible significant side effects experienced with the anthrax immunization.

The safety of our AVIP was also confirmed by an independent review of the program. Dr. Gerard N. Burrow, who serves as Special Advisor for Health Affairs for the President of Yale University, conducted the review. Dr. Burrow concluded that "the anthrax vaccine appears to be safe and offers the best available protection against wild-type anthrax as a BW agent."

With respect to efficacy, a FDA Advisory Panel stated in 1985 that there is sufficient evidence to conclude that the anthrax vaccine is effective under the limited circumstances for which this vaccine is employed. In a March 13, 1997 memorandum, the FDA confirmed that the pre-exposure administration of the FDA-licensed anthrax vaccine for the prevention of inhalation anthrax is not inconsistent with the current product label. In addition, the Committee on Infectious Diseases, American Academy of Pediatrics (1994), states that "the vaccine is effective in preventing or significantly reducing the occurrence of cutaneous and inhalation anthrax in adults."

Conducting lethal challenge studies in humans is considered unethical and, since there is no study population identified as being at high risk for inhalation anthrax, directly determining the efficacy of the vaccine in humans against aerosol exposure to anthrax spores is not possible. There have been numerous studies of the anthrax vaccine involving animal models. Several studies performed at the USAMRIID have demonstrated the efficacy of the FDA-licensed anthrax vaccine against inhalation anthrax in rhesus monkey challenge studies. These animal studies showed that the FDA-approved anthrax vaccine provided greater than 95% protection against high-dose aerosol challenge with anthrax in the monkey model. Human antibody response to the FDA-licensed vaccine provides further suggestive evidence that the FDA-licensed anthrax vaccine will protect against inhalation anthrax.

To give you a sense as to how we designed the AVIP differently, let me address three major changes from past programs – line commander ownership, risk communication, and tracking of immunizations and adverse effects. The success of this program depends on Line Commanders taking ownership of the program and making sure that their troops are immunized. As always, the medical staff support their line leadership in carrying out the medical aspects of the program. The Line has taken on this responsibility and has been a key to the remarkable success to date. Commanders, including General Shelton, Chairman of the Joint Chiefs of Staff, are often the first to take the shots. They keep track of how their units are doing in getting immunized and make sure the troops get their immunizations on a timely basis. Line Commanders are also involved in communicating the importance of this program to the health of the troops and the achievement of military missions.

With respect to risk communications, again a major change is taking place. For this and future such programs, the troops are being clearly advised up front as to why the vaccination is needed, what vaccination they are receiving, the safety and efficacy of the vaccine, and what potential adverse effects could occur. It is important that the troops understand the benefits as well as the risks, though very low, of Anthrax immunizations. When the program starts in a particular unit, troops are given the opportunity to ask questions and the Commanders and medics work with troops who have concerns about the immunization. Often this is done on an individual and personal basis. In rolling out the program and in its ongoing operation, the Department has used a wide range of communications mechanisms to reach the troops and their families. Briefings, newspapers and handouts have been used extensively. The newest area of communications has been the Internet. Each military service has established Internet web sites to address service member and family concerns regarding the AVIP and its implementation. DoD's DefenseLINK also has an anthrax web site which, with the services' web pages, provides synchronized information to all beneficiaries regarding the anthrax vaccine immunization program.

Tracking who receives vaccinations and any adverse effects is vital to a successful program. Currently, the Services use different interim automated immunization tracking systems (ITS) to record and track the anthrax immunization status of their Service members. The core information is then placed in DoD's central personnel database, the Defense Enrollment and Eligibility Reporting System (DEERS), as the system to track across all Services. These systems are used as management tools to remind Commanders and individuals about their anthrax immunization status (who needs which immunization when) and to keep track of adverse effects. Operational testing of a joint system, Preventive Health Care Application (PHCA), for use at the Service level, has occurred with worldwide deployment beginning this year. To add further emphasis to the importance of tracking immunizations, the Combatant Commands, Joint Staff, and Services began monitoring anthrax immunization status of units assigned to high threat areas as a readiness indicator.

Mr. Chairman, Representative Blagojevich, Distinguished Committee Members, we are deeply committed to protecting the health our forces and are applying the many lessons learned over the past decade. I am proud to say that the Anthrax Vaccine Immunization Program is the culmination of all those efforts and sets the standard for future efforts to protect our troops against the terrible threats of chemical and biological warfare agents. We have a terrible threat. We are fortunate to have a safe and efficacious vaccine. We would be irresponsible if we did not use it to protect our troops.

CMAT Control #
2003006-0000017

(64)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

January 3, 2003 2:45 PM

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ms. Ellen P. Embrey, DASD, Force Health Protection and Readiness

SUBJECT: Representative Oxley's Inquiry for Information on the Anthrax Vaccine Immunization Program

- Representative Oxley requested we provide a response to one of his constituents, (b)(6) regarding the Anthrax Vaccine Immunization Program. As a concerned citizen, (b)(6) has numerous concerns regarding our servicemembers and the anthrax vaccine immunization program.

- The proposed response explains AVIP policy that addresses her concerns.

RECOMMENDATION: Sign letter at TAB A.

COORDINATION: TAB C

Prepared by: COL Randolph, AVIP Office, PCDOCS # 44427 R/44440

HA/TMA Document Profile

44427

Subject:	AVIP Problem		
Author:	Oxley, Michael MOC	**Congressional Name:**	Oxley, Michael MOC
Date of Document:	10/25/2002	**Input By:**	VESPINAL
OSD # :		**Profiler's Directorate:**	Admin, HA
PR # :		**Response Signed By:**	
Organization:		**Dt Response Signed:**	
Department:		**Doc Type:**	MEMO
Assigned To:	DHS	**Application:**	DOCSIMAGE
Prepared For:	ASD	**Previous Documents:**	
Suspense Date:	1/7/2003	**Related Documents:**	
Coord Office(s):		**Notes:**	SHORT SUSP. Tasked by LTC Henselman

Beneficiary Info

Beneficiary Name:	(b)(6)
Address 1:	
Apartment #	
Phone #	
Email Address:	
City:	(b)(6)
State:	**Zip:** (b)(6)

History

Created:	1/3/2003	HA PCDOCS Adr
Edited:	1/3/2003	HA PCDOCS Adr
Status:	Available	

Retention Schedule

Type: Archive

Retention Days: 365

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DEC 10 2002 4 48PM NO 6803 P 1 2

MICHAEL G. OXLEY

COMMITTEE ON FINANCIAL SERVICES

Congress of the United States

House of Representatives

Washington, DC 20515–3501

Faxed from the Office of

Congressman Michael G. Oxley

Fourth Ohio District

To: Dr. William Winkenwerder

From: ☐ Michael G. Oxley ☐ Tim Johnson ☐ Dirk Bartlett
☐ Jim Conzelman ☒ Peter Erdman ☐ Jen Mundy
☐ Debi Deimling ☐ Jared Dilley ☐ ___

Date 12 / 10 / 2002 Pages (including cover): 2

Subject: AVIP problem

Comments:

Any help in response to this constituent's concern would be appreciated.

Thanks

(b)(6)

From: writerep
Sent: Friday, October 25, 2002 1.12 PM
To: OH04WYR
Subject: WriteRep Responses

DATE October 25, 2002 11 51 AM
NAME. (b)(6)
ADDR1-
ADDR2.
ADDR3
CITY
STATE
ZIP:
PHONE:
EMAIL.
msg:
Dear Congressman Oxley,

DOD Leg Affairs
~~703-697-6210~~
James Anderson
703 602-4491
fax
Dr. W. Kendrick

I am writing as a concerned citizen I am urging you to investigate and help stop the mandatory Anthrax Vaccine Immunization Program (AVIP) of our service men and women. Anthrax vaccine is unsafe, untested, unnecessary, unpopular, unethical, and not totally effective. Early symptoms following the first or second shot that have been reported in high numbers include headaches, malaise, respiratory distress, chills, diarrhea, fever, and abdominal cramping. Later chronic symptoms reported often after the third or fourth shot have included dizziness, chronic fatigue, chest pains, sleep disorders, memory loss, headaches, joint and muscle pain, peripheral sensory neuropathies, recurring rashes, blackouts, autoimmune diseases, swelling of limbs, collagen vascular disease, sepsis, cardiomyopathy, nausea, night sweats, cysts, tunnel vision, and seizures This information can be found at the CDC website www cdc gov/mmwr/preview/mmwrhtml/rr4915a1.htm and in the book "Anthrax. A Deadly Shot In The Dark" by Thomas S Haemstra Six people have died following anthrax immunization. Our service men and women make great sacrifices of time and sometimes their lives to defend our great nation, but they should not have to sacrifice their health because of this unsafe vaccine or risk court-martial if they refuse it Civilians are given a choice concerning this vaccine and so should our sevice men and women be given that same choice. Further research needs to be done to find a safe and effective anthrax vaccine

Sincerely,
(b)(6)

Greg:

Send FOIAs to Lynn Hemelman w/ coordinate through the AVIP folks—

Guy.

Henselman, Lynn, LTC, OASD(HA)

From: Randolph, Gaston M COL OTSG (b)(6) @otsg amedd army mil]
Sent: Wednesday, December 25, 2002 5 47 PM
To: 'lynn henselman@ha osd mil'
Subject: Draft Letter for ASD(HA) Signature
Importance: High

Lynn: As requested. GMR
-----Original Message-----
From: Cunningham, Tom T Mr Eagle
Sent: Tuesday, December 24, 2002 1:35 PM
To: Randolph, Gaston M COL OTSG
Cc: Grabenstein, John D LTC OTSG
Subject: Letter

Randy,
Attached is the final version of the (b)(6) letter
Tom

Executive Office

(b)(6)

Dear (b)(6)

Thank you for your recent e-mail concerning the Anthrax Vaccine Immunization Program (AVIP) I share your concern for our service members Preserving their health and safety is our #1 concern The Department of Defense (DoD) requires anthrax vaccination for certain service members as an added layer of protection against this potentially deadly biological agent

The threat of biological warfare has been a risk to U S forces for many years DoD analysts maintain updated threat-level evaluations, adjusting the information as necessary to reflect the risk to U S operations Based on assessment of current and past activities in such areas as Iraq and the former Soviet Union, the potential offensive biological threat facing service members makes it necessary for the DoD to have a robust biological-defense program today Anthrax is one of the deadliest biological weapons of choice

As with other vaccines, the benefits of the U S Food and Drug Administration (FDA)-licensed anthrax vaccine far outweigh any risk The Centers for Disease Control and Prevention (CDC) states that getting vaccinated is much safer than getting the diseases the vaccines prevent Such biological agents as anthrax are especially hard to detect Symptoms are delayed, and without preventive medical efforts, such as vaccination, the results can be devastating and widespread

Medical experts agree there have been no deaths found to be caused by anthrax vaccine reported among more than 2 2 million immunizations given to over 567,000 service men and women since the Anthrax Vaccine Immunization Program began in March 1998 Further, no deaths have been attributed in a cause-and-effect manner to the vaccine since the FDA licensed it over 30 years ago

Many studies establish anthrax vaccine safety From a 1958 study published in the *Bulletin of the Johns Hopkins Hospital,* to more recent studies at Fort Detrick, Maryland, evidence shows that there are no known long-term side effects to the anthrax vaccine In 2002, the National Academy of Sciences Institute of Medicine's Committee to Assess the Safety and Efficacy of the Anthrax Vaccine concluded their two-year study In their published findings, the Committee found "no evidence that people face an increased risk of experiencing life-threatening or permanently disabling adverse events immediately after receiving AVA, when compared with the general population

"Nor did it find any convincing evidence that people face elevated risk of developing adverse health effects over the longer term, although data are limited in this regard (as they are for all vaccines) "*

The IOM Committee studied data on anthrax-vaccine effectiveness and concluded "that the available evidence from studies with humans and animals, coupled with reasonable assumptions of analogy, show that AVA as licensed is an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by any known or plausible engineered strains of *B anthracis* "*

The DoD continually strives for improved vaccines and improved vaccination programs to protect the health of our force The DoD is currently collaborating with the CDC in their study to determine different ways to administer the current anthrax vaccine This study may lead to the FDA's allowing its use in fewer doses and administering it in a way that may reduce bothersome local injection-site redness, pain, swelling and itching Additionally, the DoD is partnering with the Department of Health and Human Services to develop a "next generation" anthrax vaccine, which may be as effective and safe as the current vaccine in fewer doses Both these efforts are important, but will take years to conclude Meanwhile, we must protect our service members from harm with the currently licensed, safe and effective vaccine

I trust this information addresses your concerns and I invite you to visit the AVIP's Internet Web site at http //www anthrax mil, or call the toll-free information line at 1-877-GET-VACC for more in-depth information about the anthrax-vaccine program Answers to other questions are also available by writing to avip@otsg amedd army mil

*Source "The Anthrax Vaccine Is It Safe? Does It Work?" Published in 2002 by the National Academy Press, www nap edu/catalog/10310 html

Henselman, Lynn, LTC, OASD(HA)

From: Henselman, Lynn, LTC, OASD(HA)
Sent: Friday, December 27, 2002 11 17 AM
To: Vessey, Alida, CON, OASD(HA)/TMA
Subject: RE Draft Letter for ASD(HA) Signature

Tracking:

Recipient	Read
Vessey, Alida, CON, OASD(HA)/TMA	Read 12/27/2002 11 24 AM

Would your shop be able to put the coordination package together? It should be assigned to FHP & R and prepared for Dr Winkenwerder's signature

If I should be doing something differently, please let me know

Lynn

-----Original Message-----
From: Vessey, Alida, CON, OASD(HA)/TMA
Sent: Friday, December 27, 2002 10:58 AM
To: Henselman, Lynn, LTC, OASD(HA)
Subject: RE Draft Letter for ASD(HA) Signature

I can't find it in PCDOCS Have not seen it up here

-----Original Message-----
From: Henselman, Lynn, LTC, OASD(HA)
Sent: Friday, December 27, 2002 10:39 AM
To: Vessey, Alida, CON, OASD(HA)/TMA
Subject: FW: Draft Letter for ASD(HA) Signature
Importance: High

Alida,

Is this response in PCDOCS? I have been unable to find it

Lynn
-----Original Message-----
From: Randolph, Gaston M COL OTSG [mailto:(b)(6) @otsg.amedd.army.mil]
Sent: Wednesday, December 25, 2002 5:47 PM
To: (b)(6) @ha.osd.mil'
Subject: Draft Letter for ASD(HA) Signature
Importance: High

Lynn: As requested. GMR
-----Original Message-----
From: Cunningham, Tom T Mr Eagle
Sent: Tuesday, December 24, 2002 1 35 PM
To: Randolph, Gaston M COL OTSG
Cc: Grabenstein, John D LTC OTSG
Subject: Letter

Randy,

Attached is the final version of the (b)(6) letter
Tom

"Espinal, Vicky, CIV, OASD(HA)/TMA" (b)(6) @tma.osd.mil> on 01/03/2003 10:24:44 AM

Pc Doc's
44427

To: "Rushin, Edward, DHSD" (b)(6) @deploymenthealth.osd.mil>
cc:

Subject: Hot suspense

Ed

We will be sending you a hot suspense that we received from LTC Hen Selman, suspense date will be 1/7/03. Please work asap.

Vicky Espinal
Staff Assistant
Document Management Division
(703 (b)(6)
(703 fax
(b)(6) @tma.osd.mil

SUBJECT: Representative Oxley's Inquiry for Information on the Anthrax Vaccine Immunization Program

COORDINATIONS

Dir, AVIP	COL Randy Randolph	Concur 1/3/03
Dir, PI (HA)	LTC Henselman	Concur 1/3/03

"Randolph, Gaston M COL OTSG" (b)(6) @otsg.amedd.army.mil>
on 01/04/2003 04:39:02 PM

To: (b)(6)
cc:

Subject: FW: REP OXLEY RESPONSE TO MS. HAUSHALTER

Ed:

Attached are 3 recommended (well, corrects mistakes, so important to "accept") changes using Word's Tracking Tool. I don't intend to be mean or snippy here, but these were correct in the draft I sent originally. I realize you folks made some editorial changes to express differently than me in a couple places, and I appreciate that license; however, pls don't make changes that are mistakes.

Thanks, Randy Randolph

-----Original Message-----
From: (b)(6) deploymenthealth.osd.mil
(b)(6)
Sent: Friday, January 03, 2003 1:24 PM
To: (b)(6)
Cc:
Subject: REP OXLEY RESPONSE TO MS. HAUSHALTER
Importance: High

Lynn/Randy:

Attached is the proposed response to (b)(6) regarding AVIP. If you both concur and respond via email, I will send this forward for Ms. Embrey's coordination and ASD(HA) signature.

(See attached file: Rep Oxley - AVIP Problem 1-3-03.doc)

- Rep Oxley - AVIP Problem 1-3-03.doc

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

(b)(6)

Dear (b)(6)

Thank you for your recent e-mail concerning the Anthrax Vaccine Immunization Program (AVIP). I share your concern for our servicemembers. Preserving their health and safety is our number one concern. The Department of Defense (DoD) requires anthrax vaccination for certain servicemembers as an added layer of protection against this potentially deadly biological agent.

The threat of biological warfare has been a risk to U.S. forces for many years. DoD analysts maintain updated threat-level evaluations, adjusting the information as necessary to reflect the risk to U.S. operations. Based on assessment of current and past activities in such areas as Iraq and the former Soviet Union, the potential offensive biological threat facing servicemembers makes it necessary for the DoD to have a robust biological defense program today. Anthrax is one of the deadliest biological weapons of choice.

As with other vaccines, the benefits of the U.S. Food and Drug Administration (FDA) licensed anthrax vaccine far outweigh any risk. The Centers for Disease Control and Prevention (CDC) states that getting vaccinated is much safer than getting the diseases the vaccines prevent. Biological agents such as anthrax are especially hard to detect. Symptoms are delayed, and without preventive medical efforts such as vaccination, the results can be devastating and widespread.

Medical experts agree, there have been no deaths from anthrax vaccine reported among more than 2.2 million immunizations given to over 567,000 servicemen and women since the Anthrax Vaccine Immunization Program began in March 1998. Further, no deaths have been attributed in a cause-and-effect manner to the vaccine since the FDA licensed it over 30 years ago.

Many studies establish anthrax vaccine safety. From a 1958 study published in the *Bulletin of the John Hopkins Hospital*, to more recent studies at Fort Detrick, Maryland, evidence shows that there are no long-term side effects to the anthrax vaccine. In 2002, the National Academy of Sciences, Institute of Medicine's (IOM) Committee to Assess the Safety and Efficacy of the Anthrax Vaccine, concluded their two-year study. In their published findings, the Committee found "no evidence that people face an increased risk of experiencing life-threatening or permanently disabling adverse events immediately after receiving AVA, when compared with the general population.

"Nor did it find any convincing evidence that people face elevated risk of developing adverse health effects over the long term, although data are limited in this regard (as they are for all vaccines)."*

The IOM Committee studied data on anthrax-vaccine effectiveness and concluded "that the available evidence from studies with humans and animals, coupled with reasonable assumptions of analogy, show that AVA as licensed is an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by any known plausible engineered strains of B anthracis." *

The DoD continually strives for improved vaccines and improved vaccination programs to protect the health of our forces. The DoD is currently collaborating with the CDC in their study to determine different ways to administer the current anthrax vaccine. This study may lead to the FDA's allowing its use in fewer doses and administering it in a way that may reduce bothersome local injection-site redness, pain, swelling and itching. Additionally, the DoD is partnering with the Department of Health and Human Services to develop a "next generation" anthrax vaccine, which may be as effective and safe as the current vaccine in fewer doses. Both of these efforts are important, but will take years to conclude. Meanwhile, we must protect our servicemembers from harm with the currently licensed, safe and effective vaccine.

I trust this information addresses your concerns and I invite you to visit the AVIP's Internet Website at http://www.anthrax.mil, or call the toll-free information line at 1-877-GET-VACC for more in-depth information about the anthrax-vaccine program. Answers to other questions are also available by writing to avip@otsg.amedd.army.mil.

Sincerely,

William Winkenwerder Jr., MD

Cc:
The Honorable Michael G. Oxley

* Source - "The Anthrax Vaccine, Is It Safe? Does It Work?" Published in 2002 by the National Academy Press, www.nap.edu/catalog/10310/html.

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HA/TMA Document Profile

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HA FRONT OFFICE TASKER

Assigned: 1/10/03 **Suspense Date:**1/15/03 **PCDOCS #:** 44672

From: Mr. (b)(6)

For: All DASDs

Subject: Tasker from 1/10/03 Senior Leader Meeting

Assignment:
Develop key messages to Congress to 2 pages; submit to (b)(6) and cc: (b)(6)

Completed:

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TAB A

THE FEDERAL STRATEGIC HEALTH ALLIANCE (FEDS_HEAL)

KEY MESSAGE:

FEDS_HEAL is a VA-HHS-DoD partnership that links the resources of the Veterans Health Administration (VHA) and the Department of Health and Human Services Division of Federal Occupational Health (FOH) to furnish immunizations, physical examinations, dental screening and treatment, and other specified diagnostic services to units and individuals of the Army Reserve and the Army National Guard. The underlying concept for planning the Federal Strategic Health Alliance was to create a cost-effective and accessible system of medical and dental readiness services.

FACTS:

- The downsizing of the Army's medical force structure during the 1990s created a shortfall in the infrastructure needed to meet statutory medical and dental readiness requirements for Reserve Component (RC) soldiers. The "746 Study" (Section 746 of the National Defense Authorization Act for Fiscal Year 1997) validated the shortfall in assets to support RC medical and dental readiness requirements.

- The FEDS_HEAL partnership was created through individual Memoranda of Agreement between the Office of the Chief, Army Reserve (Chief of Personnel), and FOH (Associate VP of Clinical Services), and between FOH and each of the twenty-two Veterans Integrated Service Networks.

- FEDS_HEAL is a centrally funded, locally managed health services support system. Budgeting for services remains the responsibility of the individual Reserve Component (Army National Guard and Army Reserve). The Office of the Chief, Army Reserve, and the National Guard Bureau annually allocate funding for FEDS_HEAL. Because the Defense Health Program does not cover Reserve Component medical and dental readiness services, the resources to support these activities come from Component operational funds.

- Program coordination is provided by FOH. Military units request services via an automated, web-based request system. The Office of the Chief, Army Reserve and the Surgeon's Office in the National Guard Bureau, in coordination with the Army office of the Surgeon General, review the overall performance of the Federal Strategic Health Alliance to ensure compliance with standards and equitable distribution of requirements between participants.

(b)(6)

DHSD

(b)(6)

February 26, 2002

IMPROVEMENTS IN ENVIRONMENTAL HEALTH ASSESSMENT AND HEALTH RISK MANAGEMENT

KEY MESSAGE:

The adequate identification and response to potential occupational and environmental health and safety threats is the cornerstone of insuring effective force health protection in deployments. Shortfalls during the Gulf War resulted in the creation of the U.S. Army Center for Health Prevention and Preventative Medicine to improve surveillance and monitoring in deployed settings, and the formation of the Joint Environmental Surveillance Working Group to develop uniform approaches to environmental surveillance. These organizations insure a consistent and uniform approach throughout the services.

FACTS:

- Policy and doctrine authorize occupational and environmental health and safety activities in DoD before and during deployments. Guidance documents for deployed forces insure that occupational and environmental health and safety activities are conducted in a consistent and uniform fashion.
- Medical intelligence and open source environmental/medical information are assessed before deployment. Such assessments allow identification of potential occupational and environmental health threats. This assists proper siting of base camps and the identification of appropriate countermeasures before deployment.
- Base camp assessments are conducted for occupational and environmental health and safety issues before the deployment and during operations.
- Base area assessments are applied against health-based standards and guidelines and health risk assessment and management techniques appropriate for deployed military personnel. The Institute of Medicine is currently reviewing several of these standards and guidelines to validate their use during deployments.
- Data collection, management, archiving, and reporting activities insure that information is available to unit commanders in a timely manner and that retrospective health and epidemiological studies can be conducted.
- The Deployment Health Support Directorate is assessing current deployments and practices in the area of environmental health and medical intelligence to continue improvement and refinement of policy and mission practices.

(b)(6)
DHSD
(b)(6)
October 16, 2002

GULF WAR MEDICAL LESSONS LEARNED

KEY MESSAGE: The DoD has applied medical lessons learned from the Gulf War to help protect the health of military personnel before, during, and following deployments.

- The DoD has developed and implemented a Force Health Protection (FHP) strategy that promotes and sustains the health of service members prior to deployment, protects personnel from disease and injury during deployment, and provides comprehensive follow-up treatment for deployment-related health conditions.

- The DoD has instituted a deployment health surveillance program that includes pre-deployment and post-deployment health assessments which validate individuals' medical readiness to deploy and address health concerns upon their return, along with improved occupational and environmental health surveillance programs for protecting service members' health during deployment.

- The DoD has established three deployment health centers–for health surveillance, health care, and health research–that focus on the prevention, treatment, and understanding of deployment-related health concerns.

- The DoD has improved health risk communication through the provision of regionally-specific medical intelligence, environmental risk assessments, medical threat briefings, pocket-sized health guides, and deployment-focused web sites.

- The DoD has coordinated with the VA to address deployment-related health concerns of both service members and veterans by jointly developing a Post-Deployment Health Evaluation and Management Clinical Practice Guideline (CPG), and by electronically sharing medical information through the Federal Health Information Exchange.

- The DoD has taken steps to improve deployment-related medical record keeping by developing the Composite Health Care System II (CHCS II) and the Theater Medical Information Program (TMIP), and by expanding the electronic tracking and centralized collection of immunization data.

FACTS:

- During the Gulf War, an assessment of a service member's health prior to and at the conclusion of deployment was not systematically accomplished, making it difficult to identify changes in health status which could be attributable to events that occurred during deployment. The Institute of Medicine (IOM) subsequently recommended, and Congress directed, pre- and post-deployment medical examinations to better assess the health of deployed military personnel. A DoD Directive and a DoD Instruction on joint medical surveillance were published in August 1997 and included broad direction on accomplishing pre- and post-deployment health screening assessments.

- In October and December 1998, respectively, DoD (Health Affairs) and the Joint Staff (Medical Readiness) published policy memoranda on deployment health surveillance, providing more detailed implementation guidance and specific direction on the use of standardized forms for health assessments. The Joint Staff published its concept of Force Health Protection in 1999, defining three pillars: 1) a healthy and fit force; 2) casualty prevention; and 3) casualty care and management. DoD(HA) updated its deployment health surveillance policy in October 2001 to specifically address health assessments for deploying Reserve component personnel. In February 2002, the Joint Staff (J4-MRD) published updated policy that provided standardized procedures for assessing pre- and post-deployment health and reporting diseases and non-battle injuries (DNBI), while adding guidance for conducting and reporting occupational and environmental health risk assessments.

- Following the Gulf War, the VA and the DoD established health examination registries in order to evaluate veterans and service members for illness potentially related to their service in the war. In 1998 and 2000, the Institute of Medicine recommended that post-deployment health care be re-focused to the primary-care level in order to broaden and enhance the continuity of care, foster ongoing therapeutic relationships between providers and patients, and extend this health care to encompass problems from subsequent deployments. The DoD and the VA have designed, tested, and implemented a guideline for the provision of post-deployment health care. The guideline provides a structure for the evaluation and management of service members and veterans with deployment-related concerns. It also provides access to expert clinical support to physicians and other health care professionals for patients with difficult symptoms and illnesses, and may provide a useful platform for research into post-deployment health concerns.

- The Defense Medical Surveillance System (DMSS) has been established under the Army Center for Health Promotion and Preventive Medicine (CHPPM) to provide improved DoD joint health surveillance capabilities. Operated by the Army Medical Surveillance Activity (AMSA), the DMSS database contains historical and up-to-date data on diseases and medical events (e.g., hospitalizations, ambulatory visits, and reportable diseases) as well as longitudinal data on personnel and deployments.

- The DoD now routinely deploys preventive medicine, environmental surveillance, and forward laboratory teams in support of worldwide operations. For example, CHPPM conducts pre- and during-deployment environmental health intelligence preparation of the battlefield, and performs extensive environmental assessments of operationally-selected staging areas and base sites. CHPPM also supplies environmental sampling materials for deployed forces, conducts operational risk management estimates for field commanders, and develops pocket-sized "staying healthy" guide books for deployed service members.

- Improved deployment health protection measures are being designed to counter an increasingly broad range of threats. Such measures include the fielding of new biological and chemical warfare agent detection and alarm systems; the operational testing of integrated electronic medical surveillance and emergency response

networks; current vaccines and anti-malarial drugs; and research on the next generation vaccines and pharmaceuticals.

- In addition to pre- and post-deployment health assessments, the military medical departments incorporate routine health and medical readiness appraisals to ensure service members meet and maintain health standards. A complementary effort is underway to develop standardized DoD-wide individual medical readiness indicators.

- One important health surveillance initiative prompted by post-Gulf War health issues is the monitoring of birth defects among DoD beneficiaries through establishment of a birth defects registry. Another is the use of the DoD Serum Repository for routine and pre-deployment collection and storage of serum specimens, which are subsequently available for analysis regarding military- and deployment-related health concerns.

- The Millennium Cohort Study is a comprehensive DoD health research initiative that responds to concerns about whether deployment-related exposures are associated with post-deployment health outcomes. A cross-sectional sample of 100,000 military personnel and veterans will be studied prospectively over a 21-year period.

- Tracking of immunizations was directed by DOD Instruction 6490.3, Implementation and Application of Joint Medical Surveillance for Deployments (7 August 1997). Electronic tracking of immunizations was initially implemented for the Anthrax Vaccine Immunization Program in 1998, using Service-specific automated systems. Efforts are underway by the Services to electronically track all immunizations and to centralize collection of immunization data for surveillance and research purposes.

- The Services have begun implementation of health surveillance and computerized medical record keeping during deployments, allowing for surveillance of health events as well as documentation of health care and countermeasures utilized during deployment. The Theater Medical Information Program (TMIP), which is currently undergoing testing, will gather individual medical information throughout operational deployments. This information will help to document deployment-related health problems and be shared with the VA to facilitate continuity of care for veterans.

COL John Gardner
DHSD
(b)(6)
October 23, 2002

GULF WAR LESSONS LEARNED: PROBLEMS TO SOLUTIONS

KEY MESSAGE:

The Office of the Special Assistant for Gulf War Illnesses (now the Deployment Health Support Directorate) established a lessons learned directorate in December 1998 after determining that it needed an organization that could work within the established DoD system to institutionalize lessons learned, observations, and findings from the Gulf War and subsequent deployment experiences.

FACTS:

- The Presidential Advisory Committee's Final Report validated the importance of the role of the lessons learned organization.
- The August 1998 Science and Technology Council/Presidential Review Directive-5, entitled *A National Obligation: Planning for Health Preparedness for and Readjustment of the Military, Veterans, and their Families Future Deployments,* reflected a strong commitment to implementing health-related lessons learned.
- Today, the Deployment Health Support Directorate is actively involved with the Joint Staff and Joint Forces Command to improve the overall lessons learned system.
- The Deployment Health Support Directorate has worked with Army National Guard units deploying to Bosnia in support of Peacekeeping Operations in the Balkans to identify lessons learned during the deployment as well as the pre- and post-deployment phases.
- A recent initiative of the Deployment Health Support Directorate is to establish a Medical Lessons Learned/Medical Community of Practice database. This database will ensure that medical observations/findings from operational deployments and exercises are thoroughly analyzed by medical subject matter experts and that valuable medical lessons learned are shared throughout the medical community and across service lines.

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DHSD

(b)(6)

October 17, 2002

GULF WAR ILLNESSES LESSONS LEARNED WORKING GROUP

KEY MESSAGE:

The Gulf War Illnesses Lessons Learned Working Group uses the established force development process to institutionalize solutions to issues highlighted following the Gulf War dealing with medical and training readiness, as well as nuclear, biological, chemical (NBC), and environmental hazards.

FACTS:

- Although co-chaired by the Deployment Health Support Directorate, this is an Army working group. The Army is the executive agent for NBC force development. The Army also has taken the lead in the area of environmental monitoring and occupational health for the whole force rather than just selected occupations.

- The previous Special Assistant, while he was Under Secretary of the Army, and the TRADOC commander were the driving forces behind the establishment of the Gulf War Illnesses Lessons Learned Working Group. The US Army Medical Command was and continues to be an active participant.

- The working group is comprised of representatives from operations, training, and medical functional areas to ensure the development of a complete answer.

- Solutions developed by the working group languished for over 18 months awaiting emphasis at the TRADOC level. In June 2001, the DoD IG published the Audit Report: The Gulf War Nuclear, Biological, and Chemical Lessons Learned. In a March 8, 2002, memorandum the Office of the Special Assistant for Gulf War Illnesses identified the Army's publishing of a policy memorandum which subsumed the issues being worked in response to the subject Audit Report. Subsequently, on April 19, 2002, TRADOC submitted a concept and mission analysis Force Health Protection (FHP) and Occupational and Environmental Health (OEH) Threats Implementation Plan to the Army G3.

- The incorporation of the Army's FHP and OEH Implementation Plan by TRADOC will resolve all open Gulf War NBC Lessons Learned. The plan also ensures that all future lessons are fully incorporated into the Army's doctrine, training, organizational structure, leadership, development, and materiel. Deployment Health Support Directorate will continue to monitor the implementation effort in conjunction with the TRADOC working group and likewise will serve as the point of contact for the DoD IG on any direct requests for information concerning the implementation of FHP lessons learned.

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(b)(6)
October 17, 2002

IOM FINDINGS ON GULF WAR AND HEALTH: DEPLETED URANIUM, SARIN, PYRIDOSTIGMINE BROMIDE, AND VACCINES

KEY MESSAGE:

In 2000, the Institute of Medicine (IOM) published the first of several reviews of the scientific evidence concerning the association between agents to which Gulf War veterans may have been exposed and adverse health effects. No long-term health effects were linked to depleted uranium, sarin (chemical agent), pyridostigmine bromide (chemical agent pre-treatment), or vaccines. Expected short-term health effects were linked to acute exposures to sarin and pyridostigmine. Transient acute local and systemic effects, as typically associated with vaccination, were linked to anthrax vaccine and botulinum toxoid. The IOM recognized that the evidence for or against long-term health effects, especially from low-level exposures to these agents, is insufficient, and recommended additional research and long-term follow-up of exposed populations to address this scientific uncertainty.

FACTS:

- Following the Gulf War, there were concerns that certain exposures in the Gulf may have been responsible for or contributed to illness that some veterans experienced after the Gulf War.
- The VA contracted with the IOM to study the potential health effects of several agents to which veterans may have been exposed.
- Subsequently, the Congress directed the completion of these studies in two public laws: the Veterans Programs Enhancement Act of 1998 (Public Law 105-368) and the Persian Gulf War Veterans Act of 1998 (Public Law 105-277). These laws specify the study of many biological and chemical hazards that may be associated with the health of the veterans.
- The IOM was not asked to (and did not) determine: whether a unique Gulf War syndrome exists, the level of exposures to these agents, or the potential costs of compensation.
- The IOM is now completing a study of a group of pesticides and solvents and anticipates studies of additional agents. Each report provides an assessment of the health effects that may be associated with exposures to specific agents present in the Gulf.

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October 16, 2002

DEPLOYMENT FORCE HEALTH PROTECTION

KEY MESSAGE:

Protecting the health of deployed military personnel is a paramount concern of the Department of Defense and the Office of the Assistant Secretary of Defense for Health Affairs. We are committed to ensuring that we deploy healthy military personnel, that we monitor and preserve their health while they are deployed, and that we assess their health and address their health concerns when they return.

FACTS:

- The health of service members is monitored and ensured through high medical standards at the time of accession, periodic medical and dental examinations, routine and special-purpose immunizations, and ready access to high quality health care.

- Pre-deployment health preparedness includes health risk assessments based on region-specific medical intelligence reports; individual health assessments covering specific conditions and concerns, medical protective equipment, immunizations and medications; and the establishment/updating of a deployment medical record.

- Health protection during a deployment encompasses comprehensive surveillance, risk assessments, and prevention of health hazards; weekly reporting of diseases and non-battle injuries (DNBI) and important medical events; and rapid access to medical resources both in-theater and through the aeromedical evacuation system.

- Post-deployment health protection measures include individual health assessments to promptly identify and address health conditions and concerns; medical debriefings on significant health events and exposures; placement of all deployment-related medical documents into the service member's permanent health record; and documentation and dissemination of force health protection lessons learned. The post deployment clinical practice guideline is the most recent addition to assure prompt evaluation for health concerns.

- Force health protection is also ensured through establishment of three Deployment Health Centers (Clinical, Surveillance, and Research), and the recent development of a joint DoD-VA Clinical Practice Guideline on Post-Deployment Health.

- To further demonstrate the Defense Department's continuing commitment to force health protection, we have also recently established the Deployment Health Support Directorate. This office will focus on specific measures to improve the health of deployed forces; maintain open lines of communication between DoD and service members, veterans, and their families; and serve as a bridge from the experiences of the past to the battlefields of the future.

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DHSD

(b)(6)

May 21, 2002

DOD CENTERS FOR DEPLOYMENT HEALTH

KEY MESSAGE:

Following Congressional direction, the ASD for Health Affairs directed the establishment in September 1999 of three DoD Centers for Deployment Health:

- Deployment Health **Research** Center at the Naval Health Research Center in San Diego CA
- Deployment Health **Clinical** Center at Walter Reed Army Medical Center in Washington DC
- Deployment Health **Surveillance** Center at the Army Medical Surveillance Activity on the campus of Walter Reed Army Medical Center in Washington DC

FACTS:

- The National Defense Authorization Act for Fiscal Year 1999 authorized the Secretary of Defense to "...establish a center devoted to a longitudinal study to evaluate data on the health conditions of members of the Armed Forces upon their return from deployment on military operations for the purposes of ensuring the rapid identification of any trends in diseases, illnesses, or injuries..."
- ASD Health Affairs Policy, Sep 30, 1999, www.ha.osd.mil/policies/1999/clin9928.htm
- The goal of the three DoD centers is "...to improve our ability to identify, treat, and minimize or eliminate the short- and long-term adverse effects of military service on the physical and mental health of veterans."
- The Deployment Health Research Center has been directly engaged with the VA in the IOM-recommended Millennium Cohort Study to evaluate whether deployment-related exposures are associated with post-deployment health outcomes. It also manages the national DoD Birth Defects Registry.
- The Deployment Health Clinical Center has been a leading proponent for the development of post-deployment health evaluation and management clinical practice guidelines, which have recently been implemented throughout the DoD and VA health systems.
- The Deployment Health Surveillance Center is the DoD proponent for the identification of and response to medical threats associated with deployments and, most recently, acts of terrorism.

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DHSD
(b)(6)
February 22, 2002

HEALTH EVALUATION AND ASSESSMENT REVIEW (HEAR) QUESTIONNAIRE

KEY MESSAGE:

The Health Evaluation and Assessment Review (HEAR) questionnaire is a preventive screening tool. It represents the current best practice in health assessment. Its results give DoD healthcare providers a snapshot of the patient's health, habits, and other factors that may affect overall wellness and enable providers to assess preventive service needs for each patient.

FACTS:

- The HEAR was fielded in the Preventive Health Care Application (PHCA), a computerized health maintenance system which serves as the interim solution for DoD healthcare providers to deliver and track clinical preventative services.
- PHCA functionality has been integrated into the Composite Health Care System II (CHCS II) Release 1. CHCS II is a medical and dental clinical information system that will generate and maintain a comprehensive, life-long, computer-based patient record for each Military Health System beneficiary.
- Worldwide fielding of CHCS II Release 1 will begin in the 1st quarter of FY 03.
- The paper HEAR questionnaire was originally developed by the Air Force in 1994.
- It was adopted in 1996 across the entire DoD for health assessment of active duty personnel and eligible beneficiaries.
- The PKC Corporation automated the HEAR in 1997.

(b)(6)
OSD (HA), Clinical Information Technology Program Office
(b)(6)
August 16, 2002

PRE- AND POST-DEPLOYMENT HEALTH ASSESSMENTS

KEY MESSAGE:

The DoD continues to develop a program to assess the health of servicemembers before and after they deploy to determine deployability of these individuals, allow for health interventions they may require, and track changes in their health status that may result from exposures and experiences during deployment. This program is to be part of a larger plan for standardized, longitudinal, and comprehensive health surveillance of military personnel. Fully implemented, this program is intended to be of benefit for both individual and population health.

FACTS:

- Following the Gulf War, it was apparent that the health status of deploying and redeploying service members had not always been determined or documented. This may have contributed to the difficulty in determining health status changes attributable to deployment.

- Beginning with the Bosnia deployment (1996) and formalized the following years by a directive, an instruction, and a policy statement (DoDD 6490.2 (1997), DoDI 6490.3 (1997) and DoD-HA (1998)), the DoD implemented the use of standardized forms to be administered to service members as they deploy and when they return.

- Completed health assessment forms are to be placed in the individual service members' health records with copies forwarded to the Army Medical Surveillance Activity for data entry and subsequent analysis.

- There is uncertainty as to whether forms administered immediately before and after deployments will be able to capture information suitable for all intended purposes.

(b)(6)
DHSD
(b)(6)
March 26, 2002

POST-DEPLOYMENT HEALTH CLINICAL PRACTICE GUIDELINE

KEY MESSAGE:

The DoD and the VA are implementing a clinical practice guideline for the provision of post-deployment health care in the primary care setting. This guideline applies the knowledge gained from the existing Gulf War registry programs. It requires health care providers to ask if the patient believes their medical problems might be related to a deployment, and includes strategies for health care providers to embrace these concerns.

FACTS:

- Following the Gulf War, the VA in 1992 and the DoD in 1994 established health examination registries (the Persian Gulf Registry and the Comprehensive Clinical Evaluation Program, respectively) to evaluate veterans and military personnel for illnesses possibly related to their service in the Gulf War.

- Reviews of the VA and DoD registry programs by the Institute of Medicine in 1998 and 2000 recommended that post-deployment health care be re-focused to the primary care level. This would broaden and enhance the continuity of care, foster ongoing therapeutic relationships between providers and patients, and extend this health care to encompass problems from subsequent deployments.

- The VA and the DoD developed the guidelines with the help of experienced multi-disciplinary groups and independent organizations (including RAND and the Institute of Medicine). Especially for the unexplained illnesses, the guidelines are consensus-based rather than evidence-based, since the latter is not always possible for incompletely understood illnesses.

- Additional post-deployment health guidelines in the areas of chronic fatigue, fibromyalgia, unexplained symptoms, and post-traumatic stress have been stimulated by work on this guideline and are either already in development or planned.

- The Deployment Health Clinical Center (at Walter Reed Army Medical Center) is the DoD proponent and source of consultative support for this guideline.

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DHSD

(b)(6)

May 21, 2002

RECRUIT ASSESSMENT PROGRAM

KEY MESSAGE:

- The Recruit Assessment Program (RAP) is a proposed Department of Defense (DoD) program for the routine collection of baseline demographic, medical, psychosocial, occupational, and health risk factor data from all U.S. military personnel at entry into the armed forces.

- The RAP currently utilizes an optically scannable paper questionnaire to provide data for the first building block of an electronic medical record within DoD and the Department of Veterans Affairs (VA).

- The RAP can serve several important functions, including: automating enrollment into the military health care system, improving patient care and preventive medicine efforts, and providing critical data for investigations of health problems among military personnel and veterans.

- Pilot testing at selected DoD recruit centers is nearing completion. Current results were presented to the Armed Forces Epidemiological Board (AFEB) on February 20, 2002. Based on AFEB recommendation, implementation throughout DoD can progress. With incorporation into CHCSII, the RAP could provide a substantial improvement in health care delivery. For the first time, DoD and VA physicians, public health officers, and researchers will have access to comprehensive, baseline health status data.

FACTS:

- Over the last ten years, several scientific review panels have recommended that the Department of Defense (DoD) maintain more complete and accessible medical records and collect greater health surveillance data. One specific recommendation has been for DoD to document health status before hazardous deployments. A recruit assessment program has been repeatedly singled out as a critically important component of overall military health surveillance.

- The collection of comprehensive health data at the start of military service would obviate many of the problems associated with health appraisals initiated just before a hazardous deployment. Baseline health information could provide many important benefits, particularly if integrated with health data periodically collected as part of a longitudinal health record. Because of the potential usefulness of baseline health data, the feasibility of establishing a program to collect this information is being evaluated within DoD.

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OASD(HA)/C&PP
(b)(6)
February 22, 2002

DoD BIOWARFARE IMMUNIZATIONS PROGRAM

KEY MESSAGE:

The Department of Defense established policies, assigned responsibilities, and prescribed procedures for military service members against validated biological warfare threats. It is incumbent upon commanders to identify populations at risk during deployments, determine potential health hazards and risks, and take appropriate protective measures for the protection of the force.

FACTS:

- DoD directive 6490.2 and Instruction 6490.3 require the military services and commanders to identify the populations at risk during deployments, determine potentially hazardous risks to health and take appropriate countermeasures.

- Efforts in research, development, testing, acquisition, and stockpiling of biological defense vaccines are covered in DODI 6205.3, November 1993. It provides vaccination guidance that focuses exclusively on defense against biological warfare threats and complements immunization requirements for naturally occurring endemic disease threats as outlined in DODI 6205.2, October 9, 1986.

- Army Regulation 40-562, BUMED 6230.15, Air Force Joint Instruction 48-110, and Coast Guard COMDTINST M6230.4E Immunizations and Chemoprophylaxis," November 1, 1995, provides further service specific information and guidance regarding peacetime and contingency requirements for immunization against biological warfare threats against U.S. personnel.

- The Secretary of the Army is the DoD Executive Agent for the DoD immunization program for Biological Warfare Defense.

- Research and development efforts in defending against current and emerging biological warfare threats are ongoing. Vaccines must be either licensed by the FDA or have been designated as an "Investigational New Drug."

- DepSecDef memo, dated June 28, 2002, provides for the reintroduction of the Anthrax Vaccination Immunization Program (AVIP). The USD for Personnel and Readiness memo, dated August 6, 2002, provides administrative and clinical execution guidance for this restart. ASD for Health Affairs memo, dated August 6, 2002, establishes policy on medical issues involving the anthrax vaccination.

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August 23, 2002

IMMUNIZATION DOCUMENTATION

KEY MESSAGE:

The documentation of immunizations is essential for the determination of individual and force protection and readiness, as well as for the health care of service members and veterans. While paper-based systems have been used traditionally, efforts have been made to fully automate this documentation. This would be especially advantageous for immunizations given during deployment.

FACTS:

- DoD policies require the documentation of all immunizations given to service members.[1,2] For deployments, the JCS requires immunizations to be recorded on the abbreviated medical record (DD Form 2766), supplemented as necessary by the pocket immunization record (PHS 731) and service-specific forms.[3]
- The individual services have fielded electronic immunization tracking systems:
  - The Army uses its Medical Protection System (MEDPROS) to electronically record immunizations of its service members.
  - The Navy uses its Shipboard Automated Medical System (SAMS) to electronically record immunizations of its service members, then forwards this information through the Naval Medical Information Management Center (NMIMC) to the Defense Eligibility Enrollment Reporting System (DEERS).
  - The Air Force uses its Complete Immunizations Tracking Application (AF-CITA) to record immunizations given at both medical facilities and field locations, and indicates good success with all component members.
- There are initiatives to combine or link the data from these systems for both personal and population health purposes through DEERS, the Composite Health Care System (CHCS II) and the Theater Medical Information Program (TMIP).
- We have no detailed information on the success of these documentation efforts.

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August 23, 2002

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[1] Air Force Joint Instruction 48-110, Army Regulation 40-562, Navy Bureau of Medicine and Surgery Instruction 6230.15, and Coast Guard Commandant Instruction M6230.4E, Immunizations and Chemoprophylaxis, November 1, 1995.

[2] Department of Defense Memorandum, Implementation of the Anthrax Immunization Program for the Total Force, May 18, 1998.

[3] Joint Staff Memorandum MCM-0006-02, Updated Procedures for Deployment Health Surveillance and Readiness, February 1, 2002.

VACCINE ADVERSE EVENT REPORTING SYSTEM (VAERS)

KEY MESSAGE:

- The Department of Health and Human Services established the Vaccine Adverse Event Reporting System (VAERS) in November 1990. VAERS provides a database management system for the collection and analysis of data from reports of adverse events following vaccination. VAERS is co-managed by the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA).
- DoD Medical Treatment Facilities have procedures guiding use of VAERS to report vaccine related adverse events in accordance with the Reportable Events Table (http://www.fda.gov/cber/vaers/eventtab.htm).
- Anthrax Vaccine is not included in the Reportable Events Table. However, an ASD (HA) Policy Memorandum dated OCT 15, 1999 provided guidance to the services concerning the reporting of Anthrax Vaccine related adverse events.

FACTS:

- A VAERS report form, pre-addressed to VAERS and postage-paid, is used to report pertinent information, including a narrative description of the adverse event. Forms may be obtained at http://www.fda.gov/cber/vaers/report.htm or in the Physician's Desk Reference (PDR).
- Any one can report to VAERS. VAERS reports are usually submitted by health care providers, vaccine manufacturers, and vaccine recipients (or their parents/guardians). Each report provides information that is compiled to assess vaccine safety. Complete and accurate reporting of post-vaccination events supplies public health professionals with the information they need to ensure the safest strategies of vaccine administration.
- Both the CDC and the FDA review data reported to VAERS. The CDC focuses on collective reports to detect unusual epidemiologic trends and associations. The FDA reviews individual reports to assess whether a reported event is adequately reflected in product labeling and closely monitors reporting trends for individual vaccine manufacturers and vaccine lots.
- Not all events reported to VAERS are caused by vaccinations. VAERS accepts all reports of adverse events that follow vaccination, regardless of the cause of the event. Determination of vaccine-event causal associations using VAERS data is limited by differential reporting rates, simultaneous administration of different vaccines, temporal reporting bias, and lack of background vaccination rate data. Without fully understanding these limitations, VAERS data can easily be misinterpreted.

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C&PP
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February 22, 2002

ANTHRAX VACCINE

KEY MESSAGE:

CDC sponsors the Anthrax Vaccine Research Program (AVRP) to discover whether the vaccine route can be changed and the number of doses can be reduced, while still providing protection against anthrax disease. The studies are also expected to provide more information on when a person becomes protected and the length of protection.

CDC's AVA Route-Change and Dose-Reduction Study - Evaluating intramuscular route rather than subcutaneous and evaluating protections with fewer than six shots.

Next Generation Anthrax Vaccine (NGAV)

FACTS:

Anthrax Vaccine Research Program (AVRP)

- IOM just released a report, which assesses all of CDC's research projects. This report concluded that Human Clinical Trials were the most important- top of the priority list.
- The current anthrax vaccine is injected just under the skin in a series of 6 doses over 18 months, followed by a booster dose given each year.
- Route-Change/Dose-Reduction Study is off to a good start. Human clinical trial began in May 2002 with a planned enrollment of 1560 subjects conducted over 5 study sites. The study already has 535 people enrolled- nearly 1/3 of the total. Two of the five sites have already reached 50% enrollment.
- Next Generation Anthrax Vaccine; Latest Meeting on NGAV was Tuesday Oct 22, 2002 at the CDC in Atlanta, CDR de Lara attended.
- Research for these studies is being carried out in 6 different sites around the country. Contracts were awarded totaling $22.5 million to California-based VaxGen Inc. and Britain's Avecia to test the experimental vaccine on people to see if it is safe and if protects against the deadly bacteria. Federal authorities hope that together, the two companies will pave the way toward Food and Drug Administration approval for the vaccine. Eventually, the government wants 25 million doses manufactured and added to the National Pharmaceutical Stockpile.

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Deployment Health Support Directorate
(b)(6)
October 22, 2002

DOCUMENTATION OF INDIVIDUAL ASSIGNMENT AND UNIT LOCATION DATA

KEY MESSAGE:

Knowing "who was where when" during deployments is crucial to identifying possible exposures to hazardous materials and agents. For a variety of reasons, documenting individual deployment locations is neither easy nor straightforward. It requires capturing and melding data for radically different unclassified personnel and classified operations data systems. The requirement does not align well with traditional military data needs and architectures. We continue working to refine how we track individuals and how we link location data to environmental and health information.

FACTS:

- Military personnel data systems generally do not attempt to maintain records of servicemembers' precise locations in a deployment theater. Personnel data does include units of assignment but may not reflect the unit servicemembers operated with while deployed, particularly for individual augmentees and those on temporary duty.
- Operations command and control systems typically track unit locations in near real time, but detailed data are not always automated or preserved after an operation is over.
- Reconstructing "who was where when" after the fact generally requires association of servicemembers with deployment duty units based on Service personnel data melded with available unit locations from operational reporting.
- Operations data is often sensitive and classified. None of the Service personnel data systems can handle classified information.
- We are working hard to craft improved solutions, but workable, affordable, short-term fixes have not emerged. The Defense Military Human Resources System may eventually help, but full implementation of DIMHRS is several years away.

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October 23, 2002

GLOBAL STATUS OF RESOURCES AND TRAINING SYSTEM (GSORTS)

KEY MESSAGE:

The Global Status of Resources and Training System (GSORTS) is the single Department of Defense automated readiness reporting system and the central registry of all U.S. Armed Forces operational units. As a unit readiness system, GSORTS indicates the level of selected resources and training required to undertake a mission for which a unit was organized or designed. Specifically, GSORTS provides users the ability to track location, unit readiness, activity, equipment status, and personnel status to begin identifying possible shortfalls, candidate units, and other information. GSORTS is being replaced by an enhanced version (ESORTS)

FACTS:

- GSORTS is an internal management tool used by the Chairman, Joint Chiefs of Staff, the Joint Staff, the Services, the unified commands, and the combat support agencies.
- Chairman of the Joint Chiefs Manual (CJCSM) 3150.02, 15 April 2000, describes how the commander of any reporting unit will report the unit's status in the areas of personnel, equipment on hand, equipment serviceability, and training.
- Reporting units use three methods to submit data to the Joint Staff: (1) reporting through a Service feeder system, (2) direct reporting to the database via US Message Test Format GSORTS reports, or (3) unit data entry directly to the database using a web-based input tool.
- The commander of a reporting unit determines when changes to a unit's GSORTS data are required.
- Joint Operation and Planning and Execution System (JOPES) users apply GSORTS in support of deployment planning and execution in both the deliberate and crisis response phases of joint operations. The JOPES users can access GSORTS data elements through an interface at all JOPES sites.
- The Defense Manpower Data Center maintains the official historical GSORTS data and makes it available to all GSORTS users.
- The GSORTS will be replaced by the Enhanced Status of Resources and Training System (ESORTS), which will extend coverage beyond the Services to Defense agencies and field activities. The ESORTS responds to newly published policy with full implementation awaiting development of detailed instructions.

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October 23, 2002

JOINT PERSONNEL STATUS REPORT (JPERSTAT)

KEY MESSAGE:

The Joint Personnel Status Report (JPERSTAT) provides tabulated total troop strength data to the Chairman and the other members of the Joint Chiefs of Staff for use in monitoring and evaluating the status of personnel under the operational control of a combatant commander. The JPERSTAT also provides the most current information from the field concerning casualties. The analysis of this report is used to provide information to the National Command Authority (NCA) and to address issues concerning the supported combatant commander's personnel strength, need for replacement personnel, and other personnel concerns.

FACTS:

- The supported combatant commander submits JPERSTATs to the Joint Staff's Manpower and Personnel Directorate (J-1), Personnel Readiness Division.
- When directed by the Chairman of the Joint Chiefs of Staff or the NCA, the JPERSTAT will be submitted daily to cover a 24-hour period. The Joint Staff will determine specific "report due" and "as of" times for the JPERSTAT.
- The JPERSTAT will reflect changes to personnel strength and casualties only during the period of the report. Cumulative data will not be reported.
- The JPERSTATs is classified consistent with the classification of the operation as directed by the Chairman of the Joint Chiefs of Staff.
- Primary transmission method is the Global Command and Control System (GCCS). Alternative methods are E-mail, secure facsimile, or telephone. Reports may be transmitted via the Defense Messaging System or GCCS as part of a commander's situation report (SITREP), using the SITREP message format.

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October 25, 2002

JOINT TOTAL ASSET VISIBILITY

KEY MESSAGE:

Joint Total Asset Visibility (JTAV) is the capability to provide users with timely and accurate information on the location, movement, status, and identity of units, personnel, equipment, and supplies. Information technology of JTAV fulfills a long-recognized need to leverage tracking data to increase combat capability through flexibility and agility in managing logistics and personnel. It helps the Department reduce costs and increase readiness. JTAV is a process not a product and is part of the concept called focused logistics. It is well along a path of incremental development and has proven itself in logistics visibility for US deployments in the Balkans. The personnel visibility will eventually be provided by the Defense Integrated Military Human Resources System (DIMHRS) now under development.

FACTS:

- In the past, DoD has resorted to "brute force" logistics to support warfighters. Of the 40,000 containers sent for the Gulf War, half had to be opened in theater, checked, resealed, and reinserted into the logistics system because of unknown contents or final consignees.
- The DoD has already benefited from the development and implementation of a JTAV capability. During military operations in Kosovo, most of the asset visibility short comings of Desert Storm had been overcome, and war fighters and logisticians supporting military operations were able to track materiel inside the logistics pipeline.
- JTAV data includes units, their personnel, and equipment; non-unit personnel, equipment, and supplies; and supplies and equipment in storage, transit, maintenance, or procurement.
- JTAV is accessed from the Global Combat Support System (GCSS), which it supports.
- With the termination of the Joint Personnel Asset Visibility program, which was to be a part of JTAV, DIMHRS eventually will be relied on for personnel data. In the meantime, the Personnel Tempo system (PERSTEMPO) and the Joint Personnel Status system (JPERSTAT) are among the possible interim data sources.

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October 23, 2002

PERSONNEL TEMPO (PERSTEMPO)

KEY MESSAGE:

The National Defense Authorizations Act (NDAA) for FY 2000 defined deployment and assigned the Service secretaries the responsibility for tracking and recording the number of days a service member is deployed. Further, it requires payment of high deployment per diem ($100 per day) for each day a member is deployed for 401 or more days out of the preceding 730. In addition to the dictates of NDAA 2000, OSD requires commanders to report and track activities other than those that count towards high-deployment per diem, but keep people away from their homes for 24 hours or more (e.g., individual training, hospitalization, confinement, etc.). These events, in combination with those defined by NDAA 2000, are collectively referred to as "PERSTEMPO Events."

FACTS:

- All services began tracking PERSTEMPO events on October 1, 2000.
- The Act considers a service members deployed, any day the member is performing service in a training exercise or operation at a location or under circumstances that make it impossible or infeasible for the member to spend off-duty time in the housing in which they reside.
- High operating tempo can affect unit morale, quality of life, retention, and individual readiness. For those reasons, Congress directed the senior leadership of the services to be directly involved in the management of deployments. Exceeding 182 or 220 deployment days in a year requires a general/flag officer authorization.
- The Act directs the USD (P&R) to establish—to the extent practicable—uniform standards within the Department for terminology and policies relating to deployment of units and personnel away from their assigned duty stations. The Services are required to maintain information regarding individual servicemember's event status (e.g., beginning and ending deployment dates, deployment type, operation supported, duty unit, and country location). However, due to security concerns, some of the Services are not providing specific duty location information, thus limiting the data's use for determining "who was where when."
- Due to the war on terrorism and in accordance with provisions of the initiating legislation, on October 7, 2001, the President suspended the Act's provisions mandating per diem payments. However, the Services must continue to track and report individual servicemember's PERSTEMPO events.

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October 25, 2002

DEPARTMENT OF DEFENSE READINESS REPORTING SYSTEM (DRRS)

KEY MESSAGE:

The Department of Defense Readiness Reporting Systems (DRRS) measures and reports on the readiness of military forces and the supporting infrastructure to meet missions and goals assigned by the Secretary of Defense. The DRRS will build upon the processes and readiness assessment tools used in the DoD to establish a capabilities-based, adaptive, near real-time readiness reporting system. DoD components will use the DRRS to identify critical readiness deficiencies, develop strategies for rectifying these deficiencies, and ensure they are addressed in program/budget planning and other DoD management systems. The principal focus of DRRS is to unify DoD readiness reporting under a responsive construct designed around mission essential tasks.

FACTS:

- DoD 7730.65, Department of Defense Readiness Reporting System (DRRS), June 3, 2002, established the DRRS and directs all DoD components to align their readiness reporting processes in accordance with this directive.

- The DRRS is supported by two DoD readiness management processes:
  - Senior Readiness Oversight Council (SROC) who advises the SECDEF on all matters pertaining to DoD readiness, oversees readiness-related activities provides recommendations to the SECDEF on readiness policy matters, and provides reports on current and projected readiness issues.
  - Joint Quarterly Readiness Review (JQRR) who conducts timely, scenario-based readiness assessments on a quarterly basis. The findings of the JQRR will be reported to the SROC.

- DRRS directs the development of the Enhanced Status of Resources and Training System (ESORTS). ESORTS builds upon the Global Status of Resources and Training System (GSORTS) which will provide insights into current unit and organizational readiness status and resource standards. ESORTS will highlight deficiencies in the areas of training, personnel, equipment, ordnance, and sustainment.

- DRRS establishes the requirement for a common readiness and training language throughout DoD using the Universal Joint Tasks List (UJTL).

- Mission essential tasks serve as baseline reporting and analysis construct across DoD.

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October 28, 2002

COMPOSITE HEALTH CARE SYSTEM II (CHCS II)

KEY MESSAGE:

- CHCS II is the military Computer-based Patient Record. It is an electronic clinical information system that will generate, maintain, and provide secure online access to a comprehensive and legible health record. It is the backbone of the entire suite of DoD clinical systems
- Strongly promotes military medical readiness by supporting uniform, high-quality health promotion and health care services to Military Health Service beneficiaries worldwide. It is a key enabler for Force Health Protection and Population Health Improvement, two cornerstones of military medicine. It also makes deployed Service members' health care information available for analysis and action.

FACTS:

- In September 2000, the DoD Joint Requirements Oversight Council, a review body with permanent membership comprised of all four Service Vice Chiefs and chaired by the Vice Chairman of the Joint Chiefs of Staff, approved the Operational Requirements Document for the CHCS II.
- CHCS II will be used in all DoD fixed facilities, on-board ships, and in deployed medical facilities.
- Successful integration between multiple commercial off-the-shelf applications combined with a clinician friendly interface and automated business functions has resulted in unparalleled success.
- Day-to-day use of CHCS II at home, in-garrison, is a force multiplier. It provides real-time medical readiness training on the same applications and platforms used in the field environment
- CHCS II clinical applications, in appropriately scaled-down battlefield versions, populate the Theater Medical Information Program (TMIP)
- Undergoing testing by users at Naval Medical Center Portsmouth; 1ST Medical Group, Langley Air Force Base, VA; 4th Medical Group, Seymour-Johnson Air Force Base Clinic, NC; and McDonald Army Community Hospital, Ft. Eustis, VA.
- Worldwide fielding of CHCS II will begin in the 4th quarter of FY 02, after completion of a comprehensive operational test and evaluation process.
- Functional capabilities of CHCS II include:
  - Allows users to view patient demographics, work status information, and appointment status
  - Allows documentation of the exam through the use of point and click templates, and cut and paste functions
  - Speeds order entry: laboratory, radiology, pathology tests, medications, education and consults
  - Retrieves results: laboratory, pathology, and radiology; displays abnormal results in a visually distinct manner
  - Alerts users when priority results require action

- Identifies potential drug allergies and other problems
- Tracks and stores allergy information
- Tracks consultations
- Displays medical problem lists including description, status, onset, and source.
- Allows users to view, add, and modify patient immunization data
- Automates tracking and viewing of patient wellness reminders and schedules for health screening, prevention, and safety counseling
- Captures self-reported data on satisfaction, pre and post deployment information, Health Evaluation Assessment Report, Occupational Health and others
- Provides users with need-to-know access to patient record; audit trails identify and record actions by user

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OSD (HA), Clinical Information Technology Program Office

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February 20, 2002

GOVERNMENT COMPUTER-BASED PATIENT RECORD (GCPR)

KEY MESSAGE:

- The GCPR is a collaborative effort of the Department of Defense (DoD), the Department of Veterans Affairs (VA), and the Indian Health Service (IHS) that will markedly enhance the continuity of care to our nation's veterans.

- DoD and VA have collaborated extensively to deliver a near-term solution (NTS) that will enable DoD to transmit the following protected health and demographic information on service members upon separation and on those previously separated, should electronic information exist, to VA via GCPR data repository:

  - patient name
  - category
  - social security number
  - date of birth
  - outpatient pharmacy data
  - sex
  - race
  - address
  - marital status
  - radiology results
  - religion
  - primary language
  - laboratory results

- DoD is transmitting health information on approximately 3.7 million separated service members to the VA.

FACTS:

- GCPR will be compliant with HIPAA and the Privacy Act of 1974.
- User testing of GCPR is underway, demonstrating DoD's ability to collect and transfer protected electronic health information to the GCPR data repository and VA's ability to access the information. Alpha testing at the VA Medical Center Dan Diego, CA is complete. Beta testing began in January 2002 and is scheduled to be completed in the second quarter of Fiscal Year (FY) 2002.
- Following the successful completion of the Beta testing and evaluation, enterprise-wide use of the NTS within VA is anticipated in the third quarter of FY 2002.
- Periodic CHCS extractions will occur based on separate input from the Defense Manpower Data Center.
- DoD has followed congressional direction regarding project funding; DoD spent $6M on GCPR in FY01 and has programmed approximately $6M annually for FY02-07.
- DoD and VA have conducted joint acquisitions, are sharing contract vehicles and coordinating GCPR funding, and have developed a process to efficiently transfer funds between agencies.
- Each agency has assigned GCPR project leadership to a seasoned, experienced, professional program manager.
- Northup-Grumman Corporation (NGC) and Science Application International Corporation (SAIC) are strong members of the GCPR partnership. GCPR Program In Process Review with DOD, VA, NGC, and SAIC is conducted monthly.
- Status of the GCPR is reported to the ASD (HA) and the Under Secretary for Health, Department of Veterans Affairs at the VA/DoD Executive Council meetings.

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OSD(HA), Executive Information/Decision Support Program Office

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February 19, 2002

STATUS OF DEFENSE INTEGRATED HUMAN RESOURCES SYSTEM (DIMHRS)

KEY MESSAGE:

- DIMHRS will revolutionize personnel and pay management and be based on complete business process reengineering. All Services and components have participated in the effort.
- DIMHRS is a single, fully integrated, all Service, all component military personnel and pay system that supports the entire life cycle of military personnel, from initial entry through separation and retirement and beyond, (supporting other agencies in obtaining military personnel information needed to provide benefits) and through mobilization and demobilization, deployment and redeployment.
- DIMHRS grew out of Defense Science Board Task Force recommendations that were adopted by the Department in 1996.
- DIMHRS, which will be the largest personnel system in the world, will use the PeopleSoft COTS Human Resources product and will implement standard business rules and data with an initial operating capability expected in 2004.
- DIMHRS will consolidate the operations of (and eliminate) 80 Service specific, stovepipe systems.
- The Department of the Navy is the Acquisition Agent for DIMHRS and the Joint Program Management Office has been established at the Information Technology Center in New Orleans.

FACTS:

- The DIMHRS project is currently expecting a Milestone B decision in July 2002, at which point full development can begin.
- The recently re-baselined and accelerated its acquisition strategy and is fully funded for the new strategy.
- A Request for Proposal (RFP) is scheduled for release in early February for a contractor to support Development and Implementation. Three vendors will be selected initially to work with the project through July and a single vendor will be selected in August.
- The program is currently focused on a Comprehensive Analysis to identify any gaps in the capabilities of the COTS product relative to the DoD mission requirements.

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Joint Requirements & Integration, OUSD(P&R)PI
(b)(6)
January 11, 2002

Combat Stress Control Programs Policy

DEPLOYMENT HEALTH SURVEILLANCE AND READINESS POLICY

KEY MESSAGE:

Establishes uniform and standardized health surveillance and readiness procedures for all deployments

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.

- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.

- Joint Staff Memorandum MCM-251-98, Dec 4, 1998

- http://amsa.army.mil/documents/JCS_PDFs/joint-staff-letter.pdf

- If these procedures are not codified in plans or deployment orders, they do not occur. To date, inclusion is spotty.

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February 20, 2002

DOD CENTERS FOR DEPLOYMENT HEALTH POLICY

KEY MESSAGE:

Created a research center at the Naval Health Research Center, San Diego, converted a clinical center at Walter Reed Army Medical Center, and provided for continuing medical surveillance through the Defense Medical Surveillance System. Improved our ability to identify, treat, and minimize or eliminate the short- and long-term adverse effects of military service on the physical and mental health of veterans. Centers provide an annual report to the ASD(HA) on status and progress, limitations, and accomplishments.

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.

- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.

- ASD Health Affairs Policy, Sep 30, 1999

www.ha.osd.mil/policies/1999/clin9928.htm

- Although there may be some analysis of the questionnaires, it is not comprehensive, nor have the DoD or the services asked for it. In general, the questionnaires are merely archived.

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February 20, 2002

DOD SAFETY AND OCCUPATIONAL HEALTH PROGRAM POLICY

KEY MESSAGE:

Updated DoD policies and procedures on risk management, aviation safety, ground safety, traffic safety, occupational safety and occupational health. Excludes explosive safety and fire prevention, which are covered elsewhere.

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.

- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.

- DoD Instruction 6055.1, Aug 19, 1998

- www.dtic.mil/whs/directives/corres/html/60551.htm

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January 16, 2003

IMPLEMENTATION AND APPLICATION OF JOINT MEDICAL SURVEILLANCE FOR DEPLOYMENTS POLICY

KEY MESSAGE:

Implements policy, procedures, and assigns responsibilities for joint military medical surveillance in support of all applicable military objectives. Describes routine military medical surveillance activities during major deployment, or deployments in which there is a significant risk of health problems, as identified by the Chairman of the Joint Chiefs of Staff in coordination with the Assistant Secretary of Defense for Health Affairs.

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.

- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.

- DoD Instruction 6490.3, Aug 7, 1997

- www.dtic.mil/whs/directives/corres/html/64903.htm

The program only addresses deployments OCONUS or 30 days or more to areas without established health facilities. This misses most short term and special operating forces deployments. In addition, medical surveillance questionnaire completion is not always enforced, and once completed, they are not comprehensively analyzed for trends.

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February 20, 2002

IMPLEMENTATION OF POST-DEPLOYMENT HEALTH CLINICAL PRACTICE GUIDELINE POLICY

KEY MESSAGE:

Provides a structure for primary care providers to evaluate and manage patients with deployment related health concerns including family members of recently deployed personnel.

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.

- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.

- ASD Health Affairs Policy, Dec 7, 2000

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February 20, 2002

JOINT MEDICAL SURVEILLANCE POLICY

KEY MESSAGE:

Establishes policy and assigns responsibility for routine joint medical surveillance of all Military Service members during active Federal service, especially military deployments. Designates the Secretary of the Army as the DoD Executive Agent for the Department of Defense and for the maintenance of the Armed Forces Serum Repository

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.

- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.

- DoD Directive 6490.2, Aug 30, 1997

- www.dtic.mil/whs/directives/corres/html/64902.htm

- The program only addresses deployments OCONUS or 30 days or more to areas without established health facilities. This misses most short term and special operating forces deployments. In addition, medical surveillance questionnaire completion is not always enforced, and once completed, they are not comprehensively analyzed for trends.

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MAJOR DOD FORCE HEALTH PROTECTION POLICIES

KEY MESSAGE:

Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible. FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; and rapidly stabilize, treat, and evacuate casualties. Finally, upon return from deployment, effectively evaluate and treat deployment related concerns.

FACTS:

Policy initiatives directed at achieving FHP goals follow:

Policy Type/Number	Title	Date
DoD Directive 6490.2	Joint Medical Surveillance: Establishes policy and assigns responsibility for routine joint medical surveillance of all Military Service members during active Federal service, especially military deployments. Designates the Secretary of the Army as the DoD Executive Agent for the Department of Defense and for the maintenance of the Armed Forces Serum Repository http://www.dtic.mil/whs/directives/corres/html/64902.htm	Aug 30, 1997
DoD Instruction 6490.3	Implementation and Application of Joint Medical Surveillance for Deployments: Implements policy, procedures, and assigns responsibilities for joint military medical surveillance in support of all applicable military objectives. Describes routine military medical surveillance activities during major deployment, or deployments in which there is a significant risk of health problems, as identified by the Chairman of the Joint Chiefs of Staff in coordination with the Assistant Secretary of Defense for Health Affairs. http://www.dtic.mil/whs/directives/corres/html/64903.htm	Aug 7, 1997

Joint Staff Memorandum MCM-006-02	*Updated Procedures for Deployment Health Surveillance and Readiness* Provides standardized procedures for assessing health readiness and conducting health surveillance (including occupational and environmental health surveillance procedures) in support of all military deployments. This memorandum supersedes the health surveillance reporting procedures contained in MCM-251-98, and supports the implementation of DoDD 6490.2 and DoDI 6490.3, and ASD(HA) policy memorandum of Oct. 5, 2001, on deployment health assessments and blood samples. http://chppm-www.apgea.army.mil/deployment/MCM-0006-02%201FEB2002.pdf	Feb. 1, 2002
Joint Staff Memorandum MCM-251-98	*Deployment Health Surveillance and Readiness:* Establishes uniform and standardized health surveillance and readiness procedures for all deployments. http://amsa.army.mil/documents/JCS_PDFs/joint-staff-letter.pdf	Dec 4, 1998
ASD Health Affairs Policy	*Updated Policy for Pre- and Post-Deployment Health Assessments and Blood Samples* Updates the Oct. 6, 1998, memorandum on same issue to include: Deployment-related health assessments and blood sample collections shall be required for all Reserve component personnel called to active duty for 30 days or more; and Copies of completed health assessment forms (DD Forms 2795 [Pre-deployment] and 2796 [Post-deployment] shall be forwarded to the Army Medical Surveillance Activity.) http://www.tricare.osd.mil/policy/ha01pol/01_017.pdf	Oct. 25, 2001

ASD Health Affairs Policy	Policy for Pre- and Post-Deployment Health Assessment and Blood Samples: Pre-Deployment Health: Required assessments at home station or at mobilization processing stations before deployment, and post-deployment assessments to be administered in the theater of operation before redeployment to either home station or a mobilization processing station. Deployment-Related Blood Samples: The pre- and post-deployment-related blood sample collections required by DoD Instruction 6490.3 shall be met by routine participation in Service programs for periodic or pre-deployment screening for human immunodeficiency virus (HIV) infection. If an HIV screening sample has not been collected within the 12 months before deployment, a pre-deployment blood sample is required for the purposes of screening for HIV and for meeting the requirement for a pre-deployment blood sample. Pre-deployment-related blood samples, if required, shall be collected at home stations or at mobilization processing stations before deployment. http://www.ha.osd.mil/policies/1999/clin9902.htm	Oct 6, 1998
DoD Directive 4715.1	Environmental Security: Establishes policy for environmental security within the Department of Defense. Establishes the Defense Environmental Security Council (DESC); the Environment, Safety, and Occupational Health Policy Board (ESOHPB); and the DESC Committee structure. Establishes the Armed Forces Pest Management Board (AFPMB), consisting of the AFPMB Council and Committee structure, the Directorate, and the Defense Pest Management Information Analysis Center (DPMIAC). http://www.dtic.mil/whs/directives/corres/html/47151.htm	Feb 24, 1996
DoD Directive 6490.5	Combat Stress Control Programs: This Directive establishes policy and assigns responsibilities for developing CSC programs within the Military Services, the Combatant Commands and Joint Service Operations. It also ensures appropriate prevention and management of Combat Stress Reaction (CSR) casualties to preserve mission effectiveness and warfighting, and to minimize the short- and long-term adverse effects of combat on the physical, psychological, intellectual and social health of Service members. http://www.dtic.mil/whs/directives/corres/html/64905.htm	Feb 23, 1999

DoD Directive 6205.3	DoD Immunization Program for Biological Warfare Defense: This Directive establishes policy, assigns responsibilities, and prescribes procedures for members of the Department of Defense against validated biological warfare threats, and prioritization of research, development, testing, acquisition, and stockpiling of biological defense vaccines. Second, it provides vaccination guidance that focuses exclusively on defense against biological warfare threats and complements immunization requirements for naturally occurring endemic disease threats. Third, it addresses peacetime and contingency requirements for immunization against biological warfare threats against U.S. personnel. Fourth, it designates the Secretary of the Army as the "DoD Executive Agent" for the DoD Immunization program for Biological Warfare Defense. Finally, it provides direction on levels of acquisition and stockpiling of biological defense vaccines and prioritizes research and development efforts in defending against current and emerging biological warfare threats. http://www.dtic.mil/whs/directives/corres/html/62053.htm	Nov 26, 1993
DoD Instruction 6055.1	DoD Safety and Occupational Health Program: Updated DoD policies and procedures on risk management, aviation safety, ground safety, traffic safety, occupational safety and occupational health. Excludes explosive safety and fire prevention, which are covered elsewhere. http://www.dtic.mil/whs/directives/corres/html/60551.htm	Aug 19, 1998
ASD Health Affairs Policy	Policy for National Surveillance for Birth Defects Among Department of Defense Health Care Beneficiaries: Appointed Naval Health Research Center, San Diego, to conduct surveillance for major birth defects among DoD beneficiary infants born in both military and civilian medical facilities and provide incidence rates of newly diagnosed cases for births and fetal demises. This will be accomplished by establishing surveillance for birth defects among DoD health care beneficiaries through a scientifically sound, cost-effective hybrid birth defects registry. http://www.ha.osd.mil/policies/1999/clin9906.htm	Nov 17, 1998

ASD Health Affairs Policy	Establishment of DoD Centers for Deployment Health: Created a research center at the Naval Health Research Center, San Diego, converted a clinical center at Walter Reed Army Medical Center, and provided for continuing medical surveillance through the Defense Medical Surveillance System. Improved our ability to identify, treat, and minimize or eliminate the short- and long-term adverse effects of military service on the physical and mental health of veterans. Centers provide an annual report to the ASD(HA) on status and progress, limitations, and accomplishments. http://www.ha.osd.mil/policies/1999/clin9928.htm	Sep 30, 1999
DoD Directive 6200.2	Use of Investigational New Drugs for Force Health Protection: This Directive establishes policy and assigns responsibility for compliance with pertinent references for the use of investigational new drugs for force health protection, and designates the Secretary of the Army as the DoD Executive Agent for the use of investigational new drugs for force health protection. http://www.dtic.mil/whs/directives/corres/html/62002.htm	Aug 1, 2000
ASD Health Affairs Policy	Implementation of Post-Deployment Health Clinical PracticeGuideline: Provides a structure for primary care providers to evaluate and manage patients with deployment related health concerns including family members of recently deployed personnel.	Dec 7, 2000

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POLICY – DoD IMMUNIZATION PROGRAM FOR BIOLOGICAL WARFARE DEFENSE

KEY MESSAGE:

A Directive establishes policy, assigns responsibilities, and prescribes procedures for members of the Department of Defense against validated biological warfare threats, and prioritization of research, development, testing, acquisition, and stockpiling of biological defense vaccines.

It provides vaccination guidance that focuses exclusively on defense against biological warfare threats and complements immunization requirements for natural endemic disease threats.

It addresses peacetime and contingency requirements for immunization against biological warfare threats against U.S. personnel. Fourth, it designates the Secretary of the Army as the "DoD Executive Agent" for the DoD Immunization program for Biological Warfare Defense.

It provides direction on levels of acquisition and stockpiling of biological defense vaccines and prioritizes research and development efforts in defending against current and emerging biological warfare threats.

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.
- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.
- DoD has developed a Smallpox Response Plan. Coordination currently in progress within the Department should be complete within 30 days. The Smallpox Response Plan is designed to enable our Military Health System to effectively respond to a Smallpox outbreak.
- DoD Directive 6205.3, Nov 26, 1993. This policy is being updated to reflect anthrax and investigational new drugs.
- www.dtic.mil/whs/directives/corres/html/62053.htm

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USE OF INVESTIGATIONAL NEW DRUGS FOR FORCE HEALTH PROTECTION POLICY

KEY MESSAGE:

Directives establishes policy and assigns responsibility for compliance with pertinent references for the use of investigational new drugs for force health protection, and designates the Secretary of the Army as the DoD Executive Agent for the use of investigational new drugs for force health protection.

FACTS:

- Public Law 105-261, the Strom Thurmond National Defense Authorization Act For Fiscal Year 1999, amended section 1107 of title 10, United States Code by specifying that only the President may waive the requirement for informed consent to administer an investigational new drug (IND) or drug unapproved for its applied use to a member of the armed forces. The law further specifies the conditions under which the President may grant such a waiver and that the Secretary of Defense is the only official who may request such a waiver. When a waiver is granted by the President, the Secretary must notify the chairman and ranking minority members of the four congressional committees most concerned with defense. The President may grant a waiver only if he/she determines, in writing, that obtaining consent is not feasible, is contrary to the best interests of the member, or is not in the interests of national security.

- Executive Order 13139, 30 September 1999, spells out the manner in which the above requirements will be executed. The Order indicates the steps by which the Secretary will develop a waiver request for the President, perform the necessary congressional and public notifications, and monitor the adherence to the provisions of the order and other regulations. The Order also spells out requirements for training and informing military personnel and commanders about the use of the investigational drug.

- In making determination to waive the informed consent requirement, the President must apply the standards set forth by relevant FDA regulations (21 CFR 50.23). This includes 1) Service member is confronted by a life-threatening situation, 2) no FDA approved alternative method exists, 3) and the SECDEF has determined that waiver is in the best interest of the forces at risk.

- DoD Directive 6200.2, August 1, 2000 establishes policy and assigns responsibility for carrying out the requirements of the law and the Executive Order.

- DoD scientists are developing research protocols for various IND products, such as Pyridostigmine Bromide (PB).

- www.dticmil/whs/directives/corres/html/62002.htm

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PRE- AND POST-DEPLOYMENT HEALTH ASSESSMENT AND BLOOD SAMPLES POLICY

KEY MESSAGE:

Pre-Deployment Health: Required assessments at home station or at mobilization processing stations before deployment, and post-deployment assessments to be administered in the theater of operation before redeployment to either home station or a mobilization processing station.

Deployment-Related Blood Samples: The pre- and post-deployment-related blood sample collections required by DoD Instruction 6490.3 shall be met by routine participation in Service programs for periodic or pre-deployment screening for human immunodeficiency virus (HIV) infection. If an HIV screening sample has not been collected within the 12 months before deployment, a pre-deployment blood sample is required for the purposes of screening for HIV and for meeting the requirement for a pre-deployment blood sample. Pre-deployment-related blood samples, if required, shall be collected at home stations or at mobilization processing stations before deployment.

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.

- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.

- ASD Health Affairs Policy, Oct 6, 1998

- www.ha.osd.mil/policies/1999/clin9902.htm

- This implements the DoDD 6490.2 and DoDI 6490.3 from August 1997, but the program only addresses deployments OCONUS or 30 days or more to areas without established health facilities. This misses most short term and special operating forces deployments. In addition, medical surveillance questionnaire completion is not always enforced, and once completed, they are not comprehensively analyzed for trends.

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February 20, 2002

TAB B

ENVIRONMENTAL AND HEALTH EFFECTS FROM DEPLETED URANIUM (DU) USE ON THE BATTLEFIELD

KEY MESSAGE:

Depleted Uranium (DU) is the superior heavy metal for defeating enemy armored vehicles and for defending US armored vehicles. In response to public concerns about possible health effects in areas where DU was used in combat, the United Nations Environment Programme, the World Health Organization, European Commission, the United Kingdom Royal Society and the United Kingdom Ministry of Defense evaluated areas in the Balkans where DU was used. Common conclusions were that no widespread environmental contamination and no health impact on the local population or deployed personnel is expected.

FACTS:

- Depleted uranium's density, high melting point, high tensile strength, pyrophoric properties, and ability to self sharpen as it penetrates a target make it particularly favorable for use in weapons.
- Like any heavy metal (uranium, lead, tungsten, etc.), DU has chemical toxicity properties that, in high doses, can cause poisoning and health effects. Radioactivity of DU is 40 percent lower than that of natural uranium.
- The Institute of Medicine found limited/suggestive evidence of no association between DU exposure and lung cancer (below 0.200 Sieverts cumulative internal dose) or clinically significant renal dysfunction. The study stated that there were inadequate or insufficient data to determine whether an association exists between exposure to uranium and a variety of health conditions, including lymphatic cancer, bone cancer, nervous system disease, nonmalignant respiratory disease, and other health outcomes (e.g., gastrointestinal disease).
- Reviews of literature on health effects of natural uranium or DU by the Department of Human Services' Agency for Toxic Substances and Disease Registry and the RAND Corporation support the conclusion that DU is unlikely to be the cause of undiagnosed symptoms in Gulf War veterans.
- The Baltimore Veterans Affairs Medical Center has been monitoring approximately 60 Gulf War veterans involved with DU friendly fire incidents. Approximately 20 in this group still have DU fragments in their bodies. While they have higher than normal urine uranium levels, none have adverse health effects due to the chemical or radiological properties of DU.
- The U.S. Army conducted a Capstone test to measure DU aerosol levels and residue after Abrams tanks and Bradley fighting vehicles are struck by DU rounds. The data will strengthen the validity of the OSD(HA) funded DU health risk assessment.
- Iraq maintains that DU munitions used in the Gulf War caused severe health and environmental damage in Iraq and has raised the issue with the UN Security Council.

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ENVIRONMENTAL SURVEILLANCE CAPABILITIES IN SUPPORT OF FORCE HEALTH PROTECTION REQUIREMENTS

KEY MESSAGE:

To identify the populations at risk during deployments, determine potentially hazardous exposures such as environmental contaminants and the appropriate protective measures, and conduct an overall assessment of troop health, the U.S. Army Center for Health Promotion and Preventive Medicine provides environmental surveillance related capabilities as part of its goal to develop and implement a joint service environmental surveillance capability.

FACTS:

- Department of Defense Directive 6490.2 and Instruction 6490.3 require the military services and commanders to identify the populations at risk during deployments, determine potentially hazardous exposures such as environmental contaminants and the appropriate protective measures, and conduct an overall assessment of troop health. The Joint Staff Memorandum, MCM-0006-02 (effective March 1, 2002), supersedes and updates MCM-251-98 and provides standardized procedures for assessing health readiness and conducting health surveillance (including environmental surveillance) in support of all military deployments. Servicemembers who deploy in support of Operation Enduring Freedom are currently covered by the requirements of the CJCS memorandum.

- The environmental surveillance activities in Bosnia (Operation Joint Forge) and Bosnia-Herzegovina (Operations Joint Endeavor and Operation Joint Guard) have been the most comprehensive of any conducted during a U.S. Forces deployment to date.

- This surveillance has been conducted primarily by deployed military preventive medicine detachments, the U.S. Army 520th Theater Army Medical Laboratory, and personnel from the U.S. Army Center for Health Promotion and Preventive Medicine.

- Environmental surveillance activities have led to a number of preventive medicine accomplishments that include: pre-deployment environmental health site evaluations; ambient air environmental health risk assessments; water quality surveillance and assessments; industrial activity/hazard assessments; and continuing sampling.

- Historical environmental data from Operations Desert Focus (in Saudi Arabia) Southern Watch (in Southwest Asia/Iraq), and Desert Thunder (in the Persian Gulf) have been compiled. Environmental health surveillance assessments are ongoing for Camp Doha, Kuwait, and Eskan Village, Saudi Arabia.

- The United States Army Center for Health Promotion and Preventive Medicine is continuing occupational and environmental health surveillance measures in support of Department of Defense medical units deployed for Operation Enduring Freedom. Examples include collaboration with Armed Forces Medical Intelligence Center to prepare industrial hazard assessments for base camps and forward operating bases, to provide deployed medical units

with occupational and environmental health surveillance equipment sets to Army and Navy medical detachments and Army Special Operations units, and to conduct operational risk management estimates for base camps and forward operating bases where occupational and environmental health surveillance field samples have been collected and analyzed.

- The Joint Environmental Surveillance Working Group (JESWG) formed to review, develop, and recommend functional aspects of environmental health surveillance policy for consideration by the Joint Preventive Medicine Policy Group developed an Occupational and Environmental Health Surveillance (OEHS) White Paper. The White Paper identifies numerous areas for which policy opportunities should be pursued. DASD (FHP&R) recently gave approval to DHSD to pursue six of these opportunities during FY 03: (1) enhancement of Joint Occupational and Environmental Surveillance Operations; (2) further definition of the roles of service preventive medicine units relating to chemical, biological, radiological, nuclear, and high explosive (CBRNE) agents; (3) setting OEHS training requirements; (4) establishment of an OEHS science and technology strategy; (5) enhancement of health risk communication procedures; and (6) the appropriate documentation of occupational and environmental exposures in service personnel medical records.

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GUIDANCE ON THE USE AND MANAGEMENT OF PESTICIDES IN DEPLOYED SETTINGS

KEY MESSAGE:

The use of pesticides has been shown to be a highly effective deterrent to vector borne diseases in a deployed setting. Unfortunately, improper use and application of certain pesticides during the Gulf War may have resulted in overexposures and may have contributed to the adverse health effects reported by some veterans. A post-war investigation by the Deployment Health Support Directorate (then Office of the Special Assistant for Gulf War Illnesses) showed the need to improve record keeping, training, logistics, and applications of DoD pesticide work records. Improvements in record keeping practices, training, and the proper use of personal protective equipment during the application of pesticides have been implemented to reduce the health risks associated with these compounds.

FACTS:

- The final report of the investigation will be published in winter 2003.
- DoD has developed a new policy for the procurement of pesticides by local purchase during contingency operations.
- Policy and guidance on pesticide use and management has been revised. New pesticide application recordkeeping practices are being implemented. The Joint Staff Memorandum MCM-0006-02 requires documentation of the types, concentrations, amounts, application methods, dates and times, locations, and the personnel potentially exposed to hazardous substances.
- DoD has eliminated the use of some pesticides and has established new guidance on practices associated with the use of specific pesticides. For example, most uses of chlorpyrifos, bendiocarb, and diazinon are being phased out in line with USEPA regulatory changes, and DoD has eliminated the use of the delousing powder lindane and published guidance on other methods that can be effectively used.
- New training requirements involving the use of effective personal protective measures are being implemented.
- The dissemination of pesticide-related guidance and information has been improved. The Armed Forces Pest Management Board, as DoD's responsible agency has created a website that posts the latest advances and guidance in the effective and safe use of pesticides in a deployed setting.

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IMPROVED DEPLETED URANIUM TRAINING

KEY MESSAGE:

The DoD recognizes it is essential that all military personnel receive training on the possible medical hazards of depleted uranium. The Gulf War was the first offensive and defensive use of depleted uranium (DU) in combat, and only personnel on platforms using DU were trained. In early 1999, a tri-Service DU working group met and made recommendations for total force training. Today, each of the Services use a tiered DU awareness training program. DoD and VA healthcare providers have seen and have available a DU training video.

FACTS:

- DoD and the Services need to ensure that all deployable personnel know what DU is, how it is used, how they might encounter it on the battlefield, the hazard this presents, and how to prevent or minimize personal exposures.

- The Army is the lead agency in DoD for defining DU's hazard potential and for providing guidance and training pertaining to exposure to DU on the battlefield.

- The Army's policy is that all soldiers will receive DU awareness training (Tier I) with additional specialized training provided to those with occupation specialties that involve battle damage assessment and repair and maintenance of tracked and wheeled vehicles (Tier II) and to officer and enlisted Chemical soldiers (Tier III). The DU training program, fielded in July 1999, focuses on force health protection and operational effectiveness. The Army is currently reviewing its training support packages.

- Each of the three tiers of the Army's DU training program is supported by a training support package available to all units from the Army Chemical School at Ft. Leonard Wood, MO.

- The Marine Corps also uses a three-level DU training program. Both the Marines and Navy use a Service-specific variant of the Army's DU Awareness Training video.

- The Air Force program calls for all personnel on mobility status to receive DU awareness training and has incorporated DU awareness guidance in the Nuclear, Biological, and Chemical handbook carried by all deploying personnel.

- The US Army Medical Command has provided updated DU awareness training to military caregivers in DoD and the Veterans Administration by means of a training video. The video is distributed to medical units worldwide.

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October 15, 2002

MEDICAL FOLLOW-UP OF VETERANS WITH HIGHEST DEPLETED URANIUM EXPOSURES

KEY MESSAGE:

The highest exposure to depleted uranium during the Gulf War occurred during friendly fire incidents in which US combat vehicles were struck by DU munitions fired from US tanks. Soldiers riding in or on these vehicles may have been exposed to DU by fragments embedding in their bodies, inhalation and ingestion of DU particles, and wound contamination. The Baltimore VA Medical Center began a voluntary program to monitor these DU-exposed veterans in 1993. While many of these veterans have medical problems resulting from their physical injuries, the medical evaluators report that none are sick from DU's chemical or radiological toxicity.

FACTS:

- Depleted uranium is a heavy metal (1.7 times as dense as lead) by-product of the uranium enrichment process and is 40% less radioactive than natural uranium.
- The major health concerns associated with DU relate to its chemical properties as a heavy metal rather than to its radioactivity. Very high exposure and absorption of uranium can cause kidney (renal) harm.
- The VA evaluates veterans in this voluntary program every two years to determine if their exposure to DU is affecting their health.
- In 1998, DoD and VA recommended urine uranium evaluations for veterans exposed to DU while working in contaminated vehicles for extended periods. Urine uranium tests were also made available to any Gulf War veteran who wanted one.
- Only the veterans with DU fragments in their bodies have elevated urine uranium levels. No significant relationship was found between kidney function and urine uranium values in the program participants.
- Individuals with normal urine uranium levels now are unlikely to develop any DU-related toxicity in the future, regardless of what their DU exposure may have been in the Gulf War.
- Individuals with elevated levels of urine uranium ten years after the Gulf War have not developed kidney abnormalities, cancers, or any other uranium-related adverse outcome.
- The DU Medical Follow-up Program will continue to monitor those individuals with elevated urine uranium levels to enable early detection of any adverse health effects due to their continued exposure to embedded DU fragments.
- These findings are consistent with assessments conducted by the World Health Organization, United Nations Environment Programme, European Commission, European Parliament, United Kingdom Royal Society, and United Kingdom Ministry of Defense. No widespread environmental contamination and no health impact on the local population or deployed personnel are expected.

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October 15, 2002

GAO REPORT ON COALITION WARFARE CHEMICAL AND BIOLOGICAL PROTECTION

KEY MESSAGE:

- The GAO found that the United States, the United Kingdom, and France assessed intelligence differently, came to different conclusions on Iraq's chemical and biological threat, and took different force health protection measures.
- GAO concluded "The disparity in the numbers of illnesses reported by the three countries' veterans does not point unambiguously to any single causative agent."

FACTS:

- Responding to a Shays' subcommittee request, GAO produced a report in 2001 contrasting US, British, and French approaches to Gulf War NBC issues. There has been speculation that France had less Gulf War illness than the US or UK because of these different approaches. OSAGWI (DHSD) pointed out to GAO the flaws in the draft study noted above.
- The GAO conclusion that the French had relatively fewer health complaints than the US or UK may be premature pending the results of French outreach efforts, and future French epidemiological studies of self-reported illnesses. French forces relied more on protective measures than on medicines and vaccinations. However, not all US forces took medicines and vaccines. Some took them on command, some voluntarily, and some not at all.
- The French told us their Gulf War illnesses incidence might appear lower because all their deployers were career military; no Gulf veteran retired before maximum pension years (those with symptoms got desk jobs) making it appear they had no Gulf War illnesses; and France has free health care considered first rate so access to care was not an issue.
- The United Kingdom (UK) told us their Gulf War illnesses experience mirrored ours with a 3-6 month delay equating to a delay in UK news media focus and that UK law allows suing the military for service-connected medical conditions if treatment might have been inadequate.
- The GAO claimed the US had mandatory drug and vaccine use, the UK had voluntary use, and France did not use vaccines for specific diseases, relying more on protective gear and collective protection.
- Other issues raised by the GAO report included differing NBC threat assessments, minimal "spontaneous" sharing of national NBC threat assessments, higher claimed US CW detector thresholds (not clear what they compared), and differing national approaches to NBC protection.
- DHSD has been active with the UK Gulf War office, which has a full-time liaison officer with DoD/DVA. Our contacts with the French have been very much less successful.

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November 22, 2002

ENVIRONMENTAL SECURITY POLICY

KEY MESSAGE:

Establishes policy for environmental security within the Department of Defense. Establishes the Defense Environmental Security Council (DESC); the Environment, Safety, and Occupational Health Policy Board (ESOHPB); and the DESC Committee structure.

Establishes the Armed Forces Pest Management Board, consisting of a Council and Committee structure, the Directorate, and the Defense Pest Management Information Analysis Center.

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.

- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.

- DoD Directive 4715.1, Feb 24, 1996

- www.dtic.mil/whs/directives/corres/html/47151.htm

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DEFENSE MEDICAL SURVEILLANCE SYSTEM (DMSS) AND THE ARMY MEDICAL SURVEILLANCE ACTIVITY

KEY MESSAGE:

Medical surveillance is defined as the routine and systematic collection, analysis, interpretation, and reporting of population-based data for the purposes of detecting, characterizing, and countering threats to the health, fitness, and well being of populations. In military settings, medical surveillance is required to develop and maintain healthy, fit, and operationally effective forces and to ensure their "total protection" during training and operational missions.

FACTS:

- **AMSA**: The Army Medical Surveillance Activity (AMSA) was established in 1994 as part of the Directorate of Epidemiology and Disease Surveillance, U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM). The AMSA staff includes information systems specialists, database managers, programmers, analysts, statisticians, epidemiologists, preventive medicine physicians, and public health officers from each of the three Services. In March 1997, the Assistant Secretary of Defense for Health Affairs (ASD-HA) directed that the Army establish and operate a Defense Medical Surveillance System (DMSS) by transitioning the current capability of the Army Medical Surveillance System (AMSS). AMSA coordinated the development of and now operates the DMSS.

- **DMSS**: The Defense Medical Surveillance System (DMSS) is the corporate executive information system for medical surveillance decision support in the EI/DS business area of the Military Health System (MHS). The DMSS receives and integrates standardized data from multiple individual Service and DoD sources worldwide (figure 1). The "engine" of the DMSS is a continuously growing relational database of up-to-date and historical data related to medical events (e.g., hospitalizations, outpatient visits, reportable diseases, HIV results, health risk appraisals, immunizations, deaths); personal characteristics (e.g., rank, military occupation, demographic factors); and military experiences (e.g., deployments, assignments) of all Army, Navy, Air Force, and Marine service members over their entire military careers. There are currently more than 200 million rows of data regarding more than 7.0 million service members in the on-line DMSS database.

- **DMED**: The Defense Medical Epidemiology Database (DMED) application provides authorized users worldwide (through the Internet) with real-time access to user-definable queries of a subset of data (non-privacy) contained within the DMSS. The DMED application (version 3.3) can be downloaded from AMSA's home page (http://amsa.army.mil).

- **Reports**: The AMSA/DMSS produces data summaries, epidemiologic analyses, and special reports for policy makers, medical planners, health care practitioners, and researchers worldwide. The Medical Surveillance Monthly Report (MSMR) is the principal vehicle of AMSA/DMSS for the routine dissemination of medical surveillance information of broad interest. The MSMR publishes summaries of notifiable diseases, trends of special surveillance interest (e.g., deployment-related morbidity), and field reports of outbreaks and

isolated cases with special public health or military operational significance. Current and previous issues of the MSMR are accessible from AMSA's home page (http://amsa.army.mil).

- **Serum Repository**: AMSA and the DMSS provide the sole link between medical surveillance data (e.g., personnel, military experience, medical outcomes) and specimens in the DoD Serum Repository. The DoD Serum Repository, the largest of its kind in the world, contains more than 27 million frozen archived serum specimens from members of all the military services.

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U.S. Army Center for Health Promotion and Preventive Medicine
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February 21, 2002

DISEASE AND NON-BATTLE INJURY (DNBI) SURVEILLANCE

KEY MESSAGE:

DNBI data is being collected for military deployments as part of the comprehensive Defense Medical Surveillance System (DMSS). The U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) accumulates and integrates standardized DNBI data from the Services' medical surveillance programs.

FACTS:

- During Operation Desert Shield/Desert Storm in the Gulf, and to a lesser extent Operation Joint Endeavor in the Balkans, DNBI and related medical surveillance information was neither standardized among the Services nor consistently reported for centralized data collection and analysis.

- Agencies such as the Institute of Medicine (IOM) and the General Accounting Office (GAO) have reported on deficiencies involving the collection, maintenance, and transfer of accurate surveillance data on medical incidents, potential exposures to health risks, and troop locations during deployments.

- Consensus on DNBI reportable events was achieved through the Tri-Service Joint Preventive Medicine Policy Group (JPMPG) and disseminated through a DOD (Health Affairs) policy memorandum in November 1998.

- The ability of the VA to fulfill its role in serving veterans, conducting medical research, and providing backup to DoD in times of war will be enhanced as DOD increases its medical surveillance capability.

- DoD has several information technology initiatives under development to improve the reliability of medical surveillance/DNBI information. These include the patient visibility and health surveillance components of the Theater Medical Information Program (TMIP) and the Global Expeditionary Medical System (GEMS).

- While DoD has made progress in developing medical surveillance policy and implementing medical surveillance programs, some information technology initiatives to support medical surveillance are several years away from full implementation.

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DHSD
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February 22, 2002

MEDICAL LOGISTICS IMPROVEMENTS

KEY MESSAGE:

Facility Management, Materiel Management, Equipment Management, and Technology Management will all soon be handled by one integrated system. The Defense Medical Logistics Standard Support program is a partnership involving wholesale medical logistics, medical information management, medical information technology, and numerous user communities. The implementation of business process innovations decreases costs and improves the responsiveness of medical logistics support to fixed military treatment facilities and deployed forces around the world

FACTS:

- The Defense Medical Logistics Standard Support is being developed and deployed in three major releases. Release 1, currently deployed to 110 sites worldwide, consists of the first increments of materiel management and facility management sites. Release 2, has been developed and consists of the second increments of materiel management and facility management sites. Release 3, will enables the Services to turn off Service unique medical logistics legacy systems and will deploy the only increment of equipment and technology management sites.

- A Clinger-Cohen certification supports the Milestone III approval for worldwide deployment of Defense Medical Logistics Standard Support program Release 2. The Clinger-Cohen Act has been designed to help ensure that investments in information technology provide measurable improvements in mission performance. A key to using information technology to enable improvements in DoD 's operations and procedures is establishing processes through which executive leadership can align business processes and resources to mission goals and strategic objectives.

- The Military Health System Management/Information Technology Program organizational structure provides the governance for the oversight and management of the Military Health System information technology portfolio. This governance process also is intended to ensure compliance with the Government Performance and Results Act, Clinger-Cohen Act of 1996, and DoD acquisition and management regulations.

- Critical elements of this structure include senior management oversight, Military Health System Chief Information Officer leadership, and senior managers for both IT and IM that are responsible for executing and monitoring the portfolio investment plans and are accountable to senior managers and the Military Health System Chief Information Officer.

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February 20, 2002

MEDICAL SURVEILLANCE SYSTEMS

KEY MESSAGE:

The Department of Defense is developing improved medical surveillance systems to expand force health protection capabilities.

FACTS:

- **Global Emerging Infections Surveillance and Response System (GEIS).** The DoD-GEIS was established in response to a 1996 Presidential Directive expanding the mission of DoD to include support of global surveillance, training, research, and response to emerging infectious disease threats. The system encompasses a network of overseas DoD health surveillance laboratories, along with service-specific preventive medicine activities such as the Army Medical Research Institute of Infectious Diseases, the Walter Reed Army Institute of Research, the Navy Medical Research Center, the Navy Health Research Center, and the Air Force Global Surveillance Office. DoD-GEIS is an international military-civilian medical surveillance partnership with strong ties to the Centers for Disease Control and the World Health Organization. The Army is the DoD Executive Agent for GEIS.

- **Electronic Surveillance System for the Early Notification of Community Based Epidemics (ESSENCE).** ESSENCE was developed by the DoD-GEIS and provides disease surveillance capability to over 400 DoD medical treatment facilities. The system acquires, analyzes, and disseminates (via a secure web site) aggregated data gathered daily by the DoD Ambulatory Data System.

- **Lightweight Epidemiology Advanced Detection and Emergency Response System (LEADERS).** LEADERS is a commercially developed disease surveillance program sponsored by the Air Force Surgeon General's Office. The system captures laboratory, radiology, pharmacy, and ambulatory data directly from medical treatment facilities (MTFs) in real-time via encrypted downloads. Surveillance algorithms are backed by a data-mining suite that looks for new or unusual disease trends which are then reported via a secure web site. MTF personnel are alerted and LEADERS provides tools to help confirm, respond, report, and track these trends.

- **Global Expeditionary Medical System (GEMS).** GEMS is an Air Force-sponsored deployable health management and medical surveillance tool. It includes a Patient Encounter Module (PEM) that allows the front-line medic to electronically record and track individual patient assessments. A Theater Epidemiological Module (TEM) provides the Joint Task Force Surgeon with automated surveillance and reporting of deployed force health and readiness.

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28 May 2002

MILITARY MEDICAL SURVEILLANCE RELATED TO OPERATION ENDURING FREEDOM

KEY MESSAGE:

Procedures are standardized for assessing health readiness and conducting deployment health surveillance. Deployment health surveillance information is forwarded to the Defense Medical Surveillance System health data repository, which is managed by the Army Medical Surveillance Activity. Instructions require the combatant command to determine the need for deployment-specific medical countermeasures including immunizations, chemoprophylactic medications, and other individual personal protective measures.

The United States Army Center for Health Promotion and Preventive Medicine (USACHPPM) is continuing occupational and environmental health surveillance measures in support of combat commanders and Department of Defense medical units deployed for Operation Enduring Freedom.

FACTS:

- DoDD 6490.2, "Joint Medical Surveillance," and DoDI 6490.3, "Implementation and Application of Joint Medical Surveillance for Deployments" set out health surveillance requirements. An ASD (HA) memorandum dated October 25, 2001, updates the policy for pre-deployment and post-deployment health assessments and blood samples.

- A CJCS memorandum, MCM-251-98, "Deployment Health Surveillance and Readiness" spelled out the conceptual framework for force health protection with health surveillance as a critical component. CJCS Memorandum MCM-0006-02 (effective March 1, 2002) supersedes and updates MCM-251-98 and provides standardized procedures for assessing health readiness and conducting health surveillance in support of all military deployments. Servicemembers who deploy in support of Operation Enduring Freedom are currently covered by the requirements of the CJCS memorandum.

- USACHPPM conducts pre-deployment and during-deployment environmental health intelligence preparation of the battlefield for Operation Enduring Freedom through the development of industrial hazard assessments for base camps and forward operating bases. The Center collaborates with the Armed Forces Medical Intelligence Center in producing these assessments, which are classified.

- USACHPPM is providing deployed medical units with occupational and environmental health surveillance equipment sets to Army and Navy Medical Detachments and Army Special Operations units. The sets contain sampling equipment, media, and administrative supplies, so that air, water, and soil field samples can be collected.

- The Center is conducting operational risk management estimates for base camps and forward operating bases where occupational and environmental health surveillance field samples have been collected and analyzed. This aspect involves the assimilation and comparison of the

analyzed field sample results to military exposure guidelines, where any identified medical and/or health threats are assessed.

- In summary, the Center supports Force Health Protection measures outlined in Department of Defense Joint Medical Surveillance Directives and U.S. Central Command Force Health Protection guidance.

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August 14, 2002

THEATER MEDICAL INFORMATION PROGRAM (TMIP)

KEY MESSAGE:

- TMIP is an information technology system that supports the medical readiness of deployed combat forces anywhere, anytime, and in support of any mission. It brings an integrated suite of automated medical information systems to the battlefield in direct support of the warfighter.
- Its overarching "fight like you train" philosophy reduces the fog and friction of deployed operations by maintaining the same look, feel, and function found in familiar in-garrison applications. This reduces training requirements, reduces errors, and improves casualty care.

FACTS:

- Includes multiple Command and Control, Medical Logistics, and Health Care Delivery capabilities all designed to enhance the flexibility of commanders, right-size the logistics footprint of deployed medical operations, improve the survivability the sick and injured, and multiply the overall effectiveness of U.S. military power.
- Serves as the medical component of the Global Combat Support System. Medical data generated at battlefield locations is transmitted to a central theater database, which can then be viewed for command and control of the theater medical battlefield.
- Integrates existing medical information systems to capture the deployed patient's medical record; this same information is then accessible both at home and abroad.
- Aggregates medical information from all levels of care supporting situational awareness and preventive medicine needs for operational forces.
- Biological and chemical exposures can be identified as a result of trend analysis.
- Tracks and reports patient location during evacuation from theater to stateside hospital.
- TMIP functional capabilities include:
  - Medical logistics
  - Immunization tracking
  - Structured text clinical encounter
  - Battle injuries and battlefield disease
  - Post-deployment surveys
  - Occupational Health/radiation exposure
  - Lab results
  - Status reporting
  - Blood management
  - Medical records
  - Symptomology
  - Sick call and physical exams
  - Consults
  - Logistics management
  - Disease and injury coding
  - Automated medical reference/library
- The integrated suite of TMIP capabilities includes:
  - Composite Health Care System (CHCS) II – Theater
  - Defense Medical Logistics Standard Support (DMLSS) System
  - Shipboard Automated Medical System (SAMS)
  - Medical Surveillance System (MSS)
  - Medical Analysis Tool (MAT)
  - Defense Blood Standard System (DBSS)
  - TRANSCOM Regulating and Command & Control Evacuation System (TRAC^{2}ES)

- Architecture complies with all DoD IT Architecture and Information Security Requirements.
- Follows an evolutionary acquisition strategy through the release of blocks of functional capability.
- Successful user testing has been completed at Fort Sam Houston, Texas and in Thailand during Exercise Cobra Gold. Additional user testing and evaluation will be performed during the summer of 2002 in Exercise Millennium Challenge, a Joint Forces Command exercise. Initial Operational Test & Evaluation is scheduled for 2002.

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OSD(HA), Theater Medical Information Program Office

(b)(6)

February 20, 2002

US DEPARTMENT OF DEFENSE GLOBAL EMERGING INFECTIONS SURVEILLANCE AND RESPONSE SYSTEM (DOD-GEIS)

KEY MESSAGE:

- The DoD recognizes the significant threat that emerging infectious diseases, both naturally occurring and those introduced by terrorists, pose to national security.
- The DoD recognizes the need for an international surveillance and response system to identify and control the emerging disease threat.
- The five regional tropical overseas laboratories of the Army and Navy are unique and essential assets in combating the emerging infectious disease threat to deployed troops specifically and to national security in general.

FACTS:

- **Establishment of DoD-GEIS.** The DoD-GEIS was established in response to Presidential Decision Directive NSTC-7, June 1996, which expanded the mission of the DoD to include support of global surveillance, training, research, and response to emerging infectious disease threats. The Directive called on DoD to strengthen its global disease reduction efforts through centralized coordination, improved preventive health programs and epidemiological capabilities, and enhanced involvement with military treatment facilities and laboratories within the United States and overseas.
- **DoD-GEIS Mission.** DoD-GEIS is to implement the Presidential Directive on emerging infections through an international, coordinated, joint service program focused on timely recognition and control of emerging and re-emerging infections. The means include systematic surveillance (especially laboratory-based surveillance), research, response, training, and capacity building. This mission is executed in two primary settings: the DoD's overseas laboratory network and the service-specific preventive medicine programs.
- **DoD-GEIS Partners.** The DoD-GEIS involves multiple military organizations to accomplish its mission, including the Walter Reed Army Institute of Research, the Navy Medical Research Center, the Naval Health Research Center, San Diego, CA; the US Air Force Global Surveillance Office, Brooks Air Force Base, TX; and the US Army Medical Research Institute of Infectious Diseases, Ft. Detrick, MD. DoD-GEIS also has strong relationships with the Centers for Disease Control and international health agencies.
- **GEIS Programs.** Building on the DoD network of international laboratories to evaluate critical force protection products (drugs, vaccines, diagnostic tests), DoD-GEIS operates a global surveillance network for the early recognition and response to emerging infections disease threats. It is strengthening the DoD's Military Health System laboratory capabilities, monitoring the health of DoD beneficiaries worldwide through near real-time syndromic surveillance, and enhancing the U.S. security through international partnerships to build regional capacity for sustained surveillance. For example, decisions regarding influenza vaccine composition have been enhanced by worldwide DoD surveillance for new influenza strains. DoD-GEIS also supports regional engagement initiatives of the unified commands by helping other countries implement electronic public health surveillance systems.

COL Patrick W. Kelley, MC
Director, DoD –GEIS
(b)(6)
April 1, 2002

USSOCOM MEDICAL SURVEILLANCE – HANDHELD DEVICE

KEY MESSAGE:

The Joint Forces Special Operations Component Commander (JFSOCC) identified a need for a handheld system to electronically capture patient care and health surveillance data at Level I and II during Special Operations Forces (SOF) deployments.

FACTS:

- A Combat Mission Needs Statement submitted by JFSOCC generated a need to effectively execute and support health surveillance requirements to protect the long and short term care of SOF forces.
- The Deployment Health Support Directorate (previously, OSAGWI) identified this as a requirement based on Desert Shield/Desert Storm lessons learned. The USSOCOM Surgeon's Office has been working with ASD(HA), the Joint Staff/J4, and service surgeons since 1999 to have such a device developed.
- Currently, the Army and the Air Force are developing one (Army/MC4, Air Force/Gems) but each is service-specific in its design and does not meet the joint standards desired by USSOCOM. The availability (approx. 2005) of the service systems does not support the near-term USSOCOM requirements. USSOCOM's intent is to have their device designed to be compatible with CHCS II/TMIP.
- USSOCOM in collaboration with the U.S. Army Center for Health Promotion and Preventive Medicine has developed a handheld system that meets all joint requirements including operational security.
- Based on a briefing given by SOCOM to the GAO on 30 Jul, 80 devices have been purchased, formatted and distributed (Jul) to SOCOM components and JSOTF surgeons.

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August 23, 2002

Medical Surveillance Programs - Providing Near Real-Time Syndromic Disease Reporting for Early Identification of Possible Biowarfare Attacks

KEY MESSAGE:

There are military medical surveillance programs which provide near real-time syndromic disease reporting and enable early identification of possible biological attacks.

FACTS:

- Reportable Medical Events- About 70 reportable medical events, including diseases due to biowarfare (BW) agent exposure, are reportable to state and military disease-control authorities. The efficiency and timeliness of reporting is variable and dependent upon disease/syndrome recognition and local MTF provider and preventive medicine cooperation for reporting.

- Syndromic Surveillance- Several initiatives monitor military medical databases to alert for spikes and trends in healthcare visits, by diagnosis (ICD-9 codes) compiled into diagnostic syndromic groups. These systems utilize routinely generated data from automated healthcare encounter records and are thus dependent upon the existence of these automated systems and by patient access to medical providers and provider recognition and recording of illness. These include ESSENCE (Electronic Surveillance System for the Early Notification of Community-based Epidemics), MDSS (Medical Data Surveillance System), and LEADERS (Lightweight Epidemiology Advanced Detection and Emergency Response System). ESSENCE II is working to expand both the types of data input to its system (e.g., pharmacy, lab, absenteeism) and the extent of population covered (i.e., civilians). The Biological Defense Initiative (BDI), an Office of Homeland Security project managed by DTRA, is working on testbed and prototype projects to implement both medical surveillance (ESSENCE, RSVP, B-SAFER) and environmental monitoring for biological-related events in U. S. cities.

- Public Health Laboratory Capability- There are DoD efforts (by GEIS and the Armed Forces Institute of Pathology, AFIP) to establish a directory of public health laboratory services to provide advice regarding resources for diagnosis of non-routine clinical and environmental specimens. CDC has developed the Laboratory Response Network (LRN) to allow for standardized laboratory confirmation of biowarfare agents (both clinical and environmental) and is expanding its network throughout the U. S. and DoD. Theater laboratory capability will be essential in deployed environments.

- Deployment Environmental Surveillance- CHPPM has established the Deployment Environmental Surveillance Program (DESP) to archive environmental, industrial, and biologic exposures for deployed forces. The utility of these systems for biowarfare agent detection is as yet unclear, although special studies have been conducted regarding chemical agent exposures.

- Automated Deployment Medical Surveillance- TMIP is developing MHS clinical automation systems which will include surveillance capabilities. An interim system is being implemented via a JMeWS (joint medical workstation) server on the SIPRNET using MDSS for syndromic surveillance analysis and Watch Board to supply a medical command operational picture.

- DNBI Reporting- JCS has systems in place which monitor disease and non-battle injury (DNBI) in deployed forces on at least a weekly basis, with established baselines and trend analysis being accomplished locally. This will be automated with TMIP and the JMeWS server implementations.

- Mortality Surveillance- The DoD Medical Mortality Registry is operational at the Office of the Armed Forces Medical Examiner, AFIP, and monitors deaths in DoD active duty members on a daily basis. Those which are unexplained, of infectious origin, or suspicious are immediately investigated and DoD officials notified. The DoD Casualty System identifies military deaths and manages disposition of the remains, notification of families, and family assistance regarding benefits, etc. However, it does not address circumstances or cause of death

COL John Gardner
DHSD
(b)(6)
January 8, 2003

TAB D

DOD AND VA COOPERATION

KEY MESSAGE:

- The DoD and VA continue to cooperate in their response to the concerns of veterans on several issues including, physical evaluations, potential treatment regimens, research efforts, documentation support and outreach efforts

FACTS:

- **Physical evaluations:** The VA and DoD offered comparable comprehensive exam programs to ensure Gulf War veterans' access to care. The VA's program began in 1992; the DoD's program in 1994. As of September 30, 2001, approximately 41,000 have completed the DoD exam and approximately 74,000 have participate in the VA's Persian Gulf Registry program. In February this year, both exam programs will be expanded to include all deployers. The clinical practice guidelines will assist DoD and VA health care providers in screening and evaluating servicemembers with health concerns following deployment.

- **Treatment Trials:** Two treatment trials, Exercise-Behavioral Therapy (EBT) and Antibiotic Treatment Trial (ABT), have been conducted at 36 different Veterans Affairs and DoD medical facilities nationwide. The EBT study examines whether aerobic exercise and cognitive behavioral therapy will improve the life for ill Gulf War veterans. Exercise with or without behavioral therapy produced benefits for unexplained symptoms. Behavioral therapy alone did not. The Antibiotic Treatment Trial tests the theory that ill Gulf War veterans who test positive for an organism called *Mycoplasma fermentans incognitus* will feel better after receiving antibiotic treatment with doxycycline. Results of these treatment trials have shown no apparent benefit from 12 months of doxycycline when compared to placebo for unexplained symptoms in persons with a positive polymerase chain reaction (PCR) for mycoplasma.

- **Research Efforts (Millennium Cohort Study):** An example of research collaboration is the Millenium Cohort Study. The departments of Defense and Veterans Affairs will study the health of 140,000 servicemembers, throughout their military careers and after they leave the service. The Millennium Cohort Study is designed to evaluate the impact of military deployments on various measures of health over time, including medically unexplained symptoms and chronic diseases such as cancer, heart disease, and diabetes. One of the many lessons of the Gulf War is that the lack of ongoing, population-based, longitudinal health studies has limited the ability to identify deployment-related health outcomes. When researchers want to learn whether a medical condition is occurring at a higher-than-expected rate among veterans of a particular conflict, it can be quite difficult to determine what the "expected" incidence of that ailment really is. The cohort study will serve as a foundation upon which other routinely captured medical and deployment data can be added to answer future questions about the health risks of military deployment, military occupations, and general military service.

- **Research Efforts (ALS):** A second example of research cooperation between the departments of Defense, Veterans Affairs and Health and Human Services is work related to studies on amyotrophic lateral sclerosis (ALS) and a possible connection to Gulf War service. This study is one of 193 research projects to study the possible causes of illnesses among Gulf War veterans and the third study of ALS. The study addresses the relative rates

of ALS in Gulf War veterans serving between August 2, 1990, and July 31, 1991, compared to personnel on active duty at the time who did not deploy to the Gulf. Preliminary information on ALS cases was collected by clinicians at VA and DoD in 1998 and 1999. The DoD data identified 15 patients and the combined DoD/VA data identified 28 patients with possible ALS among the 697,000 servicemembers deployed to the Gulf War. The prevalence rate – a snapshot in time – of ALS in the United States is estimated to be between six to eight cases per 100,000 population. The incidence rate – a rate over time – is one per 100,000 per year. While the current ALS study does not address the cause of ALS, this work could not have been completed without the cooperative effort between government agencies.

- **Research Efforts (Depleted Uranium):** Another example of research cooperation is the voluntary Veterans Affairs depleted uranium medical follow-up program began in 1993-1994 with the medical evaluations of 33 friendly-fire depleted uranium-exposed veterans, many with embedded depleted uranium fragments. In 1998, the VA and DoD coordinated an expanded program to assess Gulf War veterans who were in or on vehicles when they were struck by depleted uranium and those who immediately entered the vehicles to rescue soldiers. Also included were soldiers who worked in or around contaminated vehicles. As a result of DoD's contact with these individuals in 1999, an additional 29 soldiers volunteered for the surveillance program. Some Gulf War veterans with concerns about possible exposure to depleted uranium have also been tested.

- **Documentation Support:** In August 2000, the VA asked the DoD for help in obtaining information needed to clarify claims information from servicemembers who believed they might have been exposed to harmful substances during their participation in Shipboard Hazard and Defense (SHAD) exercises. Specifically, VA claims experts needed to know what type of substances veterans may have been exposed to, and when they may have been exposed. The simulants or agents used, dates of the tests and which vessels were involved are key to determine if there should be a concern today. The Defense Department began an investigation to determine medical information associated with these tests which may assist the VA in making these determinations. The process has been painstaking. Paper and microfiche records have been combed by hand, important bits of information pieced together and added to a list of materials which then had to go through the Pentagon's declassification process. This investigation has required the close cooperation of the VA, the Military Veterans Health Coordinating Board, the Assistant Secretaries for Manpower and Reserve Affairs of the Army and Navy, and elements of the Office of the Secretary of Defense. The Under Secretary of the Army also worked to expeditiously declassify needed documentation.

- **Outreach:** Representatives from the Department of Veterans Affairs have participated in various DoD outreach efforts since 1998. Local VA subject-matter experts attended nearly 20 town hall meetings organized by the then-DoD Special Assistant for Gulf War Illnesses. They fielded VA-related questions, provided one-on-one counseling when needed and helped link veterans with local resources. At the national level, representatives from the VA Central Office have participated in DoD's monthly Veterans and Military Service Organization meetings, which have focused on Gulf War illnesses. Their participation has improved Interagency communication with key stakeholders.

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February 26, 2002

DOD-VA COLLABORATION

KEY MESSAGE:

The Department of Defense (DoD) and the Department of Veterans Affairs (VA) are building a more collaborative relationship to improve the well-being of military service members and veterans.

- First (quarterly) meeting of the **DoD-VA Executive and Health Benefits Councils** held on 11 Feb 02. Agenda included standardized billing and reimbursements, joint procurement, computerized patient records, and coordination of capital investments.
- The two councils will work together to improve coordination in such areas as health care services, benefits delivery, information sharing, and capital asset coordination.
- These cooperative efforts will improve services through new initiatives and increased efficiencies that will benefit military personnel, veterans, and taxpayers.

FACTS:

- DoD-VA **sharing** was formalized in May 1982 with passage of the *VA and DoD Health Resources and Emergency Operations Act (Sharing Act)* to promote more cost effective use of federal health resources and more efficient delivery of care. Sharing activities include local MTF-VAMC agreements, joint ventures, national initiatives (e.g., joint separation physical exams), and other efforts (e.g., joint purchasing)
- DoD-VA **joint ventures** (shared medical facilities) began in Albuquerque in 1987 and today include sites at Las Vegas, Northern California, Anchorage, El Paso, Honolulu, Oklahoma City, and Key West.
- DoD-VA **Executive Council** was established by Drs. Joseph and Kizer in 1987; now includes working groups for clinical practice guidelines, patient safety, pharmacy, medical-surgical supplies, financial management, information systems, geriatric care, financial management, benefits coordination, and joint facilities/resource sharing.
- **GAO report** (May 2000) identified large numbers of sharing agreements but found activity concentrated under relatively few agreements at a few facilities. It suggested that evolving health care systems required rethinking of resource sharing strategies.
- **Barriers** to DoD-VA collaboration include mission, cultural, and population differences; DoD entitlement to care v. VA priority for care; DoD primary care focus v. VA specialty care focus; differing financial, IM/IT, and personnel systems; and the uncertain role of the VA under TRICARE
- **President's Task Force** to Improve Health Care Delivery for Our Nation's Veterans (May 2001) was established to improve benefits and services, review barriers and challenges, and identify opportunities for improved resource utilization. Work groups address leadership,

benefit services, IM/IT, facilities, pharmaceuticals, procurement, and resources/budgeting. Interim report due July 2002; final report due May 2003.

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DHSD-MR

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February 20, 2002

DOD-VA COOPERATION ON RESEARCH

KEY MESSAGE:

The departments of Defense and Veterans Affairs are cooperating in funding studies to help evaluate the impact of deployments on health. In collaborative project, the departments of Defense and Veterans Affairs will study the health of 140,000 servicemembers, throughout their military careers and after they leave the service. This "Millennium Cohort Study" is designed to evaluate the impact of military deployments on various measures of health over time, including medically unexplained symptoms and chronic diseases such as cancer, heart disease and diabetes.

FACTS:

- One of the many lessons of the Gulf War is that the lack of ongoing, population-based longitudinal health studies has limited the ability to identify deployment-related health outcomes. When researchers want to learn whether a medical condition is occurring at a higher-than-expected rate among veterans of a particular conflict, it can be quite difficult to determine what the expected incidence of that ailment really is. The cohort study will serve as a foundation upon which other routinely captured medical and deployment data can be added to answer future questions about the health risks of military deployment, military occupations, and general military service.

- The voluntary Veterans Affairs Depleted Uranium Medical Follow-up Program began in 1993-1994 with the medical evaluations of 33 friendly-fire DU-exposed veterans, many with embedded depleted uranium fragments. In 1998, the VA and DoD coordinated to enlarge the program to assess Gulf War veterans who were in or on vehicles when they were struck by depleted uranium and those who immediately entered the vehicles to rescue soldiers. Also included were soldiers who worked in or around contaminated vehicles. As a result of DoD's contacting these individuals in 1999, an additional 29 soldiers volunteered for the surveillance program. Some Gulf War veterans with concerns about possible exposure to depleted uranium have also been tested.

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February 20, 2002

DOD-VA COOPERATION ON SEPARATION PHYSICAL EXAMINATIONS

KEY MESSAGE:

DoD and the VA have collaborated on a joint initiative to conduct a single, standardized physical examination when a servicemember separates from military service and desires to file a claim for service-connected disability compensation. The initiative is called "Benefits Delivery at Discharge." It provides a discharge examination that meets the needs of both departments and allows the VA to quickly process claims. The goal of the program is to adjudicate claims within 30 days of the date of discharge.

FACTS:

- This initiative was pilot tested with the Army beginning in 1995 for servicemembers retiring or being medically separated from the military
- A joint DoD-VA memorandum of understanding (MOU) was signed in May 1998, and a DoD Health Affairs policy memorandum was published in September 1998.
- Arrangements for pre-discharge physical examination and claims processing are negotiated locally between VA regional offices and medical centers and DoD medical treatment facilities. There are approximately 30 VA regional offices and 140 military installations, including two overseas, participating in the program.
- Each year, approximately 200,000 servicemembers separate from active service. In FY 2001, approximately 27,000 servicemembers participated in the "Benefits Delivery at Discharge" program.
- Improved coordination between the DoD and the VA is also the focus of a newly established (May 2001) "President's Task Force to Improve Health Care Delivery for Our Nation's Veterans." The goals of the task force's two-year study are to improve access to veterans' benefits and to strengthen VA-DoD partnerships for health care services.

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February 26, 2002

DOD-VA COOPERATION ON PROJECT DESERET TESTING

KEY MESSAGE:

The departments of Defense and Veterans Affairs are cooperating in providing information on past chemical and biological tests, specifically tests planned and directed by the Deseret Test Center, to assist veterans making benefits claims.

FACTS:

- In August 2000, the VA asked the DoD for help in obtaining information needed to clarify claims information from servicemembers who believed they might have been exposed to harmful substances during their participation in a series of tests known as Shipboard Hazards and Defense (SHAD).

- Specifically, VA claims experts needed to know what type of substances veterans may have been exposed to, and when they may have been exposed. The simulants or agents used, dates of the tests and which vessels were involved are key to determine if there should be a concern today.

- The Defense Department began an investigation to determine medical information associated with these tests which may assist the VA in making these determinations. The process has been painstaking. Paper and microfiche records have been combed by hand, important bits of information pieced together and added to a list of materials which then had to go through the Pentagon's declassification process.

- In the course of the investigation, Defense Department investigators discovered that SHAD was a part of a larger testing program directed by the Deseret Test Center at Ft. Douglas, Utah between 1962 and 1973. In the mid-1960s the Deseret Test Center moved to Dugway Proving Ground, Utah. DoD passes all medically relevant information on each Project Deseret test to the VA, both ship-based and land-based testing.

- This investigation has required the close cooperation of the VA, the Military Veterans Health Coordinating Board, the Assistant Secretaries for Manpower and Reserve Affairs of the Army and Navy, and elements of the Office of the Secretary of Defense. The Under Secretary of the Army also worked to expeditiously declassify needed documentation.

(b)(6)

DHSD

(b)(6)

September 9, 2002

DOD-VA COOPERATION ON TREATMENT TRIALS

KEY MESSAGE:

The departments of Defense and Veterans Affairs are cooperating in evaluating treatment protocols for Gulf War veterans.

FACTS:

- Two treatment trials, Exercise-Behavioral Therapy (EBT) and Antibiotic Treatment Trial (ABT) have been conducted at 36 different VA and DoD medical facilities nationwide.

- The EBT study examines whether aerobic exercise and cognitive behavioral therapy will improve the life for ill Gulf War veterans. Exercise with or without behavioral therapy produced benefits for unexplained symptoms. Behavioral therapy alone did not.

- The Antibiotic Treatment Trial tests the theory that ill Gulf War veterans who test positive for an organism called *Mycoplasma fermentans incognitus* will feel better after receiving antibiotic treatment with doxycycline. Results of these treatment trials are have shown no apparent benefit from 12 months of doxycycline when compared to placebo for unexplained symptoms in persons with a positive PCR for mycoplasma.

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DHSD

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February 20, 2002

DoD-VA INFORMATION TECHNOLOGY SHARING

KEY MESSAGE:

- The Department of Defense (DoD) and the Department of Veterans Affairs (VA) are aggressively pursuing a number of information management and technology initiatives that will significantly enhance the ability of the departments to share appropriate health information securely. Joint efforts include:
  - Government Computer-based Patient Record (GCPR)—DoD and VA are collaborating closely to develop this vehicle that enables DoD to transfer health information to VA on service members upon separation and on service members previously separated.
  - DoD Transportation Command Regulating and Command Control Evacuation System (TRAC2ES)—provides global patient evacuation planning in an integrated system that VA is using to submit bed reporting and contingency data, providing a complete picture of medical resource availability.
  - DoD/VA are evaluating the compatibility of their health information architecture standards (technical, communications, security, systems) to foster systems interoperability and information sharing.

FACTS:

Current DoD/VA Information Technology Sharing Initiatives

- Map & Gap Health Information Architecture Standards—A 2001 comparison of DoD/VA technical standards found that ninety-six percent of the categories have the same or compatible standards or have no impact on interoperability.
- GCPR—User testing of the near term solution (NTS) is underway. Following successful completion, enterprise-wide use of the NTS within VA is anticipated in the third quarter of FY 2002. DoD is in the process of transmitting information on approximately 3.7 million separated service members to the VA.
- TRICARE Online—An enterprise-wide secure Internet portal for use by DoD beneficiaries worldwide. It provides information on health, medical facilities and providers and increases patient access to health care. VA's pilot health portal is using the same health information content provider.
- Consolidated Mail Outpatient Pharmacy (CMOP) – Progressing toward enabling DoD to use CMOP.
- TRAC2ES– Facilitates the decision process of evacuating military casualties from a combat theater to a source of definitive medical care in the Continental United States.

Opportunities for DoD/VA Information Technology Sharing – In Exploration

- Pharmacy Data Transaction Service—Allows DoD to build a medication profile for all patients. DoD/VA are evaluating sharing this service to improve VA quality of prescription services and enhance patient safety by reducing the likelihood of adverse drug-drug interactions, therapeutic overlaps, and duplicate treatments.
- Composite Health Care System II—The military Computer-based Patient Record will generate, maintain, and provide secure online access to a comprehensive and legible health

record. Developing a joint central clinical data repository will allow DoD/VA authorized users to access comprehensive patient information, perform analyses, and add to data.

- Centralized Credentials Quality Assurance System—DoD's central database for provider information supports the management of adverse privileging actions and risk management tracking. DoD/VA sharing of electronic provider information will result in improved patient access and the quality of healthcare.
- Defense Medical Logistics Standard System—DoD's award-winning, state-of-the-art technical solution improves medical logistics responsiveness at reduced costs and provides a high quality, integrated system. Potentially can meet VA medical logistics automated information management system needs and become the "bolt" on the logistics element of their Enterprise Resource Planning system.

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TRICARE Management Activity/Information Management Technology & Reengineering
(b)(6)
February 20, 2002

UNITED KINGDOM – UNITED STATES COOPERATION

KEY MESSAGE:

Exchange of medical research information and collaboration on Gulf War investigations with the UK have been ongoing since June 1995. The two governments have closely monitored each other's research and investigative efforts to avoid duplication and to ensure that neither is surprised by the revelations of the other. In addition, our respective public affairs offices maintain close contact to share items of mutual interest.

FACTS:

- The UK's Gulf Veterans' Illnesses Unit (GVIU) was formally established in 1997 to investigate possible causes of Gulf War veterans' illnesses and serve as a central coordinating body within the UK Ministry of Defence for all treatment, research, and investigative efforts.
- The UK Ministry of Defence has provided a medical officer as liaison on Gulf War Illnesses issues since 1997. The current liaison officer is Captain Surgeon David Brown.
- The Deployment Health Support Directorate (formerly the Office of the Special Assistant for Gulf War Illnesses) has an extensive history of cooperating with the GVIU on investigations related to events of the Gulf War.
  - Our first major collaboration was the Kuwait Girls' School case investigation. The GVIU located records, which could not be found in the United States, and provided access to British subjects who had played critical roles in the event. The case narrative was published as a joint document.
  - The GVIU contributed to our major investigation of possible exposures in Al Jubayl by providing information about British units in proximity to US forces.
  - We assisted the GVIU in telling the Khamisiyah story to their veterans by mapping locations of United Kingdom units relative to the possible hazard areas.
  - The GVIU also coordinated on most of our published Gulf War narratives, and we have on occasion reviewed and commented on their Gulf War papers.
  - We provide a link to the United Kingdom Ministry of Defence's web site via our GulfLINK web site (Related Sites).
- As the only two forces who used depleted uranium during the Gulf War, the US and UK have cooperated in research on the material's effects and in risk communication efforts.
- The UK has also cooperated in locating and sharing records of US and multipartite chemical and biological vulnerability testing in support of Project SHAD declassification efforts.
- The UK has a Military Assessment Programme to evaluate military Gulf War veterans as does the Department of Defense's Comprehensive Clinical Evaluation Program.

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DHSD

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March 18, 2002

GULF WAR ILLNESSES RESEARCH AND MULTIPLE CHEMICAL SENSITIVITY

KEY MESSAGE:

- The Departments of Defense, Veterans Affairs, and Health and Human Services have cooperated on over $200 million of research related to illnesses of Gulf War veterans, including some projects that focused on multiple chemical sensitivity.

FACTS:

- The following table summarizes the allocation of government funds for research into Gulf War illnesses and related topics:

Funding for Research FY'94-'02 in $Millions

Department	FY'94	FY'95	FY'96	FY'97	FY'98	FY'99	FY'00	FY'01	FY'94-'01	FY'02
DoD	$6.5	$11.0	$11.9	$28.9	$13.2	$23.5	$24.8	$22.0	$141.8	$12.0
VA	$1.2	$2.3	$3.9	$2.8	$4.7	$9.0	$12.0	$8.4	$44.3	$3.7
HHS	$0.0	$2.5	$1.6	$0.0	$1.6	$1.6	$1.6	$1.0	$10.0	$0.8
Total	$7.7	$15.8	$17.4	$31.7	$19.5	$34.2	$38.4	$31.4	$196.1	$16.5

- Funded government research related to multiple chemical sensitivity and Gulf War illnesses includes:

HHS-1	$ 3.544M	Health Assessment of Persian Gulf War Veterans from Iowa – Publications 1 and 2
DoD-39	$ 1.173M	A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces – Publications 3 and 4
VA-5	$ 2.927M	East Orange Environmental Hazards Research Center Program – Publications 5 and 6
VA-4	$ 2.829M	Boston Environmental Hazards Research Center Program Publications 7 and 8
VA-48	$ 0.327M	Cross-Sensitization as a CNS Model for Chemical Intolerance
DoD-133	$ 0.884M	(new in 2002)

- For most of these research projects, only a small part of the effort dealt specifically with multiple chemical sensitivity. The last two named projects (VA-48 and DoD-133) are predominantly dedicated to multiple chemical sensitivity.

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November 22, 2002

JOINT PERSONNEL ASSET VISIBILITY (JPAV)

KEY MESSAGE:

The JPAV was intended to be one component of the Joint Total Asset Visibility system providing users with timely and accurate information on the location, movement, status, and identity of units, personnel, equipment, and supplies. However, **this program has been abandoned** as a personnel asset visibility tool in favor of other approaches that eventually will include the Defense Integrated Military Human Resources System (DIMHRS) under development to replace all Service personnel data systems.

FACTS:

- JPAV was intended to operate in a classified environment and integrate with all Service personnel systems including PersTempo interfaces. Its data will would have been archived by the Defense Manpower Data Center.
- JPAV was intended to include data for duty unit location during operations and exercises and will capture the start and end of deployments.
- Military Services would have used existing systems to feed JPAV.
- Demonstration tools were developed for active duty forces but not for the reserve components, civilians, contractors, host nation support, noncombatants, or repatriated POWs.
- Funding for development of implementing software tools ran out at the end of FY 01 and was not renewed.
- Besides DIMHRS, other near-term candidates for adaptation to fulfill personnel asset visibility requirements in lieu of JPAV include the Personnel Tempo system (PERSTEMPO) and the Joint Personnel Status system (JPERSTAT).

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October 23, 2002

BIRTH DEFECTS IN THE OFFSPRING OF DEPLOYED VETERANS

KEY MESSAGE:

Reproductive health is an appropriate and important concern among military personnel and their families, who are mostly people in their childbearing years. Reflecting the importance of this concern, the Department of Defense has instituted a national DoD Birth Defects Registry to track such events in the DoD health care system.

FACTS:

- The Center for Deployment Health Research at the Naval Health Research Center in San Diego, California, manages the Birth Defects Registry.
- The Registry was established in 1998.
- Eight studies have examined the occurrence of birth defects in the children of Gulf War veterans. Six found no difference in the rates of birth defects between offspring of GW veterans and contemporaries who did not deploy to the Gulf. These six used medical records or examinations to identify the defects. The two other studies, which found an increased rate of birth defects in children of gulf War veterans, were based on veterans' self-reports. No medical verification of birth defects was attempted.
- The largest US military study (Cowan, D.N., et. al., "The Risk of Birth Defects Among Children of Persian Gulf War Veterans," *New England Journal of Medicine*, 1997, 336:1650-1656) involved slightly more than 75,000 live births. It found that 7.45% of births to GW veterans and non-deployers were associated with a birth defect and the risk of severe birth defects was 1.85%. There were no statistical differences in the rates of 26 major birth defects. These rates are similar to those reported in civilian populations.

COL O'Donnell
DHSD
(b)(6)
February 22, 2002

CDC CONFERENCE: THE HEALTH IMPACT OF CHEMICAL EXPOSURES DURING THE GULF WAR: A RESEARCH PLANNING CONFERENCE

KEY MESSAGE:

Congress requested that HHS examine the role of chemical exposures in the illnesses being reported by Gulf War veterans. It believed it would be useful to support research in the areas of multiple chemical sensitivity, the definition of individual genetic differences in the ability to metabolize environmental agents commonly encountered during the Gulf War, and the development of a better understanding of how multiple exposures of chemicals interact to exert their toxicity. Congress emphasized the need for treatment trials that use treatment approaches being developed in the public and private sectors for illnesses resulting from chemical and other environmental exposures.

The CDC sponsored the conference from February 28 through March 2, 1999. DoD scientists made presentations at this conference and had the opportunity to meet with other government and non-government scientists, veterans, activists, and media representatives.

A direct result of this conference was the CDC's support for a Memorandum of Agreement with DoD, which made possible the creation of the Medsearch web site.

FACTS:

- The background document on Gulf War research prepared for the conference and the Final Report on the conference are informative documents posted on the CDC web site and referenced on the Medsearch web site.
- Crucial Congressional support for this conference came from members who are strong supporters of the unproven hypothesis called multiple chemical sensitivity (MCS). Numerous well-known advocates for MCS attended or made presentations at the conference.

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Deployment Health Support Directorate

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October 22, 2002

MEDSEARCH

KEY MESSAGE:

In June 2002, the DoD, the CDC, and the Department of Veterans Affairs, launched MEDSEARCH. Veterans and service members can now find information about the federally funded Gulf War medical research at one central web site.

The idea for the on line medical library came as a recommendation from a CDC conference in 1999.

FACTS:

- MEDSEARCH is at: http://www.gulflink.osd.mil/medsearch/.
- A variety of agencies have helped with content on Medsearch by contributing documents. The VA and its Research Working Group have tracked just about all the work done related to Gulf War illnesses. Other contributions and assistance have come from the CDC, the Deployment Health Clinical Center at Walter Reed Army Medical Center, and the Medical Research and Material Command.
- All of the actual research articles have been peer reviewed
- The site also features plain language topics so that a layperson can readily find what he or she is looking for. For example, data on neurological disorders is listed under "Brain and nervous system." There are topics listed that are not available at other medical sources. For example, under environmental and occupational hazards one can find pesticides and depleted uranium, topics that the average HMO may not have much information on, but that Gulf War veterans are keenly interested in.
- To make sure the web site is user friendly and fills the need it was created to fill, the development team has met with groups of people who make up the intended audience for the web site. Four such gatherings made up of veterans, veterans families and active duty explored the web site in its formative stages and offered valuable feedback for improvement.

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Deployment Health Support
(b)(6)
October 21, 2002

OFFICE OF THE SPECIAL ASSISTANT FOR GULF WAR ILLNESSES (OSAGWI) CURRENT MISSION AND STRUCTURE

KEY MESSAGE:

DoD established the Office of the Special Assistant for Gulf War Illnesses (OSAGWI) in November 1996. In April 2001, it became the Office of the Special Assistant for Gulf War Illnesses, Medical Readiness, and Military Support, and in October 2001, it became the Deployment Health Support Directorate (DHSD). This directorate supports the Special Assistant and continues the mission of assisting Gulf War veterans, facilitating force health protection initiatives, and coordinating health-related deployment issues between the ASD(HA) and the military departments. The Directorate is committed to developing and disseminating information in a relevant and timely manner to incorporate lessons from previous deployments.

FACTS:

- The Deputy Secretary of Defense established the Office of the Special Assistant for Gulf War Illnesses on November 12, 1996, with a three-part mission to ensure that:
  - Veterans of the Gulf War received appropriate care,
  - The Department of Defense was doing everything possible to understand and explain Gulf War illnesses,
  - The Department of Defense put into place all required military doctrine, and personnel procedures to ensure our forces are protected in the future.
- On April 5, 2001, the Deputy Secretary of Defense re-designated the office as the Office of the Special Assistant for Gulf War Illnesses, Medical Readiness, and Military Deployments. The appointment of the Acting Assistant Secretary of Defense for Health Affairs as the special assistant integrated the experience and expertise of OSAGWI as a permanent asset to focus on deployment health for all deployments.
- On October 2, 2001, the Under Secretary of Defense (Personnel and Readiness) reorganized support to the special assistant by creating the Deployment Health Support Directorate in the TRICARE Management Activity. Its mission is to:
  - Promote implementation of DoD programs & policy to protect the health of all those involved in deployments.
  - Assess deployments for traditional and non-traditional threats to health and assure rapid integration of force health protection lessons learned.
  - Actively conduct outreach programs to keep servicemembers, their families, veterans, service organization and the American public informed of DoD efforts to protect the health of the force.

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DHSD
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February 20, 2002

VETERANS' DATA MANAGMENT (VDM) TEAM

KEY MESSAGE:

The Veterans Data Management section of the Deployment Health Support Directorate is a phone center created to facilitate trust and communication between Gulf War veterans and the Department of Defense using Customer Relations Management and best business practices.

VDM contact managers provide veterans, family members, and the public with factual information about all deployments, both past and ongoing, on a daily basis. Contact managers, who are veterans themselves, provide a host of information about a variety of topics related to veteran and deployment issues.

FACTS:

- VDM was created in December 1996 in response to veterans' concerns about illnesses believed to be caused by their Gulf War service.
- VDM contact managers were a focal point for the Gulf War illnesses investigations, obtaining first hand information and documentation from Gulf War veterans. The process involved veterans in a significant and meaningful way and established for the Gulf War veteran a single point of contact with our office.
- Since 1996, contact managers have communicated with more than 17,000 veterans, family members, and the public addressing their concerns and issues. Today, many individuals continue to speak to contact managers on a periodic basis.
- In 2000, contact managers began to answer questions and concerns from veterans, family members, and the public about past and current deployment health issues.
- Contact managers act as a conduit for the individual and other federal and private organizations (e.g., the Department of Veterans Affairs, the American Legion, etc.) where veterans, family members, and the public can receive the assistance.
- The staff is available 12 hours each workday from 9:00 a.m. to 9:00 p.m. In the event of significant veteran or public interest, these hours may be expanded.

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February 20, 2002

DEPLOYMENT HEALTH SUPPORT DIRECTORATE
OUTREACH TO SERVICEMEMBERS, VETERANS, AND THEIR FAMILIES

KEY MESSAGE:

DoD is working to ensure veterans of the Gulf War have access to appropriate care. It is doing everything possible to understand and explain Gulf War illnesses and is informing the veterans and the public of progress and findings through outreach efforts. In addition, DoD is putting into place all required military doctrine, personnel and medical policies and procedures to minimize any future problem from exposure to biological and chemical agents and other environmental hazards.

FACTS:

- An outreach program was developed, using a multi-media approach, that included displays, briefings, Internet demonstrations, brochures and other handout materials to provide accurate information, dispel rumors, and educate the public on health and force protection issues resulting from the Gulf War.

- In its first year, the outreach program conducted in conjunction with the American Legion and Veterans of Foreign Wars veteran's service organizations. Using public forums – "town hall meetings" – outreaches were conducted in 13 major metropolitan areas.

- To ensure that the active duty, National Guard, Reserves, military health care providers, and family members received information on Gulf War issues, total force outreach programs were conducted at 96 military installations and their surrounding communities worldwide. Additionally, briefing teams provided exhibits at 81 conferences hosted by veterans, service, military support, and health organization associations.

- Since outreach began in 1997, these programs provided the opportunity to reach out to more than 70 thousand active duty military personnel, reserve component members, veterans, family members, military health care providers, and the general public.

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February 20, 2002

NATIONAL SURVEILLANCE FOR BIRTH DEFECTS AMONG DEPARTMENT OF DEFESE HEALTH CARE BENEFICIARIES POLICY

KEY MESSAGE:

Appointed Naval Health Research Center, San Diego, to conduct surveillance for major birth defects among DoD beneficiary infants born in both military and civilian medical facilities and provide incidence rates of newly diagnosed cases for births and fetal demises. This will be accomplished by establishing surveillance for birth defects among DoD health care beneficiaries through a scientifically sound, cost-effective hybrid birth defects registry.

FACTS:

- Based on lessons learned following the Gulf War, the DoD implemented a number of policy changes designed to improve the delivery of health care to active duty personnel. Using the Force Health Protection (FHP) strategy, the overarching goal is to protect the health of military members from medical and environmental hazards associated with military service to the maximum extent possible.

- FHP is an evolving strategy that seeks to balance the Military Health System's responsibilities to promote and sustain health and wellness throughout each person's military service; prevent acute and chronic illnesses and injuries during training and deployment; rapidly stabilize, treat, and evacuate casualties; effectively evaluate and treat deployment related concerns upon return from deployment.

- ASD Health Affairs Policy, November 17, 1998

- www.ha.osd.mil/policies/1999/clin9906.htm

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February 20, 2002

#2003013-000012

(66)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

January 23, 2003, 3:15 PM

FOR: Ellen P. Embrey, DASD, Force Health Protection and Readiness

FROM: COL Terry Rauch, EO, DASD(HA)FHP&R

SUBJECT: Investigational New Drugs (IND) for Force Health Protection

- TAB B is a draft letter to the Commissioner, FDA regarding IND for force health protection.
- TAB C is a letter to the ASD(HA) from the Commissioner, FDA, December 13, 2002.
- TAB D is a letter from the ASD(HA) to the Commission, FDA, November 20, 2002.

RECOMMENDATION: Sign the memo at TAB A.

COORDINATION: TAB E

Prepared by: (b)(6) FHP/R Program Director, Health Science Policy,
(b)(6) PCDOCS# 44537/R 45241

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

JAN 2 8 2003

HEALTH AFFAIRS

MEMORANDUM FOR ~~DEPUTY~~ ASSISTANT TO THE SECRETARY OF DEFENSE (CHEMICAL & BIOLOGICAL DEFENSE)

SUBJECT: Interface with the FDA for Use of Particular IND Products

Dr. Winkenwerder spoke to the Commissioner of the Food and Drug Administration (FDA) and subsequently wrote him a letter on November 20, 2002 (attached). The purpose was to thank the FDA for their efforts since September 11, 2001, to approve drugs and vaccines needed for treatment or prophylaxis of bioterrorism threats and to note that there were several issues that impact our ability for formulate deployment plans for Investigational New Drug (IND) medical products. Specifically, those issues regarding pyridostigmine bromide, botulinum pentavalent toxoid vaccine, and label concerns regarding Anthrax Vaccine Adsorbed (AVA) post exposure with antibiotics and Cidofovir for treatment of smallpox.

The Commissioner of the FDA sent a letter of response dated December 13, 2002 (attached), regarding the use of IND for prophylaxis or treatment to maximize military force health protection capabilities as the war on terrorism and potential new contingencies progress.

Dr. Winkenwerder is sending a response back to the FDA noting that DoD remains eager to work with the FDA to resolve some remaining concerns. Specifically:

a. Pyridostigmine bromide (PB): On January 6, 2003, DoD submitted a New Drug Application (NDA) for PB. Approval of the NDA would eliminate DoD concerns for use of PB under the IND. We await word from FDA Center for Drug Evaluation and Research (CDER) on the approval of the PB NDA.

b. Botulinum pentavalent (BT) toxoid vaccine: We must find a means to provide a limited amount of BT to special units. We are reviewing any other potentially feasible options to address the threat of botulinum toxin. We asked the FDA to continue their stated commitment to work with us to find a resolution to this critically important issue. If this is not a safety issue, can there be a label change or a revision of the informed consent form to allow those who consent to have access to this potentially life saving product?

c. Anthrax vaccine and Cidofovir: FDA replied suggesting that we consider submitting a waiver request with appropriate justification. We agree. We must make such a submission for both of these INDs.

The purpose of this memorandum is to ask you to task the Program Executive Officer for Bio Defense to work with the FDA and USA Medical Research and Materiel Command in an expeditious manner to get approval to use BT in a limited manner for some troops and to provide the required request for waiver for the AVA Post Exposure IND label requirement and the Cidofovir IND label requirement for treatment of smallpox.

My POC is Colonel Terry **Rauch,** who may be reached at (b)(6), **email:** (b)(6)**@ha.osd.mil.** Thank you in advance for your willingness to see rapid resolution of these matters.

Sincerely,

Ellen Embrey
Deputy Assistant Secretary of Defense
Force Health Protection and Readiness

Attachments:
As stated

THE ASSISTANT SECRETARY OF DEFENSE

1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

Mark B. McClellan, M.D., Ph.D.
Commissioner of Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. McClellan:

This is a follow-up to your letter of December 13, 2002, regarding the use of investigational new drugs (INDs) for prophylaxis or treatment to maximize military force health protection capabilities as the war on terrorism and potential new contingencies progress. Thank you and the staff of the Food and Drug Administration (FDA) for your quick response to my letter of November 20, 2002.

DoD remains eager to accelerate approval of several high priority new drug applications which could be required for use in a contingency. Again, first among these is the approval of pyridostigmine bromide as a nerve agent pre-treatment against soman and tabun. Second is the approval of Anthrax Vaccine Absorbed (AVA) as a post-exposure treatment with antibiotics. These continue to be are our high priority concerns.

Unresolved issues remain that currently impact our ability to formulate deployment plans for the following JND medical products in priority order: Pyridostigmine Bromide; Botulinum Pentavalent Toxoid Vaccine; Anthrax vaccine for post-exposure treatment, and Cidofovir as a post exposure treatment for smallpox. Let me discuss the status of these and other issues since your letter. Specifically:

a. Pyridostigmine bromide: An amendedIND protocol was submitted to the FDA on January 6, 2003. This IND protocol included the informed consent language worked out between DoD and HHS/FDA. However, as you know, the execution of an IND protocol during active military operations is highly problematic. Also, on January 6, 2003, DoD submitted a new drug application (NDA) for PB. Approval of the NDA would eliminate DoD concerns for use of PB under the IND, and is extremely important. We await word from FDA on the approval of the PB NDA.

b. Botulinum pentavalent toxoid vaccine (BT): DoD submitted the additional potency assay data in December, 2002. At a meeting between DoD and FDA on December 18, 2002, FDA noted that this product is on "voluntary clinical hold." FDA stated the potency data show the product is unusable, and reminded the DoD that the protocol remains on voluntary clinical hold, absent additional supporting data. We must find a means to provide a limited amount of BT to special units. We are reviewing any other potentially feasible options to address the threat of botulinum toxin. We ask that you continue your stated commitment to work with us to find a resolution to this critically important issue.

c. Anthrax vaccine and Cidofovir: Both products are currently licensed for other indications; however, DoD will be using them under IND for unapproved indications (postexposure prophylaxis of anthrax, and smallpox infection, respectively). We requested a simplified process for re-labeling of the vials in which we would overlabel the vials with an "IND use only" sticker or a waiver of this requirement. Your reply suggests that we consider submitting a waiver request, with appropriate justification. We agree. We will make such a submission for both of these INDs.

I have asked Colonel Terry Rauch of my office to act as the responsible official to accept your offer of assistance in coordinating DoD-FDA interactions. Colonel Rauch can be reached at (b)(6), (b)(6) @ha.osd.mil. Thank you for your efforts to effect rapid resolution of these matters.

Sincerely,

William Winkenwerder Jr., MD

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

December 13, 2002

William Wmkenwerder, Jr, M D.
Assistant Secretary of Defense, Health Affairs
Washington, D C 20301-1200

Dear Dr Wmkenwerder

Thank you for your November 20 letter concermng use of products under IND for prophylaxis or treatment m the military setting and for your kind words on FDA's efforts since September 11, 2001. I agree that it is valuable for both our agencies to put DoD priorities in writing I will address each of your issues m order as presented m your letter

(a) Pyridostigmine bromide FDA continues to have concerns about DoD's proposed method of informed consent for the pyridostigmine bromide trial FDA and HI-IS legal counsel remain committed to workmg with DoD's counsel to fashion a legally supportable solution in a timely manner

(b) Pentavalent botulinum toxoid (PBT) vaccme FDA is m receipt of the October 22, 2002, submission by DoD to IND 3723, containing lot release information for PBT vaccine lots PBT 003 and PBT 004 This information was submitted pursuant to FDA's Center for Biologics Evaluation and Research (CBER) request in telephone conversations with DoD representatives on February 14, 2002, and October 10, 2002

For PBT lot 003, summary potency data for serotypes A, C, and E were reported as inconclusive, while the results for serotypes B and D were found to be below specifications. Serotypes D and E failed the resistance to challenge test For PBT lot 004, summary potency data for serotypes A, B, C, and E were reported as mconclustve, while the results for serotype D were reported to be below specifications In the resistance to challenge assay, serotypes B, D, and E were reported to be below specifications

Further, mtenm clmical immunogenicity data submitted to IND 3723 on April 16, 2001, have raised concerns about the ability of PBT lots 003 and 004 to induce a persistent antibody response m subjects immunized with this product

FDA is concerned that military personnel may no longer be adequately protected from *C botulinum* toxins through administration of PBT because of rapidly decreasing clinical antibody titers and potency data that are either below specifications or have inconclusive results for all 5 serotypes In order to fully assess whether immunization with current lots of PBT may offer protective benefit under a military contmgency, we have requested

from DoD representatives the details of the potency assay data, including assay procedures and investigation reports, and the clinical immunogenicity data derived from the use of these lots Once CBER has the opportunity to review these data, this should allow an assessment of whether it is acceptable to relabel the remaining vials of PBT vaccine and/or to change the consent form to reflect a trivalent vaccine We are committed to working with you to make this important assessment

(c) Anthrax vaccine and Cidofovir Investigational products should be labeled as described in 21 CFR 312 6 Alternatively, a sponsor may request that FDA waive applicable requirements set forth in the IND regulations, including labeling for an investigational new drug (21 CFR 3 12 10) A waiver request must contain certain information described in 21 CFR 312 10 Please note that if FDA were to grant such a waver with respect to the labeling of a product to be used for investigational purposes but that remains labeled for its licensed use, FDA would be prepared, in this particular instance, to exercise its discretion and not object to the product's shipment for investigational use The Agency would be prepared to do so if DoD provides adequate information to end-users and to subjects concerning the investigational status and use of the product in question In addition, an adequate procedure for recording the disposition of the product would need to be in place, m accordance with 21 CFR 3 12 62(a)

FDA can work with, and provide guidance to, DoD on this matter Please also note that if DoD does "over-label" either anthrax vaccine or cidofovir for investigational use, DoD may not be able to change the labeling back to that representing either product's approved use unless FDA approves a supplement for additional relabeling

Lastly, I would mention that FDA's Office of Counterterrorism (OCT) in the Office of the Commissioner, specifically Dr (b)(6) email (b)(6) @oc fda gov), can serve as an FDA point of contact for your office and help coordinate FDA actions on DoD inquiries Colonel Rauch should feel free to contact her at any time (b)(6) also has a DoD liaison officer, (b)(6) (b)(6), Ph D , currently detailed to OCT. who can assist m these DoD priority issues Matters relating to specific product applications, such as INDs/IDEs, NDAs, or BLAs, should be discussed with the appropnate FDA Center

We look forward to working with you and your staff to resoive these issues and maximize health protection for our military forces

Sincerely,

Mark B McClellan, M D , Ph D
Commissioner of Food and Drugs

FORCE HEALTH PROTECTION & READINESS
DEPLOYMENT HEALTH SUPPORT DIRECTORATE

CMAT #: 3013-02
PCDOCS# 44537
Date: 1-13-03

Action Tasking // Internal Routing Sheet

		Action	Info	Comments
	ASD (HA)/Special Assistant			
	Director FHP/R & DHSD (DIR)			
	FHP/R ACTION OFFICE (b)(6) (Lead)	X		
	(Assist)			
	Deputy Director DHS (DEP)			
	DHS ACTION OFFICE _____ (Lead)			
	_____ (Assist)			
	DHS Operations Support Office (OSO)			
	DHS Editorial Review (ER)			
	☐ COMEBACK COPY TO _____ DHS AMB ☐ GET CMAT # WHEN SIGNED ☐ CHRON ALE			

SUSPENSE: ~~1-15-03~~ 1-16-03

Prepare reply for signature of:
☐ Director
☐ _____

Hot

Comments:

Products Under IND for Prophylaxis or Treatment - SEE ASD (HA) note

☐ Congress	☐ Oversight	☐ FOIA	☐ OSD	☐ WBM	☐ VSO/MSO	☐ Outgoing
☒ Ltr to ASD HA	☐ IR	☐ E-Mail	☐ OGA	☐ Other	☐ PCDOCS	☐ Veteran

KEYWORDS: FDA

CMAT Control #
2003013-0000012

HA/TMA Document Profile

44537

Subject: Products Under IND for Prophylaxis or Treatment

Author: (b)(6) M.D., Ph.D.
Date of Document: 12/13/2002
OSD # :
PR # :
Organization: Department of Health and Human
Department:
Assigned To: DHS
Prepared For: ASD
Suspense Date: 1/16/2003
Coord Office(s):

Congressional Name:
Input By: (b)(6)
Profiler's Directorate: Admin, HA
Response Signed By:
Dt Response Signed:
Doc Type: LETTER
Application: DOCSIMAGE
Previous Documents:
Related Documents:

Notes: SHORT SUSPENSE. REMARKS FROM DR. WINKENWERDER ATTACHED.

Beneficiary Info
Beneficiary Name:
Address 1:
Apartment #
Phone #
Email Address:
city:
State: **Zip:**

History
Created: 1/7/2003 HA PCDOCS Adr
Edited: 1/7/2003 HA PCDOCS Adr
Status: Available

Retention Schedule
Type: Archive
Retention Days: 365

☐ **From External Source?**

Access Control
☒ Secure Document
☐ **Enable** Content Searching

44537

To: Ms. Embrey's office 6 Jan 03

For evaluation and action, based upon response of FDA. I would like our action plan, based on this letter, within 8 business days.

Bill

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 203014200

HEALTH AFFAIRS

NOV 20 2002

Mark B. McClellan, M.D., Ph.D.
Commissioner of Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. McClellan: Mark

This is a follow-up to our phone conversation on November 18.2002, regarding the use of investigational new drugs (IND) for prophylaxis or treatment to maximize military force health protection capabilities as the war on terrorism and potential new contingencies progress.

First, let me thank you and the staff of the Food and Drug Administration (FDA) far the efforts since September 11.2001, to approve drugs and vaccines needed for treatment or prophylaxis of biotarorism threats. FDA's approval of BioPort's Biologics License Application Supplement has been instrumental in assuring the provision of vaccine necessary for the protection of our forces against tbis threat. Moreover, the licensing of the vaccinia vaccine (Dryvax) was of immense importance to DoD, as was the approval of doxycyclii and penicillin for post exposure treatment of inhalation anthrax. We have a strong relationship on which to build for the future.

DoD is eager to accelerate approval of several high priority new drug applications which could be required for use in a contingency. First among these is the approval of pyridostigmine bromide as a nerve agent pre-treatment against soman and tabun. Second is the approval of Anthrax Vaccine Absorbed (AVA) as a post-exposure treatment with antibiotics. These are our hi& priori@ concerns.

There are several unresolved issues that currently impact our ability to foimuiste deployment plans for the following IND medical products in priority order: Pyridostigmine Bromide; Botulinum Pentavalent Toxoid Vaccine; Anthrax vaccine for post-exposure treatment, and Cidofovir as a post exposure treatment for smallpox. Specifically:

a. rPyridostigmine bromide: A new protocol has been submitted to the FDA. Although it has not been placed on clinical hold, the FDA has expressed issues with the proposed method of informed consent. The informed consent issue is currently being discussed between DoD legal counsel and Health and Human Services legal counsel. This discussion hss been ongoing for the past month and must be resolved to finalize the plans for fielding the drug.

b. Botulinum pentavalent toxoid vaccine: Two of the five subtypes (D and E) have recently failed potency testing. The issue that requires your assistance is whether it will be necessary to relabel the remaining vials and change the informed consent form to reflect a trivalent vaccine.

c. Anthrax vaccine and Cidofovir: Both products are currently licensed, however, DoD will be using them under IND for unapproved indications (postexposure prophylaxis of Anthrax, and Smallpox infection, respectively). We request you consider a simplified process for re-labeling of the vials in which we would overlabel the vials with an "IND use only" sticker or a waiver of this requirement.

I wanted to document a clear understanding of the priorities of the Department in achieving results needed by our country in the months ahead. My office stands ready to convene an interagency meeting with appropriate representatives from the FDA to facilitate effective resolutions to these issues. My point of contact is Colonel Terry Rauch, who may be reached at (b)(6) email (b)(6) @ha.osd.mil. I look forward to our work together. Thank you in advance for your willingness to see rapid resolution of these matters.

Sincerely.

Bill

William Winkenwerder, Jr.. MD

(b)(6) CON, OASD(HA)/TMA" <(b)(6) @tma.osd.mil> on 11/20/2002 01:30:40 PM

To: (b)(6) @OSAGWI
cc: (b)(6) /TMA" <(b)(6) @tma.osd.mil>

Subject: IND Pkg

Hi Ed,
Just FYI. Dr. Winkenwerder signed the IND package today. I faxed to the FDA and mailed out the original as well. I am sending comeback copy to you through DMD/Sky5. The signed document is scanned in PCDOCS at 43160. Have a great day!

(b)(6)
Document Management Division
Phone: (b)(6)
Fax:

SUBJECT: Investigational New Drugs for Force Health Protection

COORDINATIONS

USAMMDA	COL Jeffrey Gere	1/23/03 Recommends coord with DATSD(CBD)
DATSD(CBD)	LTC (b)(6)	Concur 1/23/03 with changes
DoD, OGC	Mr. (b)(6)	Concur 1/23/03
XO, DASD(FHP&R)	COL Rauch	_____
Bucket Supervisor	Col Cunningham	_____

(b)(6) **CIV, OASD/HA**

From: (b)(6), Mr, DoD OGC
Sent: Friday, January 17, 2003 9:11 AM
To: (b)(6), CIV, OASD/HA
Subject: RE: DRAFT Memo to DATSD(CBD) re FDA ltr on INDs

O.K. with me. -- JC

-----Original Message-----
From: (b)(6), CIV, OASD/HA
Sent: Thursday, January 16, 2003 2:45 PM
To: (b)(6)
Subject: DRAFT Memo to DATSD(CBD) re FDA ltr on INDs

Attached is my first draft of the requested memo to DR. Winegar concerning a tasking to work with FDA for BT IND approval and to provide a waiver for label for AVA Post Exposure and for label for Cidofovir. Sal

<< File: FDA Embrey to Winegar IND Jan 16 03.doc >>

(b)(6)
Program Director, Health Science Policy
Office of the Assistant Secretary of Defense
(Health Affairs) Force Health Protection & Readiness
Washington, DC 20301-1200
Phone (b)(6)
FAX

(b)(6) CIV, OASD/HA

From: (b)(6) LTC, OSD-ATL
Sent: Thursday, January 23, 2003 12:16 PM
To: (b)(6)
cc:
Subject: RE: Interface with FDA for Use of Particular IND Products Draft Memo

Sal:

First off, neither of us attended the bot meeting yesterday, so I'm not sure whether this memo is OBE or not. Maybe COL Rauch could clue us in. Having said that, the issues are still being worked irregardless of the memo.

Assuming the memo is still needed, here are some further comments:

Acronyms should be spelled out the first time used.

Dr. Winegar will task the PEO - but added that they need to collaborate with/work with MRMC to develop the BT data.

Dr. Winegar believes that MRMC should have the lead on the INDs, unless we come up with a compelling reason for someone else to have the lead.

In regards to reviewing the INDs – Dr. Winegar stated that it's MRMC for the IRB level, and then the Army SG for the HSRRB. Dr. Winegar's comments: adding these steps makes it clear that cooperation is needed and that it won't happen overnight!

Bob

Lieutenant Colonel (b)(6)
phone: (b)(6)
e-mail (b)(6)@osd.mil

-----Original Message-----
From: (b)(6) CIV, OASD/HA
Sent: Wednesday, January 22, 2003 5:52 PM
To: (b)(6)
Cc:
(b)(6)
Subject: RE: Interface with FDA for Use of Particular IND Products Draft Memo

LTC (b)(6) Thanks for the returned on my call. Attached is a revised draft based on our conversation. Is this OK. Please review and comment. (b)(6)

<< File: FDA Embrey to Winegar IND Jan 23 03.doc >>

-----Original Message-----
From: (b)(6) CIV, OASD/HA
Sent: Friday, January 17, 2003 5:23 PM
To: (b)(6)
Cc:
Subject: Interface with FDA for Use of Particular IND Products Draft Memo

Dr. Winegar: Attached is a draft memo to you from Ms. Embrey. Can you have your staff review and comment before it gets signed and sent. Thanks. VR Sal Cirone

<< File: FDA Embrey to Winegar IND Jan 16 03.doc >>

(b)(6)
Program Director, Health Science Policy
Office of the Assistant Secretary of Defense
(Health Affairs) Force Health Protection & Readiness
Washington, DC 20301-1200
Phone: (b)(6)
FAX:

(b)(6) **CIV, OASD/HA**

From: (b)(6) @DET.AMEDD.ARMY.MIL]
Sent: Friday, January 17, 2003 12:06 PM
To: (b)(6)
cc:
Subject: RE: DRAFT Memo to DATSD(CBD) re FDA ltr on INDs

Sal, I dont have anything specific re: the memo. I would suggest you coordinate with AJW prior to sending it. I suspect that she will turn to JPO/CBMS, and that their response will be that they do not have AVA or cidofovir in their developmental programs so therefore do not have any responsibility for them. They might be willing to help on the bot toxoid; Im not a vaccinologist but Im not sure what else can be done right now. The statement in the letter says "we must find a means to provide a limited amount of BT to special units". When we briefed AJW a few weeks ago, we told her that 1) bot toxoid is dead in the water and is not available for the current operation in SWA, and 2) that even if it were to be made available, it is already too late. The dosing regimen requires doses at 0, 2 and 12 weeks. It is generally recognized that antibody levels are not sufficient for protection until after the third dose. So even if we started tomorrow we could not have people fully immunized until mid April. I am not sure this fact is clear to Dr. Winkenwerder. Maybe you should make sure he understands that before he decides to fall on his sword over this. Jeff

-----Original Message-----
From: (b)(6) @ha.osd.mil]
Sent: Friday, January 17, 2003 11:29 AM
To: (b)(6)
Cc:
Subject: FW: DRAFT Memo to DATSD(CBD) re FDA ltr on INDs

Jeff: Attached is a draft memo to Dr. AJW. Re INDs. Can you review and comment? I cant get these to COL Davies -- the system keeps rejecting his address. Can you forward for his comment/concurrence? Thanks. Sal Cirone

-----Original Message-----
From: (b)(6) CN, OASD/HA
Sent: Thursday, January 16, 2003 2:45 PM
To: (b)(6)
Subject: DRAFT Memo to DATSD(CBD) re FDA ltr on INDs

Attached is my first draft of the requested memo to DR. Winegar concerning a tasking to work with FDA for BT IND approval and to provide a waiver for label for AVA Post Exposure and for label for Cidofovir. Sal

<<FDA Embrey to Winegar IND Jan 16 03.doc>>

(b)(6)
Program Director, Health Science Policy
Office of the Assistant Secretary of Defense
(Health Affairs) Force Health Protection & Readiness
Washington, DC 20301-1200
Phone: (b)(6)
FAX:

#20030130000012

(b)(6) **CIV, OASD/HA**

From: (b)(6) @DET.AMEDD.ARMY.MIL]
Sent: Thursday, January 16, 2003 2:50 PM
To: (b)(6)
Cc:
Subject: RE: FDA ltr re-write

my suggestion is red = add "informed consent" to page 1, para 4, sentence 2.
Accepted! CHANGE MADE 01/16/03 Cme

-----Original Message-----
From: (b)(6) @ha.osd.mil]
Sent: Thursday, January 16, 2003 1:41 PM
To: (b)(6)
Cc: (b)(6)
Subject: FW: FDA ltr re-write

COL Gere and COL Davies: Attached below is a draft memo from Dr. Winkenwerder to the Commissioner of the FDA. COL Gere, LTC (b)(6) and Dr. (b)(helped in the initial draft --- however -- there have been changes made by my supervisors. This draft letter makes COL Rauch the POC vice MG Martinez-Lopez because the front office wanted to keep the POC within HA. It also changes the Bot Tox paragraph because the front office wants to pursue a path or plan to get some type of BT approval for a limited number of Servicemembers, similar to giving it to lab workers who might be in need of protection. It is my understanding that HA received a brief on this last week and COL Burnette indicated that there were other possibilities -- although not very optimistic -- with lots 5&6 . In that regard I have been asked to draft a memo to the DATSD(CBD) to request that she task the appropriate organizations to work to FDA to find a solution to this issue. Also the paragraph on the AVA Post Exposure IND and the Cidofovir IND has been changed to reflect the FDA suggestion for a waiver. The memo to the DATSD(CBD) will also request that she task the appropriate organization to prepare and submit the IND waivers to FDA. Finally I have been asked to draft a memo to OTSG Army to develop a plan for Rx only since the PB may be licensed and require prescription use only.

I would like your concurrence on the letter below to the FDA. My suspense is today.

-----Original Message-----
From: (b)(6) CIV, OASD/HA
Sent: Thursday, January 16, 2003 1:07 PM
To: (b)(6)
Cc:
Subject: FW: FDA ltr re-write

Terry: This is the copy which I will make final. I changed the last paragraph to appoint you as POC as Dr. Winkenwerder asked for the first letter. I will draft a memo from Ms Embrey to Dr. Winegar to ask her to task MRMC to work with the FDA on both the Bot Tox and the waivers. I will draft a memo from Ms. Embrey to OTSG Army to quickly develop a plan for RX only use of Nerve Agent Pretreatments and Antidotes. Sal

<<FDA Winkenwerder IND Jan 16 03.doc>>

-----Original Message-----

From: (b)(6)

Sent: Thursday, January 16, 2003 10:27 AM

To: (b)(6)

Cc:

Subject: FDA ltr re-write

Terry: Attached is a re-write with Mr. Casciotti's changes. I have added a few sentences to the BT paragraph to include Ms. Embrey's concern. Can both of you review what I have and comment? When I get something close to final, I would like to send it back to MRMC for their information. I'll also include COL Neal Burnette since he is the one who will have to work with USAMRMC on the lots five and six to see what we can do. Sal

<< File: FDA Winkenwerder IND Jan 16 03.doc >>

(b)(6)

Program Director, Health Science Policy

Office of the Assistant Secretary of Defense

(Health Affairs) Force Health Protection & Readiness

Washington, DC 20301-1200

Phone: (b)(6)

FAX:

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON. DC 20301-I 200

HEALTH AFFAIRS

ACTION MEMO

January 3, 2003 2:45 PM

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ms. Ellen P. Embrey, DASD (Force Health Protection and Readiness)
//s// 1-6-03

SUBJECT: Representative Oxley's Inquiry for Information on the Anthrax Vaccine Immunization Program

- Representative Oxley requested we provide a response to one of his constituents, (b)(6) regarding the Anthrax Vaccine Immunization Program (AVTP)(TAB B). As a concerned citizen, (b)(6) has numerous concerns regarding our servicemembers and the AVIP.

- The proposed response explains AVIP policy that addresses her concerns.

RECOMMENDATION: That the ASD (HA) sign the letter at TAB A.

COORDINATION: TAB C

Prepared by: COL Randolph, Dir, AVTP, (b)(6), PCDOCS # 44427/R44440

(b)(6)

From: writerep
Sent: Friday, October 25.2002 1.12 PM
TO: OH04WYR
Subject: WriteRep Responses

DATE October 25, 2002 11 51 AM
NAME.
ADDR1.
ADDR2.
ADDR3
CITY
STATE
ZIP:
PHONE:
EMAIL.
msg:
(b)(6)

DOD Leg Affairs
~~703-697-6210~~
Jane Anderson
(b)(6)
fax
(b)(6)
Dr. W. Kerkvliet
WW

Dear Congressman Oxley,

I am writing as a concerned citizen I am urging you to investigate and help stop the mandatory Anthrax Vaccine Immunization Program (AVIP) of our service men and women. Anthrax vaccine is unsafe, untested, unnecessary, unpopular, unethical, and not totally effective. *Early* symptoms following the first or second shot that have been reported in high numbers include headaches, malaise, respiratory distress, chills, diarrhea, fever, and abdominal cramping. Later chronic symptoms reported often after the third or fourth shot have included dizziness, chronic fatigue, chest pains, sleep disorders, memory loss, headaches, joint and muscle pain, peripheral sensory neuropathies, recurring rashes, blackouts, autoimmune diseases, swelling of limbs, collagen vascular disease, sepsis, cardiomyopathy, nausea, night sweats, cysts, tunnel vision, and seizures This information *can be* found at the CDC website www cdc gov/mmwr/preview/mmwrhtml/rr4915a1.htm and in the book "Anthrax. A Deadly Shot In The Dark" by Thomas S Haematxa Six people have died following anthrax immunization. Our service men and women make great sacrifices of time and sometimes their lives to defend our great nation, but they should not have to sacrifice their health because of this *unsafe* vaccine or risk court-martial if they refuse it Civilians are given a choice concerning this vaccine and So should our sevice men and women be given that same choice. Further research needs to be done to find a safe and effective anthrax vaccine

Sincerely,
(b)(6)

MICHAEL G OXLEY
COMMITTEE ON
FINANCIAL SERVICES

Congress of the United States

House of Representatives

Washington, DC 20515-5501

Faxed from the Office of

Congressman Michael G. Oxley

Fourth Ohio District

To: Dr. William Winkenwerder

From: ☐ Michael G Oxley ☐ Tim Johnson ☐ Dirk Bartlett
☐ Jim Conzelman ☒ Peter Erdman ☐ Jen Mundy
☐ Debi Deimling ☐ Jared Dilley ☐ _____

Date 12 / 10 / 2002 Pages (including cover). 2

Subject: AVIP problem

Comments:

Any help in response to this constituent's concern would be appreciated.

Thanks

SUBJECT: Representative Oxley's Inquiry for Information on the Anthrax Vaccine Immunization Program

COORDINATIONS

Dir, PI (HA)	LTC (b)(6)	Concur 1/3/03
CoS, HA	Ms. (b)(6)	_____
PDASD (HA)	Mr.	_____

TRICARE

TRICARE Management Activity

DOCUMENT MANAGEMENT DIVISION
ADMIN OFFICE

ACTION OFFICE FHP+R DATE 1/10/03 PCDOCS # 44427

The attached correspondence is returned for the following reason(s):

- [x] Distribution
- [ ] Coordination
- [ ] Revision
- [ ] Correct Signature Block
- [ ] Correct Envelope Size
- [ ] Correct Letterhead
- [ ] Provide Original/Supporting Documents
- [ ] Provide SD 391
- [x] Retain for your Files

Additional Comments:

Signed letter scanned. Orig returned for dist and copy for file.

Def

Health Affairs

ROUTING AND TRANSMITTAL SHEET

TRICARE Management Activity

	Sign	Coord		Sign	Coord
____ ASD, HA	✓		____ Dir, TMA		
____ PDASD, HA					
____ DASD, C&PP			____ CMO		
____ DASD, FHP&R			____ Dir, DHS		
____ DASD, HB&FP			____ CFO		
____ DASD, HPA			____ COO		
			____ Dir, TRICARE Operations		
____ CIO, MHS			____ Dir, IMT&R		
____ OGC, DoD			____ OGC, TMA		
____ LA					
____ CoS, HA		✓	____ Dir, A&M		
____ Military Assistant			____ CoS, TMA		
1/3/03 Dir, PI, HA		✓	____ Dir, PI, TMA		
____ Dir, P&S			____ Dir, Admin		
____ Other (Specify)			____ Other (Specify)		

DMD (SKY) ____ Date: ____ **DMD (PNT)** A Date: 1/7/03

late Received: 1703 **Suspense Date:** 1/7/03

Subject: AVIP Problem

PCDOCS #: 144277R44440 **OSD/P&R #:** NA

AO: Col Randolph **Office:** FMR **Phone #:** (b)(6)

VOTES:

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

JAN - 9 2003

(b)(6)

Dear (b)(6)

Thank you for your e-mail concerning the Anthrax Vaccine Immunization Program (AVIP). I share your concern for our servicemembers. Preserving their health and safety is our number one concern. The Department of Defense (DoD) requires anthrax vaccination for certain servicemembers as an added layer of protection against this potentially deadly biological agent.

The threat of biological warfare has been a risk to U.S. forces for many years. The DoD analysts maintain updated threat-level evaluations, adjusting the information as necessary to reflect the risk to U.S. operations. Based on assessment of current and past activities in such areas as Iraq and the former Soviet Union, the potential offensive biological threat facing servicemembers makes it necessary for the DoD to have a robust biological defense program today. Anthrax is one of the deadliest biological weapons of choice.

As with other vaccines, the benefits of the U.S. Food and Drug Administration (FDA) licensed anthrax vaccine far outweigh any risk. The Centers for Disease Control and Prevention (CDC) states that receiving the vaccination is much safer than getting the diseases the vaccines prevent. Biological agents such as anthrax are especially hard to detect because symptoms are delayed. Without preventive medical efforts such as vaccination, the results can be devastating and widespread.

Medical experts agree, there have been no deaths from anthrax vaccine reported among more than 2.2 million immunizations given to over 567,000 Service men and women since the AVIP began in March 1998. Further, no deaths have been attributed in a cause-and-effect manner to the vaccine since the FDA licensed it over 30 years ago.

Many studies establish anthrax vaccine safety. From a 19.58 study published in the *Bulletin of the John Hopkins Hospital,* to more recent studies at Fort Detrick, Maryland, evidence shows there are no long-term side effects to the anthrax vaccine. In 2002, the National Academy of Sciences, Institute of Medicine (IOM) Committee to Assess the Safety and Efficacy of the Anthrax Vaccine, concluded their two-year study. In their published findings, the Committee found no evidence that people face an increased risk of experiencing life-threatening or permanently disabling adverse events immediately after receiving AVA, when compared with the general population.

Nor did it find any convincing evidence that people face elevated risk of developing adverse health effects over the long term, although data are limited in this regard (as they are for all vaccines).*

The IOM Committee studied data on anthrax-vaccine effectiveness and concluded "that the available evidence from studies with humans and animals, coupled with reasonable assumptions of analogy, show that AVA as licensed is an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by any known plausible engineered strains of B anthracis."*

The DoD continually strives for improved vaccines and improved vaccination programs to protect the health of our forces. The DoD is currently collaborating with the CDC in their study to determine different ways to administer the current anthrax vaccine. This study may lead to the FDA's allowing its use in fewer doses and administering it in a way that may reduce bothersome local injection-site redness, pain, swelling and itching. Additionally, the DoD is partnering with the Department of Health and Human Services to develop a "next generation" anthrax vaccine, which may be as effective and safe as the current vaccine in fewer doses. Both of these efforts are important, but will take years to conclude. Meanwhile, we must protect our servicemembers from harm with the currently licensed, safe and effective vaccine.

I trust this information addresses your concerns and I invite you to visit the AVIP's Internet Website at http://www.anthrax.mil, or call the toll-free information line at 1-877-GET-VACC for more in-depth information about the anthrax-vaccine program. Answers to other questions are also available by writing to avip@otsg.amedd.army.mil.

Sincerely,

William Winkenwerder, Jr., MD

cc:
The Honorable Michael G. Oxley

* Source - "The Anthrax Vaccine, Is It Safe? Does It Work?" Published in 2002 by the National Academy Press, www.nap.edu/catalog/10310/html.

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1 200

HEALTH AFFAIRS

JAN - 9 2003

(b)(6)

Dear (b)(6)

Thank you for your e-mail concerning the Anthrax Vaccine Immunization Program (AVIP). I share your concern for our servicemembers. Preserving their health and safety is our number one concern. The Department of Defense (DoD) requires anthrax vaccination for certain servicemembers as an added layer of protection against this potentially deadly biological agent.

The threat of biological warfare has been a risk to U.S. forces for many years. The DoD analysts maintain updated threat-level evaluations, adjusting the information as necessary to reflect the risk to U.S. operations. Based on assessment of current and past activities in such areas as Iraq and the former Soviet Union, the potential offensive biological threat facing servicemembers makes it necessary for the DoD to have a robust biological defense program today. Anthrax is one of the deadliest biological weapons of choice.

As with other vaccines, the benefits of the U.S. Food and Drug Administration (FDA) licensed anthrax vaccine far outweigh any risk. The Centers for Disease Control and Prevention (CDC) states that receiving the vaccination is much safer than getting the diseases the vaccines prevent. Biological agents such as anthrax are especially hard to detect because symptoms are delayed. Without preventive medical efforts such as vaccination, the results can be devastating and widespread.

Medical experts agree, there have been no deaths from anthrax vaccine reported among more than 2.2 million immunizations given to over 567,000 Service men and women since the AVIP began in March 1998. Further, no deaths have been attributed in a cause-and-effect manner to the vaccine since the FDA licensed it over 30 years ago.

Many studies establish anthrax vaccine safety. From a 1958 study published in the *Bulletin of the John Hopkins Hospital,* to more recent studies at Fort Detrick, Maryland, evidence shows there are no long-term side effects to the anthrax vaccine. In 2002, the National Academy of Sciences, Institute of Medicine (IOM) Committee to Assess the Safety and Efficacy of the Anthrax Vaccine, concluded their two-year study. In their published findings, the Committee found no evidence that people face an increased risk of experiencing life-threatening or permanently disabling adverse events immediately after receiving AVA, when compared with the general population.

Nor did it find any convincing evidence that people face elevated risk of developing adverse health effects over the long term, although data are limited in this regard (as they are for all vaccines).*

The IOM Committee studied data on anthrax-vaccine effectiveness and concluded "that the available evidence from studies with humans and animals, coupled with reasonable assumptions of analogy, show that AVA as licensed is an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by any known plausible engineered strains of B anthracis."*

The DoD continually strives for improved vaccines and improved vaccination programs to protect the health of our forces. The DoD is currently collaborating with the CDC in their study to determine different ways to administer the current anthrax vaccine. This study may lead to the FDA's allowing its use in fewer doses and administering it in a way that may reduce bothersome local injection-site redness, pain, swelling and itching. Additionally, the DoD is partnering with the Department of Health and Human Services to develop a "next generation" anthrax vaccine, which may be as effective and safe as the current vaccine in fewer doses. Both of these efforts are important, but will take years to conclude. Meanwhile, we must protect our servicemembers from harm with the currently licensed, safe and effective vaccine.

I trust this information addresses your concerns and I invite you to visit the AVIP's Internet Website at http://www.anthrax.mil, or call the toll-free information line at 1-877-GET-VACC for more in-depth information about the anthrax-vaccine program. Answers to other questions are also available by writing to avip@otsg.amedd.army.mil.

Sincerely,

William Winkenwerder, Jr., MD

cc:
The Honorable Michael G. Oxley

* Source - "The Anthrax Vaccine, Is It Safe? Does It Work?" Published in 2002 by the National Academy Press, www.nap.edu/catalog/10310/html.

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OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

MEMORANDUM FOR ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ms. Ellen P. Embrey, DASD, Force Health Protection and Readiness

SUBJECT: Expanding Responsibility of the Anthrax Vaccine Immunization Program to Support the Milinary Biological Warfare Vaccine Program

REFERENCES: (a) Deputy Secretary of Defense Memorandum of June 282002, "Reintroduction of the Anthrax Vaccine Immunization Program (AVIP)" (TAB B)

(b) Deputy Secretary of Defense Memorandum (S) of December 12, 2002, "(U) Stage 2 Smallpox Vaccination Implementation" (NOT ATTACHED - CLASSIFIED)

(c) DoD Directive 6205.3, "DoD Immunization Program for Biological Warfare Defense," November 26, 1993 (TAB B)

(d) DoD Directive 5100.88, "DoD Executive Agent," September 3, 2002 (TAB B)

- References (a) and (b) have continued the Secretary of the Army Executive Agency responsibilities for the Anthrax Vaccine Immunization Program (AVIP) and established similar responsibilities for the Smallpox Vaccination Program (SVP). Bioterrorism preparedness and readiness to address biological warfare threats of military significance make vaccine program management a top Force Health Protection priority.

- As the DoD Executive Agent for AVIP, the Army has demonstrated outstanding management, synchronization, and implementation of the anthrax and smallpox immunization programs. Therefore it's necessary to expand the AVIP Agency to support a Military Vaccine Agency (MILVAX), addressing all vaccine implementation requirements.

- Accordingly, I recommend that you request the Secretary of the Army, in accordance with references (a) through (d), to immediately transition the AVIP Agency to the Military Vaccine Agency, and include support for the Smallpox Vaccination Program.

RECOMMENDATION: That the ASD (HA) sign memo at TAB A.

COORDINATION: TAB C

ATTACHMENTS:
As stated

Prepared by: COL Perry Kendrick, FHP/R, (b)(6), PCDOCS# 45275, 45273

TAB A

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1 200

HEALTH AFFAIRS

MEMORANDUM FOR SECRETARY OF THE ARMY

SUBJECT: Expanding responsibility of the Anthrax Vaccine Immunization Program to Support the Military Biological Warfare Vaccine Program

REFERENCES: (a) Deputy Secretary of Defense Memorandum of June 28, 2002, "Reintroduction of the Anthrax Vaccine Immunization Program (AVIP)"

(b) Deputy Secretary of Defense Memorandum (S) of December 12, 2002, "(U) Stage 2 Smallpox Vaccination Implementation"

(c) DoD Directive 6205.3, "DoD Immunization Program for Biological Warfare Defense," November 26, 1993

(d) DoD Directive 5100.88, "DoD Executive Agent," September 3, 2002

In references (a) and (b) the Deputy Secretary of Defense continued the Secretary of the Army Executive Agency responsibilities for the AVIP and established similar responsibilities for the Smallpox Vaccination Program (SVP). Bioterrorism preparedness and readiness to address naturally occurring diseases of military significance makes vaccine program management a top Force Health Protection priority. As the DoD Executive Agent for AVIP, the Army has demonstrated outstanding management, coordination, synchronization, and implementation of a joint Service-level immunization program.

Accordingly, I recommend that the Secretary of the Army, in accordance with references (a) through (c) begin immediately transitioning the AVIP Agency to undertake this larger role with support to the Smallpox Vaccination Program. Consistent with reference (d), I will recommend that the Deputy Secretary of Defense further expand the Executive Agency responsibili to include support for all Bioweapon vaccine program implementations through the Military Vaccine Agency.

William Winkenwerder Jr., MD

TAB B

Ref A

DEPUTY SECRETARY OF DEFENSE
1010 DEFENSE PENTAGON
WASHINGTON, DC 20301-1010

JUN 28 202

MEMORANDUM FOR SECRETARIES OF THE MILITARY DEPARTMENTS
CHAIRMAN OF THE JOINT CHIEFS OF STAFF
UNDER SECRETARIES OF DEFENSE
ASSISTANT SECRETARIES OF DEFENSE
GENERAL COUNSEL, DEF'ARTMENT OFDEFENSE
INSPECTOR GENERAL, DEPARTMENT OF DEFENSE
DIRECTORS OF DEFENSE AGENCIES
COMMANDANT OFTHEUS COAST GUARD

SUBJECT: Reintroduction of the Anthrax Vaccine Immunization Program (AVIP)

Food and Drug Administration (FDA) approval of the manufacturer's renovated facility restores the availability of anthrax vaccine. FDA has determined that the current anthrax vaccine is safe and effective in protecting against all forms of anthrax infection, a scientific conclusion recently supported by the Institute of Medicine.

Current intelligence assessments indicate that the anthrax threat to Department of Defense (DoD) forces is real. The Department's goal is to protect all forces against anthrax as a part of the Department's Force Health Protection program. Steps are being taken by the Department to ensure protection of U.S. service- and DoD personnel against the threat of anthrax and other potential bioweapon agents, including improved intelligence, detection, and surveillance capabilities, protective clothing and equipment, and new generation vaccines and other medical countermeasures.

At this time, the DoD will resume an Anthrax Vaccine Immunization Program (AW) consistent with FDA guidelines and the best practice of medicine, beginning with military personnel, and Emergency-Essential DoD civilians and contractors, at higher risk whose performance is essential for certain mission critical capabilities. Vaccination is mandatory for these personnel. except as provided under applicable medical and administrative exemption policies.

The scope of the AW shall encompass personnel assigned to or deployed for more than 15 days in higher threat areas whose performance is essential for certain mission critical capabilities. Near-term AVTP implementation may also include other personnel determined by the Assistant Secretary of Defense for Health Affairs, in consultation with the Chairman of the Joint Chiefs of Staff, to be at higher

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risk of exposure to anthrax as conditions change. Vaccinations shall begin, to the extent feasible, 45 days prior to deployment or arrival in higher threat areas.

For personnel who are covered under this new policy, who had previously begun the six shot series but had not completed it, resumption of their vaccination series will begin immediately. For personnel whose six sbot series was interrupted, but who are not covered under the new policy, completion of their vaccination series will be deferred until further notice; resumption will begin when feasible, subject to availability of vaccine. Personnel currently being immunized—designated special mission units, manufacturing and DoD research personnel, and Congressionally mandated anthrax vaccine researchers—will continue with their scheduled vaccinations and annual booster shots.

The Under Secretary OF Defense for Personnel and Readiness shall issue policy guidance on the medical and administrative aspects of the AVIP. Effective program implementation continues to be the responsibility of the Secretary of the Amy as the Executive Agent for the AVIP and the designated senior military officers of the services*

Paul Wolfowitz

Ref C

Department of Defense

DIRECTIVE

NUMBER 6205.3
November 26, 1993

ASD(NS&CP)

SUBJECT: DoD Immunization Program for Biological Warfare Defense

References: (a) Title 10, United States Code
(b) DoD Instruction 6205.2, "Immunization Requirements," October 9, 1986
(c) AR 40-562/NAVMEDCOMINST 6230.3/AFR 161-13/CG COMDTINST M6230.4D, "Immunizations and Chemoprophylaxis," November 7, 1988
(d) DoD Directive 5 136.1, "Assistant Secretary of Defense for Health Affairs," December 2, 1992
(e) through (g), see enclosure 1

1. PURPOSE

This Directive:

1.1. Establishes policy, assigns responsibilities, and prescribes procedures for members of the Department of Defense against validated biological warfare threats, and prioritization of research, development, testing, acquisition, and stockpiling of biological defense vaccines under reference (a).

1.2. Provides vaccination guidance that focuses exclusively on defense against biological warfare threats and complements immunization requirements for naturally occurring endemic disease threats outlined in references (b) and (c).

1.3. Addresses peacetime and contingency requirements for immunization against biological warfare threats against U.S. personnel.

1.4. Designates the Secretary of the Army as the "DoD Executive Agent" for the

DoD Immunization Program for Biological Warfare Defense.

1.5. Provides direction on levels of acquisition and stockpiling of biological defense vaccines and prioritizes research and development efforts in defending against current and emerging biological warfare threats.

2. APPLICABILITY AND SCOPE

This Directive applies to:

2.1. The Office of the Secretary of Defense, the Military Departments (including their National Guards), the Chairman of the Joint Chiefs of Staff, the Unified Commands, and the Defense Agencies (hereafter referred to collectively as "the DoD Components"). The term "Military Services," as used herein, refers to the Army, the Navy, the Air Force, and the Marine Corps.

2.2. Essential DoD civilian personnel, and personnel of other Federal Departments, when assigned as part of the U.S. Armed Forces.

3. DEFINITIONS

Terms used in this Directive are defined in enclosure 2.

4. POLICY

It is DoD policy that:

4.1. For immunization, the following personnel, subject to special exceptions approved by the Chairman of the Joint Chiefs of Staff, should be immunized against validated biological warfare threat agents, for which suitable vaccines are available, in sufficient time to develop immunity before deployment to high-threat areas:

4.1.1. Personnel assigned to high-threat areas.

4.1.2. Personnel predesignated for immediate contingency deployment (crisis response).

4.1.3. Personnel identified and scheduled for deployment on an imminent or ongoing contingency operation to a high-threat area.

4.2. For vaccine research, development, testing, evaluation, acquisition, and stockpiling, efforts for the improvement of existing vaccines and the development of new vaccines against all validated biological warfare threat agents shall be integrated and prioritized. The Department of Defense shall develop a capability to acquire and stockpile adequate quantities of vaccines to protect the programmed force against all validated biological warfare threats.

5. RESPONSIBILITIES

5.1. The Under Secretary of Defense for Acquisition and Technology shall ensure the coordination and integration of the DoD Immunization Program for Biological Warfare Defense with all acquisition-related elements of the DoD Biological Defense Program.

5.2. The Under Secretary of Defense for Policy shall review all facets of the DoD Immunization Program for Biological Warfare Defense to ensure that it is consistent with DoD policy and is adequately integrated into overall DoD biological defense policies.

5.3. The Assistant Secretary of Defense for Health Affairs shall:

5.3.1. Serve as the advisor to the Secretary of Defense as in DoD Directive 5 136.1 (reference (d)) on the DoD Immunization Program for Biological Warfare Defense.

5.3.2. In consultation with the DoD Executive Agent, the Secretaries of the Military Departments, and the Chair of the Armed Forces Epidemiological Board, identify vaccines available to protect against biological threat agents designated by the Chairman of the Joint Chiefs of Staff and recommend appropriate immunization protocols.

5.3.3. Issue instructions to the Military Departments and the other appropriate DoD Components on the immunization of DoD personnel, under the guidelines of this Directive, and monitor and evaluate the implementation of those instructions.

5.4. The Secretary of the Army, as the DoD Executive Agent for the Immunization Program for Biological Warfare Defense, shall:

5.4.1. Besides those responsibilities in the Deputy Secretary of Defense Memorandum and the Joint Service Agreement (references (e) and (f)), do the following to enhance the DoD Immunization Program for Biological Warfare Defense, and report ammally through the Assistant Secretary of Defense for Health Affairs (ASD(HA)) to the Secretary of Defense the capability to carryout those policies:

5.4.1.1. Vaccine Research and Development

5.4.1.1.1. Priorities developed in coordination with the ASD(HA), the Chairman of the Joint Chiefs of Staff, and the Secretaries of the Military Departments shall include the development of vaccines against validated biological warfare threat agents for which none exist, improvement of vaccines that are unacceptable in the time they take to produce immunity or in the level of immunity they produce or are inadequate because of the number of doses required to achieve. immunity, assessment of the effectiveness of vaccines against biological warfare threat agents in their likely modes of use (e.g., aerosols), and development of multivalent vaccines that will produce protective immunity after a single vaccination. Vaccines must be either licensed by the Food and Drug Administration (FDA) or have been designated, under FDA requirements, "for use as investigational new drugs (INDs)," as in 21 CFR 50 (reference (g)).

5.4.1.2. Vaccine Acquistion and Stockpiling

5.4.1.2.1. Develop and maintain a DoD capability to acquire and stockpile adequate quantities of vaccines to protect the programmed force against all validated biological warfare threat agents for which suitable vaccines exist.

5.4.1.2.1. On an annual basis, provide information and recommendations, in coordination with the Secretaries of the Military Departments and the Chair of the Armed Forces Epidemiological Board, to the ASD(HA) on vaccines to acquire and appropriate immunization schedules that include reimmunization required to develop and maintain protective immunity. Those recommendations should include, but not be limited to the following:

5.4.1.2.1.1. All relevant data on the effectiveness of each vaccine against the corresponding biological warfare threat agent.

5.4.1.2.1.2. The expected type, frequency, and severity of vaccine-associated adverse reactions.

5.4.2. Serve as the focal point for the submission of information **from** the Services, as specified by subsection **5.5.,** below, and monitor the Services' implementation of the **DoD Immunization** Program for Biological Warfare Defense. Recommend appropriate changes and improvements to the ***Secretary*** of Defense through the **ASD(HA),** and the Secretaries of the Military Departments. Report to the Secretary of Defense annually on the Immunization Program for Biological Warfare Defense.

5.4.3. The Executive Agent Acquisition Executive (AE) shall plan, program, and budget for biological defense. The AE shall coordinate directly with the **ASD(HA),** the Under Secretary of Defense for Policy, the Under Secretary of Defense for Acquisition, the Secretaries of the Departments, and other offices as required to ensure program integration.

5.5. The Secretaries of the **Military** Departments shall:

5.5.1. Implement, monitor, **evaluate,** and document the **DoD** Immunization Program for Biological Warfare Defense in their Department and establish procedures for coordinating and reporting the following **information** to the Executive Agent:

5.5.1.1. The identification, reporting, and epidemiologic **evaluation** of vaccine-associated adverse reactions, in accordance with FDA requirements.

5.5.1.2. The collection and forwarding of data required by the Executive Agent needed to meet requirements of the FDA for products that are the **INDs.**

5.5.2. Transmit the instructions of the **ASD(HA)** about the immunization program for biological **warfare** defense to subordinate units.

5.5.3. Program and budget for the required vaccinations for members of their Department and provide **the DoD** Executive Agent with projected program requirements.

5.6. The Chairman of the Joint Chiefs of **Staff,** in consultation with the Commanders of the Unified Commands; the Chiefs of the Military Services; and the Director, Defense Intelligence Agency **(DIA),** annually and as required, shall validate and prioritize the biological warfare threats to **DoD** personnel and forward that list to the **DoD** Executive Agent through the **ASD(HA).**

5.7. The Commanders of the Unified Commands, **annually** and as required, shall

provide the Chairman of the Joint Chiefs of Staff with their assessment of the biological warfare threats to their theaters.

5.8. The Chair of the Armed Forces Epidemiological Board, in consultation with the DoD Executive Agent and the Secretaries of the Military Departments, annually and as required, shall identify to the ASD(HA) vaccines available to protect against validated biological warfare threat agents, and recommend appropriate immunization protocols.

6. PROCEDURES

The DoD Immunization Program for Biological Warfare Defense shall be conducted, as follows:

6.1. The Commanders of the Unified Commands, annually and as required, shall provide the Chairman of the Joint Chiefs of Staff with their assessment of the biological warfare threats to their theater.

6.2. The Chairman of the Joint Chiefs of Staff, in consultation with the Commanders of the Unified Commands; the Chiefs of the Military Services; and the Director, DIA, annually, shall validate and prioritize the biological warfare threats to DoD personnel and forward them to the DoD Executive Agent through the ASD(HA).

6.3. Within 30 days of receiving the validated and prioritized biological warfare threat list from the Chairman of the Joint Chiefs of Staff, the DoD Executive Agent shall, in consultation with the Secretaries of the Military Departments and the Chair of the Armed Forces Epidemiology Board, provide recommendations to the ASD(HA) on vaccines and immunization protocols necessary to enhance protection against validated biological warfare threat agents.

6.4. Within 30 days of receiving the coordinated recommendations of the DoD Executive Agent, the ASD(HA) shall direct the Secretaries of the Military Departments to begin immunization of the specified DoD personnel against specific biological warfare threat agents.

6.5. For biological threats for which the only available vaccine is an ND, it shall be administered under 21 CFR 50 and 312 (reference (g)) and the established ND protocol and/or other applicable legal procedures.

7. INFORMATION REQUIREMENTS

The annual reporting requirements in section 5., above, have been assigned Report Control Symbol DD-POL(A) 1921.

8. EFFECTIVE DATE AND IMPLEMENTATION

This Directive is effective immediately. The Secretaries of the Military Departments shall forward one copy of implementing documents to the Assistant Secretary of Defense for Health Affairs within 120 days.

William J. Perry
Deputy Secretary of Defense

Enclosures - 2
1. References
2. Definitions

El. ENCLOSURE 1

REFERENCES. continued

(e) Deputy Secretary of Defense Memorandum, "Biological Warfare Defense Program," August **26, 1991**

(f) Joint Service Agreement, "Joint Service Coordination of Chemical Warfare and Chemical-Biological Defense Requirements, Research, Development, and Acquisition," July **5, 1984**

(g) Title 21, Code of Federal Regulations, Parts 50, "Informed Consent of Human Subjects," and 3 12, "Investigational New Drug Application," current edition

E2. ENCLOSURE 2

DEFINITIONS

E2.1.1. Biological Warfare **Agent.** A microorganism or biological toxin intended to cause disease, injury, or death in humans.

E2.1.2. **Biological** Warfare Threat. A biological materiel planned to be deployed to produce casualties in humans.

E2.1.3. High-Threat Area. A geographic area in the proximity of a nation or nations considered to pose a potential biological threat to **DoD** personnel by the Chairman of the Joint Chiefs of Staff in consultation with the Commanders in Chief of the Unified Commands and the Director, DIA.

E2.1.4. Immunity. The capacity to resist the effects of exposure to a specific biological agent or toxin.

E2.1.5. Immunization. The process of rendering an individual immune. **Immunization** refers to "the administration of a vaccine to stimulate the immune system to produce an immune response (active immunization)." That process may require weeks to months and administration of multiple doses of vaccine.

E2.1.6. Programmed Force. The **DoD** active and Reserve force approved by the Secretary of Defense in the Future Years Defense **Program.**

E2.1.7. Vaccination. The administration of a vaccine to an individual for inducing immunity.

E2.1.8. Vaccine. A preparation that contains one or more components of a biological agent or toxin and induces an immune response against that agent when administered to an individual.

E2.1.9. Validated Biological Warfare Threat Agent. A biological warfare agent that is validated as a threat to **DoD** personnel by the Chairman of the Joint Chiefs of Staff, in consultation with the Commanders of the Unified and Specified Commands; the Chiefs of the Military Services; and the Director, DIA.

Ref D

Department of Defense

DIRECTIVE

NUMBER 5100.88
September 3, 2002

DA&M

SUBJECT: DoD Executive Agent

References: (a) Title 10, United States Code
(b) DoD Instruction 4000.19, "**Interservice** and Intragovernmental Support," August **9, 1995**
(c) DoD 5025. 1-M, "**DoD** Directives System **Procedures," current** edition
(d) DoD Directive 5100.3, "Support of the Headquarters of Combatant and Subordinate Joint **Commands," November 15, 1999**
(e) through (g), see enclosure 1

1. PURPOSE

Pursuant to the authority of the Secretary of Defense under reference (a), this Directive:

1.1. Provides a DOD-wide definition of **DoD** Executive Agent.

1.2. Provides **DoD** approval authority for assigning **DoD** Executive Agent responsibilities, functions, **and** authorities within the Department of Defense.

1.3. Prescribes the policy for the management and control of **DoD** Executive Agent assignments and arrangements associated with such assignments within the Department of Defense.

1.4. Provides for the exchange of information between **DoD** Executive Agents and the **DoD** Components regarding resources **and** the quality of support throughout the full range of operations.

2. APPLICABILITY

This Directive applies to the Office of the Secretary of Defense; the Military Departments; the Chairman of the Joint Chiefs of Staff; the Combatant Commands; the Office of the Inspector General, Department of Defense; the Defense Agencies; the DoD Field Activities; and all other organizational entities within the Department of Defense (hereafter collectively referred to as "the DoD Components").

3. DEFINITIONS

As used in this Directive, the following terms have the meaning set forth below:

3.1. DoD Executive Agent. The Head of a DoD Component to whom the Secretary of Defense or the Deputy Secretary of Defense has assigned specific responsibilities, functions, and authorities to provide defined levels of support for operational missions, or administrative or other designated activities that involve two or more of the DoD Components. The nature and scope of the DoD Executive Agents responsibilities, functions, and authorities shall:

3.1.1. Be prescribed at the time of assignment.

3.1.2. Remain in effect until the Secretary of Defense or the Deputy Secretary of Defense revokes or supersedes them.

3.2. OSD Principal Staff Assistants. The Under Secretaries of Defense, the Director of Defense Research and Engineering, the Assistant Secretaries of Defense, the General Counsel of the Department of Defense, the Assistants to the Secretary and Deputy Secretary of Defense, and the OSD Directors or equivalents, who report directly to the Secretary of Defense or Deputy Secretary of Defense.

4. POLICY

It is DoD policy that:

4.1. The DoD Executive Agent designation shall be conferred when

4.1.1. No existing means to accomplish DoD objectives exists.

4.1.2. DoD resources need to be focused on a specific area or areas of responsibility in order to minimize duplication or redundancy, or

4.1.3. Such designation is required by law, Executive Order, or Government-wide regulation.

4.2. **Only** the Secretary of Defense or the Deputy Secretary of Defense may designate a **DoD** Executive Agent and assign associated responsibilities, functions, and authorities within the Department of Defense.

4.3. The Head of a **DoD** Component shall be designated as a **DoD** Executive Agent The **DoD** Executive Agent may delegate, to a subordinate designee within that official's Component, the authority to act on that official's behalf for any or **all** of those **DoD** Executive Agent responsibilities, functions, and authorities assigned by the Secretary of Defense or the Deputy Secretary of Defense. The **DoD** Executive Agent, or subordinate designee, may arrange for and execute inter-Service support agreements, in accordance with **DoD** Instruction 4000.19 (reference **(b)),** memoranda of understanding, and other necessary arrangements, as required, to fulfill assigned **DoD** Executive Agent responsibilities, functions, and authorities.

4.4. Within the scope of assigned responsibilities and functions, the **DoD** Executive Agent's authority takes precedence over the authority of other **DoD** Component officials performing related or collateral joint or multi-component support responsibilities and functions.

4.5. **The DoD** Executive Agent assignments and arrangements associated with such assignments shall be identified in a **DoD** issuance in accordance with reference (c). **The** issuance shall:

4.5.1. Cite the Secretary of Defense's or the Deputy Secretary of Defense's authority assigning **DoD** Executive Agency.

4.5.2. Identify the responsibilities, functions, relationships, and authorities of the **DoD** Executive Agent.

4.5.3. Identify **funding** and other resource arrangements for the **DoD** Executive Agent to carry out assigned responsibilities, functions, and authorities.

4.5.4. Specify other **DoD** Components, if any, that provide operational missions or administrative or other designated activities in support of the **DoD** Executive Agent.

4.6. The **DoD** Executive Agency arrangements shall be structured in a manner that permits the effective and efficient accomplishment of assigned responsibilities, functions, and authorities.

4.7. The **DoD** Executive Agent funding methods and resource requirements, including force structure to the extent permitted by law, shall be included as a part of the Planning, Programming, Budgeting and Execution process.

4.8. The performance of **DoD** Executive Agents shall be assessed periodically for continued need, currency, effectiveness, and efficiency in satisfying end user requirements.

4.9. There shall be **an** approved list of **DoD** Executive Agent designations.

4.10. Procedures governing the establishment, disestablishment, modification, and execution of **DoD** Executive Agent assignments and associated arrangements shall be established.

4.11. The funding and costs **in** support of each **DoD** Executive Agent assignment and associated arrangements shall be identified separately and shall be visible within the **DoD** budget.

5. RESPONSIBILITIES AND FUNCTIONS

5.1. The Director of Administration **and** Management, Office of the **Secretary** of Defense, shall:

5.1.1. Develop policy on **DoD** Executive Agent assignments and arrangements associated with such **assignments** for approval by the Secretary of Defense or the Deputy Secretary of Defense; oversee the implementation of the policy throughout the Department of Defense; and, issue guidelines, as appropriate, to define further the policies, responsibilities and functions, and authorities contained in this Directive.

5.1.2. Coordinate on all **DoD** issuances that assign or modify **DoD** Executive Agent designations.

5.1.3. Develop, maintain, monitor, revise, **and** make available to all the **DoD** Components, the list of **DoD** Executive **Agent designations** approved by the Secretary of Defense or the Deputy Secretary of Defense.

51.4. Issue **DoD** issuances implementing this Directive.

5.2. The DoD Executive Agents shall:

5.2.1. Execute **DoD** Executive Agent responsibilities, consistent with applicable law, **DoD** Directive 5 100.3 (reference (d)), **DoD** Directive 5 100.73 (reference (e)), and this Directive.

5.2.2. Ensure proper coordination with the **DoD** Components for the responsibilities and activities assigned to provide continuous, sustainable, **and** global support as required by end users. Ensure effective planning throughout operations by developing a coordinated process and support plans for transition from peacetime to wartime **and/or** contingency operations.

5.2.3. Identify requirements and resources, including force structure to the extent permitted by law, necessary to execute assigned responsibilities and functions. Submit these requirements to the cognizant Head of the **DoD** Component to be included in their respective budget **documenation.**

5.2.4. Monitor resources used in performing assigned responsibilities and functions.

5.2.5. Develop, maintain, and report results of performance of **DoD** Executive Agent responsibilities and functions, as may be required by law, Secretary of Defense decision, or other Congressional requirements.

5.2.6. Obtain reports and information, consistent with **DoD** Directive 8910.1 (reference **(f)),** as necessary, to carry out assigned **DoD** Executive Agent responsibilities, functions, and authorities.

5.2.7. Establish, maintain and preserve information as records, consistent with **DoD** Directive 5015.2 (reference (g)), that document the transaction of business and mission of the **DoD** Executive Agent.

5.2.8. Designate a focal point to coordinate matters regarding assigned**DoD** Executive Agent responsibilities, functions, and authorities.

5.3. The OSD Principal Staff Assistants shall:

5.3.1. Oversee the activities of **DoD** Executive Agents in their functional areas of responsibility.

5.3.2. Assess periodically, but not less than every three years, DoD Executive Agent assignments and arrangements associated with such assignments, under their cognizance for continued need, currency, and effectiveness and efficiency in satisfying end user requirements. Recommend establishment, continuation, modification, or cancellation of those DoD Executive Agent assignments and arrangements associated with such assignments, under their cognizance, as appropriate.

5.3.3. Designate a focal point to implement the guidance contained in this Directive and to coordinate matters regarding identification, control, and evaluation of the DoD Executive Agent assignments and arrangements associated with such assignments within their area of cognizance.

5.4. The Heads of the DoD Components, when receiving DoD Executive Agent support, shall:

5.4.1. Provide estimates of requirements and associated resources to the designated DoD Executive Agent on a timely basis.

5.4.2. Assess, as required, DoD Executive Agent support for effectiveness and efficiency in meeting requirements and make appropriate recommendations for improvement.

5.4.3. Designate a focal point to coordinate matters regarding the establishment of new, the identification of existing, and the control and evaluation of DoD Executive Agent support arrangements.

5.5. The Chairman of the Joint Chiefs of Staff shall:

5.5.1. Coordinate with the OSD Principal Staff Assistants and the Heads of the DoD Components to monitor DoD Executive Agent assignments and arrangements associated with such assignments for impact on the full range of operations.

5.5.2. Communicate, to the Combatant Commanders, DoD Executive Agent assignments and arrangements associated with such assignments in order to support and facilitate national military objectives throughout the full range of operations.

5.6. The Under Secretary of Defense (Comptroller) shall:

5.6.1. Ensure that the **DoD** Component budget submissions, including requirements supporting **DoD** Executive Agent assignments and arrangements associated with such assignments, are integrated into the **DoD** Planning, Programming, and Budgeting System.

5.6.2. Ensure that all **funds** and costs required to support **DoD** Executive Agent **assignments** and the arrangements associated with such assignments are displayed separately and justified in the **FYDP** and the budget exhibit submissions of de **Heads** of the **DoD** Components exercising **DoD** Executive Agent responsibilities and **functions.**

5.7. The General Counsel of the Department of Defense shall coordinate on all **DoD** issuances that assign or modify **DoD** Executive Agent designations, and provide legal counsel and advice, as appropriate, to implement this Directive.

6.. EFFECTIVE DATE

6.1. **This** Directive is effective immediately.

6.2. This Directive does not revise, modify, or rescind any **DoD** Executive Agent assignments and their implementing arrangements in existence as of the effective date of this Directive.

Paul Wolfowitz
Deputy **Secretary** of Defense

Enclosures - 1
El. References, continued

El. ENCLOSURE 1

REFERENCES, continued

(e) DoD Directive 5100.73, "Major Department of Defense Headquarters Activities," May 13, 1999
(f) DoD Directive 89 10.1, "Management and Control of Information Requirements," June 11, 1993
(g) DoD Directive 5015.2, "DoD Records Management Program," March 6, 2000

Tab C

SUBJECT: Expanding Responsibility of the Anthrax Vaccine Immunization Program to Support the Military Biological Warfare Vaccine Program

COORDINATIONS

MILVAX	COL Randy Randolph	_____
DoD, OGC	Mr. John Casciotti	Concur 1/17/03
CoS (HA)	Ms. Diana Tabler	_____
PDASD (HA)	Mr. Wyatt	_____

(b)(6)

01/17/2003 08:56 AM

To: (b)(6) **@osd.pentagon.mil,** (b)(6) **@otsg.amedd.army.mil**
cc:

Subject: REQUEST FOR COORDINATION - Expanding Responsibility of the Anthrax Vaccine Immunization to Support the Military Biological Warfare Vaccine Program
Document is Permanently Archived

John / COL Randolph,

Colonel **Rauch** asked that you review the attached drafts for **ASD(HA)** and **USD(PR)** signature.


MILVAX USD PR Action Memo 1-15


MILVAX ASD HA Action Memo 1-15

(b)(6)
Chief, Action Management Branch
Deployment Health Support Directorate
(b)(6)

(b)(6)

01/21/2003 10:22 AM

To: (b)(6) @otsg.amedd.army.mil
cc: (b)(6) @ha.osd.mil

Subject: REQUEST FOR COORDINATION - Expanding Responsibility of the Anthrax Vaccine Immunization to Support the Military Biological Warfare Vaccine Program
Document is Permanently Archived

Colonel,

Have you had a chance to review both packages? (b)(6) recommaneded changes have been incorporated and are attached. MILVAX USD PR Action Memo 1-15

MILVAX ASD HA Action Memo 1-15

His changes were only to DSD package. At your convenience please.

---------- Forwarded by (b)(6) /OSAGWI on 01/21/2003 10:22 AM ----------

(b)(6)

01/17/2003 08:56 AM

To: (b)(6) @osd.pentagon.mil (b)(6) @otsg.amedd.army.mil
cc:

Subject: REQUEST FOR COORDINATION - Expanding Responsibility of the Anthrax Vaccine Immunization to Support the Military Biological Warfare Vaccine Program
Document is Permanently Archived

John / COL Randolph,

Colonel **Rauch** asked that you review the attached drafts for **ASD(HA)** and **USD(PR)** signature.

MILVAX USD PR Action Memo 1-15 MILVAX ASD HA Action Memo I-15

(b)(6)
Chief, Action Management Branch
Deployment Health Support Directorate
(b)(6)

(b)(6)
Chief, Action Management Branch
Deployment Health Support Directorate
(b)(6)

(69)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

January 31, 2002, 3:00 P.M.

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ms. Ellen P. Embrey, DASD, Force Health Protection and Readiness

SUBJECT: DoD National Vaccine Healthcare Center (VHC) Network Advisory Board Charter

- TAB A is a request for coordination on the draft charter, DoD National Vaccine Healthcare Center Network Advisory Board (VHC NAB).

- Attached at TAB B is the proposed charter, which establishes the VHC network and the board membership. The board functions as a consultative panel of experts that convenes for the review of VHC NAB issues and makes recommendations to the Assistant Secretary of Defense for Health Affairs.

- The VHC network, along with the NAB, is a collaborative effort between the Department of Defense and the Centers for Disease Control and Prevention, to establish a system for monitoring vaccine adverse events occurring among members of the armed forces. See information paper attached at TAB B.

- Coordination of the draft charter by addressees is requested no later than March 7, 2003.

RECOMMENDATION: That ASD(HA) sign memo at TAB A.

COORDINATIONS: (TAB C)

Attachments:
As stated

Prepared by: CDR (b)(6), DHSD, (b)(6)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

January 31, 2002, 3:00 P.M.

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ms. Ellen P. Embrey, DASD, Force Health Protection and Readiness

SUBJECT: DoD National Vaccine Healthcare Center (VHC) Network Advisory Board Charter

- TAB A is a request for coordination on the draft charter, DoD National Vaccine Healthcare Center Network Advisory Board (VHC NAB).

- Attached at TAB B is the proposed charter, which establishes the VHC network and the board membership. The board functions as a consultative panel of experts that convenes for the review of VHC NAB issues and makes recommendations to the Assistant Secretary of Defense for Health Affairs.

- The VHC network, along with the NAB, is a collaborative effort between the Department of Defense and the Centers for Disease Control and Prevention, to establish a system for monitoring vaccine adverse events occurring among members of the armed forces. See information paper attached at TAB B.

- Coordination of the draft charter by addressees is requested no later than March 7, 2003.

RECOMMENDATION: That ASD(HA) sign memo at TAB A.

COORDINATIONS: (TAB C)

Attachments:
As stated

Prepared by: CDR (b)(6), DHSD, (b)(6), 45729

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (M&RA)
ASSISTANT SECRETARY OF THE NAVY (M&RA)
ASSISTANT SECRETARY OF THE AIR FORCE (M&RA)
JOINT STAFF SURGEON
DIRECTOR, HEALTH AND SAFETY, US COAST GUARD
PRESIDENT, ARMED FORCES EPIDEMIOLOGY BOARD

SUBJECT: Draft charter for the DoD National Vaccine Healthcare Center Advisory Board

I request coordination no later than noon Friday, March 7, 2003, on the draft charter for the DoD National Vaccine Healthcare Center Network Advisory Board (VHC NAB), (Attachment #1).

This charter establishes the VHC NAB, which provides consultative expertise for the review of network mission specific issues and makes recommendations to the Assistant Secretary of Defense for Health Affairs.

I have enclosed an information paper on the DoD NationalVaccine Healthcare Center Network for your information, (Attachment #2).

If you have questions regarding this matter, please contact Commander (b)(6) (b)(6), e-mail (b)(6)@deploymenthealth.osd.mil. Forward your coordination (TAB D) to (b)(6).

William Winkenwerder Jr., MD

Attachments:
As stated

CHARTER

DoD National Vaccine Healthcare Center Network Advisory Board

1. **PURPOSE:** The DoD Vaccine Healthcare Center Network Advisory Board (VHC NAB) provides consultative expertise for the review of network mission specific questions and makes recommendations to the Assistant Secretary of Defense for Health Affairs, ASD(HA). The ASD(HA) shall appoint a Director, DoD National Vaccine Healthcare Center Network to chair the NAB. The NAB provides periodic oversight recommendations regarding the VHC network program and proposes changes in the mission or functions of the network.

2. **BACKGROUND:** The VHC network is a collaborative effort between the Department of Defense and the Centers for Disease Control and Prevention that fulfills Section 751 of the National Defense Authorization Act of 2001. This Act instructs the Secretary of Defense to establish guidelines under which servicemembers "may obtain access to a Department of Defense Center of Excellence treatment facility for expedited treatment and follow up" [10USC 1110(2)(b)(3)] as part of establishing "a system for monitoring adverse events of members of the armed forces to the anthrax vaccine" [10USC 1110(2)(b)(1)]. The network will function as allergy-immunology Centers of Excellence and be accessible to DoD beneficiaries and providers either directly or on a referral basis. As the network matures, it will develop the structure and tools to support a vaccine safety assessment program from surveillance and enhanced vaccine adverse events reporting to case management of complex adverse events. Emphasis will be placed on standardization of clinical and educational programs that focus on healthcare provider and beneficiary understanding of immunizations and vaccine safety. Clinical research partnerships will be developed to validate clinical guidelines and support improvements in vaccine healthcare delivery. The first of 15 planned regional centers opened in Washington, DC, at Walter Reed Army Medical Center on September 6, 2001.

   Historically the DoD has depended on the Armed Forces Epidemiological Board (AFEB) for vaccine advice and guidance, just as the Department of Health and Human Services has depended on the Advisory Committee on Immunization Practices (ACIP). Representation on the NAB by members of both the AFEB and ACIP bring scientific credibility and institutional independence to the oversight and recommendations provided to the ASD(HA) and the Director, National Vaccine Healthcare Center Network.

3. **GOALS:** The VHC NAB goals include but are not limited to:

   - Providing review of programs, tools and research developed by the VHC network.
   - Providing guidance and recommendations on how to best optimize collaborative efforts between government and civilian agencies with the VHC network.
   - Assisting and directing the VHC network in providing its services to personnel in order to enhance vaccine use, primarily for the military in operational settings.
   - Consulting and reviewing clinical-management issues, protocols, and other vaccine-delivery issues for the VHC network.

4. **MEMBERSHIP:** Voting members will consist of the Chair, the Surgeons General of the Military Services, the Director, Health and Safety of the U. S. Coast Guard, and representatives from the ACIP and the AFEB. Subcommittees, either continuing or ad hoc, shall be established as needed as working groups of the NAB to assist in performing its functions. When necessary, each subcommittee may request the advice of non-voting consultants to provide the requisite balance in viewpoints through breadth of expertise. Representatives to the NAB should include board-certified specialists in the fields of immunology, infectious disease, pediatrics, family medicine, and operational medicine. The membership will include:

Director, DoD National Vaccine Healthcare Center Network	Chair
Member of the Advisory Committee on Immunization Practices	Member
Member of the Advisory Committee on Immunization Practices	Member
Member of the Armed Forces Epidemiological Board	Member
Member of the Armed Forces Epidemiological Board	Member
Representative from the Centers for Disease Control and Prevention	Member
Academic Immunology/Immunization/Vaccine Safety Expert	Member
Academic Immunology/Immunization/Vaccine Safety Expert	Member
Representative , Assistant Secretary for Health, Department of Health and Human Services	Ex-Officio Representative
Representative, Surgeon General of the Army	Ex-Officio Representative
Representative, Surgeon General of the Navy	Ex-Officio Representative
Representative, Surgeon General of the Air Force	Ex-Officio Representative
Representative, Marine Corps Surgeon	Ex-Officio Representative
Representative, Health and Safety of the U. S. Coast Guard	Ex-Officio Representative
Representative. TRICARE Management Activity	Ex-Officio Representative
Representative, Under Secretary for Health Department of Veterans Affairs	Ex-Officio Representative
Executive Secretary	
Staff Assistant	

5. **MEETINGS:** Bi-annual meetings with additional meetings as requested by Chair.

   SUBCOMMITTEES: Continuing or ad hoc subcommittees shall be established as needed. Subcommittees shall be represented on the parent NAB. The chair of the NAB shall appoint voting members and designate one to serve as the chairperson. When necessary, a subcommittee may request the advice of non-voting consultants in order to enable it to carry on its work while providing the requisite balance in viewpoints through breadth of expertise.

6. **SUPPORT AGENCY:** The Surgeon General, Department of the Army shall be responsible for providing administrative and staff support for operation of the NAB through the Walter Reed National Vaccine Healthcare Center Network. Administrative support is defined as budgeting, funding, fiscal control, manpower control and utilization, personnel administration, security administration, space, facilities, supplies and administrative services.

7. **INDIVIDUAL PROCUREMENTS:** The NAB is not authorized to advise on individual procurements. No matter shall be assigned to the NAB for its consideration that would require any member of the NAB or Subcommittees to participate personally and substantially in the conduct of any specific procurement, or place him or her in the position of acting as a "procurement official," as that term is defined pursuant to law.

8. **DELIVERABLES.** Written minutes from meetings to include consensus statements on clinical and research issues brought to the committee.

9. **DURATION OF DOD NATIONAL VACCINE HEALTHCARE CENTER NETWORK CLINICAL ADVISORY BOARD.** The Charter of the DoD National Vaccine Healthcare Center Network Clinical Advisory Board is subject to renewal two (2) years from the date of this charter and every two years thereafter unless abolished by re-issuance or cancellation.

William Winkenwerder Jr., MD

ASD(HA) Approval Date:

Information Paper

DoD National Vaccine Healthcare Center Network

ISSUE

The National Vaccine Healthcare Center Network (VHC) is a collaborative effort between the Department of Defense (DoD) and the Centers for Disease Control and Prevention (CDC) /National Immunization Program (NIP) to provide compliance with HR 4205 by permitting DoD to fulfill the requirements set forth in Section 735 paragraph (d) "system for monitoring adverse reactions of the anthrax vaccine." In addition to providing compliance with existing legislation, the network offers DoD, in collaboration with the CDC, a means to establish an overall system for monitoring adverse events for all vaccines. It also provides a capability for DoD to respond to the rapidly evolving current and future vaccine health care needs.

Current resourcing does not accommodate the needs of the proposed network. Additional manpower requirements are projected for the Allergy-Immunology Department of the Walter Reed Army Medical Center as workload to support this initiative increases.

The Anthrax Vaccination Immunization Program has highlighted areas of improvement in the military vaccination system that must be addressed. These include:

1. Response to servicemembers who express concern that they may have suffered adverse events to vaccinations;
2. Training of immunization supervisory providers, nursing personnel and technicians;
3. Understanding of the Vaccine Adverse Events Reporting System (VAERS) and individual provider responsibilities to submit the VAERS-1 form in cases of adverse events temporally associated with vaccination;
4. Provider understanding of what constitutes an adverse event that occurs with a temporal relationship to a vaccination;
5. In-depth VAERS reporting to include follow-up VAERS on persistent medical problems that adversely impact on quality of life or result in disability;
6. Provider understanding of balanced risk communication (in a high anxiety, low trust environment) in relation to anthrax vaccine specifically and immunizations in general;
7. Policy and resourcing for implementation of quality standards regarding administration of vaccines within the DoD;
8. Medical resources for the diagnosis, treatment and long term follow-up of patients with complex, chronic, multi-system diseases such as chronic fatigue syndrome with onset temporally associated with an anthrax immunization event.

NATIONAL VHC NETWORK VISION

The VHC is a network of regional vaccine health-related clinical programs aimed at facilitating the health care of military members and DoD beneficiaries that involve vaccines and other therapeutic modalities that improve personal immune protection and "immune readiness." The VHC network is dedicated to continuous performance improvement of immunization and immune therapy health care delivery, from education and research to management of adverse

reactions for all DoD beneficiaries. The VHC network will become a strategically located collection of centers of excellence for military vaccine quality care as well as support for enterprise-wide quality improvements in immunization health care delivery in general. As a platform from which to conduct vaccine studies and as the cornerstone for the CDC/DoD partnership to enhance vaccine safety, efficacy, and acceptability, the VHC network has the potential to become a national resource for the validation of vaccine safety and ongoing surveillance of post-marketing vaccine-related adverse events.

VHC NETWORK MISSION STATEMENT

In order to provide this clinical support and leadership for immune readiness, the VHC network will work in partnership with the CDC and other agencies to develop programs that are dedicated to the highest quality and safety of all immunizations and preventive medicine services. This CDC/DoD collaboration is designed to 1) improve the safety and quality of the delivery of vaccines to military personnel and DoD/VA beneficiaries, 2) improve the reporting of vaccine-related adverse events in military personnel and DoD/VA beneficiaries, 3) improve the quality of clinical management and follow-up of beneficiaries who suffer vaccine-related adverse events, 4) improve military personnel level of satisfaction with their vaccine-related health care services, follow-up experiences, and patient advocacy, and 5) improve beneficiary and vaccine provider knowledge, understanding, and acceptance of immunization requirements.

VHC NETWORK COLLABORATIVE GOALS

The VHC Network will assess and enhance:

- The quality of delivery of immunizations to military personnel and DoD beneficiaries.
- The level of reporting vaccine-related adverse events in the military healthcare system.
- Clinical management and follow-up of vaccine related adverse events and the level of patient advocacy provided to military personnel and beneficiaries who suffer vaccine-related adverse events.
- The knowledge, attitudes, and beliefs of military personnel, DoD beneficiaries and providers regarding immunization requirements.
- The number of trained support personnel for immunization health care improvements.

BACKGROUND

Immunizations in general are the cornerstone of "immune readiness" for servicemembers and beneficiaries, both at home and abroad. Immunizations from the beginning have been the most cost-effective disease prevention public health interventions in 20th and 21st century medicine, only exceeded in efficacy by clean water and proper waste disposal. Biological warfare and terrorism are serious threats both within and outside the United States with new and more difficult challenges facing numerous organizations (beside the military) involved in disease and disaster prevention. Even under the worst criticism regarding efficacy, the anthrax vaccination program is a better preventive strategy for the defense against biological warfare and terrorism threats than any other available strategy. A framework for the delivery of multiple immunizations exists throughout the military health care system. However, it has not been standardized or resourced adequately for the many challenges that have developed over the past 15 years.

The entire vaccine world, both within and outside governmental institutions, has been faced with increasing numbers of issues that challenge the credibility and trust in the immunization health care delivery system. The 1990's were a decade of increasing public concern regarding the safety of vaccines in general and distrust of government organizations and the established medical community, particularly in relation to how individuals with adverse reactions to vaccines are cared for and supported. Examples of just some of the issues are summarized below:

- **Live oral polio vaccine.** There have been cases of paralytic polio in previously healthy children caused by this vaccine. As a result, the public's perceptions of risk associated with traditional immunizations in general have steadily increased. The policy of using live oral polio vaccine in infants has changed as a consequence to further reduce risk. The National Vaccine Compensation Act, directed toward childhood vaccine injury compensation, does NOT address adults with vaccine-related morbidity and thereby has failed to engender confidence in vaccine safety for some sectors.
- **Swine "flu" vaccine.** In the 1970's, this vaccine caused neurological disease complications resulting in persistent distrust of the very safe current influenza vaccine.
- **First generation hepatitis B vaccine.** This vaccine was derived from a blood product (plasma) and there was a perceived risk of HIV transmission that was resolved by recombinant vaccine generations of today. There was never any data to support the concerns about transmission risk. New concerns about this vaccine have arisen from hair loss to questions regarding the risk of thimerosal and mercury accumulation.
- **Infant rotavirus vaccine.** This vaccine was recalled one year after FDA licensing due to over 100 cases of bowel obstruction and several deaths linked potentially to the vaccine.
- **Neonatal hepatitis B vaccine.** Policy for this vaccine has been changed recently due to new concerns about thimerosal content and possible mercury morbidity (birth and 2 month visit with multiple vaccines exceeding the EPA levels of safety 0.1 mcg/kg/day). There is no data regarding actual harm caused by the vaccine or thimerosal, but national and international policy has moved to a recommendation to modify all vaccines in regard to preservative content. This may result in higher costs of vaccines and decreased availability, particularly in developing countries.
- **Measles and hepatitis B vaccines.** These vaccines have been the subject of increasing suspicion as etiologic factors in autism, multiple sclerosis, diabetes, autoimmune disease, etc. Clear data is lacking to support the validity of these fears, yet data alone has not been an adequate response to managing the public's concerns.
- **HIV transmission and immunizations.** There continues to be a belief that immunizations contributed to or even caused the HIV epidemic in Africa and other developing countries.

There appears to be a trend nationally of negative perceptions feeding the distrust of vaccines in general. The negative factors challenging public trust in vaccines are occurring at a time when distrust of traditional medicine is also growing and there is an increasing trend toward the public's desire for alternative or complementary medicine. Moreover, there are increasing demands for freedom of individual choice in health care. The response to the anthrax vaccine immunization program partially reflects the background issues surrounding vaccines in general.

The deficiencies of immunization health care within the DoD have been reviewed in a recent report to the Armed Forces Epidemiological Board: **Vaccines in the Military: A DoD-Wide Review of Vaccine Policy and Practice.** A Report for the Armed Forces Epidemiological Board (AFEB), April 1999; AFEB Infectious Disease Control Subcommittee: "Deficiencies of the current approach to the delivery of vaccines in the DoD" (page 72-77). In addition, the National Vaccine Advisory Committee has recently published a subcommittee report on improved standards for quality adult immunization programs in non-traditional sites that challenges all health care systems to address vaccine delivery and resourcing of quality standards implementation. (**Adult Immunization Programs in Nontraditional Settings: Quality Standards and Guidance for Program Evaluation.** MMWR 2000;49(RR-1)(Mar 24);1-13. www.cdc.gov/epo/mmwr/preview/mmwrhtml/rr4901a1.htm) The existing health care system has not been resourced to meet the complexities and resource requirements of 21st century immunization health care delivery.

In the context of these standards and national concerns, there is a renewed emphasis on vaccine adverse events reporting or the VAERS system — specifically, developing a more visible outreach for quality improvements in VAERS reporting and follow-up. Anthrax is an older vaccine and post marketing surveillance for adverse events is critical to the credibility of the program. Vaccines are prescription drugs. All prescription drugs are associated with adverse reactions or side effects at a minimum rate of one to two percent. Drug-related medical problems, including those associated with vaccines, should be treated proactively, recognizing that causality can frequently not be proven or disproved. This is a part of doing business and trust is built if the resources to care for the problems are available and credible.

STATUS OUTLINE

1. VHC Structure

The VHC Network has one Lead VHC located at Walter Reed Army Medical Center, responsible for the co-ordination and development of policies, tools, education materials and standard operating procedures for all VHC sites, and Regional VHCs. Initial training of Regional VHC personnel will be the responsibility of the Lead VHC. The Lead VHC will co-ordinate its efforts with existing DoD organizations dedicated to quality immunization services within the services and the Veteran's Administration.

The Lead VHC reports to DoD and the CDC. DoD, through the Army as the executive agent, will provide command and control and administrative support of the entire VHC program. The current organizational framework for the VHC network includes the North Atlantic Regional Medical Command (NARMC) as the Regional Command servicing the Lead VHC; the Walter Reed Army Medical Center as the hosting agency for the Lead VHC; and the Allergy-Immunology Department of Walter Reed Army Medical Center as internal subject matter experts. The Lead VHC will report to the DoD through this chain. The Lead VHC reports to the CDC through the National Immunization Program (NIP). Within the NIP there will be a cell of personnel to provide program management and data management to the overall VHC Network program. Future co-ordination with the VA and civilian centers developed for comparable issues will be a developmental requirement.

There are potentially more than 600 DoD immunization sites worldwide in need of support. Categorization of support requirements within each region and for individual sites must first be identified for comprehensive standardization of practice, educational support, assistance with VAERS reporting, and case management of complex adverse events related patients. To support this effort, the number of VHC sites required throughout the DoD potentially exceeds 16. The scope of work and extent of outreach within each region remains to be defined. The regional VHCs are under the command and control of the Lead VHC, and all data collected will be reported through the lead VHC. Personnel for the lead VHC and the first regional VHC are in training. Both the lead VHC and the NARMC VHC are located at WRAMC

FACILITIES

Providing adequate facilities for the VHC mission within DoD facilities requires resourcing of renovations and structural adaptations to accommodate personnel and automation requirements. Since the VHC function is to provide a visible and accessible service center and "safe haven" for vaccine related reporting and problem solving, both for providers and patients, location of the VHC within existing military treatment facilities is essential. Initial renovations for the Lead and NARMC regional VHC was completed in May of 2001. The facilities include a service center, clinical evaluation spaces to include facilities for specialized testing and vaccine dose challenges, and a 16-seat learning laboratory/classroom integrated with the existing TRISERVICE Immunization-Allergy-Asthma Specialist School.

INITIAL PRIORITIES

The initial phase of the VHC initiative, involving the NARMC regional scope, will focus on the development of a core training program for personnel involved (currently 9 weeks, including risk communication and clinical expertise development) with subsequent outreach to immunization sites within the region. The outreach will include assessment of compliance with new quality standards for immunization services and assessment of training and resource requirements to include development of support programs to these sites. Support programs will include but are not limited to the following:

1. Reviewing and/or assisting in the development of standardized operating procedures that incorporate the new quality standards for immunization services and facilitate VAERS reporting of vaccine related adverse events;
2. Developing mechanisms to provide support for case management of patients with prolonged or more severe adverse events temporally associated with anthrax vaccine specifically and military required vaccines in general;
3. Assisting in the development of local educational resources to include annual update training in vaccine related health care issues to include adverse events information;
4. Developing an enhanced communication network in order to allow for bi-directional information exchange relevant to immunization issues; and
5. Establishing systematic surveys for data necessary for identifying needs for improved VAERS and quality immunization services.

The establishment of a template of standard operating procedures (SOPs) for a regional VHC is a core requirement of the first year scope of work for review and maturation in other regional endeavors to include service specific needs. Each region will be permitted the flexibility to tailor its SOPs in order to meet the specific requirements of its provider and patient population. These SOPs must be living documents in order to respond to the changing vaccine scenarios for the future, but should be coordinated within the Lead VHC in order to foster inter-service consistency for immunization health care.

During VHC regional outreach, personnel will actively perform follow-up on patients with anthrax vaccine-related adverse events to include initial evaluations and reporting of persons not previously captured in the VAERS system.

Personnel will participate in surveys of attitudes, knowledge and beliefs among servicemembers, providers and other beneficiary groups regarding anthrax vaccine, specifically, and other vaccines in general. Focus will be placed on the development of communication and education programs that address the needs of the DoD community.

All initiatives will be developed in collaboration with the CDC/NIP and in coordination with existing DoD functions.

SUBJECT: Draft Charter: Vaccine Healthcare Center Network Advisory Board)

COORDINATION

	Concur	Non-concur
Assistant Sec of the Army (M&RA)	_____	_____
Assistant Sec of the Navy (M&RA)	_____	_____
Assistant Sec of the Air Force (M&RA)	_____	_____
Joint Staff Surgeon	_____	_____
Director, Health and Safety, USCG	_____	_____
President, Armed Forces Epidemiology Board	_____	_____

POC: CDR (b)(6), DHSD, Phone: ((b)(6) Fax: (b)(6)

70

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-I 200

HEALTH AFFAIRS

ACTION MEMO

February/, 2003, 6:00 P.M.

FOR: UNDER SECRETARY OF DEFENSE (PERSONNEL AND READINESS)

FROM: Dr. William Winkenwerder Jr., Assistant Secretary of Defense (Health Affairs)

SUBJECT: Annual Report to Congress on Separations Resulting From Refusal to Participate in the Anthrax Immunization Program

- Section 75 1 of National Defense Authorization Act for 2001 requires the SECDEF to submit an annual report to Congress on the separations that have resulted from servicemembers who refused to participate in the Anthrax Vaccine Immunization Program (AVIP).
- This year's annual report, due not later than April 1, 2003, must include the number of members separated categorized by military department, grade, and active duty or reserve status.
- TAB A is a draft memorandum requesting the Services provide the required information, which will be compiled and used in the 2003 Separations Report to Congress.

RECOMMENDATION: Sign memorandum at TAB A

COORDINATION: TAB B

Attachments:
As stated

Prepared by: CDR (b)(6), DHSD, (b)(6), PCDOCS# 45870

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND READINESS

MEMORANDUM FOR SECRETARY OF THE ARMY (M&RA)
SECRETARY OF THE NAVY (M&RA)
SECRETARY OF THE AIR FORCE (M&RA)

SUBJECT: Annual Report to Congress on Separations Resulting From Refusal to Participate in the Anthrax Immunization Program

Section 75 1 of the National Defense Authorization Act for 2001 requires the Secretary of Defense to submit an annual report to Congress on service separations that have resulted from members who refused to participate in the Anthrax Vaccination Immunization Program.

This report must include the number of members separated, branch of service, grade, and active duty or reserve status. This report covers the timeframe from January 1, 2002 through December 3 1, 2002.

Thank you for your attention to this matter. Please provide information no later than 12:00 noon, Friday, March 7, 2003, to the ASD (HA) point of contact, CDR (b)(6) at (b)(6).

David SC. Chu

Cc:
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force

Annual Report to Congress on Separations Resulting From Refusal to Participate in the Anthrax Immunization Program

COORDINATION

DASD(FHP&R)	Ms. Ellen Embrey,	Concur 02/11/03
PI, (HA)	LTC (b)(6)	Concur 02/12/03
DoD, OGC	Mr. (b)(6)	Concur 02/12/03
Chief of Staff, ASD(HA)	Ms. (b)(6)	
PDASD(HA)	Mr. (b)(6)	EMW 02/19/03

TRICARE

TRICARE Management Activity

DOCUMENT MANAGEMENT DIVISION
ADMIN OFFICE

ACTION OFFICE DHS DATE 3-21-03 PCDOCS # 46171
(B) 45870

The attached correspondence is returned for the following reason(s):

- ☑ Distribution
- ☐ Coordination
- ☐ Revision
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- ☐ Provide Original/Supporting Documents
- ☐ Provide SD 391
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Additional Comments:

Signed Response Scanned into PCDocs # 46171

Health Affairs

ROUTING AND TRANSMITTAL SHEET

TRICARE Management Activity

	Sign	Coord		Sign	Coord
_____ ASD, HA		✓	_____ Dir, TMA		
_____ PDASD, HA					
_____ DASD, C&PP			_____ CMO		
_____ DASD, FHP&R			_____ Dir, DHS		
_____ DASD, HB&FP			_____ CFO		
_____ DASD, HPA			_____ COO		
			_____ Dir, Regional Operations/PEO		
_____ CIO, MHS			_____ Dir, IMT&R		
2/12/03 OGC, DoD		✓	_____ OGC, TMA		
_____ LA					
_____ CoS, HA		✓	_____ Dir, A&M		
_____ Military Assistant			_____ CoS, TMA		
_____ Dir, PI, HA			_____ Dir, PI, TMA		
_____ Dir, P&S			_____ Dir, Admin		
_____ Other (Specify)			_____ Other (Specify)		

DMD (SKY) ~~[illegible]~~ Date: ~~2/13/03~~ **DMD (PNT)** [illegible] Date: 2/13/03

Date Received: 2/13/03 **Suspense Date:** _____

Subject: Annual Report to Congress on Separations Resulting From Refusal to Participate in the Anthrax Immunization Program

PCDOCS #: 45870 **OSD/P&R #:** _____

AO: CDR (b)(6) **Office:** DHSD **Phone #:** (b)(6)

NOTES:

CMAT Control # 71
2003044-0000037

[Categorical Listing] [Numerical Listing]

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, D.C 20301-1200

HEALTH AFFAIRS

15 OCT 1999

MEMORANDUM FOR SURGEON GENERAL OF THE ARMY
SURGEON GENERAL OF THE NAVY
SURGEON GENERAL OF THE AIR FORCE

SUBJECT: : Policy for Reporting Adverse Events Associated with the Anthrax Vaccine

This memorandum establishes the Department of Defense (DoD) Anthrax Vaccine Immunization Program (AVIP) policy for reporting requirements on adverse events possibly related to the anthrax vaccine adsorbed (AVA).

Requirements for Generating a Vaccine Adverse Event Reporting System (VAERS) Form VAERS-1

For the purposes of reporting anthrax vaccine adverse events, a Form VAERS-1 (Attachment 1) must be completed and submitted using Service reporting procedures for those events resulting in a hospital admission or time lost from duty for greater than 24 hours or for those events suspected to have resulted from contamination of a vaccine lot. Further, health care providers are encouraged to report other adverse events that in the provider's professional judgment appear to be unexpected in nature or severity. In addition, the patient or a health care provider may submit a Form VAERS-1 directly to the Food and Drug Administration (FDA) for any possible adverse event. To obtain Form VAERS-1, contact the FDA at 1-800-822-7967 or visit the FDA web site www.fda.gov/cber/vaers/vaers.htm. Additional VAERS statistics are available from the National Technical Information Services (NTIS) at 1-800-553-6847.

A supplemental form (Attachment 2), specifically for use in connection with anthrax vaccine adverse event reporting, will be used by the Services' reportable disease project officers to verify completeness of and to classify each Form VAERS-1. The Services will submit a copy of the Form VAERS-1 and a supplemental form to the Army Medical Surveillance Activity (AMSA), U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM). The AMSA will serve as the central repository and will monitor all Form VAERS-1 submitted. The AMSA will coordinate the results of these reports directly with the DoD AVIP Agency, Office of the Army Surgeon General (OTSG), and the Services' Surgeons General.

Service Reporting Procedures

Army: All reports of anthrax vaccine adverse events are submitted by the chief of preventive medicine through the Army's automated reportable disease system to AMSA. These reports are consolidated daily into the Defense Medical Surveillance System (DMSS). In addition, a Form VAERS-1 is submitted to the chairman of the supporting medical treatment facility's (MTF) Pharmacy and Therapeutics Committee. Reports are submitted by the chairman, MTF Pharmacy and Therapeutics Committee, to the FDA's Vaccine Adverse Event Reporting System and copies of the Form VAERS-1 are

provided to the reportable disease project officer at AMSA, DSN: 662-0471 or commercial: 202-782-0471.

Navy: All reports of anthrax vaccine adverse events are submitted by the preventive medicine department or the senior medical officer through the Navy Disease Reporting System (NDRS) to the Navy Environmental Health Center (NEHC). These reports are consolidated monthly into the DMSS. In addition, a Form VAERS-1 is submitted by the health care provider to the FDA's Vaccine Adverse Event Reporting System and a copy to the reportable disease project officer at NEHC DSN: 864-5603 or commercial 757-462-5500. NEHC forwards a copy of the Form VAERS-1 and the supplemental form to AMSA.

Air Force: All reports of anthrax vaccine adverse events are submitted by the military health care provider to the Force Health Protection and Surveillance Branch, IERA/RSRH, 2513 Kennedy Circle, Brooks AFB, TX 78235-5123, DSN 240-3471 (commercial: 210-536-4371), FAX DSN 240-6841 (commercial: 210-536-6841). If the incident is life threatening or a death has occurred, the report will be made by telephone within 24 hours to IERA/RSRH. These reports are consolidated monthly into DMSS. A Form VAERS-1 is submitted to the FDA's Vaccine Adverse Event Reporting System and a copy to the Force Health Protection and Surveillance Branch. A copy of the Form VAERS-1 and supplemental form are sent to AMSA. Copies are also provided to the local Pharmacy and Therapeutic Committee, major command clinical points of contact, and the Air Force Medical Operations Agency (AFMOA).

Timeliness of Form VAERS-1 Reporting

A copy of Form VAERS-1 should be submitted to each Service's reportable disease project officer (AMSA, NEHC, IERA/RSRH) within seven days of the occurrence of the adverse event. The reportable disease project officer is responsible for verifying the completeness of the information on each report and completing an anthrax vaccine adverse event supplemental form (Attachment 2) prior to sending the report to AMSA. The reportable disease project officer has seven days from receipt to submit the copy of Form VAERS-1 and a completed supplemental form to AMSA so that consolidated DoD reporting can be provided to the AVIP Agency, OTSG.

Adverse events that are deemed life-threatening (such as anaphylaxis), result in death, or are suspected to be the result of contaminated lots must be reported telephonically to each Services' reportable disease project officer within 24 hours of the occurrence of the event. Each reportable disease project officer has an additional 24 hours to notify AMSA of the occurrence. Hard copy reports of the event should follow the initial telephonic report.

Classification of the Form VAERS-1

Each Service's reportable disease project officer is responsible for classifying Form VAERS-1 reports based on the information submitted and any other supplemental information necessary to complete a report and make a determination. The following classification system will be used to classify each report on the supplemental form:

Local Reactions:

Mild local reactions involve local erythema and induration of 1-2 cm diameter that may increase in size to 3-5 cm. Usual onset is within 24 hours and the reaction subsides by 48 hours. Reactions tend to increase in severity by the fifth injection, then decrease in severity with subsequent doses. Mild reactions may occur in up to 30 percent of recipients.

Moderate local reactions involve local erythema, induration, and pruritus involving an area more than 5 cm diameter. Subcutaneous nodules may occur at the injection site and persist for several weeks. Moderate reactions occur in up to 4 percent of recipients.

Large local reactions can consist of extensive edema from the site of injection extending past the elbow to possibly involving the forearm, in addition to local inflammatory reaction, focal rash, itching, and subcutaneous nodules. Large local reactions occur less frequently.

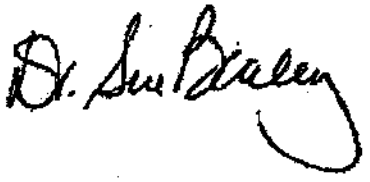
Systemic Reactions:

Systemic reactions usually are characterized by malaise, myalgia, arthralgia, and fatigue. The individual may have generalized rash and pruritis, dyspnea, and fever. Focal swelling and itching may appear at areas other than injection site. A simple headache may last a short duration and is treatable. Chills and fever are rare. Immediate reactions are suggestive of anaphylaxis. Systemic reactions rarely occur (< 0.2% injections).

Report to the Executive Agent of AVIP

AMSA is responsible for forwarding to the DoD AVIP Agency a weekly summary of the reported anthrax vaccine adverse events. This summary will compile the reports of anthrax vaccine adverse events submitted by each Service. The classification system maintains consistency of anthrax vaccine adverse event reporting within the DoD.

This policy provides guidance to support the Department's AVIP through improving vaccine adverse event reporting procedures of the Services' instruction "Immunization and Chemoprophylaxis" (AFJI 48-110, AR 40-62, BUMEDINST 6230.15, CG COMDTINST M6230.4E) of November 1, 1995. This policy is effective immediately and shall be included in all Service and Joint Staff plans and policies for the AVIP and for joint medical surveillance and force health protection



Dr. Sue Bailey

Attachments:
1. Form VAERS-1(FDA), Vaccine Adverse Event Reporting System
2. Anthrax Vaccine Adverse Event Supplemental Form

[Top]
Last update: 12/10/1999

CMAT Control #
2003044-0000038

(72)

[Numerical Listing]

HEALTH AFFAIRS

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

16 May 2000

MEMORANDUM FOR SECRETARY OF THE ARMY SECRETARY OF THE NAVY SECRETARY OF THE AIR FORCE AIR FORCE (M,RA,I&E)

SUBJECT: Policy on Adherence to the Anthrax Vaccine Immunization Schedule and Medical Exemptions to Anthrax Vaccination

This memorandum is intended to provide policy guidance on the following medical issues: compliance with FDA-approved vaccine guidelines on the scheduling and administration of anthrax vaccine; the medical exemptions to anthrax vaccination; and the reporting of adverse events associated with the anthrax vaccine.

Dosage Schedule.

The Commissioner of the Food and Drug Administration (FDA) recently expressed concern over reports that some members of the Armed Forces in both Active and Reserve components are receiving their anthrax vaccine doses substantially later than called for by the schedule approved by the Food and Drug Administration (FDA), as described in the vaccine manufacturer's package insert. As stated clearly in all Anthrax Vaccine Immunization Program (AVIP) policies, full immunization requires six doses administered at 0, 2, and 4 weeks, and at 6, 12, and 18 months, to complete the primary series. This schedule is the only schedule approved by the FDA at this time.

All reasonable steps should be taken to ensure that shots are given on or as close as possible to the recommended schedule. As stated in my memorandum of September 11, 1998 (HA Policy No. 98-045), doses of the vaccine should not be administered on a compressed or accelerated schedule (for example, shorter intervals between doses or more doses than required).

Continued senior leadership attention is necessary to assure proper implementation of the program. Administration of the vaccination schedule at the unit command level requires, at a minimum, notification to the recipient of the date, time, and location for the next scheduled shot, the availability of the next shot at the proper time, and implementation of a procedure to recall the patient if he or she does not appear as scheduled. Higher command levels should monitor and provide appropriate follow-up to ensure compliance. Accurate documentation in both individual medical records and Service-specific automated immunization tracking systems will greatly aid this effort. Attention should be directed to those units having a significant percentage of the second and third doses being administered more than seven days late, and the fourth, fifth, or sixth doses being given more than 30 days late.

To ensure uniformity of practice, in cases in which a dose is received beyond the scheduled date, administration of the next shot in the series should be based on the interval of time between doses, as indicated on the FDA-approved schedule. The approved dosing intervals 2 are: two weeks between doses 1 and 2; two weeks between doses 2 and 3; five months between doses 3 and 4; six months between doses 4 and 5; and six months between doses 5 and 6. For example, if dose 3 is received six weeks after dose 2

(rather than the normally scheduled two weeks), dose 4 should be given five months after dose 3. There are no data to support reduced immune effectiveness of the vaccine if doses are given later than the scheduled time but doses given too early may result in reduce immune responses.

Medical Exemptions.

The granting of medical exemptions is a medical function that can only be performed by a privileged health care provider. Such individual exemptions should be applied only when medically warranted, with the overall health and welfare of the patient clearly in mind. The granting of medical exemptions should be based on potential benefits versus risks and should always take into consideration the immediate threat assessment.

Temporary medical exemptions are warranted in the five situations listed below.

(1) Immunosuppressive Therapy. Individuals receiving systemic corticosteroid therapy, other immunosuppressive drug therapies, or radiation therapy, may be in a state of temporary immunodeficiency. Because of potential suppression of the immune response, these individuals should be deferred from receiving the anthrax vaccine until immune function returns, as determined by the attending physician.

(2) Acute Illnesses. Serious acute diseases or acute injuries may be potentially aggravated by anthrax vaccination or can lead to more severe side effects with immunization. This includes any acute febrile illnesses. Vaccinations may resume, as determined by the attending physician.

(3) Post-surgery. Post-surgical situations may warrant temporary vaccination deferment in order to ensure full recovery through convalescence. The timeframe when vaccinations may resume following a surgical procedure will be again be determined by the patient's attending physician.

(4) Pregnancy. Anthrax vaccine should be deferred until after pregnancy. Because anthrax immunization is largely based on occupational risk, vaccination should resume with full assumption of duties following pregnancy, unless a longer post-partum interval is medically indicated, and be in accordance with current DoD and Service policies.

(5) Other Conditions. In situations where a medical condition is in the process of being evaluated or treated, a temporary deferral of anthrax vaccination may be warranted. This would include significant vaccine-associated reactions that are being evaluated. The timeframe for deferral will be determined by the attending physician, and in accordance with current DoD and Service policies.

3 Situations warranting a permanent medical exemption include: severe reaction to a previous anthrax vaccination, where it has been determined that further vaccination will seriously endanger the health status of the patient; and Human Immunodeficiency Virus (HIV) infection and other chronic immunodeficiencies, where the immune response may be unpredictable and such individuals would not be deployed to a high threat area.

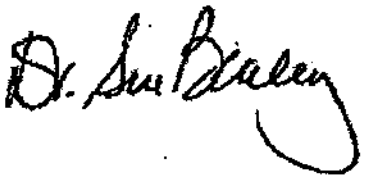
If an individual's case is complex or not readily definable, an allergist/immunologist, or other appropriate medical specialist, should be consulted before any exemption is granted. If a permanent deferment from further immunizations is indicated, appropriate DoD and Service policies will be pursued for the granting of such exemptions. Medical records will be accurately and appropriately annotated pertaining to any temporary or permanent exemptions. Health care providers will periodically review exemptions, to assure that they continue to be valid.

Adverse Events.

As provided in HA Policy No. 99-031, "Policy for Reporting Adverse Events Associated with the Anthrax Vaccine," 15 October 1999, any serious adverse reaction temporally associated with receipt of a dose of anthrax vaccine should be immediately evaluated by a privileged health care provider and any specialists, if indicated. The clinical practice guidelines available on the AVIP web site (www.anthrax.osd.mil). can also be consulted.

Vaccine Adverse Event Reporting System (VAERS) reports shall be filed using Service reporting procedures for those events resulting in hospital admission or lost duty time or work greater than 24 hours or from those events suspected to have resulted from contamination of a vaccine lot. Further, health care providers are encouraged to report other adverse events that in the provider's professional judgment appears to be unexpected in nature or severity. In other situations in which the patient wishes to submit a Form VAERS-1 report, the health care provider will assist the patient in completion of the reporting form. VAERS-1 form reports may be obtained by accessing the AVIP web site or by calling the FDA at 1-800-822-7967.

These policies are effective immediately and should be communicated to appropriate commanders, health care providers, and others involved in the implementation of the AVIP.



Dr. Sue Bailey

Attachment:
As stated

cc:
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force

CLINICAL GUIDELINES
FOR MANAGING ADVERSE EVENTS AFTER VACCINATION

February 2001 edition

1. Purpose: To help medical personnel individually manage and document adverse events after vaccination. Based on clinical experience with adverse-drug-reaction management with vaccines in general, treatment and reporting recommendations are offered here. Adapt these guidelines to individual clinical cases, according to the judgment and scope-of-practice of the health-care provider.

2. Adverse Events After Vaccination: Most people tolerate vaccination without significant side effects. But adverse events may occur after vaccination, sometimes requiring treatment to relieve symptoms. Although many side effects respond to self-medication, people experiencing a reaction should advise a health-care provider before the next dose of the same vaccine. Several studies indicate that women are more likely than men to experience temporary injection-site reactions and systemic symptoms that typically resolve on their own.

a. *Injection-site reactions*, such as redness and swelling. These reactions are not unusual. Antibiotics are not typically warranted to treat injection-site reactions. Anthrax vaccine, administered subcutaneously, is associated with a high frequency of nodules (also called knots or lumps). Although mild to moderate local reactions can be self-medicated, worsening local reactions should be reported to a health-care provider and documented in the medical record, before the next dose.

b. *Systemic events* such as immediate hypersensitivity, fever, or muscle aches. Systemic events are less common than injection-site reactions, and may or may not be caused by the vaccine. Systemic events may appear later after vaccination than injection-site reactions.

c. Some events are caused by vaccination. Others simply coincide in time and may be unrelated to the vaccine. The frequency of the events listed in the attached tables is not uniform. Some are common, while others are rare, if they occur at all. Events may occur that are not listed. Regardless, it is paramount for health-care providers to provide the best care possible for the person in need, regardless of causality. Identify and document clinical problems that follow vaccination before the next dose. Vaccination should be considered in the differential diagnosis, as biologically appropriate. When planning future actions, assess the risk-benefit ratio for continued vaccination versus medical exemption.

d. While most reactions after vaccination require no treatment, some people may need further evaluation, therapy, and/or exemption from further doses of the vaccine. Document all adverse events requiring pre-vaccination treatment, post-vaccination treatment, relief from work, hospitalization, or other medical care on the Service's clinical-encounter form. Report as discussed below.

3. Treatment Guidelines—See algorithms depicted in Figures 1, 2, and 3, plus companion tables with text-based details. Based on published literature and clinical experience, these guidelines are divided into two major groups: injection-site reactions and systemic events. Consider relevant footnotes. Patients may present with symptoms corresponding to more than one category.

4. VAERS Reporting:

a. Adverse events after vaccination are reported to the Vaccine Adverse Event Reporting System (VAERS) using Form VAERS-1. DoD and the Coast Guard require submission of Form VAERS-1, *at a minimum*, for adverse events after vaccination that involve hospitalization, a life-threatening event (such as anaphylaxis), loss of duty of 24 hours or longer, or an event related to suspected contamination of a vaccine vial. These are minimum requirements. Clinicians are encouraged to report all other clinically relevant adverse events after administration of any vaccine or medication to VAERS or MedWatch.

b. Clinicians who file Form VAERS-1 are not making a determination that the two events are causally linked. Ideally, initial VAERS forms should be submitted by primary-care providers, with follow-up VAERS forms filed by subspecialists as additional information comes to light. Anyone identifying a qualifying case, and uncertain whether a Form VAERS-1 was submitted previously, should submit one.

c. If the patient considers his or her adverse event significant and due to the vaccine, the clinician should file a Form VAERS-1 report. Vaccine recipients may complete VAERS forms themselves and submit them directly to the FDA. Reporting by a health-care provider is preferred, to enhance the quality and completeness of the clinical data reported.

d. Form VAERS-1 may be downloaded from the Service surveillance centers, or from www.anthrax.osd.mil/vaers/vaers.htm. Additionally, one may obtain VAERS forms by contacting VAERS at 1-800-822-7967 or www.vaers.org.

e. Attach pertinent information from the vaccine recipient's medical record to the Form VAERS-1 report. Forward the original Form VAERS-1 and attachments to VAERS, P.O. Box 1100, Rockville, MD 20849-1100. At the same time, send a copy of the Form VAERS-1 and attachments through the local Preventive Medicine or Preventive Health Officer, as applicable, to the Service surveillance center (Annex A). Reports also should be submitted to the local pharmacy-and-therapeutics (P&T) committee, because institutions have an accreditation requirement to encourage adverse-drug-reaction reporting. Do not delay reporting while awaiting a P&T committee meeting. Pharmacists can assist in filing Form VAERS-1.

f. The Department of Defense forwards all Form VAERS-1 reports to the FDA and the CDC without screening or restriction. All Form VAERS-1 reports on anthrax vaccine are reviewed for causality by an independent civilian committee, known as the Anthrax Vaccine Expert Committee (AVEC), under the auspices of the U.S. Department of Health and Human Services.

g. Granting administrative exemptions is a non-medical function, usually controlled by an individual's unit. Granting medical exemptions is a medical function performed by a credentialed health-care provider. Medical exemptions should be applied only when medically warranted. If the case is complex or not readily definable, a clinical summary should be sent to the regional clinical subject matter expert or group for review. Medical records of Service Members who disagree with a given provider or consultant's recommendations regarding the exemption should be referred for a second opinion to a provider or consultant group with experience in vaccine adverse reaction management. Review exemptions periodically to confirm continued applicability.

5. Referrals:

a. If additional clinical consultation is needed to assess a patient's condition, the primary-care provider should first perform the initial clinical work-up appropriate to the presenting symptoms. Temporary medical exemptions may be granted by primary-care providers pending referral to a subspecialist appropriate to the individual's clinical condition (e.g., dermatology, neurology, otolaryngology, rheumatology, allergy/immunology).

b. Subspecialists may grant indefinite medical exemptions. Multidisciplinary consultations may be appropriate in some circumstances.

6. Exemption Codes: Use the following exemption codes for electronic tracking of vaccinations (www.mods.asmr.com/mods/forceman/appendix_c.html).

a. Good medical practices for the management of an adverse drug reaction apply to the evaluation of any adverse event after vaccination. Good medical practices also apply to the medical-decision process for granting exemptions or continuing to vaccinate in the face of an adverse event potentially linked to vaccine administration.

b. Medical Exemption Codes:

Code	Meaning	Explanation or Example	Duration
MI	Medical, Immune	Evidence of immunity (e.g., serologic antibody test); documented previous infection (e.g., chickenpox)	Indefinite
MR	Medical, Reactive	Severe adverse reaction after immunization (e.g., anaphylaxis). Code can be reversed if an alternate form of prophylaxis is available. Probably warrants VAERS report	Indefinite
MT	Medical, Temporary	Pregnancy, hospitalization, temporary immune suppression, convalescent leave, any temporary contraindication to immunization	Specified period
MP	Medical, Permanent	HIV infection, pre-existing allergy, permanent immune suppression. Can be reversed if the condition changes.	Indefinite
MD	Medical, Declined	Declination of optional vaccines (not applicable to anthrax vaccine), religious waivers	Indefinite
MS	Medical, Supply	Exempt due to lack of vaccine supply	Indefinite

c. Administrative Exemption Codes:

Code	Meaning	Explanation or Example	Duration
AD	Administrative, Deceased	Service member is deceased	Indefinite
AL	Administrative, Emergency Leave	Service member is on emergency leave	Max 1 month
AM	Administrative, Missing	Missing in action, prisoner of war	Indefinite
AP	Administrative, PCS	Permanent change of station	Max 3 months
AR	Administrative, Refusal	UCMJ Actions	Until resolution
AS	Administrative, Separation	Discharge, separation, retirement	
AT	Administrative, Temporary	AWOL, legal action pending	Max 3 months

7. Acknowledgements & Revisions:

a. This revision, the second edition of these guidelines, is issued by the Anthrax Vaccine Immunization Program (AVIP) Agency, within the Office of The Army Surgeon General, Falls Church, Virginia. The guidelines were developed based on published literature and clinical consensus, beginning at the Biological Warfare Defense Immunizations Conference, 25-27 May 1999. The major authors of this document are LTC (b)(6), COL Renata Engler, LTC (b)(6) LTC (b)(6), along with clinicians from the medical departments of the U.S. Army, Navy, Marine Corps, Air Force, and Coast Guard.

b. This document will be revised periodically, based on clinical experience and epidemiological data. This document provides general guidelines to adapt to individual clinical cases, according to the judgment and scope-of-practice of each health-care provider.

c. Forward suggestions for improvements to this document to LTC (b)(6), Anthrax Vaccine Immunization Program Agency, fax (b)(6), e-mail (b)(6)@amedd.army.mil. Medical command channels will disseminate revisions periodically, which will be posted on the AVIP website, www.anthrax.osd.mil.

8. Selected Bibliography on Anthrax & Other Vaccines:

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Annex A. Service Surveillance Centers

Army Medical Surveillance Activity
Bldg T-20, Rm 213 (Attn: MCHB-EDS)
6825 16th Street, N.W.
Washington, DC 20307-5000
Phone: 202-782-0471 (DSN 662)
Fax: 202-782-0612
http://amsa.army.mil/AMSA/amsa_home.htm

Navy Environmental Health Center
2510 Walmer Ave
Norfolk, VA 23513-2617
Phone: 757-462-5500 (DSN 253), after hours 757-621-1967
Fax: 757- 444-9691
http://www-nehc.med.navy.mil/

Air Force Force Health Protection and Surveillance Branch
Institute for Environment, Safety and Occupational Health (ESOH) Risk Analysis
2513 Kennedy Circle
Brooks AFB, TX 78235-5123
Phone: 210-536-5454 (DSN 240)
Fax: 210-536-6841
http://iera.satx.disa.mil/iera/index.html

Coast Guard Headquarters Directorate of Health and Safety
Commandant (G-WKH)
2100 Second Street SW
Washington, DC 20593
Phone: 202-267-1098
Fax: 202-267-4338

Table 1A: Localized Reactions (LR) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Local (Injection-Site) Reactions (LR) typically involve changes at the injection site with contiguous spread. Signs of inflammation (e.g., itching, redness, heat, swelling) may be present, with occasional bruising. Record specific observations, along with a photo, if needed to preserve the image. Biopsy may be warranted in some cases (e.g., scaling, crusting).	Remote electronic consultation (e.g., telephonic, e-mail, telemedicine) can be used to request assistance. Reassure vaccine recipient that local reactions typically resolve and do NOT result in long-term disease. Although some of these reactions may mimic cellulitis, antibiotic therapy is not warranted for post-vaccination inflammation.	Unless LR was very large or complicated, Service Member usually can proceed with subsequent doses. Credentialled health-care providers may make clinical decisions to alleviate future discomfort for individual Service Members who develop large or persistent injection-site reactions.[8]	Most local reactions require no treatment. Topical or oral treatment to control symptoms depends on reaction severity. Complications may warrant consultation with a specialist. May benefit from treatment and/or pretreatment programs.[1,2] VAERS reporting discussed in text.
Subcutaneous Nodules (LR1): • Usually painless with no redness or heat at the site • Usually present within 1-2 days of the injection, may persist for weeks, gradually dissipating	Record size (in mm) of nodule in longest diameter and duration of palpable presence. Usually requires no treatment. Reassure vaccine recipient that these are common and will resolve spontaneously.	Proceed with subsequent doses at different site (e.g., contralateral side, antero-lateral thigh). Anthrax: For unusually large, bothersome or persistent nodules, consider route.	Do not inject into or through nodule. If painful, consider topical corticosteroid cream or ointment applied 2 to 3 times per day for as long as symptoms persist. Dermatology consult if persistent (> 4 to 6 months).
Local Redness or Swelling (LR2): • < 30 mm in longest diameter • "Mild"	Usually requires no treatment. Resolves within < 72 hours in most cases. Reassure.	Proceed with subsequent doses.	May benefit from topical steroid therapy or antihistamines, if itching is present.[1]
Local Redness or Swelling 30 to 50 mm (LR3): • 30 to 50 mm in longest diameter • "Mild"	May warrant treatment. Rash management noted in LR8.	Proceed. Consider topical corticosteroids and/or antihistamines just after injection.[1,2]	May benefit from topical corticosteroids and/or antihistamines just after injection.[1,2]

Table 1B: Localized Reactions (LR) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Local Redness or Swelling 50 to 120 mm, but NOT extending below elbow (LR4): • Patient may exhibit concern about progression and risk from next injection • "Moderate"	Treat with topical therapy, analgesics, antihistamines to prevent complications or progression. May benefit from short course of oral prednisone, if symptoms persist or worsen. Consider consultation with next level of care.[7] Rash management noted in LR8.	Consider consultation with next level of care,[7] before proceeding with next dose. Consider pre-treatment options. Anthrax: Consider route.[8]	Consider treatment before or at time of next vaccination.[1,2,3] Avoid simultaneous vaccination.
Local Redness or Swelling > 120 mm without complications (LR5): • "Large – Simple"	Rash management noted in LR8.	Consider consult with next level of care.[7] Temporary exemption may be warranted. Consider pretreatment options.[1,2] Anthrax: Consider route and/or interval.[8]	If repeats or worsens, consider temporary exemption, pending consultation. Consider pretreatment.[1,2,3] Encourage submission of Form VAERS-1. Avoid simultaneous vaccination.
Local Redness or Swelling > 120 mm or extending below elbow (LR6): • "Large – Complicated" • Peri-articular soft-tissue swelling, soreness, stiffness may be present • May occur with systemic symptoms Note: May see swelling at or below wrist. Consider possibility of gravitational settling of edema.	Provide treatment by physician. Consider potent topical and/or oral corticosteroids to prevent complications or progression.[1] Seek consultation, as needed. If reaction occurs after ≥ 2 doses, may be immune (i.e., a "hyper-responder," although booster doses may still be needed). Rash management noted in LR8.	Give temporary exemption, pending consultation. Anthrax: Consider route and/or interval.[8] Avoid simultaneous vaccination.	If repetitive or worsening, may merit a temporary exemption from subsequent vaccination, pending consultation. Benefit-risk ratio may merit pretreatment trial.[1,2,3] Encourage submission of Form VAERS-1.

Table 1C: Localized Reactions (LR) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Numbness, Burning, or Tingling At or Distal to Injection Site (LR7_): • 7a. Prolonged lack of sensation (numbness, hypesthesia, anesthesia) near or over injection site • 7b. Burning or painful sensation (dysesthesia) near or over injection site • 7c. Tingling, altered, cold, or other sensation without stimulus (paresthesia) near or over injection site • 7d. Any unusual sensation distal to injection site If physical exam and/or nerve studies establish diagnosis of focal neurologic disease (e.g., ulnar nerve neuropathy, see SE14.	Record detailed description, size of area affected. No specific treatment. Usually resolves in < 1 to 2 weeks. Reassure. May benefit from topical corticosteroids.	Reinforce avoiding injection over triceps. Proceed with subsequent doses at different site, to avoid ulnar nerve. Anthrax: Consider route.[8]	Value of topical anti-inflammatory therapy not established. Encourage submission of Form VAERS-1. Avoid simultaneous vaccination.
Focal Rash At or Near Injection Site (LR8): • May involve vesicles or papules	May treat with topical steroid cream and new-generation antihistamine.[1] May be associated with LR3, LR4, LR5, LR6, or other categories.	After rash resolves, continue doses. Give temporary exemption, pending consultation. Obtain photo and consider biopsy.	If etiology is not clear or rash is slow to resolve, consult with dermatologist. Avoid simultaneous vaccination.
Other Events At or Near Injection Site (LR-xx)	Treat according to clinical condition. Seek consultation, as appropriate.	Base decision on complete medical evaluation and consideration of benefit-risk ratio.	

Table 2A: Systemic Events (SE) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Systemic Events (SE): Symptoms and signs of illness after vaccination. Any reaction that does not involve the injection site. Temporal relationship does NOT prove a cause-effect relationship, particularly if multiple vaccines were given and/or other specific diagnoses of illness have occurred.	Health-care provider should provide appropriate diagnostic evaluation. In some cases, give pretreatment to avert symptoms with next vaccination, to avoid morbidity, but allowing for continued vaccination.	If mild and self-limited, may proceed with next dose. Avoid multiple vaccines in one session for this patient, if possible. Credentialled health-care providers may make clinical decisions to alleviate future discomfort for individual Service Members who develop substantial or persistent reactions.[8]	VAERS reporting discussed in text.
Myalgias and/or Arthralgias (SE1a) **Arthritis** (SE1b) • Primary • Secondary (exacerbation of existing condition)	Acetaminophen or NSAIDs may be administered. Pretreatment may be necessary.	Subsequent doses can usually be given. Anthrax: For symptoms persisting > 96 h, seek specialty consultation; consider route.[8]	If persistent, start work-up to rule out other etiologies. Consult, if needed. VAERS report encouraged when symptoms persist > 48 hours.

Table 2B: Systemic Events (SE) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Mild "Viral"-Like Symptoms (SE2a): At least three of the following, lasting < 96 hours: • Fever (100° to 102.5°F (adolescent/adult) or 104°F (children)) [oral equivalent] • Anorexia • Nausea • Myalgia • Arthralgia • Malaise • Fatigue • Light-headedness (colloquial "dizziness," but not true vertigo. See also SE19b) • Headache (including photophobia or aching eyes) But without (or only one) symptom referable to either the respiratory (SE17) or gastrointestinal tract (SE18). May be associated with moderate or large local reactions. Usually resolves spontaneously with no treatment or with analgesics and rest. ========== **"Flu"-like or "Viral"-like,** not otherwise specified (SE2b)	Options include antihistamines and analgesics to prevent complications or progression.	Proceed with next dose, in most cases..[2,4] For fever > 102.5°F (adolescent / adult) or 104°F (children) [oral equivalent], consider benefit-risk ratio for continuing doses if patient or provider is concerned about risk with future doses.	Consider treatment before or at time of next vaccination, particularly if large local reaction as well.[1,2,4]
Severe and/or Prolonged Nonspecific Symptoms (sometimes called severe or prolonged "viral"-like illness) (SE3) • Includes temperature > 102.5°F (adolescent/adult) or 104°F (children) [oral equivalent] • Includes temperature > 100.5°F and/or systemic symptoms lasting > 96 hours	May benefit from short course of oral prednisone, if not stabilized. May warrant consultation.[5] Evaluate for coincident disease, treat appropriately. High temperatures warrant consultation.	Consult with next level of care. Consider temporary exemption, pending consultation. If unexplained by other causes, may warrant contraindication.	VAERS report encouraged, if no other cause identified. Avoid simultaneous vaccination.

Table 2C: Systemic Events (SE) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Headaches (SE4): • Usually bitemporal without migraine features, "tension" type or dominant feature of "flu"-like syndrome • Usually resolve in several days	Acetaminophen 650 to 1000 mg orally every 4 to 6 hours or ibuprofen 600 to 800 mg orally every 8 hours (or other non-steroidal anti-inflammatory drugs, NSAIDs); can start this treatment 1 hour before next dose.[5]	Proceed with next dose, unless worsening pattern. Anthrax: For symptoms persisting > 96 h, consider route.[8]	Pretreatment generally effective. If pattern worsens, give temporary exemption, pending consultation with neurology. If referred, neurologist should submit follow-up VAERS.
Nausea and/or Vomiting (SE5): • No other signs or symptoms of anaphylaxis • Usually resolves without treatment • Can be vasovagal	Usually resolves without treatment, but standard anti-emetics and even (sedating) antihistamines may provide relief.	Proceed with next dose, with precautions for a vasovagal reaction. Anthrax: For symptoms persisting > 96 h, consider route.[8]	Not reproducible from one injection to the next on initial observations, unless part of vasovagal reaction. Typically, no predictive value for more serious reaction.
Syncope or Near-Syncope (Fainting, Light-headedness) Shortly After Vaccination (SE6): • May be accompanied by prolonged malaise • Fainting or near-fainting with signs of vasovagal reaction (diaphoresis, nausea, vomiting, usually bradycardia, widening pulse pressure and/or frank hypotension) • May result in a fall with secondary injury • Asking people before vaccination about this predisposition may avoid injury	Position in sitting or supine position with legs elevated, head down. • Rarely requires atropine to reverse profound bradycardia • Encourage hydration as soon as stabilized and before future injections • Advise that future injections be given in supine position	Proceed, but with precautions as outlined under treatment. Anthrax: If syncope or near-syncope was related to pain or burning at injection site after injection, consider route.[8]	Occurs in about 1% of healthy, fit adults. Procedures when giving injections of any kind should anticipate this reaction, to avoid traumatic injury.

Table 2D: Systemic Events (SE) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Tinnitus (SE7): • New onset ringing in the ears developing within less than 1 to 2 weeks after an injection • Other cause unlikely (e.g., neurogenic hearing loss from noise injury)	Therapy for nasal congestion may help in some cases. If symptoms persist > 1 to 2 weeks, consult with ear-nose-throat (ENT) specialist.	Consider temporary exemption, pending routine consultation with specialist.	No well-defined association with any vaccine recognized at this time. If event recurs with later dose, give temporary exemption, pending consultation.
Focal or Limited Skin Reaction, not near most recent injection site (SE8): Take photo while acute (or have local dermatologist and/or allergist evaluate)	Treat as indicated. Consult with dermatology, if symptoms persist.	Subsequent doses can usually be given.	May be a rash, erythema, bruising, swelling, etc., at a distance from most recent injection site, such as at previous injection site. May be unrelated to vaccination.
Generalized Skin Reaction (pruritic or non-pruritic), not suggestive of anaphylaxis (SE9): • Maculopapular or target lesions • Must involve skin sites remote from injection site, not just on the injection arm • Take photo while acute (or have local dermatologist and/or allergist evaluate)	Cetirizine 10 mg daily or other second-generation antihistamines. Consider high-dose prednisone (50 to 60 mg daily for 5 to 7 days with rapid taper) if severe.[1,2] If rash is early erythema multiforme, Stevens-Johnson, or toxic epidermal necrolysis, see section SE10. Longer therapy may be needed. Note: accurate diagnosis may call for skin biopsy.	Consider temporary exemption, pending routine consultation with specialist.	In rare circumstances, additional vaccine doses may result in a more serious generalized skin reaction. Additional doses should be given with caution after expert evaluation and consideration of benefit/risk ratio. Encourage submission of Form VAERS-1.

Table 2E: Systemic Events (SE) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Diffuse Blistering Dermatitis and/or Mucositis (SE10): • Erythema multiforme • Stevens-Johnson syndrome • Toxic epidermal necrolysis • Others (fixed drug eruptions, etc.)	Treat acutely, record visually with photo; immediate dermatology and allergy consultation for full treatment program and follow-up. Accurate diagnosis may call for skin biopsy.	Give temporary exemption, pending consultation.	Submit Form VAERS-1. There are no safety data for challenge dosing and/or desensitization of these types of potentially life-threatening skin reactions.
Anaphylaxis, Generalized Allergic Reaction: onset typically within the first few hours after vaccination (SE11): • **Anaphylaxis:** Watery eyes, nasal congestion, general itching, hives, coughing, throat tightness, wheezing, short of breath, light-headed, rapid heart rate, hypotension, anxiety reaction ("sense of doom"), nausea, vomiting, diarrhea, loss of bladder or bowel control with loss of consciousness • **Generalized rash, itching and shortness of breath:** Treat as anaphylaxis, unless immediate evidence of other cause.	Potentially life-threatening allergic reaction, treat immediately with epinephrine. Oral corticosteroid therapy prevents delayed-phase anaphylaxis, which can also become life threatening. Admit to hospital if laryngeal edema or other life-threatening condition is present. Physician or physician assistant evaluation required.	Give temporary exemption, pending consultation with allergist.	Submit Form VAERS-1. Seek allergy consult.[4] Review benefit-risk ratio carefully with patient. Consult patient regarding treatment options and further vaccination under controlled desensitization conditions. Avoid simultaneous vaccination.
Angioedema/Swelling – Diffuse or distant from injection site, with or without pruritus within 2 weeks of vaccination (SE12): • If onset immediate (within ~ 2 hours after injection) may be early cutaneous presentation of serious anaphylactic reaction (see SE11) • If delayed onset (typically within 2 to 3 weeks), consider serum sickness	If initial manifestation is consistent with anaphylaxis, treat as in SE11. If onset > 4 hours, consider treating with corticosteroids and anti-histamines for 5 to 7 days. Note risk of relapse of serum sickness, if steroids are tapered too quickly. Evaluate with CBC, ESR, CRP, LFTs, and UA. Store serum sample before steroid therapy.	Give temporary exemption, pending consultation with allergist.	Submit Form VAERS-1. Seek allergy consult.[4] Review benefit-risk ratio carefully with patient. Consult patient regarding treatment options and further vaccination under controlled desensitization conditions.

Table 2F: Systemic Events (SE) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Neurologic Disease, Severe (SE13): Possible diagnoses include: • Peripheral neuropathy, nonfocal • Encephalopathy • Guillain-Barré syndrome • Progressive focal neurologic disease (see also SE14) Assumes no other etiologic factor	Consult with neurology for diagnosis and treatment. Some cases may benefit from rapid treatment with high-dose intravenous immunoglobulin.	Give temporary exemption, pending consultation with neurology.	Submit Form VAERS-1. Consider risk for recurrent reaction before administering additional doses.
Focal Neurologic Disease (SE14): • Cranial nerve palsy • Neuropathy/neuritis • Radiculopathy • Paresthesias / blepharospasms • Optic neuritis • Ulnar nerve neuropathy (if diagnosis based on physical exam and/or nerve studies. If by symptoms only, give precedence to LR7 group)	Consider compression or trauma to ulnar nerve due to act of injection. Perform clinical work-up. Consult with neurology.	Give temporary exemption, pending consultation with neurology. Emphasize injection in deltoid rather than triceps area.	Submit Form VAERS-1. If persistent, specific treatment may be necessary after neurology consultation.
Prolonged Fatigue (> 60 days)[6] (SE15): < 50% functionality (work, recreation, school), compared to before vaccination • Loss of exercise tolerance • Non-restful sleep a frequent feature • Reduced concentration, decreased memory, as seen in many other chronic illnesses and/or depression	Treat and consult appropriately before 60-day threshold. Consult with specialty center with expertise in chronic fatigue and related syndromes.	Give temporary exemption, pending consultation.	Currently no recognized association with any vaccine. Cases are often eventually linked with other diagnoses. Close follow-up and sequential evaluations may be warranted. Submit Form VAERS-1.

Table 2G: Systemic Events (SE) After Vaccination: February 2001

(Note: The probability of events listed in these tables is not uniform. Some are quite common. Others occur rarely, if at all)

Adverse Event Definitions & Evaluation	Treatment & Management	Future Doses	Comments
Acute Anxiety Response (SE16):	Educate. Reassure. Treat according to clinical condition.	Anthrax: If response related to burning at injection site or related events, consider route.[8]	Some personnel may benefit from psychiatry consultation to assist with diagnosis and management.
Respiratory Illness (SE17): symptoms such as cough, coryza, congestion, sore throat and rhinorrhea with or without accompanying systemic symptoms	Treat symptomatically. If symptoms persist ≥ 2 weeks, consider other etiologies.	Proceed with next dose, in most cases.[2,4]	Contrast with SE2a. Some patients may jointly experience SE17 and SE2a.
Gastrointestinal Illness (SE18): symptoms such as vomiting and/or diarrhea, with or without accompanying systemic symptoms (e.g., loose stool, abdominal pain, gas, indigestion). Note that category SE5 includes uncomplicated nausea and/or vomiting.	Treat symptomatically. Treat symptomatically. If symptoms persist ≥ 2 weeks, consider other etiologies.	Proceed with next dose, in most cases.[2,4]	Contrast with SE2a. Some patients may jointly experience SE18 and SE2a.
Dizziness (SE19a) **"True" Vertigo** (SE19b) • Dysequilibrium characterized by spinning or impulsion, often with nystagmus	An agent such as meclizine or scopolamine may help symptoms of vertigo.	As clinically appropriate.	
Idiosyncratic Response(s) to Live Vaccine(s) (SE20), for example: • Rash after measles, rubella, varicella vaccines • Fever after yellow-fever vaccine • Abdominal cramps, diarrhea after oral typhoid vaccine	As clinically appropriate.	As clinically appropriate.	
Other Systemic Events (SE-xx)	Treat according to clinical condition. Seek consults, as appropriate.	Base decision on complete medical evaluation and consideration of benefit-risk ratio.	

1 - **Treatment program for moderate to large local reactions:**
- Apply topical corticosteroid cream or ointment at least 2 to 3 times per day until reaction has resolved. Rarely requires oral corticosteroids (e.g., prednisone at 1 mg/kg or 50 to 60 mg per day for 3 to 4 days, tapering off by 10 to 20 mg per day over the next 2 to 4 days). Avoid unprotected sun exposure at the treated sites and use sunscreen aggressively.
- If itching is present, use second-generation antihistamines such as fexofenadine (*Allegra®*) 60 mg twice daily or cetirizine (*Zyrtec®*) 10 mg daily. If not available, use first-generation antihistamines, recognizing sedating side effects.
- If swelling extends below elbow, a sling may be useful. Some vaccine recipients may benefit from an ice pack within first 24 hours.

2 - **Pretreatment program to prevent future large local reactions:**
- If localized itching was a dominant feature, pretreat with a second-generation antihistamine such as fexofenadine (*Allegra®*) 60 mg twice daily (at least 2 doses prior to the next injection) or cetirizine (*Zyrtec®*) 10 mg daily (at least 2 doses before next injection), continuing for 48 to 72 hours after the injection (longer if local reaction persists or reflares). If not available, use first-generation antihistamines, recognizing their sedating side effects.
- Avoid unprotected sun exposure at the treated site for at least 1 to 2 weeks and use sunscreen aggressively. For at least 3 to 4 days, avoid strenuous exercise using the arm that has received the vaccination.

3 - **Comment:** Some vaccine recipients will tolerate these types of reactions less well than others, and may be apprehensive about the health risk from the next injection. Careful education and/or willingness to consult with specialists may prevent unnecessary polarization or potential refusal of subsequent vaccinations. Because most of these vaccine recipients can receive additional doses safely, it is important to avoid unnecessary indefinite exemptions, considering the threat and mortality risk of weaponized anthrax.

4 - **Prototype Allergy-Immunology Evaluation:** Anthrax vaccine skin testing (full-strength prick test, 1:1,000 then 1:100 volume/volume dilution intradermal) with both prick and intradermal histamine (histamine base: prick test 1 mg/ml, intradermal 0.1 mg/ml) and diluent controls (sodium chloride 0.9%). If patient understands risks and benefits of further vaccination and seeks desensitization, provide progressive dose challenge without pretreatment initially, treat any reactions appropriately, and pretreat subsequent doses as needed. Save serum from before and 3 to 4 weeks after procedure, to evaluate immune response later. Serum can be sent to central repository or local medical treatment facility (MTF) serum bank. Use generic consent form for serum collection for patient care, but specifying permission for subsequent use of sera for anonymous retrospective research.

5 - **Treatment program for mild to moderate systemic events:** Symptomatic treatment to prevent recurrence of adverse events has been very effective for many vaccines, including anthrax vaccine.

6 - **Prolonged fatigue** linked to vaccination is extremely rare, and has not been characterized as a well-defined vaccine-related adverse event. However, if the patient so desires, Form VAERS-1 may be filed. In many cases, other diagnoses are made when more extensive evaluation and follow-up occurs.

7 - **Next level of care** indicates review by provider with more specialized scope of practice.

8 – **Route and Interval:** DoD and USCG policy is to administer anthrax vaccine using the subcutaneous route, as described in the manufacturer's product labeling ("package insert"). This policy, however, does not preclude a physician or other credentialled health-care provider from making clinical decisions to alleviate future discomfort for an individual Service Member who developed a large or

persistent injection-site reaction or experienced a significant systemic event after an earlier dose of anthrax vaccine. Information to be given to these Service Members appears on the following page.

According to the guidelines of the Advisory Committee on Immunization Practices (ACIP. Use of anthrax vaccine in the United States. *MMWR* 2000;49(RR-15)(Dec 15):1-20, http://www.cdc.gov/mmwr/PDF/rr/rr4915.pdf or http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4915a1.htm):

"At this time, ACIP cannot recommend changes in vaccine administration because of the preliminary nature of this information. However, the data in this report do support some flexibility in the route and timing of anthrax vaccination under special circumstances. As with other licensed vaccines, no data indicate that increasing the interval between doses adversely affects immunogenicity or safety. Therefore, interruption of the vaccination schedule does not require restarting the entire series of anthrax vaccine or the addition of extra doses."

Regarding immunogenicity considerations in individualizing medical treatment: "Because of the complexity of a six-dose primary vaccination schedule and frequency of local injection-site reactions (see Vaccine Safety), studies are under way to assess the immunogenicity of schedules with a reduced number of doses and with intramuscular (IM) administration rather than subcutaneous administration. Immunogenicity data were collected from military personnel who had a prolonged interval between the first and second doses of anthrax vaccine in the U.S. military anthrax vaccination program. Antibody to PA was measured by enzyme-linked immunosorbent assay (ELISA) at 7 weeks after the first dose. Geometric mean titers increased from 450 µg/mL among those who received the second vaccine dose 2 weeks after the first (the recommended schedule, n = 22), to 1,225 for those vaccinated at a 3-week interval (n = 19), and 1,860 for those vaccinated at a 4-week interval (n = 12). Differences in titer between the routine and prolonged intervals were statistically significant ($p < 0.01$)."

Regarding immunogenicity and safety considerations in individualizing medical treatment: "...a small randomized study was conducted among military personnel to compare the licensed regimen (subcutaneous injections at 0, 2, and 4 weeks, n = 28) and alternate regimens (subcutaneous [n = 23] or intramuscular [n=22] injections at 0 and 4 weeks). Immunogenicity outcomes measured at 8 weeks after the first dose included geometric mean IgG concentrations and the proportion of subjects seroconverting (defined by an anti-PA IgG concentration of $\geq$ 25 µg/mL). In addition, the occurrence of local and systemic adverse events was determined. IgG concentrations were similar between the routine and alternate schedule groups (routine: 478 µg/mL; subcutaneous at 0 and 4 weeks: 625 µg/mL; intramuscular at 0 and 4 weeks: 482 µg/mL). All study participants seroconverted except for one of 21 in the intramuscular (injections at 0 and 4 weeks) group. Systemic adverse events were uncommon and similar for the intramuscular and subcutaneous groups. All local reactions (i.e., tenderness, erythema, warmth, induration, and subcutaneous nodules) were significantly more common following subcutaneous vaccination. Comparison of the three vaccination series indicated no significant differences between the proportion of subjects experiencing local reactions for the two subcutaneous regimens but significantly fewer subcutaneous nodules ($p < 0.001$) and significantly less erythema ($p = 0.001$) in the group vaccinated intramuscularly (P. Pittman, personal communication, USAMRIID, Ft. Detrick, MD)."

ANTHRAX VACCINE IMMUNIZATION PROGRAM
INFORMATION PAPER

SUBJECT: Route of Administration for Anthrax Vaccine 1 February 2001

1. PURPOSE. To describe an alternate route for administrating anthrax vaccine.

2. FACTS.

a. The US government license (approved by the Food and Drug Administration (FDA)) for anthrax vaccine is based on injecting the vaccine subcutaneously, about ½-inch under the skin. Subcutaneous (SC) injections place the vaccine in fatty tissue between the skin and underlying muscle. The anthrax vaccine was 92.5% effective in preventing anthrax infection when injected subcutaneously in a key study (Brachman, 1962; FDA, 1985).

b. In a small study, people given anthrax vaccine SC or IM were compared for antibody levels and side effects. The two groups developed roughly the same amount of antibodies. But people vaccinated by the SC route were more likely to develop tenderness, redness, warmth, swelling, or lumps at the injection site, compared to people vaccinated by the IM route. Other information shows that anthrax-fighting antibody levels are somewhat higher when the intervals between anthrax vaccinations are prolonged a few weeks longer than usual. These data come from the US Army Medical Research Institute of Infectious Diseases (USAMRIID), Fort Detrick, MD (ACIP, 2000).

c. Although it is DoD policy to follow the FDA-approved method of SC injections, this policy does not prevent a physician or other authorized health-care provider from making a clinical decision to use an IM injection in a special case. A special case could be to alleviate future discomfort for an individual Service Member who developed a large or persistent injection-site reaction or experienced a significant systemic event after an earlier dose of anthrax vaccine given by SC injection. In such a special case, IM administration is not prohibited if the health-care provider believes the injection will provide appropriate vaccine protection and reduce side effects, and informs the patient of the special circumstances.

d. The independent civilian panel known as the Advisory Committee on Immunization Practices reported that available data "do support some flexibility in the route and timing of anthrax vaccination under special circumstances. As with other licensed vaccines, no data indicate that increasing the interval between doses adversely affects immunogenicity or safety."

3. REFERENCES.

a. Brachman PS, Gold H, Plotkin SA, Fekety FR, Werrin M, Ingraham NR. Field evaluation of a human anthrax vaccine. *American Journal of Public Health* 1962;52:432-45. http://www.anthrax.osd.mil/site_files/articles/indexclinical/brachman.pdf.

b. Food & Drug Administration. Biological products; Bacterial vaccines and toxoids; Implementation of efficacy review. *Federal Register* 1985;50:51002-117. http://www.anthrax.osd.mil/Site_Files/articles/Indexclinical/Fed_register.htm.

c. Advisory Committee on Immunization Practices. Use of anthrax vaccine in the United States. *Morbidity & Mortality Weekly Report* 2000;49(RR-15):1-20. www.cdc.gov/mmwr/PDF/rr/rr4915.pdf.

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Approved by COL Randolph

MANAGING ADVERSE EVENTS AFTER VACCINATION

Service Member Receives Vaccine

***If in yellow or red zone, avoid simultaneous administration with other vaccines.**

LOCAL REACTION
(More common in women than men)

NO REACTION	MILD LOCAL REACTION: Redness < 50 mm diameter, pain, swelling, itching; lump / nodule (LR1, LR2, LR3)	MODERATE LOCAL REACTION: Redness 50-120mm diameter, pain, swelling, itching; lump / nodule; numbness, tingling; burning (LR4, LR7)*	LARGE LOCAL REACTION, ± COMPLICATIONS: Redness >120 mm, pain, swelling to or below elbow; local rash (LR5, LR6, LR8)*
Document. Educate.	Document. Educate. Offer topical corticosteroids, antihistamines, analgesics.[1,2]	Document. Educate. Treat within first 24 h with topical corticosteroids, antihistamines, +/- NSAIDs for pain.[1,3] Avoid strenuous exercise.	Document. Educate. Take photo. Consider consultation with next level of care. Treat symptoms: Steroids, antihistamines, +/- NSAIDs for pain.[3] Encourage VAERS report. Avoid strenuous exercise.
Continue to screen for exclusion criteria (e.g., steroid therapy, pregnancy). Continue series as scheduled.	Continue series as scheduled. Avoid strenuous exercise for 24 to 48 h after next dose to avoid aggravating local reaction.	For moderate reaction, continue series. Before next dose, consider issues of pretreatment,[1,2,3,7] route,[8] or interval.[9] If reactions to later doses decrease, continue. If reactions recur, persist, or worsen: Reevaluate, consider temporary exemption pending consultation.	

Clinical guidelines for managing adverse events after vaccination: *Version February 2001.* This document provides general guidance, to adapt to individual clinical cases. Use with companion tables. Patients may present with symptoms corresponding to more than one category. Revisions to this document will be disseminated via medical command channels and posted on AVIP site, www.anthrax.osd.mil. The probability of events on this chart is not uniform: some are quite common and some are rare. See cover sheet for details.

Submit Form VAERS-1 as warranted. Must be submitted for hospitalization, loss of duty ≥ 24 h, or suspected vial contamination. Other events may also be reported. Presumption of causation is not required to submit Form VAERS-1. Forms available at www.anthrax.osd.mil/vaers/vaers.htm.

MANAGING ADVERSE EVENTS AFTER VACCINATION

Service Member Receives Vaccine

***If in yellow or red zone, avoid simultaneous administration with other vaccines.**

SYSTEMIC EVENT

Myalgias, arthralgias, arthritis; headaches; syncope or near syncope; anxiety response. (SE1, SE4, SE6, SE16) *

"Flu"- or Viral-Like Symptom Groups:

Viral-Like	Respiratory	Gastrointestinal
< 96 h; 3 of these: Temp 100.5-102.5°F (adolescent/adult) or 104°F (children), anorexia/nausea, myalgia/arthralgia, malaise/fatigue, light-headedness, headache (SE2a) (but not SE17 or 18)	Cough, coryza or rhinorrhea, congestion, sore throat. (SE17)	Nausa, vomiting; diarrhea, abdom. pain, gas, indigestion. (SE5, SE18)

***Severe / prolonged*:**
≥ 96 h or T > 102.5 or 104°F (SE3) *

Other events: Fatigue > 60 days; Tinnitus; Vertigo; idiosyncratic events after live vaccines (SE7, SE15, SE19, SE20) *

Document. Educate. Consult as needed. Consider pre/post-treatment NSAID.[1-5] Headache: acetaminophen , ibuprofen, *et cetera*.[1-5]

Document. Treat symptoms.[1,3,5] Educate.

Treat acute event. Document. Educate.

For mild to moderate event(s), continue. Before next dose, consider issues of pretreatment,[3,5,7] route,[8] or interval.[8] If tolerates next dose, continue series. If event(s) recur or worsen: Reevaluate; consider temporary exemption and VAERS report, pending consultation.

For mild to moderate event(s), continue. If event(s) recur or worsen: Reevaluate; consider temporary exemption and VAERS report, pending consultation.

Prompt consult.* Give temporary exemption pending consultation. VAERS report.

Clinical guidelines for managing adverse events after vaccination: *Version February 2001.* This document provides general guidance, to adapt to individual clinical cases. Use with companion tables. Patients may present with symptoms corresponding to more than one category. Revisions to this document will be disseminated via medical command channels and posted on AVIP site, www.anthrax.osd.mil. The probability of events on this chart is not uniform: some are quite common and some are rare. See cover sheet for details.

Submit Form VAERS-1 as warranted. Must be submitted for hospitalization, loss of duty ≥ 24 h, or suspected vial contamination. Other events may also be reported. Presumption of causation is not required to submit Form VAERS-1. Forms available at www.anthrax.osd.mil/vaers/vaers.htm.

MANAGING ADVERSE EVENTS AFTER VACCINATION

Service Member Receives Vaccine

*If in yellow or red zone, avoid simultaneous administration with other vaccines.

SYSTEMIC EVENT

Anaphylaxis, systemic allergic reaction; Angioedema or swelling, Serum sickness (SE11, SE12)*	Other skin disorders: Focal or limited; Generalized skin disorder; Diffuse blistering dermatitis and/or mucositis (SE8, SE9, SE10)*	Neurologic disorder: Peripheral neuropathy; Encephalopathy, Guillain-Barré, Focal neurologic disease (SE13, SE14)*	Other systemic disorder presenting or worsening in temporal association with vaccine
Treat acute event. Document. Educate.	Treat. Document. Educate. Take photo(s). Consider biopsy.	Treat. Document. Educate.	Treat. Document. Educate.
Prompt allergy consultation.[4] Give temporary exemption. Submit VAERS report. Grant indefinite exemption, if warranted.	Immediate or prompt dermatology or other consultation. Give temporary exemption. Submit VAERS report. Grant indefinite exemption, if warranted.	Prompt neurology consultation. Give temporary exemption. Submit VAERS report. Grant indefinite exemption, if warranted.	Seek consultation, as appropriate. Consider temporary exemption.[5] Submit VAERS report. Grant indefinite exemption, if warranted.

Clinical guidelines for managing adverse events after vaccination: *Version February 2001.* This document provides general guidance, to adapt to individual clinical cases. Use with companion tables. Patients may present with symptoms corresponding to more than one category. Revisions to this document will be disseminated via medical command channels and posted on AVIP site, www.anthrax.osd.mil. The probability of events on this chart is not uniform; some are quite common and some are rare. See cover sheet for details.

Submit Form VAERS-1 as warranted. Must be submitted for hospitalization, loss of duty ≥ 24 h, or suspected vial contamination. Other events may also be reported. Presumption of causation is not required to submit Form VAERS-1. Forms available at www.anthrax.osd.mil/vaers/vaers.htm.

CMAT Control #
2003052-0000002

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

74

HEALTH AFFAIRS

ACTION MEMO

February 25, 2003, 10:00 A.M.

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ellen P. Embrey, DASD, Force Health Protection and Readiness

SUBJECT: Designation of US Coast Guard's National Strike Force as an Anthrax Vaccine Immunization Program (AVIP) Priority 1 Designated Special Mission Unit.

- Attached at TAB A is a draft memorandum that designates the US Coast Guard's National Strike Force as a Designated Special Mission Unit and therefore an AVIP priority-1 unit under current DoD policy and implementation plans.
- These National Strike Force teams provide critical response and decontamination support to facilities contaminated with anthrax spores. Most notably, this unit deployed and supported the decontamination of the Hart building in Washington, DC in Fall 2001.
- The Under Secretary of Defense (P&R) policy memorandum dated August 6, 2002, gives the ASD (HA) authority to identify other personnel as mission critical and therefore requiring immunization with the anthrax vaccine.
- This request has been coordinated with the AVIP-MILVAX office, giving full concurrence.

RECOMMENDATION: That ASD(HA) sign memo at TAB A.

COORDINATION: TAB B

Attachments:
As stated

Prepared by: CDR (b)(6), DHSD/ODASD(FHP&R), (b)(6), DCDOS #46306

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

MEMORANDUM FOR DIRECTOR, THE JOINT STAFF
COMMANDANT OF THE US COAST GUARD

SUBJECT: Designation of US Coast Guard's National Strike Force as an Anthrax Vaccine Immunization Program (AVIP) Priority 1 Designated Special Mission Unit.

REFERENCE: Under Secretary of Defense for Personnel and Readiness Memorandum, "Policy on Administrative Issues Related to the Anthrax Vaccine Immunization Program (AVIP), August 6, 2002."

By direction of the Undersecretary of Defense for Personnel and Readiness, the Assistant Secretary of Defense for Health Affairs may deem additional personnel occupationally at higher risk for exposure to anthrax and their performance essential for mission critical capabilities.

The increasing threat of the use of weapons of mass destruction makes it essential that we have a critical response and decontamination capability like the US Coast Guard's National Strike Force.

As such, the US Coast Guard's National Strike Force is designated as an Anthrax Vaccine Immunization Program (AVIP) Designated Special Mission Unit and subject to priority-1 anthrax immunization plans.

This designation is effective immediately. COL Gaston Randolph, Director of the AVIP-MILVAX Agency is the point of contact for any question on this matter. He can be contacted at (b)(6).

William Winkenwerder Jr. MD

Subject: Designation of US Coast Guard's National Strike Force as an Anthrax Vaccine Immunization Program (AVIP) Priority 1 Designated Special Mission Unit.

COORDINATION

COL Gaston Randolph, US Army
Director, MILVAX-AVIP Agency

20 February 2003

(b)(6)
02/21/2003 08:28 AM

To: (b)(6) OSAGWI@OSAGWI, (b)(6) @OSAGWI
cc:

Subject: FW: AVIP Special Mission Unit designation

(b)(
COL Randolph has made some changes to the AVIP Spec Mission Unit package. See attachment below. Please incorporate into final if has not already gone out.

I haven't seen this before.

Thanks
(b)(6)

---------- Forwarded by (b)(6) on 02/21/2003 08:29 AM ----------

"Randolph, Gaston M COL OTSG" (b)(6) @otsg.amedd.army.mil>
on 02/20/2003 08:49:50 PM

To: (b)(6) @deploymenthealth.osd.mil" (b)(6) @deploymenthealth.osd.mil>
cc:

Subject: FW: AVIP Special Mission Unit designation

I made a couple recommended changes using Word's Tracking Tool. Randy

-----Original Message-----
From: (b)(6) deploymenthealth.osd.mil
(b)(6) @deploymenthealth.osd.mil]
Sent: Thursday, February 20, 2003 2:46 PM
To: (b)(6) @otsg.amedd.army.mil
Subject: AVIP Special Mission Unit designation

COL,
Here is a rough for the USCG AVIP' Special Mission Unit designation. Please let me know if there are any glaring errors. Our admin folks are checking the "Memorandum for" line. Please let me know if you see any glaring errors. Thanks sir.

V/R,
(b)(6)

(See attached file: AVIP Designated Special Mission Unit 20 Feb 03.doc)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

February 26, 2003, 2:30

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ellen P. Embrey, DASD, Force Health Protection and Readiness **//s//02/25/03**

SUBJECT: Designation of U.S. Coast Guard's National Strike Force as an Anthrax Vaccine Immunization Program (AVIP) Priority 1 Designated Special Mission Unit

- Attached at TAB A is a memorandum that designates the U.S. Coast Guard's National Strike Force as a Designated Special Mission Unit and therefore an AVIP priority-1 unit under current DoD policy and implementation plans.

- These National Strike Force teams provide critical response and decontamination support to facilities contaminated with anthrax spores. Most notably, this unit deployed and supported the decontamination of the Hart building in Washington, DC in Fall 2001.

- The Under Secretary of Defense (P&R) policy memorandum dated August 6, 2002, gives the ASD (HA) authority to identify other personnel as mission critical and therefore requiring immunization with the anthrax vaccine.

- This request has been coordinated with the AVIP-MILVAX office, giving full concurrence (TAB B).

RECOMMENDATION: That the ASD (HA) sign memo at TAB A.

COORDINATION: TAB C

+ Joint Staff
MG James Hawkins
Vice Director, Joint Staff
5 Feb 03.

+ Dr. Anna J. Winegar (OSD)

Attachments:
As stated

Prepared by: CDR (b)(6) DHSD/OASD (FHP&R) (b)(6)
PCDOCS# 46306

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

MAR 1 8 2003

MEMORANDUM FOR DIRECTOR, THE JOINT STAFF
COMMANDANT OF THE U.S. COAST GUARD

SUBJECT: Designation of U.S. Coast Guard's National Strike Force for Anthrax Vaccine Immunization Program (AVIP)

REFERENCE: Deputy Secretary of Defense "Reintroduction of the Anthrax Vaccine Immunization Program (AVIP)," June 28, 2002

The referenced memorandum authorizes inclusion in the AVIP of additional personnel at higher risk of exposure to anthrax based on performance of critical capabilities.

The increasing threat of the use of weapons of mass destruction makes it essential that we have a critical response and decontamination capability like the U.S. Coast Guard's National Strike Force.

Therefore, I approve inclusion of the U.S. Coast Guard's National Strike Force, involving approximately 213 active duty members, in current AVIP implementation. Execution of the AVIP for these personnel is under the authority of the Commandant of the Coast Guard.

This determination is effective immediately. COL Gaston Randolph, Director of the AVIP-MILVAX Agency is the point of contact for any question on this matter. He can be contacted at (703) 681-5101.

William Winkenwerder, Jr., MD

cc:
Surgeon General of the Army

THE JOINT STAFF
WASHINGTON, DC

Reply ZIP Code:
20318-0300

DJSM-0100-03
05 February 2003

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

Subject: Designation of US Coast Guard's National Strike Force as an Anthrax Vaccination Immunization Program (AVIP) Special Mission Unit

1. The US Coast Guard has requested that the members of its National Strike Force be designated as a Special Mission Unit (Priority 1) under the DOD AVIP (enclosure).

2. The Coast Guard has assigned 213 active duty personnel into three National Strike Teams (NSTs) capable of providing critical response and decontamination support to facilities contaminated with anthrax spores. In the past, this unit has deployed and supported activities such as decontamination of the Hart building in Washington, D.C. The Coast Guard has stated that the NSTs will continue to respond to anthrax contamination in the foreseeable future.

3. This request was coordinated with the Army as the executive agency for the DOD Immunization Program for Biological Warfare Defense.

4. I concur in this request and recommend that the USCG National Strike Force be designated as a special mission unit and that all personnel assigned to this unit receive anthrax immunizations based on that priority.

JAMES A. HAWKINS
Major General, USAF
Vice Director, Joint Staff

Enclosure

Copy to:
Commandant, US Coast Guard

U S Department of Transportation
United States Coast Guard

Commandant
United States Coast Guard

2100 Second Street, S W
Washington, DC 20593-0001
Staff Symbol G-WK
Phone (202) 267-1098
Fax (202) 267-4512
Email

6230

DEC 13 2002

MEMORANDUM

TJ BARRETT
Acting

From THOMAS H COLLINS
COMDT (G-C)

Reply to G-WK
Attn of. RADM Joyce Johnson
202-267-1098

To Department of Defense, Joint Staff, ATTN Joint Staff Surgeon

Subj DESIGNATION OF U.S COAST GUARD'S NATIONAL STRIKE FORCE AS AN AVIP SPECIAL MISSION UNIT

Ref (a) COMDTINST M6230 3A, Coast Guard Anthrax Vaccine Immunization Program (AVIP), page 2
(b) CDC document, Antimicrobial Prophylaxis to Prevent Anthrax Among Decontamination/Cleanup workers Responding to an Intentional Distribution of *Bacillus anthracis*, dtd 22 Oct 01

1 I request that the U S Coast Guard's National Strike Force be designated as an AVIP Special Mission Unit As per reference (a), this will mandate anthrax immunization as a priority 1 unit The U S Coast Guard's National Strike Force includes 213 deployable active duty members divided into three different response teams (National Strike Teams (NSTs)). One mission performed in October-December 2001 was to respond to and perform decontamination efforts in areas known to be contaminated with anthrax Under current mission profiles, the NSTs will respond to anthrax contamination sites for the foreseeable future

2 Reference (b) describes the potential for breaches of protection and the contamination of workers using appropriate personal protection equipment Due to this potential for increased exposure during repeated deployments into contaminated anthrax areas, we request Anthrax vaccine to immunize Strike Team members that are at-risk of exposure due to mission requirements Designation as a Special Mission Unit will allow these at-risk military members to receive licensed anthrax vaccine IAW reference (a), thus ensuring maximum protection for our personnel with the potential to be repeatedly exposed to anthrax contaminated sites.

3 It is our intention to utilize only NST members who have been immunized with the anthrax vaccine as our primary responders to anthrax decontamination sites in the future. Currently, only six Strike Team personnel have begun the anthrax vaccine series Immunizing all Strike Team personnel will ensure that we are ready to respond immediately to any future anthrax contamination site Current projections to start most personnel with three doses of vaccine and bring those previously started in the program up-to-date would require 633 doses

4 My Point of Contact for this matter is RADM Joyce M Johnson at (202) 267-1098

#

Designation of US Coast Guard's National Strike Force as an Anthrax Vaccine Immunization Program (AVIP) Priority 1 Designated Special Mission Unit.

COORDINATION

COL Gaston Randolph, US Army	20 February 2003
Director, MILVAX-AVIP Agency	concur
OGC	as revised 3/4/03
DATSD (CBD)	13 Mar

Designation of US Coast Guard's National Strike Force as an Anthrax Vaccine Immunization Program (AVIP) Priority 1 Designated Special Mission Unit.

COORDINATION

COL Gaston Randolph, US Army	20 February 2003
Director, MILVAX-AVIP Agency	concur
OGC	(b)(6)

as revised 3/4/03

****
*** TX REPORT ***
****

TRANSMISSION OK

TX/RX NO	1874
CONNECTION TEL	(b)(6)
SUBADDRESS	
CONNECTION ID	
ST. TIME	03/26 09:07
USAGE T	00'21
PGS. SENT	2
RESULT	OK

Deployments Health Support Directorate
5113 Leesburg Pike, Suite 901
Falls Church, Virginia 22041
(703) (b)(6)
Fax: (703)

FACSIMILE TRANSMITTAL SHEET 3/26/03 8:42:42 AM

TO: COMMANDANT

FROM: (b)(6)

ORGANIZATION: U.S. COAST GUARD

FAX NUMBER: (b)(6)

TOTAL NO. OF PAGES INCLUDING COVER: 2

PHONE NUMBER: (b)(6)

SENDER'S PHONE NUMBER: (b)(6)

SUBJECT: DESIGNATION OF US COAST GUARD NATIONAL STRIKE FORCE FOR ANTHRAX VACCINE IMMUNIZATION PROGRAM (AVIP)

☐ URGENT ☐ FOR REVIEW ☐ PLEASE COMMENT ☐ PLEASE REPLY ☐ PLEASE RECYCLE

NOTES/COMMENTS:

Please confirm receipt

****
*** TX REPORT ***
****

TRANSMISSION OK

TX/RX NO	1873
CONNECTION TEL	(b)(6)
SUBADDRESS	
CONNECTION ID	JOINT STAFF SG
ST. TIME	03/26 09:05
USAGE T	00'44
PGS. SENT	2
RESULT	OK

Deployments Health Support Directorate
5113 Leesburg Pike, Suite 901
Falls Church, Virginia 22041
(703) (b)(6)
Fax: (703)

FACSIMILE TRANSMITTAL SHEET 3/26/03 9:03:54 AM

TO: SURGEON GENERAL ***FROM:*** (b)(6)

ORGANIZATION: JOINT STAFF SURGEON

FAX NUMBER: (b)(6)

TOTAL NO. OF PAGES INCLUDING COVER: 2

PHONE NUMBER: (b)(6)

SENDER'S PHONE NUMBER: (b)(6)

SUBJECT: DESIGNATION OF US COAST GUARD NATIONAL STRIKE FORCE FOR ANTHRAX VACCINE IMMUNIZATION PROGRAM (AVIP)

☐ URGENT ☐ FOR REVIEW ☐ PLEASE COMMENT ☐ PLEASE REPLY ☐ PLEASE RECYCLE

NOTES/COMMENTS:

Please confirm receipt

(b)(6)

Forward to MS Embassy Office
FORAC:
(1) Prepare package w/
response to DJS and
implementing document (i/
FRP+R, concurs).
(2) Coord action w/ MICVAX

Dir. W wants turnaround NLT
20 FEB — based on the date
of the USCG originating
document.

(b)(6)

DOCUMENT MANAGEMENT DIVISION
ADMIN OFFICE

TRICARE
TRICARE Management Activity

ACTION OFFICE OHS **DATE** 3-20-03 **PCDOCS #** 45855
(R) 46306

The attached correspondence is returned for the following reason(s):

- ☑ **Distribution**
- ☐ **Coordination**
- ☐ **Revision**
- ☐ **Correct Signature Block**
- ☐ **Correct Envelope Size**
- ☐ **Correct Letterhead**
- ☐ **Provide Original/Supporting Documents**
- ☐ **Provide SD 391**
- ☑ **Retain for your Files**

(b)(6)

3/25

Fax copy of memo and attachment to Dir Joint Staff and Commandant Coast Guard — copy for Delara and Col Adams

(b)(6)

Additional Comments:

Signed response Scanned into PCDocs #45855

Health Affairs

ROUTING AND TRANSMITTAL SHEET

TRICARE Management Activity

	Sign	Coord		Sign	Coord
3/3/03 ASD, HA BW	✓		____ Dir, TMA		
____ PDASD, HA					
____ DASD, C&PP			____ CMO		
____ DASD, FHP&R			____ Dir, DHS		
____ DASD, HB&FP			____ CFO		
____ DASD, HPA			____ COO		
			____ Dir, Regional Operations/PEO		
____ CIO, MHS			____ Dir, IMT&R		
3/4/03 OGC, DoD		✓	____ OGC, TMA		
____ LA					
____ CoS, HA		✓	____ Dir, A&M		
____ Military Assistant			____ CoS, TMA		
____ Dir, PI, HA			____ Dir, PI, TMA		
____ Dir, P&S TAB C			____ Dir, Admin		
3/3/03 Other (Specify) Dr. Johnson-Winegar		✓	____ Other (Specify)		

DMD (SKY) ____ Date: 2/27/03 **DMD (PNT)** ____ Date: 2/27/03

Date Received: 2/26/03 **Suspense Date:** ____

Subject: Designation of US Coast Guard's National Strike Force as an Anthrax Vaccine Immunization Program Priority 1 Designated Special Mission Unit

PCDOCS #: 46306, 46599 **OSD/P&R #:** ____

AO: COR (b)(6) **Office:** DHS **Phone #** (b)(6)

NOTES:

Please call Anita or Greg
for pick up.
(703) 697-8979

(75)

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

OCT 19 2001

HEALTH AFFAIRS

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY
(MANPOWER AND RESERVE AFFAIRS)
ASSISTANT SECRETARY OF THE NAVY
(MANPOWER AND RESERVE AFFAIRS)
ASSISTANT SECRETARY OF THE AIR FORCE
(MANPOWER AND RESERVE AFFAIRS)
EXECUTIVE DIRECTOR, TRICARE MANAGEMENT ACTIVITY

SUBJECT: Policy on Prophylaxis and Treatment for Anthrax Exposures

This policy provides guidance for prescribing antibiotics for post-exposure prophylaxis for anthrax. This guidance is applicable to all DoD providers. The recent isolation of anthrax in several different locales in the U.S. has highlighted the need for policy guidance concerning the dispensing of antibiotics to those who are concerned that they may have been exposed to anthrax or who fear they might be exposed in the future. Current guidelines from the Centers for Disease Control and Prevention (CDC) recommend that physicians not prescribe antibiotics for anthrax at this time unless there is credible evidence to support the possibility of exposure. Providers should work with local public health officials in cases of suspected exposure, and prescribe antibiotics in accordance with current CDC guidelines.

A focus upon identification and tracking of suspected exposures will help to ensure that those exposed receive appropriate care and follow-up. Preventive measures, such as prophylactic antibiotics, are not without risk, and in the absence of any evidence of a release of a biologic agent, currently have no benefit. Inappropriate use of antibiotics will lead to increased antibiotic resistance among microorganisms causing common bacterial infections (e.g., otitis media, pneumonia) and may result in serious adverse effects (e.g., *Clostridium difficile* colitis, allergic reactions, interactions with other medications). Given the risks associated with inappropriate antibiotic use and since medications from the national stockpile would be rapidly available for prophylaxis of exposed persons following a confirmed bioterrorist event, physicians should refrain from prescribing antibiotics for patients for current use or to stockpile for the future.

DoD providers should prescribe antibiotics for patient use as prophylaxis against biological agents only if there is clinical suspicion of exposure to anthrax, or there has been confirmation by local public health officials that such prescribing is indicated. Similarly, military facility pharmacies should dispense such prescriptions only under these circumstances. All suspected exposures to biologic agents must be reported to local preventive medicine, public health and law enforcement officials immediately so that appropriate investigation and any necessary control measures may begin.

Language for ACIP to consider regarding AVA
Ocotber 25, 2001

1.Recommendations for further clarification of relative efficacy of 60 day antibiotic post-exposure prophylaxis vs at least 30 days of antibiotics + 3 doses of anthrax vaccine

Current
Because of the potential persistence of spores following a possible aerosol exposure, antibiotic therapy
should be continued for at least 30 days if used alone, and although supporting data are less definitive, longer antibiotic therapy
(up to 42--60 days) might be indicated. If vaccine is available, antibiotics can be discontinued after three doses of vaccine have
been administered according to the standard schedule (0, 2, and 4 weeks)

Need to discuss
Basis for current recommendation of 60 days of abx or 30 days abx + 3 doses vaccine is the Friedlander 1992 study. On the basis of this data alone, both strategies appear to be effective, and the evidence for additional efficacy of vaccine+abx is from one monkey only. In light of current vaccine shortages, would it be best to recommend only 60 days abx for postexposure, and shift vaccine resources to pre-exposure prophylaxis (see point # 3)?

2. Recommendations for anthrax vaccine studies in pediatric populations

IND contingency protocol approved by CDC IRB Oct 5th indicates that
vaccine can be used post-exposure for pediatric populations. Shall we include as part of ACIP research agenda?

3. Prioritization of populations for pre-exposure anthrax vaccination
- **based on current epidemiology &**
- **potential wider scale threat**

Current
Bioterrorism Preparedness

Although groups initially considered for preexposure vaccination for bioterrorism preparedness included emergency first
responders, federal responders, medical practitioners, and private citizens, vaccination of these groups is not recommended.
Recommendations regarding preexposure vaccination should be based on a calculable risk assessment. At present, the target

population for a bioterrorist release of B. anthracis cannot be predetermined, and the risk of exposure cannot be calculated. In addition, studies suggest an extremely low risk for exposure related to secondary aerosolization of previously settled B. anthracis spores (28,83). Because of these factors, preexposure vaccination for the above groups is not recommended. For the military and other select populations or for groups for which a calculable risk can be assessed, preexposure vaccination may be indicated.

Options other than preexposure vaccination are available to protect personnel working in an area of a known previous release of B. anthracis. If concern exists that persons entering an area of a previous release might be at risk for exposure from a re-release of a primary aerosol of the organism or exposure from a high concentration of settled spores in a specific area, initiation of prophylaxis should be considered with antibiotics alone or in combination with vaccine as is outlined in the section on postexposure prophylaxis.

Revised:
According to the Advisory Committee on Immunization Practices, routine vaccination with anthrax vaccine, adsorbed (AVA) is indicated for persons engaged a) in work involving production quantities or concentrations of *B. anthracis* cultures and b) in activities with a high potential for aerosol production. Laboratorians using standard Biosafety Level 2 practices in the routine processing of clinical samples are not at increased risk for exposure to *B. anthracis* spores.

However, ACIP recommendations do not address the issue of vaccination of persons handling environmental specimens in outbreak settings. Standard BSL2 practices may be insufficient for processing and handling these specimens. Because of the ongoing threat of exposure to anthrax spores, vaccination of these workers is appropriate, with the highest priority for vaccination of workers in laboratories and decontamination crews handling specimens from areas where anthrax has been documented.

The next priority of persons considered for vaccination would be public health and law enforcement teams expected to respond to anthrax investigations. Additionally, if it is determined that an ongoing risk of bioterrorist threats using *B anthracis* exists, it would be appropriate to vaccinate firefighters, police, hazmat and EMT personnel in large metropolitan areas to be able to respond to and stabilize an emergency large scale outbreak.

P&R MEETING RE GAO/IG REPORTS (Mr. Mayberry):

1. COL Diniega, LTC (b)(6), MAJ (b) attended as representative of Dr. (b)(6) (ASDHA not DASD-HOP)

2. 4 reports to HA as lead:
   - Bioterrorism—Research Activities and Preparedness Activities, Sep 2001 (WEB)
   - Medical Readiness – Clarification of Expectations (Draft, Jul 2001; HA Response drafted by CDR (b)(6) 14 Aug 01) ~~(SECRET)~~
   - AVIP and USAF, NG (WEB)
   - ROK MTF CB preparedness (CLASSIFIED)

3. Format:
   PROBLEM IDENTIFIED IN REPORT:

   ACTIONS TAKEN TO DATE:

   CURRENT STATUS (Identify shortfalls, if any):

   HAVE REQUIREMENTS CHANGED SINCE 9/11/01? (Policy/resources/requirements issues?)

4. Draft responses in by Noon, Mon. Report to Dr. Chu by Thu. Meeting Mon or Tue

5. Actions:

   AVIP and RCs – LTC (b)(6)
   Fed Rsch/Preparedness – COL D. (called Mr (b)(6) as much bigger than HA) ~~(Sat/Sun)~~
   Med Readiness – CDR (b)(response good. Must be reformatted
   MTFs in ROK – COL Thompson trying to get report. Probably need Service responses. Probably should go to TMA as involves many peacetime care issues/facilities.

6. Proposed actions:
   COL Baken, HOP POC/Coordinator: farm out work w/ COL Driscoll
   Rest of HOP - support

PROBLEM IDENTIFIED IN REPORT:

ACTIONS TAKEN TO DATE:

CURRENT STATUS (Identify shortfalls, if any):

HAVE REQUIREMENTS CHANGED SINCE 9/11/01? (Policy/resources/requirements issues?)

(76)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

March 6, 2003, 4:00 P.M.

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ms. Ellen P. Embrey, DASD, Force Health Protection and Readiness

SUBJECT: Request for Exception to Policy for Priority II Anthrax Vaccinations for Selected Air Force Air Mobility Command (AMC) Personnel.

- Per USD(P&R) policy memo, August 6, 2002, a request for exception to policy requires recommendation from the Combatant Commander, with final approval from ASD(HA) in consultation with the Chairman of the Joint Chiefs of Staff.

- The Director, Joint Staff endorsed a recommendation by the Air Force to vaccinate certain AMC personnel against anthrax as an exception to policy (TAB B). This request includes 4,250 personnel, including strategic airlift crews, Ravens, and tactical airlift control elements (TALCEs). For the purpose of determining impact to overall supply, 12,750 doses (4,250 x 3 inoculations) is the planning figure.

- The Joint Staff recommended approval of this request in its entirety; however, the MILVAX-AVIP agency is concerned that all personnel under the requested exception to policy would be immediately vaccinated. They recommend phasing vaccinations to start at the time the person is actually placed on orders to high threat area.

- The Deputy for Chemical and Biological Defense non-concurs with immediately immunizing the entire 4,250 AMC personnel outlined in the request. He recommends vaccinations for these individuals after notification of deployment to a high-risk area.

- Given stockpile concerns, it is reasonable to approve immediate vaccination of strategic airlift crews now, and approve vaccination of Raven and TALCE personnel only when placed on orders to a designated high threat area.

RECOMMENDATION: Approve phased vaccination by signing memo at TAB A.

COORDINATION: TAB C

Attachments:
As stated

Prepared by: CDR (b)(6) DHSD/ODASD(FHP&R), (b)(6) 46714, 46715

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

MAR 10 2003

MEMORANDUM FOR DIRECTOR, THE JOINT STAFF
COMMANDER, AIR MOBILITY COMMAND

SUBJECT: Request for Exception to Policy for Priority II Anthrax Vaccinations for Selected AMC Personnel

REFERENCE: Under Secretary of Defense (Personnel and Readiness) memorandum, "Policy on Administrative Issues Related to the Anthrax Vaccine Immunization Program (AVIP)," August 6, 2002

In accordance with the above reference, an exception to policy is approved for Tactical Airlift Control Elements (TALCEs), Strategic Airlift Aircrew Members, and Security Forces Ravens to be immediately vaccinated against anthrax.

Execution of this vaccination program is per previously published clinical and administrative guidelines and consistent with existing Service implementation plans. The Secretary of the Army remains the Executive Agent for the Anthrax Vaccine Immunization Program (AVIP). Questions regarding this matter shall be directed to COL Gaston Randolph, Director of the MILVAX-AVIP agency. He can be reached at (703) 681-5101.

William Winkenwerder, Jr.

William Winkenwerder, Jr., MD

****
*** TX REPORT ***
****

TRANSMISSION OK

TX/RX NO	1776
CONNECTION TEL	(b)(6)
SUBADDRESS	
CONNECTION ID	
ST. TIME	03/12 13:12
USAGE T	00'47
PGS. SENT	2
RESULT	OK

Deployments Health Support Directorate
5113 Leesburg Pike, Suite 901
Falls Church, Virginia 22041
(703) (b)(6)
Fax: (703)

FACSIMILE TRANSMITTAL SHEET 3/12/03 1:11:27 PM

TO: ***AMC COMMANER*** ***FROM:*** (b)(6)

ORGANIZATION:

FAX NUMBER: (b)(6) ***TOTAL NO. OF PAGES INCLUDING COVER:*** 2

PHONE NUMBER: (b)(6) ***SENDER'S PHONE NUMBER:*** (b)(6)

SUBJECT: REQUEST FOR EXCEPTION TO POLICY FOR PRIORITY II ANTHRAX VACCINATIONS FOR SELECTED AIR FORCE AIR MOBILITY COMMAND (AMC) PERSONNEL

☐ URGENT ☐ FOR REVIEW ☐ PLEASE COMMENT ☐ PLEASE REPLY ☐ PLEASE RECYCLE

NOTES/COMMENTS:

46025

THE JOINT STAFF
WASHINGTON, DC

Reply ZIP Code
20318-0300

DJSM-0109-03
06 February 2003

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

Subject. Exception to Policy for Priority II Anthrax Vaccinations for Selected AMC Personnel

1. Recommend approval of AMC's request (Enclosure A) that selected personnel be approved for anthrax immunizations as an exception to policy.

2 Personnel to be vaccinated under the exception would include strategic airlift crews, Ravens (security forces that travel with the aircraft and protect crews while on the ground at foreign airfields) and tactical airlift control elements (TALCEs) -- an estimated 4,250 personnel, including Active and Reserve Component personnel.

3 Service members are expected to deploy to designated higher-threat areas (HTAs) for more than 15 cumulative days in a 12-month period and are at heightened risk of anthrax exposure This request is supported by USCENTCOM, USEUCOM and USTRANSCOM

4. The Army, as the executive agent for the DOD Immunization Program for Biological Warfare Defense, concurred with critical comment (Enclosure B) Although vaccination of personnel who are in an HTA for cumulative deployments of greater than 15 days in a 12-month period was supported, the Army indicated that vaccinations should begin on an individual basis when the individual is first notified of a deployment or deploys into one of the HTAs for the first time

5 While this approach may be feasible for some Active Component personnel, significant advance planning is required to administer vaccinations to Reserve Component personnel Combined with the relatively short notice inherent in many airlift missions, it seems prudent to give the AMC commander discretion to vaccinate these personnel prior to actual notice of a deployment if it is deemed that they have a high probability of being deployed to an HTA. Furthermore, many of these personnel are expected to require smallpox immunizations under the current smallpox vaccination policy, and it will be much simpler logistically to administer both vaccinations at the same time.

6 TALCE personnel are subject to deployment at less than 12 hours notice to austere fields where medical logistic support to conduct vaccinations is often lacking. Therefore, immediate vaccination of those who are deemed to have a high probability of deploying to an HTA should be authorized.

7 Other Active personnel who have deployed to one of the designated HTAs within the past 12 months should also be authorized for immediate vaccination All other personnel should begin vaccinations as soon as they are designated for deployment to an HTA

8. The Joint Staff points of contact for this issue are (b)(6) (b)(6) (b)(6)

JAMES A. HAWKINS
Major General, USAF
Vice Director, Joint Staff

Enclosures

Copy to
HQ USAF, Attn Deputy Chief of Staff for Air and Space Operations

DEPARTMENT OF THE AIR FORCE
HEADQUARTERS UNITED STATES AIR FORCE
WASHINGTON DC

AFODM 001-03
16 Jan 03

MEMORANDUM FOR DIRECTOR, JOINT STAFF

SUBJECT Exception to Policy for Priority II Anthrax Vaccinations for Selected AMC Personnel

Request Joint Staff action on the attached Exception to Policy (ETP) request from AMC/SG (Attachment 1) Current DoD policy for requesting ETP for Priority II anthrax vaccinations requires recommendation from Combatant Commander, with final approval from ASD/HA in consultation with the Chairman, Joint Chiefs of Staff (USD/P&R Memo, 6 Aug 02) (Attachment 2)

Current DoD policy for Priority II anthrax vaccination requires personnel to be assigned or deployed to a higher threat area (HTA) greater than 15 consecutive days AMC strategic airlift aircrews, Ravens and Tactical Airlift Control Elements (TALCEs) are not usually in a HTA greater than 15 *consecutive* days, and therefore, are not authorized to receive anthrax vaccine under Priority Group II However, since many of the designated AMC personnel are in a HTA greater than 15 *cumulative* days, their risk for possible anthrax exposure is increased Therefore, request an ETP for AMC strategic airlift aircrews, Ravens and TALCEs (an estimated 4,250 personnel, including AD and ARC personnel) to receive anthrax vaccine now

Air Staff POCs on this issue are Brig Gen Robert Smolen, HQ USAF/XON (DSN (b)(6), e-mail (b)(6) @pentagon af mil) and Col Deneice Van Hook, HQ USAF/SGZP (DSN (b)(6) e-mail (b)(6) @pentagon af mil)

Attachments
1 AMC Request for ETP w/ Bulleted Point Paper
2 6 Aug 02 USD/P&R Memo

RONALD E. KEYS, Lt Gen, USAF
Deputy Chief of Staff
Air & Space Operations

DEPARTMENT OF THE AIR FORCE
HEADQUARTERS AIR MOBILITY COMMAND

29 OCT 2002

MEMORANDUM FOR HQ AFMOA/SG

FROM: HQ AMC/SG
203 West Losey Street, Suite 1600
Scott AFB IL 62225-5219

SUBJECT: Request for Strategic Airlift Mission Exception to Policy Anthrax Vaccine Implementation Plan (AVIP)

1. Strategic air mobility assets routinely transit geographic areas identified as higher threat areas (HTAs) for anthrax, but are not included in the Air Force AVIP plan. Due to their unique missions, AMC/SG requests an Exception to Policy, in accordance with Annex B of the Air Force AVIP 2002 Implementation Plan. AMC has identified three specific missions for ETPs: Tactical Airlift Control Elements (TALCEs), Strategic Airlift Aircrew Members, and Ravens.

2. TALCFs, including their associated Global Reach Liaison (GRL) teams, are subject to rapid deployment (less than 12 hours notice) to austere fields in HTAs on average for 45 days. TALCEs lack adequate pre-deployment time to provide an initial anthrax vaccination series (i.e. shots 1, 2 and 3). Additionally, they often lack the medical logistics support necessary to vaccinate in the field due to their far forward laydown. Because of their mission criticality and logistical circumstances, TALCEs should be identified as Priority Two personnel.

3. Due to the nature of strategic airlift, aircrew members assigned to this mission are unlikely to remain in place for 15 days or longer, but can be reasonably expected to exceed 15 cumulative days in a 12-month period. IAW with instructions in Annex B of the Air Force AVIP 2002 plan, request that AMC and AMC gained C-5, C-17, C-141, and special airlift mission (C-32, C-37, C-40) crewmembers be granted an ETP to initiate immediate anthrax vaccination. In addition, ETP to vaccinate Security Forces Ravens is also requested. Ravens are specially trained security forces that travel with these aircraft and protect them while on the ground at foreign airfields. These flyers and security forces should be identified as Priority Two personnel.

4. The Command Surgeon, Headquarters Air Mobility Command, estimates the total number of affected personnel as 4,250. Please refer to the attached point paper for further details. Should your staff have any questions, my POC is Lt Col (b)(6) DSN (b)(6) or (b)(6) @scott.af.mil

CHARLES B. GREEN
Brigadier General, USAF, MC, CFS
Command Surgeon

Attachment:
AVIP ETP Point Paper

POINT PAPER

ON

ANTHRAX VACCINE FOR STRATEGIC AIRLIFTERS

- The Air Force AVIP 2002 Implementation Plan directs anthrax vaccination for personnel assigned 15 consecutive days or longer to Higher Threat Areas (HTAs)
  - AVIP Plan specifically identifies vaccination policy for special missions and those assigned to HTAs and deployed as part of AEF buckets
  - AVIP Plan does not address those military personnel frequently transiting HTAs but not residing for ≥ 15 consecutive days – a frequent occurrence for strategic airlifters
  - AVIP Plan Annex B allows MAJCOM to submit Exception to Policy (ETP)
    - Plan specifically suggests strategic airlift personnel be considered for ETP when personnel can be expected to accumulate 15 days in a 12-month period
- C-5, C-17, C-141 and special airlift mission crewmembers routinely fly into the HTAs and are expected to exceed 15 days in a 12-month period It would be appropriate to vaccinate them based on their frequent exposure/rotation through these HTA
- Ravens, security forces accompanying these aircraft, provide aircraft security at off-station airfields, are also expected to exceed 15 days cumulative days in HTAs, and require similar anthrax vaccine protection
- Tactical Airlift Control Elements (TALCEs) and Global Reach Laydown teams provide initial aerial port, aircraft maintenance, and C2 for strategic airlift at far forward bases
  - Demanding mission has 12-hour deployment notice for 45-day missions
  - Do not have robust medical support, including routine access to vaccinations
  - They are AEF enablers, not tied to an AEF bucket, subject to deployment at any time
- Based on AMC functional inputs, AMC/SG estimates total AMC and AMC-gained personnel included in these proposals to be 4,250
  - Aircrew (1,000 Active Duty/ 2,350 Air Reserve Component), Ravens (250/220), TALCEs (430 all AD)
- Recommendation. Identify Strategic Airlift Aircrew, Ravens, and TALCEs as AVIP priority two personnel for immediate vaccination to adequately protect them prior to deployment

Lt Col (b)(6) /AMC/SGPA/DSN (b)(6) @scott.af.mil/dob/18 Oct 02

HEADQUARTERS DEPARTMENT OF THE ARMY
ASSISTANT DEPUTY TO THE ARMY OPERATIONS DEPUTY
(JOINT AFFAIRS)
OFFICE OF JOINT AND DEFENSE AFFAIRS

03 FEB 2003

ARMY PLANNER DACS-ZD-JDA
Memorandum Number 085-03

MEMORANDUM FOR SECRETARY, JOINT STAFF, ATTN: J-4 (Health Service Support Division), LTC Jones

SUBJECT: Exception to Policy for Anthrax Vaccination for Selected AMC Personnel. (SJS 03-00355)

1. Concur only subject to the following critical comment

2. Critical comment We agree that certain personnel of the USAF Air Mobility Command (AMC) may be at increased risk of *Bacillus anthracis* exposure based on cumulative deployments of greater than 15 days in a twelve-month period; however, anthrax vaccinations should not begin to the entire force of 4,250 personnel immediately on approval of this request. Vaccinations should only begin on an individual basis, when that individual is first notified of deployment or deploys into one of the CJCS-designated High Threat Areas (HTA) for the first time Any deviation from this concept will result in a non-concurrence.

Rationale: The alert status of AMC's subject personnel does not justify immediate vaccination Their alert status is no different than other Services' alert forces (e.g., Division Ready Brigades within Army Divisions), which are not being vaccinated. Rather, on notice of actual deployment these forces begin vaccinating if they fall within the other parameters of the DoD Anthrax Vaccine Immunization Program policy.

Further, current DoD contingency AVA requirements, coupled with competing AVA requests from both U S Federal Agencies and foreign nations, constrain DoD's anthrax vaccine supplies until May 03

3 POC is COL Randy Randolph or MAJ (b)(6), at (b)(6)

RANDY C WRIGHT
Colonel, GS
Deputy to the ADCSOPS (JA)

OPTIONAL FORM 99 (7-90)
FAX TRANSMITTAL # of pages ▶
(b)(6) (b)(6)
Phone # (b)(6)
Fax #

HEADQUARTERS DEPARTMENT OF THE ARMY
Assistant Deputy Chief of Staff for Operations and Plans
(Joint Affairs)

ARMY PLANNER DAMO-ZC
MEMORANDUM NO.

MEMORANDUM FOR SECRETARY, JOINT STAFF, ATTN: J-4 (Health Service Support Division), (b)(6)

SUBJECT: Exception to Policy for Anthrax Vaccination for Selected AMC Personnel, Joint Staff Action Number JSJ 03-00355

1. Concur subject to the following critical comment.

2. Critical comment. Concur that subject servicemembers of the US Air Force Air Mobility Command (AMC) may be at increased risk of *Bacillus anthracis* exposure based on cumulative deployments of greater than 15 days in a twelve-month period; however, anthrax vaccinations should not begin to the entire force of 4,250 servicemembers immediately on approval. They should begin in each individual when that individual first is notified of deployment or deploys into one of the CJCS-designated High Threat Areas (HTA) for the first time. Any deviation from this concept will result in a non-concurrence.

Rationale: Although we agree conceptually that subject forces may be at increased risk to exposure, we disagree that vaccinations to all individual servicemembers in the entire subject forces should be started immediately. Rather, the anthrax vaccination 6-dose series should start in each individual only when each individual servicemember in the subject forces has deployment orders into one of the 14 CJCS-designated HTA countries. The alert status of AMC's subject forces should not justify immediate vaccination—their alert status is no different than other Services' alert forces (e.g., Division Ready Brigades within Army Divisions), which are not being vaccinated. Rather, on notice of deployment these forces begin vaccinating if they fall within the other parameters of the DoD Anthrax Vaccine Immunization Program policy.

Further, current DoD contingency AVA requirements, coupled with competing AVA requests from both U.S. Federal Agencies and foreign nations, constrain DoD's anthrax vaccine supplies until May 03.

3. POC is COL Randy Randolph or MAJ (b)(6), at (b)(6).

ASSISTANT TO THE SECRETARY OF DEFENSE
3050 DEFENSE PENTAGON
WASHINGTON, DC 20301-3050

NUCLEAR AND CHEMICAL
AND BIOLOGICAL DEFENSE
PROGRAMS

MEMORANDUM FOR DEPUTY ASSISTANT SECRETARY OF DEFENSE
FOR FORCE HEALTH PROTECTION AND
READINESS

SUBJECT: *Request for Exception to Policy – Anthrax Immunizations for* Selected Air Force Air Mobility Command (AMC) Personnel

I cannot concur with your request for exception to policy to immediately immunize 4,250 selected Air Force Air Mobility Command (AMC) personnel. Vaccinations should begin only for individuals who are notified they are to deploy into one of the designated high threat areas and not for all AMC personnel at this time. Anthrax vaccine supplies are very limited and a six shot series for 4,250 personnel requires 25,500 doses of vaccine.

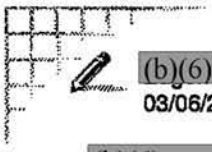
for Steve E Lawrence COL, USA
Anna Johnson-Winegar, Ph.D.
Deputy for Chemical/Biological Defense

Attachments:
As Stated

SUBJECT: Exception to Policy for Priority-2 Anthrax Vaccinations for Selected AMC Personnel

COORDINATION

Director, MILVAX-AVIP Agency	Concur with critical comments
USD (AT&L)	Non-concur with comments
DUSD (TSP&CP)	Concur



(b)(6)
03/06/2003 09:50 AM

To: (b)(6) OSAGWI@OSAGWI
cc:

Subject: FW: Exception to Policy for Selected AMC Personnel

cc

---------- Forwarded by (b)(6) OSAGWI on 03/06/2003 09:53 AM ----------

(b)(6) on 03/05/2003 05:15:33 PM

To: (b)(6)

cc:

Protection and Readiness, OASD/HA" <Ellen.Embrey@ha.osd.mil>

Subject: FW: Exception to Policy for Selected AMC Personnel

Guys: I spoke at length with the author of this request today. It is prudent to approve this request in its entirety. I made some modifying language. Please review for consistency.

Please process to get thru to Dr W by Friday, 7 Mar. Thanks much.

-----Original Message-----
From: (b)(6) deploymenthealth.osd.mil
(b)(6) deploymenthealth.osd.mil]
Sent: Wednesday, March 05, 2003 3:10 PM
To: (b)(6) @ha.osd.mil
Subject: Exception to Policy for Selected AMC Personnel

Sir,
ETP package as discussed.

v/r,
(b)(6)

---------- Forwarded by (b)(6) /OSAGWI on 03/05/2003 03:12 PM ----------

(b)(6)
03/05/2003 03:08 PM

FILE

DMMC Control #
2003066-0000

77

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

FEB 2 7 2003

HEALTH AFFAIRS

MEMORANDUM FOR DATSD (NUCLEAR, CHEMICAL & BIOLOGICAL DEFENSE PROGRAMS)

SUBJECT: Increased Production of Anthrax Vaccine Adsorbed (AVA)

Thank you for your memo dated February 20, 2003, subject as above (TAB 1), and the summary of the Joint Vaccine Acquisition Program (JVAP) office's review of options to increase production of AVA by BioPort Corporation. Their conclusions that BioPort can potentially increase near-term production by 20-percent would certainly enhance our readiness of US forces and domestic preparedness.

Your memo clearly outlines the steps and estimated timeline BioPort must take to accomplish this increased production. I know you, your staff, and the JVAP office are very committed to realizing this new AVA production target, as well providing the necessary oversight, support and assistance to BioPort for achieving this objective. I am very anxious to being receiving the increased AVA production in order to meet the growing demand for the vaccine.

I request a regular progress report towards the completion of this increased production initiative so that my office might stay informed of the situation and can better plan the distribution and use of this limited resource.

William Winkenwerder, Jr., MD

Attachment:
As stated

cc:
USD (P&R)
USD (AT&L)
PDUSD (P&R)
ASD (ISP)
ATSD (NCB)
DASD (FHP&R)
DUSD (TSP&CP)
SURG GEN, US ARMY
DIR, MILVAX/OTSG

ASSISTANT TO THE SECRETARY OF DEFENSE
3050 DEFENSE PENTAGON
WASHINGTON, DC 20301-3050

NUCLEAR AND CHEMICAL
AND BIOLOGICAL DEFENSE
PROGRAMS

FEB 20 [illegible]

MEMORANDUM FOR ASSISTANT SECRETARY OF DEFENSE
(HEALTH AFFAIRS)
DEPUTY UNDER SECRETARY OF DEFENSE
(TECHNOLOGY SECURITY POLICY AND
COUNTERPROLIFERATION)

SUBJECT: Increased Production of Anthrax Vaccine Adsorbed (AVA)

Per your request, the Joint Vaccine Acquisition Program (JVAP) office has reviewed options to increase production of AVA by BioPort, Inc. In the near term, BioPort can potentially increase production by approximately 20% by adding a second shift and thereby producing nine sublots per week instead of the current seven.

In order to accomplish this, additional personnel must be recruited or reassigned and trained with an estimated completion date of May 2003. Further, final installation and validation of a new water supply for "water for injection" must be completed. The estimated completion date for this is May 2003 followed by Food and Drug Administration (FDA) approval.

We will continue to monitor production progress and provide updated information on AVA doses produced by BioPort and released by the FDA.

Anna Johnson-Winegar, Ph.D.
Deputy for Chemical/Biological Defense

(78)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ms. Ellen P. Embrey, DASD, Force Health Protection and Readiness
(//s// 3-12-03 0915 Colonel Rauch)

SUBJECT: Department of Defense (DoD) Provision of Anthrax Vaccine for Federal Bureau of Investigation (FBI)

- The Assistant Director, Counterterrorism Division of the FBI requested anthrax and smallpox vaccinations to support approximately 150 personnel (TAB B).

- Personnel are integral to the FBI's mission responsible for federal law enforcement crisis response to weapons of mass destruction incidents involving US interests.

- Originally requesting anthrax and smallpox, the FBI was successful in getting smallpox vaccine from Department of Health and Human Services. However, DoD remains the primary source of anthrax vaccine.

- An interagency agreement between DoD and the FBI is required and must be completed before the request can be supported.

- DoD Directive 6205.4, Immunization of Other Than U.S. Forces for Biological Weapons Defense, reserves to the Secretary of Defense the authority to approve the provision of vaccine to non-DoD entities.

RECOMMENDATION: Sign coordination memo at TAB A, DEPSECDEF decision package that authorizes anthrax vaccine to approximately 150 members of the FBI.

COORDINATION: TAB C

Attachment:
As Stated

Prepared by: Colonel David Adams, FHP/R, (b)(6), Pedocs 46900

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ms. Ellen P. Embrey, DASD, Force Health Protection and Readiness

SUBJECT: Department of Defense (DoD) Provision of Anthrax Vaccine for Federal Bureau of Investigation (FBI)

- The Assistant Director, Counterterrorism Division of the FBI requested anthrax and smallpox vaccinations to support approximately 150 personnel (TAB B).

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- An interagency agreement between DoD and the FBI is required and must be completed before the request can be supported.

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RECOMMENDATION: Sign coordination memo at TAB A, DEPSECDEF decision package that authorizes anthrax vaccine to approximately 150 members of the FBI.

COORDINATION: TAB C

Attachment:
As Stated

Prepared by: Colonel David Adams, FHP/R, (b)(6)

THE ASSISTANT SECRETARY OF DEFENSE

1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

MEMORANDUM FOR UNDER SECRETARY OF DEFENSE (POLICY)
UNDER SECRETARY OF DEFENSE (ACQUISITION, TECHNOLOGY, AND LOGISTICS)
UNDER SECRETARY OF DEFENSE (PERSONNEL AND READINESS
GENERAL COUNSEL, DEPARTMENT OF DEFENSE

SUBJECT: Department of Defense (DoD) Provision of Anthrax Vaccine for Federal Bureau of Investigation (FBI)

The Assistant Director, Counterterrorism Division, FBI, requested anthrax vaccination for 150 personnel charged with the mission of national response in the event of an act of biological terrorism. These personnel are integral to the FBI's mission of federal law enforcement crisis response to weapons of mass destruction incidents involving U.S. interests.

Originally requesting anthrax and smallpox, the FBI was successful in getting smallpox vaccine from Department of Health and Human Services. However, DoD remains the primary source of anthrax vaccine.

DoD Directive 6205.4, Immunization of Other Than U.S. Forces for Biological Weapons Defense, reserves to the Secretary of Defense the authority to approve the provision of vaccine to non-DoD entities.

An interagency agreement is required and must be completed before the request can be supported. That interagency agreement is being developed by Office of General Counsel now.

We believe this request merits our support, as the sole source for this vaccine. Request your coordination/comment on the proposed Deputy Secretary of Defense decision package by March 14, 2003. My POC is Colonel David Adams, (b)(6).

William Winkenwerder, Jr., MD

Attachments:
As Stated

THE ASSISTANT SECRETARY OF DEFENSE

1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

DepSec Action_____

FOR: DEPUTY SECRETARY OF DEFENSE

FROM: William Winkenwerder, Jr., MD, ASD (Health Affairs)

SUBJECT: Department of Defense (DoD) Provision of Anthrax Vaccine for Federal Bureau of Investigation (FBI)

- The Assistant Director, Counterterrorism Division of the FBI requested anthrax and smallpox vaccinations to support approximately 150 personnel (TAB B).

- Personnel are integral to the FBI's mission responsible for federal law enforcement crisis response to weapons of mass destruction incidents involving U.S. interests.

- Originally requesting anthrax and smallpox, the FBI was successful in getting smallpox vaccine from Department of Health and Human Services. However, DoD remains the primary source of anthrax vaccine.

- An interagency agreement between DoD and the FBI is required and must be completed before the request can be supported.

- DoD Directive 6205.4, Immunization of Other Than U.S. Forces for Biological Weapons Defense, reserves to the Secretary of Defense the authority to approve the provision of vaccine to non-DoD entities.

RECOMMENDATION: Sign memo at TAB A authorizing anthrax vaccine to approximately 150 members of the FBI.

COORDINATION: TAB C

Attachment:
As Stated

Prepared by: Colonel David Adams, FHP/R, (b)(6)

DEPUTY SECRETARY OF DEFENSE

1010 DEFENSE PENTAGON
WASHINGTON, DC 20301-1010

MEMORANDUM FOR DIRECTOR, FEDERAL BUREAU OF INVESTIGATIONS

SUBJECT: Request for Anthrax Vaccine

I approve your request for anthrax vaccination of approximately 150 FBI personnel who are assigned national crisis response missions. This approval is subject to the terms of an interagency agreement addressing financial considerations and indemnification.

SUBJECT: Department of Defense (DoD) Provision of Anthrax Vaccine for Federal Bureau of Investigation (FBI)

COORDINATIONS

CoS (HA)	Ms. (b)(6)	_____
PDASD, HA	Mr.	_____
USD(P)	Mr. Douglas J. Feith	_____
USD(AT&L)	Mr. (b)(6)	_____
USD(P&R)	Dr. David S.C. Chu	_____
DoD, OGC	Mr. (b)(6)	_____

(79)

ANTHRAX VACCINATION IMMUNIZATION PROGRAM

April 30, 2002

Briefing Book

Ms Embrey
Deputy Assistant Secretary of Defense for Health Affairs

Table of Contents
New Anthrax Vaccine Immunization Program

Tab H

April 30, 2002 7:00 PM

New Anthrax Vaccine Immunization Program

- The Food and Drug Administration (FDA) approved BioPort's renovated facility (only US licensed manufacturer of anthrax vaccine) January 2002.

- The vaccine is safe and effective against all forms of anthrax, a conclusion determined by an Institute of Medicine independent national expert panel in February 2002.

- Vaccination 6-shot series—day 0, 2 weeks, 4 weeks, 6 months, 12 months, 18 months, and annual boosters; relatively high immunity/protection achieved with first 3 shots, but FDA licensure requires full 6 shots.[1]

- BioPort has the capability and is planning to produce approximately 2 million doses of vaccine in 2002, and 11 million total doses from 2002-2004. Approximately 500,000 doses now available.

- DoD negotiating to purchase total BioPort production for 2002-2004 for use by DoD and other federal agencies—DHHS, State, Justice/FBI, EPA and CIA (TAB 1).

- DoD believes threat of anthrax to DoD forces is real, based on current intelligence assessments.

- DoD policy for vaccine use takes into consideration: intelligence assessments; limited supply of the vaccine; complex vaccine dosing requirements; other national security requirements; and potential contingency requirements for DoD/DHHS.

    - Mandatory for military and Emergency Essential civilians and contractor personnel assigned/deployed/deployable for more than 15 days in higher threat areas whose performance is essential for certain mission critical capabilities (TAB 2).
    - Exemptions for certain medical conditions and administrative situations (e.g., separation being processed).

---

[1] CDC study underway to determine possible use of fewer doses.

- Implementation Strategy –
  - Start immunizations now, on prioritized basis, for priority groups 1 – 3.
  - Re-assess contingency use plans for priority groups 4 – 5 in early June 2002.

- Interagency federal coordination
  - For policy of vaccine use by non-DoD federal personnel and civilians, including dependents. First meeting (March 28), second meeting (April 16).
  - Final voluntary use policy, consistent and coordinated by OHLS, expected by June.

- DoD plans to announce policy May 3, 2002—following coordination with Office of Homeland Security, OMB and Congress.

- Messages –
  - Health and safety of our men and women is our top concern.
  - Anthrax vaccine is safe and effective.
  - Threat from anthrax is deadly and real. Vaccination offers a layer of protection, in addition to antibiotics, needed for certain members of the Armed Forces.
  - DoD policy for use of vaccine is coordinated with other federal agencies, representing groups of individuals that meet the definition of being at higher risk and whose performance is essential for certain mission critical capabilities.

Prepared by: William Winkenwerder, Jr., MD, Assistant Secretary of Defense (Health Affairs), (b)(6)

Tab H

Federal Anthrax Vaccine Requirements, starting DoD Stockpile in FY02 **version: 14 Apr 02**

Program Component	DoD Vaccine Requirement, Priorities 1, 2, & 3	DoD Vaccine Requirement, Priorities 4 & 5	Vaccination of Deferred Personnel	DoD Stockpile Set-Aside	HHS Require-ment	State Dept. Require-ment	FBI Require-ment	Other Require-ments	Sum of Fed Require-ments (DoD + Others)	Released Doses by Year (80% yield)	Fraction Consumed by Federal Purchase	Cumulative Fraction Consumed
	doses	doses	doses	doses	doses	doses	doses	doses	doses	doses		
FY 2002	172,929	1,014,000	0	600,000	500,000	44,000	500	23,000	2,354,429	1,598,824	147.3%	147.3%
FY 2003	357,227	1,239,632	406,640	300,000	1,000,000	114,000	2,720	11,500	3,431,719	3,978,824	86.2%	103.7%
FY 2004	357,227	1,987,057	609,960	300,000	1,500,000	149,000	620	5,750	4,909,614	4,816,471	101.9%	102.9%
Total FY02-04	887,383	4,240,689	1,016,600	1,200,000	3,000,000	307,000	3,840	40,250	10,695,762	10,394,119	102.9%	
									difference	-301,643	-2.9%	

Assumptions

* 15-day-in-theater policy
* Priorities 1, 2, & 3 begin May 02
* Priority 4 begins Aug 02 (uses stockpile)
* AVIP resumption decision 20 Apr 02
* Priority 5 begins Jan 03
* Vaccinations for deferred personnel begin Apr 03

Federal Anthrax Vaccine Requirements, starting DoD Stockpile in FY03 **version: 14 Apr 02**

Program Component	DoD Vaccine Requirement, Priorities 1, 2, & 3	DoD Vaccine Requirement, Priorities 4 & 5	Vaccination of Deferred Personnel	DoD Stockpile Set-Aside	HHS Require-ment	State Dept. Require-ment	FBI Require-ment	Other Require-ments	Sum of Fed Require-ments (DoD + Others)	BioPort Production (based on 80% yield)	Fraction of Production Consumed by Federal Purchase	Cumulative Fraction Consumed
	doses	doses	doses	doses	doses	doses	doses	doses	doses	doses		
FY 2002	172,929	1,014,000	0	0	500,000	44,000	500	23,000	1,754,429	1,598,824	109.7%	109.7%
FY 2003	357,227	1,239,632	406,640	0	1,000,000	114,000	2,720	11,500	3,131,719	3,978,824	78.7%	87.6%
FY 2004	357,227	1,987,057	609,960	300,000	1,500,000	149,000	620	5,750	4,909,614	4,816,471	101.9%	94.2%
Total FY02-04	887,383	4,240,689	1,016,600	300,000	3,000,000	307,000	3,840	40,250	9,795,762	10,394,119	94.2%	
									difference	598,357	5.8%	

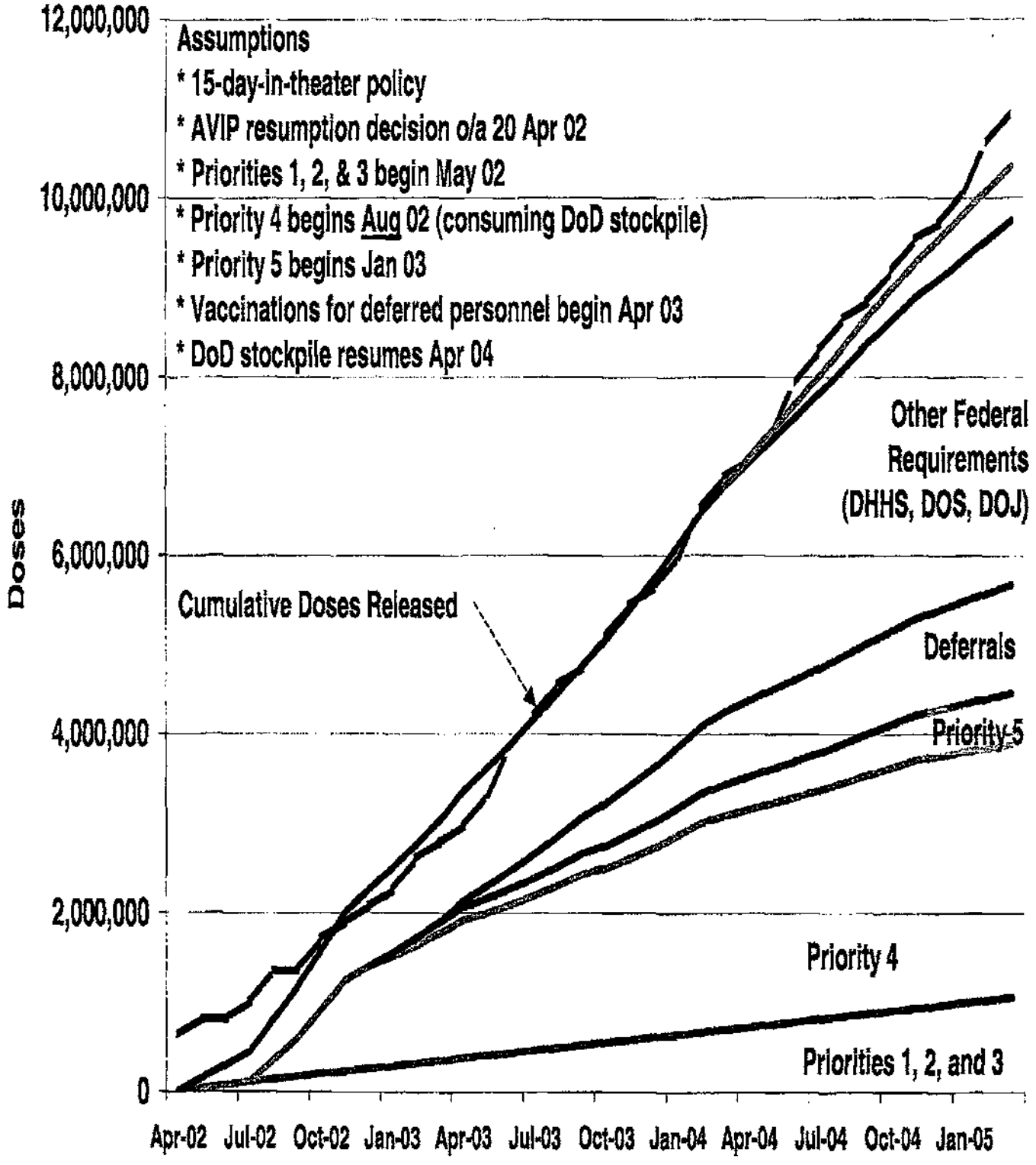
Assumptions

* 15-day-in-theater policy
* Priorities 1, 2, & 3 begin May 02
* Priority 4 begins Aug 02 (uses stockpile)
* AVIP resumption decision 20 Apr 02
* Priority 5 begins Jan 03
* Vaccinations for deferred personnel begin Apr 03
* **DoD stockpile resumes Apr 04**

Tab H

Chart 21

Joint Staff Priorities, 3-Year Observation
Cumulative Anthrax Vaccinations



AVIP Agency, DASG-HCA

4/30/02

Tab H

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

APR 25 200

MEMORANDUM FOR DEPUTY DIRECTOR, HOMELAND SECURITY

THROUGH: DEPUTY UNDER SECRETARY OF DEFENSE, POLICY SUPPORT

SUBJECT: U. S. Government Anthrax Vaccine Immunization Policy

The sole manufacturer of Anthrax Vaccine Adsorbed (AVA) recently obtained Food and Drug Administration approval of its renovated manufacturing facility. In an effort to determine the most appropriate distribution of this new supply of vaccine, the Department of Defense has initiated a series of meetings with several other federal agencies to develop a consistent U. S. Government vaccine use policy.

To date, two meetings have been held. The agencies that have participated include the Departments of State, Transportation, and Health and Human Services, as well as the Federal Bureau of Investigation, the Central Intelligence Agency and the Environmental Protection Agency. While these are not all the Cabinet-level Federal agencies that may have a need for the vaccine, outreach efforts to other agencies should continue to ensure their at risk personnel requirements are identified.

During the meetings, participating agencies came to a consensus on the need to give priority to mission essential personnel based on their risk of anthrax exposure. They generally agreed that agency policies needed to be consistent across the U.S. Government, and that requirements for vaccine needed to be prioritized based on highest risk of exposure over the next three years. For most of the agencies, higher risk and priority applies to civilian and contractor personnel assigned to higher threat areas, those employed in laboratories, and those who must investigate actual or suspected terrorist attacks. The exception is the Department of Transportation (DOT). DOT has identified its civilian senior leadership within the Office of the Secretary of Transportation as highest priority and thus to be the first to receive the vaccine within that agency. This will require additional discussion before a consistent policy can result.

The Department of Defense realizes this interagency effort may be more appropriately handled within the Health and Medical Policy Coordinating Committee within your office. Accordingly, as we discussed, I defer any further interagency efforts in this regard to your office to lead this endeavor to an appropriate conclusion.

Anticipating this, I am forwarding information describing our progress to date. Enclosed are points of contact for each of the agencies that have participated in meetings thus far, and the minutes of the meetings that occurred on March 28, 2002 and April 16, 2002. In addition, I have attached the policies provided by the Department of State, the Federal Bureau of Investigation and our own Department of Defense Directive on vaccination policy for "Other than U.S. Forces."

I would be happy to brief the interagency representatives at your next Health and Medical Policy Coordinating Committee meeting on efforts accomplished thus far. Additionally, I strongly encourage the involvement and participation of appropriate representatives of the National Security Council and the Office of Domestic Policy.

DoD anticipates announcing its own policy soon and it may be to our advantage to have begun work on a coordinated policy by that time.

I look forward to working with you on this. If you have any questions, please contact me or my Deputy Assistant Secretary for Force Health Protection and Readiness, Ms. Ellen Embrey, at (b)(6).

Sincerely,

William Winkenwerder, Jr., MD

Attachments:
As stated

ANTHRAX VACCINE IMMUNIZATION PROGRAM INTERAGENCY MEETING MINUTES
28 MARCH 2002
OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE FOR HEALTH AFFAIRS

The first in a series of US Government Interagency meetings was held to begin discussions on the identifying a consistent policy for all U. S. Government Agencies who anticipate continuing or establishing an Anthrax Vaccine Immunization Program activities. The following individuals attended.

Dr. (b)(6)
Ms.
Adn
COI
COI

Dr. (b)(6)
Dr.
Mr
Mr
Ms
Ms

DOD:

Dr. Winkenwerder welcomed the agencies and provided an overview of the current vaccine supply situation. He then discussed the need for a consistent anthrax vaccine usage policy for civilian personnel and suggested the other Federal agency establish their immunization policy based on the criteria of mission-essential personnel receiving the highest priority for vaccination. He reviewed current DoD policy for other than U.S. forces, which included other civilians and dependents. Dr. Winkenwerder requested all agencies review their agencies' vaccine requirement, forward a copy of the agency current anthrax vaccine policy and the updated version once the criteria of mission-essential is incorporated. Dr. Winkenwerder then requested that all agencies identify a point of contact for discussing legal issues to include memoranda of agreement and indemnification of the vaccine manufacturer.

(b)(5),(b)(6)

DOS

Dr. (b)(6) said the State Department program is voluntary and will continue as such. In addition, she mentioned that DoS usually immunizes the other Federal agencies' personnel who are stationed overseas. Dr. (b)(6) mentioned that the Department of State already has a proposed memorandum of agreement that is currently being reviewed by DoD.

DOT

Admiral Johnson reported that the Coast Guard is already included in the DoD military personnel number. But she would identify a DOT point of contact for the remainder of DOT.

FBI

Dr. (b)(6) mentioned that the FBI also has an Interagecy Agreement in DoD review. He expected the FBI to continue its current voluntary policy, however, they have never had a problem getting members to take the vaccine.

ACTION ITEMS

All agencies shall:

1) Review and confirm the requirement previously submitted;
2) Identify a point of contact for the discussions on indemnification and memoranda of agreement;
3) Provide copy of current anthrax vaccine immunization program policy;
4) Update current policy to incorporate a tiered approach to immunizations.

ANTHRAX VACCINE IMMUNIZATION PROGRAM INTERAGENCY MEETING MINUTES
16 APRIL 2002
DEPARTMENT OF HEALTH AND HUMAN SERVICES
BOARD HEARING ROOM

The second in a series of US Government Interagency meetings was held to review the current status of activities. The following individuals attended.

Dr. (b)(6)
(b)(6)
Dr.
Ms.
Adr
COI
COI
COI
LTC

Dr. (b)(6)
Dr.
(b)(6)
Dr. (b)(6)
Mr.
Mr.
Mr.
Mr.

DOD:

Dr. Winkenwerder discussed the DoD anthrax vaccine policy, its current status and the overall approach to accommodating other Federal agency requirements. He indicated Homeland Security wants to help coordinate interagency efforts. Dr. Winkenwerder said efforts would be made to ensure no inference that the vaccine is defective is conveyed. DoD messages will emphasize the vaccine is safe and effective and it offers a layer of protection to those who are immunized.

DHHS

Mr. (b)(6) discussed the use HHS will make of anthrax vaccine. Highest priority is for post-exposure use, with the aim of giving the vaccine as soon as possible after exposure is verified. Administration of the vaccine will occur with antibiotics. Subsequent to the 2-week and 4-week doses, antibiotics can then stop. If the B. anthracis is used more often or in a widespread manner, then the post-exposure program will grow.

Dr. (b)(6) said two requests for proposal are being published, one to develop vaccine and a second is a one-year notice that HHS will purchase the experimental vaccine.

(b)(5)

DOS

Dr. (b)(6) said the State Department program is voluntary and based on a worse case estimate that 100% of the eligible personnel elect to participate. Dr. (b)(6) said that

Tab H

Anthrax Vaccine Immunization Program (AVIP) Communications Plan

BACKGROUND:

The Department of Defense will resume the Anthrax Vaccine Immunization Program consistent with FDA guidelines and the best practice of medicine, beginning with personnel at higher risk whose performance is essential for certain mission critical capabilities. This policy, which focuses the use of the anthrax vaccine, takes into consideration use of the vaccine for other national security and civilian requirements.

OBJECTIVES:

- Enhance DoD's credibility with regard to use of the anthrax vaccine, and demonstrates commitment to health/safety of troops.
- Promote view of coordinated federal approach to vaccine use.
- Create a deterrent for the use of anthrax against US troops.
- Avoid specific information useful to adversaries.

STRATEGY:

- Inform key executive and legislative branch leaders of AVIP resumption plan prior to public announcement.
- Engage internal and external (third-party) experts to attest to the vaccine's effectiveness and explain the anthrax threat.
- Update "look and feel" of all educational materials including internet website and print media.

MESSAGES:

- The health and safety of our men and women in uniform are our top concerns.
- The anthrax vaccine is safe and effective.
- Vaccination offers a layer of protection that is needed for certain personnel at highest risk.
- The threat from anthrax is deadly and real.

Approved: _____

TACTICS AND AUDIENCES:

Audience/Outreach/ Product	Principal	Staff	Targets	Tactics	Timeline
<u>Completed</u> **Third Party Credible Sources**	Winkenwerder	HA/AVIP	Physicians & Scientists outside DoD	Teleconference and information	**Feb 8: 10:00 AM Mar 28: Fedex**
Trade Press	Winkenwerder	PA/HA/AVIP	AFIS-Rhem Times News Svc Military Update National Journal Stars & Stripes	Roundtable on Military Health System	**Feb. 22: 9:30 AM**
Internal DoD & Svc staffs	Winkenwerder	HA/AVIP	USD, ASD, JCS	Telephone calls	**ASAP**
White House	Chu/Winkenwerder	HA/AVIP	DPC/NSC	Call/brief	**3 days prior to announcement**
Homeland Security	Chu/Winkenwerder	HA/AVIP	Gov Ridge & staff	Call/brief	**3 days prior to announcement**
OMB	Wyatt	HA/AVIP	Robin Cleveland, Natl Sec Pgms	Call/brief	**3 days prior to announcement**

TACTICS AND AUDIENCES:

Audience/Outreach/ Product	Principal	Staff	Targets	Tactics	Timeline
Public Affairs Guidance	Clarke	PA/HA/AVIP	Worldwide PA Officers	Message	**2 days prior to announcement**
Congress	Winkenwerder, Moore, Abell, Wyatt, Embrey	HA/LA/AVIP	HASC, SASC, Govt Reform Sub, VA sub, indiv members	Call with offer to brief	**1-2 days prior to announcement**
Third Party Credible Sources	Winkenwerder	HA/AVIP	Physicians & Scientists outside DoD, AMA	Teleconference & information	**1 day prior to announcement**
Selected Media	Chu/Winkenwerder	PA/HA/AVIP	Wash Post, NYT, WSJ, CBS, AFIS	Embargoed 1-on-1 Interviews	**1 day prior to announcement**
Press Briefing	SecDef, Gen Myers, Chu, Gen Pace, Winkenwerder, Policy	PA/HA/AVIP	Pentagon Press Corps	Press briefing	**Day of announcement**
Press Release	Clarke	PA/HA/AVIP	All media	Press Release	**Day of announcement**
Veterans & Beneficiary Associations	Wyatt	HA/AVIP	30+ organizations	Press Release	**Day of announcement**

TACTICS AND AUDIENCES:

Audience/Outreach/ Product	Principal	Staff	Targets	Tactics	Timeline
Trade Press	Wyatt	HA/AVIP	AFIS Times News Svc Military Update US Medicine Federal Practitioner National Journal Stars & Stripes	Press Release	**Day of announcement**
Congress	Winkenwerder Svc Surgeons Gen	LA/HA/AVIP	All Offices	Packet of information, paper and disk	**Day of announcement**
Opinion Media	Winkenwerder & Policy	PA/HA/Policy	OpEd pages of major/regional newspapers	Place opinion pieces explaining anthrax vaccine safety/efficacy and threat of anthrax	**Week of announcement and/or as needed**
National, Washington & Trade Press	Winkenwerder	PA/HA/AVIP	Public, military, health professionals	One-on-one interviews	**Week of announcement and as requested**
Internal Media	Winkenwerder Svc Surgeons Gen	HA/PA/Mil Svcs	Troops and families	Bylined article	**Embargoed for week of annc't.**

TACTICS AND AUDIENCES:

Products	Principal	Staff	Targets	Tactics	Timeline
Q&A		Health Affairs			Completed
Blue Top		Public Affairs			Completed
Public Affairs Guidance		Public Affairs			Completed
Myths & Fact		Health Affairs, Public Affairs			Completed
What are people saying about anthrax? (News excerpts)		Health Affairs			Completed
Talking Points		Public Affairs			Completed
Institute of Medicine Report		Health Affairs			Completed
Armed Forces Epidemiological Board Report		Health Affairs			Completed

Tab H

DRAFT

SUBJECT: PUBLIC AFFAIRS GUIDANCE - RESUMPTION OF ANTHRAX VACCINE IMMUNIZATION PROGRAM (AVIP)

1. ALL PREVIOUS ANTHRAX VACCINE IMMUNIZATION PROGRAM PAG IS SUPERCEDED.

2. PURPOSE: THIS MESSAGE CONTAINS GUIDANCE FOR THE NEW ANTHRAX VACCINE IMMUNIZATION PROGRAM.

3. POSTURE: PUBLIC AFFAIRS POSTURE FOR ALL ASPECTS OF THE AVIP REMAINS ACTIVE. PUBLIC AFFAIRS OFFICERS ARE AUTHORIZED AND ENCOURAGED TO WIDELY DISTRIBUTE INFORMATION CONTAINED HEREIN TO INTERNAL AND EXTERNAL AUDIENCES.

4. BACKGROUND:
A. ON MAY 3, 2002, THE SECRETARY OF DEFENSE WILL ANNOUNCE AT A PRESS BRIEFING NEW IMPLEMENTING INSTRUCTIONS FOR RESUMPTION OF THE ANTHRAX VACCINE IMMUNIZATION PROGRAM. A TRANSCRIPT OF THAT BRIEFING WILL BE AVAILABLE AT WWW.DEFENSELINK.MIL.

B. THE FOLLOWING IS THE TEXT OF A DOD PRESS RELEASE THAT WILL BE ISSUED ON MAY 3, 2002 AND POSTED AT WWW.DEFENSELINK.MIL:

(QUOTE) THE SECRETARY OF DEFENSE ANNOUNCED TODAY THAT WITH THE SUCCESSFUL FOOD AND DRUG ADMINISTRATION APPROVAL OF THE RECENTLY-RENOVATED BIOPORT ANTHRAX VACCINE PRODUCTION FACILITY, ANTHRAX VACCINATION FOR SERVICEMEMBERS AND OTHER DESIGNATED PERSONNEL AT GREATEST RISK WILL RESUME. (PARA)"THE DECISION TO RESUME VACCINATION REFLECTS OUR CONCERN FOR THE HEALTH AND SAFETY OF SERVICEMEMBERS," SAID RUMSFELD. "OTHER FACTORS," HE STATED, "INCLUDED THE AVAILABILITY OF A SAFE AND EFFECTIVE VACCINE AND A REEVALUATION OF THE THREAT POSED BY POTENTIAL ADVERSARIES." VACCINATION OFFERS A LAYER OF PROTECTION IN ADDITION TO ANTIBIOTICS AND OTHER MEASURES THAT IS NEEDED FOR CERTAIN MEMBERS OF THE ARMED FORCES. RECENTLY THE NATIONAL ACADEMY OF SCIENCES' INSTITUTE OF MEDICINE CONCLUDED THAT THE CURRENT ANTHRAX VACCINE IS SAFE AND EFFECTIVE IN PROTECTING AGAINST ALL FORMS OF ANTHRAX INFECTION. (PARA) THE PROGRAM RESUMPTION WILL INCLUDE DEFENSE DEPARTMENT PERSONNEL ASSIGNED TO OR DEPLOYED FOR MORE THAN 15 DAYS IN A DESIGNATED HIGHER THREAT AREA WHOSE PERFORMANCE IS ESSENTIAL FOR CERTAIN MISSION CRITICAL CAPABILITIES. THIS PROGRAM WILL ALSO INCLUDE SELECTED HOMELAND DEFENSE MANAGEMENT PERSONNEL. (PARA)TO BEGIN SERVICEMEMBER VACCINATIONS, DOD WILL ADMINISTER RECENTLY-MANUFACTURED AND FDA-APPROVED VACCINE. THE SIX-SHOT VACCINATION SERIES MAY BE AUTHORIZED FOR OTHER DOD PERSONNEL OR IN OTHER THREAT AREAS WHEN DETERMINED TO BE AT HIGH RISK OF EXPOSURE TO ANTHRAX. THE POLICY MAY BE EXPANDED AT A FUTURE DATE TO PROVIDE SIMILAR PROTECTION AS THE THREAT DEMANDS AND EXISTING SUPPLIES ALLOW. (PARA) AS VACCINATIONS RESUME, SERVICEMEMBERS AND OTHERS IN HIGHER THREAT AREAS WHO HAD BEGUN THE SERIES OF VACCINATIONS BUT DID NOT COMPLETE THE SERIES WILL RESUME THEIR REGIMEN ACCORDING TO FDA GUIDELINES. THOSE WHO HAD BEGUN THEIR VACCINATIONS BUT NOT COMPLETED THEM AND ARE NOT IN OR ASSIGNED TO GO TO HIGHER THREAT AREAS WILL COMPLETE THE SERIES AT A LATER DATE. (PARA) SINCE JUNE 11, 2001, THE ANTHRAX VACCINE IMMUNIZATION PROGRAM HAS VACCINATED PERSONNEL IN DESIGNATED SPECIAL MISSION UNITS, ANTHRAX VACCINE RESEARCH, AND CONGRESSIONALLY MANDATED STUDIES, INCLUDING COLLABORATIVE PROJECTS WITH THE CENTERS FOR DISEASE CONTROL AND PREVENTION. (PARA) ANTHRAX REMAINS ONE OF THE TOP BIOLOGICAL WARFARE THREATS TO U.S. TROOPS. VACCINATION IS THE SAFEST AND MOST RELIABLE WAY TO PROTECT SERVICEMEMBERS FROM A POTENTIAL THREAT THAT IS HIGHLY FATAL, EVEN WITH EARLY TREATMENT. SINCE MARCH 1998, DOD HAS VACCINATED MORE THAN 524,000 SERVICEMEMBERS WITH MORE THAN TWO MILLION DOSES OF ANTHRAX VACCINE SINCE MARCH 1998. (UNQUOTE)

DRAFT

C. TALKING POINTS FOR THE ANTHRAX VACCINE IMMUNIZATION PROGRAM FOLLOW: (PARA) THE HEALTH AND SAFETY OF OUR MEN AND WOMEN IN UNIFORM ARE OUR TOP CONCERNS (PARA) THE ANTHRAX VACCINE IS SAFE AND EFFECTIVE (PARA) VACCINATION OFFERS A LAYER OF PROTECTION THAT IS NEEED FOR CERTAIN MEMBERS OF THE ARMED FORCES (PARA) THE THREAT FROM ANTHRAX IS DEADLY AND REAL (PARA) MORE INFORMATION ABOUT THE ANTHRAX VACCINE IMMUNIZATION PROGRAM IS AT HTTP://WWW.ANTHRAX.OSD.MIL/ .

5. QUESTIONS AND ANSWERS.

Q-1. HOW DO YOU INTEND TO PROTECT THE TROOPS? WHAT'S YOUR NEW ANTHRAX VACCINATION POLICY?
A-1. AT THIS TIME, THE DEPARTMENT OF DEFENSE WILL RESUME THE ANTHRAX VACCINE IMMUNIZATION PROGRAM (AVIP) CONSISTENT WITH U.S. FOOD AND DRUG ADMINISTRATION GUIDELINES AND THE BEST PRACTICE OF MEDICINE. OUR POLICY IS TO IMMUNIZE MILITARY PERSONNEL, EMERGENCY-ESSENTIAL DOD CIVILIANS AND CONTRACTOR PERSONNEL, ASSIGNED TO OR DEPLOYED FOR MORE THAN 15 DAYS IN HIGHER THREAT AREAS WHOSE PERFORMANCE IS ESSENTIAL FOR CERTAIN MISSION CRITICAL CAPABILITIES, AS WELL AS SELECTED HOMELAND CONSEQUENCE MANAGEMENT PERSONNEL.

Q-2. SO, YOU'RE CHANGING SECRETARY COHEN'S TOTAL FORCE VACCINATION POLICY?
A-2. YES. OWING TO LIMITATIONS IN VACCINE SUPPLY, WE'RE RESUMING THE ANTHRAX VACCINE IMMUNIZATION PROGRAM BY ASSURING PRIORITY FOR THOSE AT HIGHER RISK WHOSE PERFORMANCE IS ESSENTIAL FOR CERTAIN MISSION CRITICAL CAPABILITIES. (PARA) HOWEVER, PROTECTION OF ALL FORCES AGAINST ANTHRAX EXPOSURE REMAINS A CRITICAL GOAL OF THE DEPARTMENT'S FORCE HEALTH PROTECTION PROGRAM. WE ARE TAKING NECESSARY STEPS TO DEVELOP OPTIMAL PROTECTION AGAINST THE THREAT OF ANTHRAX AND OTHER POTENTIAL BIOWEAPON AGENTS, INCLUDING IMPROVED INTELLIGENCE, DETECTION, AND SURVEILLANCE CAPABILITIES, PROTECTIVE CLOTHING AND EQUIPMENT, NEW GENERATION VACCINES AND OTHER MEDICAL COUNTERMEASURES. IN ADDITION, WE HAVE STOCKPILED ANTIBIOTICS IN DISTRIBUTED LOCATIONS.

Q-3. BUT DO YOU INTEND TO VACCINATE THE TOTAL FORCE OVER THE LONG TERM?
A-3. THE DEPARTMENT WILL NOT SO MUCH FOCUS ON AN ENDSTATE—BUT RATHER WHAT WE SHOULD DO **NOW** TO PROTECT OUR PERSONNEL AT HIGHER RISK WHOSE PERFORMANCE IS ESSENTIAL FOR CERTAIN MISSION CRITICAL CAPABILITIES. OVER THE LONG TERM OUR GOAL IS TO HAVE AN EASILY ADMINISTERED VACCINE, WHICH UTILIZES THE LATEST TECHNOLOGY, THAT IS EASILY SCALABLE TO PRODUCE LARGE QUANTITIES. WE ARE WORKING TOGETHER WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES AND PRIVATE INDUSTRY TO PRODUCE SUCH A "NEXT GENERATION VACCINE." (PARA) WITH REGARD TO THE CURRENT VACCINE, THE FDA APPROVED BIOPORT'S RENOVATED VACCINE FACILITY EARLIER THIS YEAR, AND RELEASED SOME VACCINE FOR USE. BIOPORT NEEDS TO ESTABLISH A CONSISTENT AND GREATER SUPPLY OF VACCINE. SO WE'RE WATCHING BIOPORT'S PRODUCTION AND FDA'S RELEASE OF ADDITIONAL VACCINE CLOSELY. WE ARE MOVING DELIBERATELY, ONE STEP AT A TIME. WE ARE IMPLEMENTING A POLICY WE ARE HIGHLY CONFIDENT WE CAN FULLY EXECUTE.

Q-4. WHEN DO YOU EXPECT TO TAKE THE NEXT STEP? DO YOU INTEND TO EXPAND THE AVIP? A-Q-4. WE HAVE NO SCHEDULED TIMELINE TO TAKE THE NEXT STEP OR EXPAND. WE WILL MONITOR SEVERAL FACTORS: FIRST, IS SUPPLY OF THE VACCINE AS BIOPORT PRODUCTION INCREASES OVER THE COMING YEAR. SECOND, IS PROGRESS ON CURRENT RESEARCH EFFORTS. THE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) WILL SOON BEGIN A CLINICAL STUDY TO DETERMINE IF THE VACCINE CAN PROTECT EQUALLY WITH LESS THAN SIX DOSES; AND IF, BY CHANGING THE WAY WE ADMINISTER THE SHOT, FROM SUBCUTANEOUSLY (JUST UNDER THE SKIN), TO INTRAMUSCULARLY (DEEPER INTO THE MUSCLE), WE CAN REDUCE THE INJECTION SITE SWELLING, ITCHING, REDNESS AND PAIN. THE FDA WILL NEED TO APPROVE THAT CHANGE AFTER REVIEWING THE STUDY DATA. THIS EFFORT WILL LIKELY TAKE AT LEAST TWO YEARS. A THIRD FACTOR IS HOW THE THREAT OF ANTHRAX TO OUR FORCES MAY CHANGE

OVER TIME. WE WILL BE WATCHING THE CHANGING THREAT AND WORLD SITUATION CLOSELY WITH THE INTELLIGENCE COMMUNITY. (PARA) SO THE DEPARTMENT IS GOING TO KEEP OUR ATTENTION ON ALL THESE FACTORS AS THEY EVOLVE. LET'S SEE WHERE WE ARE A YEAR OR SO FROM NOW.

Q-5. WHAT ARE THESE "CERTAIN MISSION CRITICAL CAPABILITIES" IN YOUR NEW POLICY?
A-5. WE WILL NOT TALK ABOUT THESE CAPABILITIES BUT ONLY SAY THEY ARE ALL IMPORTANT IN THIS WAR WE WAGE AGAINST TERRORISM.

Q-6. WILL VACCINATIONS UNDER YOUR NEW PROGRAM BE MANDATORY?
A-6. YES. IT IS IMPORTANT THAT ALL PERSONNEL WHOSE DUTIES ARE ESSENTIAL TO THESE MISSION CRITICAL CAPABILITIES ARE VACCINATED AGAINST ANTHRAX—FOR THEIR PERSONAL PROTECTION AND FOR SUCCESS OF THE MILITARY MISSION. SO VACCINATION WILL BE MANDATORY, EXCEPT AS PROVIDED UNDER APPLICABLE MEDICAL AND ADMINISTRATIVE EXEMPTION POLICIES, SIMILAR TO THOSE WE'VE ALWAYS HAD IN PLACE.

Q-7. WHY CAN'T YOU ALLOW PERSONNEL TO CHOOSE VOLUNTARILY TO BE VACCINATED?
A-7. WE PROVIDE MANY DIFFERENT VACCINES AND MEDICAL PROCEDURES ON A MANDATORY BASIS, WHEN IT IS KNOWN THAT THE VACCINE OR MEDICAL MEASURE IS SAFE AND EFFECTIVE, AND EXPOSURE OR POSSIBLE EXPOSURE TO AN AGENT POSES A REAL RISK. ALSO, WE FIGHT AND WIN AS TEAMS—IF ONE OR SEVERAL TEAM MEMBERS IN AREAS OF HIGHER RISK ARE NOT VACCINATED AND FALL VICTIM TO ANTHRAX, THEY COULD JEOPARDIZE THE LIVES OF OTHER TEAM MEMBERS AND MISSION SUCCESS.

Q-8. WHY AREN'T YOU PROTECTING PERSONNEL DEPLOYED 15 DAYS OR LESS?
A-8. WE DIDN'T WANT TO IMPOSE THE EIGHTEEN-MONTH, SIX-DOSE SERIES WITH A YEARLY BOOSTER ON INDIVIDUALS WHOM, EXCEPT FOR THEIR LIMITED TRAVEL INTO A HIGHER RISK AREA, HAD NO CONTINUED THREAT OF EXPOSURE TO ANTHRAX.

Q-9. CAN PERSONNEL DEPLOYED 15 DAYS OR LESS VOLUNTEER TO BE VACCINATED?
A-9. IF THOSE INDIVIDUALS HAVE CONCERNS, THEY SHOULD SPEAK WITH THEIR COMMANDERS. WE RECOGNIZE THAT SOME OF OUR PERSONNEL MAY BE ON ROTATION SCHEDULES WITH DUTY TAKING THEM INTO HIGHER THREAT AREAS MULTIPLE TIMES IN A GIVEN YEAR, BRINGING CUMULATIVE TIME DEPLOYED TO MORE THAN 15 DAYS IN A GIVEN YEAR. THERE ARE ALLOWANCES IN OUR POLICIES, BY EXCEPTION, FOR COMMANDERS WITH PERSONNEL WITH THESE TYPES OF SITUATIONS.

Q-10. IN YOUR POLICY MEMO, WHAT DO YOU MEAN BY "HIGHER THREAT AREAS?"
A-10. IT REPRESENTS THE DEPARTMENT'S FOCUS ON APPLYING ITS LIMITED VACCINE SUPPLY TO THOSE PERSONNEL WHOSE DUTIES BRING THEM INTO HIGHER RISK OF ANTHRAX INFECTION, BY DEPLOYMENT LOCATION AND/OR OCCUPATION, AND TO PRESERVE MISSION CRITICAL CAPABILITIES IN THOSE AREAS. BECAUSE THE ANTHRAX THREAT HAS NOW REACHED INSIDE OUR HOMELAND, WE INTEND TO VACCINATE A LIMITED NUMBER OF SELECTED DOD UNITS THAT MAY BE ASKED TO SUPPORT DOMESTIC CONSEQUENCE MANAGEMENT.

Q-11. WHAT COUNTRIES ARE INCLUDED IN THE "HIGHER THREAT AREAS?"
A-11. WE ARE NOT GOING TO COMMENT ON THAT QUESTION.

Q-12. IS KOREA A "HIGHER THREAT AREA?" WILL YOU VACCINATE FORCES BOUND FOR KOREA?
A-12. WE ARE NOT GOING TO COMMENT ON THAT QUESTION.

Q-13. WHAT DETERMINES AN AREA OF THE WORLD OR A COUNTRY TO BE DESIGNATED "HIGHER THREAT?"
A-13. MANY FACTORS GO INTO SUCH DETERMINATIONS, INCLUDING INTELLIGENCE INFORMATION, KNOWN CAPABILITIES, AND OTHER VARIABLES.

Q-14. WHO WILL BE VACCINATED AMONG THE "SELECTED HOMELAND CONSEQUENCE MANAGEMENT PERSONNEL?"
A-14. HOMELAND CONSEQUENCE MANAGEMENT PERSONNEL INCLUDE CERTAIN PERSONNEL AND UNITS WHOSE PRIMARY DUTIES INCLUDE MISSIONS TO HELP DEFEND OUR HOMELAND. THERE ARE A RELATIVELY SMALL NUMBER OF SUCH INDIVIDUALS AND UNITS.

Q-15. WHEN WILL ANTHRAX VACCINATIONS UNDER THIS POLICY START?
A-15. WE ARE CURRENTLY VACCINATING DESIGNATED SPECIAL MISSION UNITS, AND PERSONNEL INVOLVED IN RESEARCH AND ANTHRAX VACCINE MANUFACTURING. THIS POLICY CONTINUES VACCINATION FOR THOSE PERSONS, AND ADDS AND RESUMES OTHERS AS WE ARE ABLE TO DISTRIBUTE ADEQUATE SUPPLIES OF VACCINES AND EDUCATE OUR PERSONNEL. QUITE SIMPLY, ANTHRAX VACCINATIONS UNDER THIS POLICY WILL BE ADMINISTERED TODAY, TOMORROW, NEXT WEEK, AND IN THE WEEKS AND MONTHS AHEAD.

Q-16. IT'S TAKEN YOU THREE MONTHS SINCE FDA'S BIOPORT APPROVAL TO MAKE THIS DECISION...DOES THIS IMPLY THAT THE DEPARTMENT OR THAT SECRETARY RUMSFELD HAS CONCERN ABOUT THIS VACCINE OR THIS PROGRAM?
A-16. NO. SECRETARY RUMSFELD ASKED THE DEPARTMENT TO LOOK VERY CLOSELY AT ALL ASPECTS OF THIS VACCINATION PROGRAM: THE THREAT, VACCINE SUPPLY, VACCINE SAFETY, VACCINE EFFECTIVENESS, TROOP EDUCATION, AND ONGOING AND FUTURE RESEARCH. HE DEMANDED THAT WE PULL TOGETHER LESSONS-LEARNED OVER THE PAST FOUR YEARS OF ADMINISTERING THIS PROGRAM, AND OF THE COUNTRY'S RECENT EXPERIENCE WITH ANTHRAX. WE BELIEVE OUR CURRENT POLICY IS VERY CAREFULLY CONSIDERED.

Q-17. WHAT ABOUT THE REST OF THE COUNTRY? WHO AND WHEN WILL OTHERS OUTSIDE THE DOD BE VACCINATED?
A-17. THIS POLICY IS BEING COORDINATED BY THE OFFICE OF HOMELAND SECURITY, WORKING WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES AND OTHER FEDERAL AGENCIES. THE DEPARTMENT OF DEFENSE ANTHRAX VACCINATION POLICY, AND THE AMOUNT OF VACCINE NEEDED TO IMPLEMENT THIS POLICY TAKES INTO ACCOUNT OTHER NATIONAL SECURITY CONSIDERATIONS OUTSIDE THE DEPARTMENT OF DEFENSE. WE HAVE WORKED IN CLOSE COORDINATION AND COLLABORATION WITH THESE OTHER FEDERAL AGENCIES, AND WITH THE OFFICE OF HOMELAND SECURITY.

Q-18. IS DOD PLANNING TO USE ALL OF THE ANTHRAX VACCINE PRODUCED BY BIOPORT?
A-18. NO. DOD'S POLICY WAS DEVELOPED TAKING INTO ACCOUNT OTHER NATIONAL SECURITY CONSIDERATIONS BEYOND THE NEEDS FOR MILITARY PERSONNEL. THEREFORE, A CERTAIN SIGNIFICANT AMOUNT OF THE PRODUCED VACCINE IS BEING RESERVED FOR OTHER FEDERAL AGENCIES, AND GROUPS OF INDIVIDUALS WHOSE NEED OR POTENTIAL USE OF THE VACCINE COULD BE EVALUATED BY EXPERTS AND LEADERS AT THESE AGENCIES. THESE "ROUGH REQUIREMENTS" AMOUNTS HAVE BEEN IDENTIFIED TO DOD BY THOSE AGENCIES AND DEPARTMENTS. (PARA) DOD IS NEGOTIATING AN AGREEMENT WITH BIOPORT IN WHICH DOD WILL PURCHASE ALL OF THE VACCINE PRODUCED BY BIOPORT OVER THE NEXT FEW YEARS. DOD WILL THEN RE-SELL THE AMOUNTS THAT ARE NEEDED BY OTHER FEDERAL DEPARTMENT OR AGENCIES TO THESE DEPARTMENTS AND AGENCIES.

Q-19. DOES THIS MEAN DOD WILL PROVIDE STATES OR CITIES WITH SOME OF THE VACCINE PRODUCED BY BIOPORT?
A-19. NO. THIS MATTER AND OTHERS THAT RELATE TO POSSIBLE USE OF THE VACCINE FOR CIVILIAN CONSEQUENCE MANAGEMENT OR OTHER FIRST RESPONDER PERSONNEL WILL BE CONSIDERED THROUGH POLICY THAT IS BEING COORDINATED BY THE OFFICE OF HOMELAND SECURITY WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES AND OTHER FEDERAL AGENCIES. (PARA) BECAUSE OF THE OVERALL LIMITED SUPPLY OF THE VACCINE, AND THE NEED TO RESERVE SIGNIFICANT PORTIONS FOR POSSIBLE POST-EXPOSURE USE IN A LARGE-SCALE CONTINGENCY EVENT, IT IS LIKELY THAT ONLY RELATIVELY SMALL AMOUNTS OF THE

VACCINE WILL BE AVAILABLE FOR PRE-EXPOSURE USE. POLICY CONSIDERATIONS ON THIS MATTER WILL BE EVALUATED IN THE COMING WEEKS.

Q-20. CONSIDERING THE DIRECT ATTACKS ON THE PENTAGON LAST FALL, WILL PEOPLE WORKING IN THE PENTAGON BE VACCINATED?
A-20. AT THIS TIME, WE DO NOT PLAN TO VACCINATE PERSONNEL SIMPLY BECAUSE THEY WORK IN THE PENTAGON.

Q-21. SENIOR DOD LEADERS WERE VACCINATED DURING THE PREVIOUS AVIP. WILL THEY BE VACCINATED NOW?
A-21. THE CURRENT POLICY IS TO VACCINATE PERSONNEL ASSIGNED TO OR DEPLOYED TO HIGHER RISK AREAS AND WHO PERFORM MISSION ESSENTIAL JOBS. SENIOR DOD LEADERS MEETING THAT CRITERION WILL BE VACCINATED.

Q-22. WHAT ABOUT ALL THOSE PEOPLE WHO RECEIVED ANTHRAX VACCINATIONS IN THE PAST? WILL THEY RESUME THE SIX-DOSE SERIES?
A-22. THOSE WHO FALL WITHIN THE GROUPS DEFINED BY THIS POLICY WILL RESUME AS SOON AS THEIR UNIT BEGINS VACCINATIONS—SOME MAY RESUME TODAY, TOMORROW, NEXT WEEK OR IN THE NEAR TERM WEEKS AND MONTHS AHEAD. OTHERS, NOT COVERED UNDER THE CURRENT POLICY, WILL RESUME AS SOON AS OUR ANTHRAX VACCINE SUPPLY ALLOWS.

Q-23. SO WHAT YOU'RE SAYING IS YOU DO INTEND TO RESUME ALL THOSE BEGUN BEFORE, BUT NOW DEFERRED?
A-23. YES, AS THE DEPARTMENT OF DEFENSE HAS ALWAYS SAID, WE ARE COMMITTED TO COMPLETING THE 6-DOSE SERIES FOR EVERYONE WHO BEGAN THE SERIES WHO REMAINS IN THE FORCE.

Q-24. BECAUSE OF THE ANTHRAX VACCINE IMMUNIZATION PROGRAM SLOWDOWN, IT'S BEEN A YEAR AND A HALF SINCE MY LAST DOSE OF ANTHRAX VACCINE; DO I HAVE TO START ALL OVER WITH DOSE #1?
A-24. NO. BASED ON EXPERIENCE WITH ANTHRAX VACCINE AND OTHER VACCINES, THERE IS NO NEED TO RESTART A MULTI-DOSE VACCINE SERIES. CIVILIAN MEDICAL EXPERTS ADVISING THE CENTERS FOR DISEASE CONTROL AND PREVENTION RECOMMEND THIS. EACH DOSE IS LIKE CLIMBING A SET OF STAIRS TOWARD FULL IMMUNITY.

Q-25. THE CENTERS FOR DISEASE CONTROL AND PREVENTION USE OF ANTHRAX VACCINE FOR CONGRESSIONAL AND U.S. POSTAL SERVICE WORKERS WAS CALLED "EXPERIMENTAL" AND "INVESTIGATIONAL," REQUIRING INFORMED CONSENT; WHY THEN DOES THE DEPARTMENT OF DEFENSE'S USE OF ANTHRAX VACCINE IN THE ANTHRAX VACCINE IMMUNIZATION PROGRAM NOT REQUIRE INFORMED CONSENT OF SERVICEMEMBERS?
~~A-25. THE CENTERS FOR DISEASE CONTROL AND PREVENTION OFFER OF ANTHRAX VACCINE FOR CONGRESSIONAL AND U.S. POSTAL SERVICE WORKERS USED ANTHRAX VACCINE FOR "POST EXPOSURE TREATMENT" IN THREE DOSES. THIS IS NOT A FOOD AND DRUG ADMINISTRATION LICENSED USE OF THE VACCINE, ALTHOUGH THE VACCINE ITSELF WAS, AND IS, LICENSED. THEREFORE, IN THAT CASE (POST EXPOSURE), THE VACCINE WAS ADMINISTERED UNDER AN "INVESTIGATIONAL NEW DRUG" PROTOCOL, WITH INFORMED CONSENT.~~ THE DEPARTMENT OF DEFENSE'S USE OF ANTHRAX VACCINE IN THE ANTHRAX VACCINE IMMUNIZATION PROGRAM FOR PRE-EXPOSURE PREVENTION USING SIX DOSES OVER 18 MONTHS IS CONSISTENT WITH THE FOOD AND DRUG ADMINISTRATION-LICENSED USE OF THE VACCINE. THE CENTERS FOR DISEASE CONTROL AND PREVENTION OFFER OF ANTHRAX VACCINE FOR CONGRESSIONAL AND U.S. POSTAL SERVICE WORKERS USED ANTHRAX VACCINE FOR "POST-EXPOSURE TREATMENT" IN THREE DOSES. THIS IS NOT A FOOD AND DRUG ADMINISTRATION-LICENSED USE OF THE VACCINE, ALTHOUGH THE VACCINE ITSELF WAS, AND IS, LICENSED. THEREFORE, IN THAT CASE (POST EXPOSURE), THE VACCINE WAS ADMINISTERED UNDER AN "INVESTIGATIONAL NEW DRUG" PROTOCOL, WITH INFORMED CONSENT.

Q-26. HOW MANY SERVICEMEMBERS HAVE BEEN VACCINATED?
A-26. SINCE THE BEGINNING OF THE ANTHRAX VACCINE IMMUNIZATION PROGRAM IN MARCH 1998, DEPARTMENT OF DEFENSE VACCINATED OVER 525,000 PEOPLE WITH MORE THAN 2.1 MILLION DOSES OF ANTHRAX VACCINE.

Q-27. WHY DOESN'T DOD ~~YOU~~ USE ANTIBIOTICS RATHER THAN ANTHRAX VACCINE?
A-27. THERE IS NO BETTER ROUND-THE-CLOCK PROTECTION AGAINST ANTHRAX INFECTION THAN THE ANTHRAX VACCINE. ANTIBIOTICS ARE EFFECTIVE WHEN STARTED IMMEDIATELY OR VERY SOON AFTER EXPOSURE. HOWEVER, NOT ALL EXPOSURES CAN BE PREDICTED IN ADVANCE OR EVEN DETERMINED IN VERY EARLY STAGES, PARTICULARLY IN CERTAIN MILITARY SITUATIONS. IN SUCH SITUATIONS, THE CONSEQUENCES FOR MILITARY PERSONNEL AND THEIR MISSION COULD BE VERY UNFAVORABLE. THIS IS NOT A RISK WE CAN AFFORD TO TAKE. DOD WILL THEREFORE VACCINATE AHEAD OF TIME FOR THE BEST PROTECTION.

THREAT QUESTIONS

Q-28. WHAT IS THE THREAT OF ANTHRAX USED AGAINST OUR MILITARY?
A-28. ANTHRAX IS AN ATTRACTIVE WEAPON OF MASS DESTRUCTION FOR OUR ENEMIES. IT IS HIGHLY LETHAL, RELATIVELY EASY TO PRODUCE IN LARGE QUANTITIES AND TO DEVELOP AS A WEAPON, EASILY SPREAD IN THE AIR OVER A LARGE AREA AND IT CAN BE STORED AND REMAIN DANGEROUS FOR A LONG TIME. FOR THIS REASON, ANTHRAX MAY BE THE MOST IMPORTANT BIOLOGICAL WARFARE THREAT FACING U.S. FORCES. THE INTELLIGENCE COMMUNITY BELIEVES SEVERAL COUNTRIES CURRENTLY HAVE OR ARE DEVELOPING AN OFFENSIVE BIOLOGICAL WARFARE CAPABILITY USING ANTHRAX. HOWEVER, GIVEN THE EASE WITH WHICH ANTHRAX CAN BE PRODUCED, THE THREAT COULD COME FROM ANYWHERE. FOR THAT REASON, U.S. FORCES MAY HAVE LITTLE OR NO WARNING BEFORE AN ANTHRAX ATTACK, WHICH COULD BE DELIVERED BY UNCONVENTIONAL MEANS. AS A RESULT, U.S. MILITARY FORCES AROUND THE WORLD FACE A VERY REAL THREAT OF A SURPRISE ANTHRAX ATTACK. DUE TO LIMITED SUPPLIES OF THE VACCINE AND OTHER NOTED CONSIDERATIONS, OUR CURRENT POLICY IS TO VACCINATE MILITARY AND MISSION ESSENTIAL PERSONNEL IN HIGHER RISK AREAS.

Q-29. HAS THE THREAT CHANGED SINCE THE TERRORIST ATTACKS IN FALL 2001?
A-29. THE THREAT OF ANTHRAX WEAPONS IN THE HANDS OF ADVERSARIAL COUNTRIES REMAINS. BUT ANTHRAX WAS USED AS A BIOLOGICAL WEAPON IN THE UNITED STATES IN FALL 2001 BY UNKNOWN TERRORISTS. DELIVERING ANTHRAX WAS AS SIMPLE AS PUTTING IT IN AN ENVELOPE AND DROPPING IT IN A MAILBOX.

EFFECTIVENESS QUESTIONS

Q-30. WHO SAYS ANTHRAX VACCINE IS EFFECTIVE?
A-30. THE FOOD AND DRUG ADMINISTRATION LICENSES ANTHRAX VACCINE AS A SAFE AND EFFECTIVE PREVENTION AGAINST *BACILLUS ANTHRACIS—THE* BACTERIA CAUSING ANTHRAX. THE FOOD AND DRUG ADMINISTRATION REAFFIRMED THIS POSITION IN NUMEROUS TESTIMONIES TO CONGRESSIONAL COMMITTEES OVER THE PAST THREE YEARS. BASED ON HUMAN AND ANIMAL DATA, THE NATIONAL ACADEMY OF SCIENCES' INSTITUTE OF MEDICINE CONCLUDED IN MARCH 2002 THAT ANTHRAX VACCINE IS "AN EFFECTIVE VACCINE FOR THE PROTECTION OF HUMANS AGAINST ANTHRAX, INCLUDING INHALATIONAL ANTHRAX, CAUSED BY ALL KNOWN OR PLAUSIBLE ENGINEERED STRAINS OF *BACILLUS ANTHRACIS.*"

Q-31. DOES ANTHRAX VACCINE ONLY PROTECT AGAINST CUTANEOUS ANTHRAX?
A-31. NO. THIS VACCINE PREVENTS ANTHRAX REGARDLESS OF ROUTE OF EXPOSURE. BASED ON HUMAN AND ANIMAL DATA, THE NATIONAL ACADEMY OF SCIENCES' INSTITUTE OF MEDICINE CONCLUDED IN MARCH 2002 THAT ANTHRAX VACCINE IS "AN EFFECTIVE VACCINE FOR THE

PROTECTION OF HUMANS AGAINST ANTHRAX, INCLUDING INHALATIONAL ANTHRAX, CAUSED BY ALL KNOWN OR PLAUSIBLE ENGINEERED STRAINS OF *BACILLUS ANTHRACIS*."

Q-32. WILL ANTHRAX VACCINE PROTECT AGAINST ALL STRAINS OF ANTHRAX?
A-32. YES. EVERY DISEASE-CAUSING STRAIN OF *BACILLUS ANTHRACIS* CAUSES ANTHRAX DISEASE VIA THE SAME PROTEIN. THE VACCINE PRODUCES ANTIBODIES THAT NEUTRALIZE THAT PROTEIN. THE NATIONAL ACADEMY OF SCIENCES' INSTITUTE OF MEDICINE CONCLUDED IN MARCH 2002 THAT "IT IS UNLIKELY THAT EITHER NATURALLY OCCURRING OR ANTHRAX STRAINS WITH BIOENGINEERED PROTECTIVE ANTIGEN COULD BOTH EVADE AVA [THE U.S. ANTHRAX VACCINE] AND CAUSE THE TOXICITY ASSOCIATED WITH ANTHRAX."

HEALTH AND SAFETY QUESTIONS

Q-33. HOW MANY PEOPLE WHO GET THE ANTHRAX VACCINE GET SICK?
A-33. BASED ON OVER 30 YEARS OF ANTHRAX VACCINE USE, WE KNOW THAT FROM 30 TO 60 PERCENT OF PEOPLE WHO RECEIVE ANTHRAX VACCINE WILL DEVELOP A SMALL SKIN REACTION (LESS THAN ONE INCH) AT THE INJECTION SITE. ABOUT ONE IN A HUNDRED DEVELOPS A REACTION 5 INCHES IN DIAMETER OR LARGER. THE RATE OF SIDE EFFECTS AWAY FROM THE INJECTION SITE IS ABOUT THE SAME AS FOR OTHER VACCINES: FROM 5 TO 35 PERCENT, WITH THESE EVENTS GOING AWAY WITHIN A FEW DAYS. AS THE NATIONAL ACADEMY OF SCIENCE NOTED IN THEIR MARCH 2002 REPORT, THESE RATES ARE SIMILAR TO OTHER VACCINES.

Q-34. IS IT TRUE THAT WOMEN HAVE MORE SIDE EFFECTS TO ANTHRAX VACCINE THAN MEN?
A-34. YES, WOMEN EXPERIENCE MORE SMALL SKIN REACTIONS THAN MEN. FOR SKIN REACTIONS SMALLER THAN ONE INCH IN DIAMETER, THE LIKELIHOOD IS 60 PERCENT FOR WOMEN AND 30 PERCENT FOR MEN. FOR SIDE EFFECTS AWAY FROM THE INJECTION SITE, THE RATES FOR MEN AND WOMEN ARE ABOUT THE SAME.

Q-35. DOES ANTHRAX VACCINE CAUSE SEVERE SIDE EFFECTS OR DEATH?
A-35. MEDICAL EXPERTS AGREE: NO DEATH AND ONLY RARE SERIOUS SIDE EFFECTS HAVE BEEN CAUSED BY ANTHRAX VACCINE. THE DEPARTMENT OF DEFENSE, FOOD AND DRUG ADMINISTRATION, CENTERS FOR DISEASE CONTROL AND PREVENTION, AND AN INDEPENDENT PANEL OF CIVILIAN PHYSICIANS REVIEW EVERY REPORT OF SERIOUS ILLNESS OR DEATH THAT MIGHT POSSIBLY BE ASSOCIATED WITH ANTHRAX VACCINATION. THESE GROUPS ALL AGREE THAT ANTHRAX VACCINE IS NOT ASSOCIATED WITH ANY UNEXPECTED PATTERNS OF ADVERSE EVENTS. THE NATIONAL ACADEMY OF SCIENCES' INSTITUTE OF MEDICINE REPORTED IN MARCH 2002, "THERE IS NO EVIDENCE THAT LIFE-THREATENING OR PERMANENTLY DISABLING IMMEDIATE-ONSET ADVERSE EVENTS OCCUR AT HIGHER RATES IN INDIVIDUALS WHO HAVE RECEIVED AVA [U.S. ANTHRAX VACCINE] THAN IN THE GENERAL POPULATION." IN RARE CASES, PATIENTS EXPERIENCE SERIOUS ADVERSE EFFECTS; THESE ARE TREATED AND FOLLOWED APPROPRIATELY.

Q-36. IF A SERVICEMEMBER HAS A SERIOUS REACTION AFTER ANTHRAX VACCINATION, WILL HE/SHE BE TAKEN CARE OF, OR WILL THE SERVICE JUST THROW THEM OUT?
A-36. IF A SERVICEMEMBER HAS A SERIOUS REACTION TO ANTHRAX VACCINE, HE/SHE WILL BE EXEMPTED FROM FURTHER DOSES AND WILL RECEIVE FULL MEDICAL CARE. THIS POLICY IS THE SAME POLICY AS FOR ANY VACCINATION OR ANY SERVICE-CONNECTED EVENT.

Q-37. DID ANTHRAX VACCINE CAUSE THE ILLNESSES OF GULF WAR VETERANS?
A-37. NO. THERE ARE NO ESTABLISHED CONNECTIONS BETWEEN THE ANTHRAX VACCINE AND THE PERSISTENT AND UNEXPLAINED ILLNESSES REPORTED BY SOME GULF WAR VETERANS, ALTHOUGH RESEARCH CONTINUES ON THIS ISSUE. A VERY RECENT REVIEW OF THE ANTHRAX VACCINE BY THE NATIONAL ACADEMY OF SCIENCES' INSTITUTE OF MEDICINE CONCLUDED THAT, WHILE DATA ARE LIMITED, NO CONVINCING EVIDENCE SHOWS THAT PERSONNEL WHO RECEIVED THE VACCINE HAVE ELEVATED RISKS OF LATER ON-SET HEALTH EFFECTS.

~~SCIENTISTS HAVE NOT MADE ANY CONNECTION BETWEEN U.S. MADE ANTHRAX VACCINE AND ILLNESSES OF GULF WAR VETERANS. A NUMBER OF CIVILIAN REVIEW PANELS FOUND NO SCIENTIFIC REASON TO ASSOCIATE OTHER ILLNESSES WITH ANTHRAX VACCINE.~~

Q-38. DID THE DEFENSE DEPARTMENT ADD SQUALENE TO ANTHRAX VACCINE IN 1990-91 TO STRETCH THE VACCINE SUPPLY? DOESN'T THE FINDING OF ANTI-SQUALENE ANTIBODIES IN GULF WAR VETERANS PROVE IT?
A-38. NO. SQUALENE WAS NOT ADDED TO ANY VACCINES ADMINISTERED TO GULF WAR VETERANS. FURTHER, THE NATIONAL ACADEMY OF SCIENCES FOUND THE EVIDENCE FOR THAT ANTI-SQUALENE TEST TO BE INADEQUATE AND NO SUCH LINK HAD BEEN ESTABLISHED. FOOD AND DRUG ADMINISTRATION (FDA) SCIENTISTS FOUND TRACE QUANTITIES OF SQUALENE IN ANTHRAX, DIPHTHERIA, AND TETANUS VACCINES (LESS THAN THE NATURAL LEVEL OF SQUALENE IN THE HUMAN BLOODSTREAM). THE FDA NOTES THAT THESE MINUTE QUANTITIES COULD HAVE COME FROM THE BACTERIA INVOLVED OR FROM PROCESSING DURING FDA TESTS (SQUALENE IS PRESENT IN THE OIL IN FINGERPRINTS). THE FDA CALLED SQUALENE IN VACCINES "NATURALLY OCCURRING AND SAFE."

Q-39. DIDN'T LOT XXXXX CAUSE PROBLEMS?
A-39. NO. BASED ON SELF-ADMINISTERED SURVEYS AND SPONTANEOUS REPORTS, LOT-TO-LOT COMPARISONS IN THE VARIOUS HUMAN SAFETY STUDIES PERFORMED TO DATE FOUND NO MEANINGFUL DIFFERENCES BASED ON LOT. NO VIAL OF ANTHRAX VACCINE WAS DISTRIBUTED BY THE MANUFACTURER WITHOUT LOT-SPECIFIC MANUFACTURING AND TESTING DATA, EXPLICITLY REVIEWED AND APPROVED BY THE FOOD AND DRUG ADMINISTRATION. THE DEPARTMENT OF DEFENSE USES ONLY VACCINE LOTS THAT THE FOOD AND DRUG ADMINISTRATION RELEASES AS MEETING ALL APPLICABLE STANDARDS.

VACCINE PRODUCTION, PROCUREMENT & INVENTORY QUESTIONS

Q-40. DID THE FOOD AND DRUG ADMINISTRATION REVOKE BIOPORT'S LICENSE TO MANUFACTURE ANTHRAX VACCINE?
- A-40. NO. BIOPORT'S PREDECESSOR, THE STATE OF MICHIGAN, APPROVED RENOVATIONS IN 1995 FOR THE LANSING FACILITY. IN 1997, THE FOOD AND DRUG ADMINISTRATION (FDA) ISSUED A NOTICE OF INTENT TO REVOKE LICENSE TO THE MICHIGAN MANUFACTURER. MICHIGAN RESPONDED WITHIN 30 DAYS WITH A STRATEGIC PLAN FOR COMPLIANCE TO FDA STANDARDS. THE MANUFACTURER VOLUNTARILY CLOSED THE ANTHRAX VACCINE PRODUCTION LINE IN JANUARY 1998 FOR RENOVATION. BIOPORT SUBMITTED A HIGHLY DETAILED SET OF QUALITY CONTROL DOCUMENTS TO FDA IN FALL 2001. FDA APPROVED ALL ASPECTS OF BIOPORT'S FACILITIES AND PROCESSES ON JANUARY 31, 2002. THE CURRENT SHORTAGES OF INFLUENZA, TETANUS, PNEUMOCOCCAL, AND OTHER VACCINES SUGGEST THAT THE U.S. VACCINE INDUSTRY IS STILL LABORING TO MEET FDA PRODUCTION STANDARDS.

Q-41. ISN'T ANTHRAX VACCINE BASED ON OLD (ARCHAIC) TECHNOLOGY?
A-41. ANTHRAX VACCINE WAS INVENTED USING MID-CENTURY TECHNOLOGY THAT ALSO LED TO HIGHLY SUCCESSFUL VACCINES AGAINST TETANUS, DIPHTHERIA, AND OTHER INFECTIOUS DISEASES. TODAY'S PRODUCTION OF ANTHRAX VACCINE MEETS ALL CURRENT FOOD AND DRUG ADMINISTRATION STANDARDS OF PRODUCTION.

Q-42. WHAT IS THE IMPLICATION OF THE FOOD AND DRUG ADMINISTRATION'S JANUARY 31, 2002 ACTION "APPROVING" BIOPORT?
A-42. THE FOOD AND DRUG ADMINISTRATION APPROVED THE RENOVATIONS TO BIOPORT'S ANTHRAX VACCINE MANUFACTURING FACILITIES AND PROCESSES. THE LICENSE TO MAKE ANTHRAX VACCINE HAS BEEN VALID WITHOUT INTERRUPTION SINCE 1970. BIOPORT'S LICENSE WAS AMENDED AND APPROVED BY FDA TO REFLECT THOSE NEW FACILITIES AND PROCESSES.

Q-43. HOW MUCH VACCINE DOES THE DEPARTMENT OF DEFENSE NOW HAVE?

A-43. APPROXIMATELY 500,000 DOSES OF FOOD AND DRUG ADMINISTRATION-RELEASED ANTHRAX VACCINE.

Q-44. WHAT'S THE COST PER DOSE?
A-44. CONTRACT NEGOTIATIONS ARE UNDERWAY AND COST PER DOSE WILL BE DETERMINED WITH THESE NEGOTIATIONS.

Q-45. HOW MUCH HAS THE DEPARTMENT OF DEFENSE SPENT ON THE ANTHRAX VACCINE PROGRAM?
A-45. SINCE SEPTEMBER 1998, $146M HAS BEEN OBLIGATED FOR THE ANTHRAX VACCINE PRODUCTION PROGRAM TO OBTAIN FOOD AND DRUG ADMINISTRATION LICENSURE AND PROCURE VACCINE.

Q-46. WHAT HAPPENS TO THE "OLD" VACCINE, THE LOTS THAT THE FOOD AND DRUG ADMINISTRATION DIDN'T RELEASE?
A-46. THOSE UNRELEASED, PRE-RENOVATION LOTS WILL REMAIN AS AN EMERGENCY STOCKPILE, UNTIL NEWER PRODUCTION LOTS CAN REPLACE THEM. THEY WOULD BE USED ONLY IN AN EMERGENCY AND WITH THE CONCURRENCE OF THE FOOD AND DRUG ADMINISTRATION.

Q-47. WHERE DOES THE DEPARTMENT OF DEFENSE STAND ON THE SECOND-SOURCE FOR ANTHRAX VACCINE PRODUCTION?
A-47. POTENTIAL SOURCES FOR A "NEXT GENERATION" ANTHRAX VACCINE ARE CURRENTLY BEING EXAMINED. THERE HAS BEEN INTEREST BY COMMERCIAL MANUFACTURERS IN A "SHARED LICENSE" AGREEMENT WITH BIOPORT; BUT THAT COULD TAKE TWO TO FOUR YEARS OR LONGER.

MILITARY DISCIPLINE QUESTIONS

Q-48. HOW ARE REFUSALS TO BE VACCINATED HANDLED?
A-48. WE ANTICIPATE THAT VERY FEW, IF ANY, SERVICEMEMBERS WILL REFUSE TO BE VACCINATED GIVEN ~~MORE RECENT KNOWLEDGE~~ MORE RECENT KNOWLEDGE ABOUT THE THREAT OF ANTHRAX AND ALSO ABOUT THE VALIDATED SAFETY AND EFFECTIVENESS OF THE VACCINE. HOWEVER, WE BEGIN WITH THE ASSUMPTION THAT ANY SERVICEMEMBER COVERED BY THIS NEW MANDATORY POLICY WHO REFUSES VACCINATION MAY BE UNINFORMED ABOUT THE FACTS RELATED TO THE DEADLY EFFECTS OF THE ANTHRAX AGENT AND THE SAFE PROTECTION AFFORDED BY THE VACCINE. OUR FIRST ACTION WITH THOSE WHO MIGHT REFUSE THE VACCINE WILL BE TO DETERMINE THEIR CONCERN AND PROVIDE INFORMATION.

THIS IS A FORCE HEALTH PROTECTION ISSUE. IF A SERVICE MEMBER CONTINUES TO REFUSE THE VACCINE, THEN A COMMANDER WILL MANAGE THE SITUATION AS HE OR SHE WOULD FOR ANY FAILURE TO OBEY A LAWFUL ORDER, INCLUDING EDUCATING THE MEMBERS ABOUT THE AVIP AS APPROPRIATE.
~~IF A SERVICEMEMBER CONTINUES TO REFUSE THE VACCINE AFTER REPEATED EFFORTS TO EDUCATE HIM OR HER, THEN A COMMANDER WILL MANAGE THE SITUATION AS HE OR SHE WOULD FOR ANY SITUATION OF "FAILURE TO OBEY A DIRECT AND LAWFUL ORDER." THIS IS A FORCE HEALTH PROTECTION ISSUE AND MANAGEMENT OF REFUSALS WILL BE IN ACCORDANCE WITH POLICIES OF THE RESPECTIVE SERVICES.~~

WE EXPECT SERVICEMEMBERS TO COMPLY WITH ADMINISTRATION OF THIS VACCINE AS FOR ANY OTHER MANDATORY VACCINATION. IT IS COMPARABLE TO AN ORDER TO WEAR BODY ARMOR DURING ARMED ENGAGEMENT, OR TO DON A PROTECTIVE MASK IN A SUSPECTED CHEMICAL OR BIOLOGICALLY CONTAMINATED ENVIRONMENT. ANY SERVICEMEMBER WHO DOES NOT COMPLY WITH THESE MEASURES ENDANGERS HIS/HER OWN HEALTH, AND PLACES BOTH THEIR UNIT AND MISSION ACCOMPLISHMENT AT RISK.

MILITARY AND CIVILIAN JUDGES UNIFORMLY HAVE FOUND ORDERS FOR MEMBERS TO BE VACCINATED TO BE LAWFUL ORDERS. AGAIN, WE DO NOT ANTICIPATE THIS ISSUE TO BE A MAJOR PROBLEM.

6. CONTINGENCY STATEMENT – NOT APPLICABLE.

7. MISCELLANEOUS INFORMATION – NOT APPLICABLE.

8. POINTS OF CONTACT: THE OASD (PA) IS JIM TURNER, (703)-697-5135, DSN 227-5135. THE TOLL FREE NUMBER FOR ADDITIONAL INFORMATION REGARDING THE AVIP IS 1-877-GET-VACC (1-877-438-8222) OR WEBSITE AT HTTP://WWW.ANTHRAX.OSD.MIL/.

Tab H

Executive Summary

ABSTRACT

Anthrax Vaccine Adsorbed (AVA) was licensed in 1970 to provide protection against infection with Bacillus anthracis. *AVA was initially administered on a limited basis, primarily to protect veterinarians and workers processing animal products such as hair or hides that could be contaminated with anthrax spores. In the 1990s, with growing concerns about the possible use of anthrax as a biological weapon, use of the vaccine was substantially expanded. The Department of Defense (DoD) vaccinated some of the military personnel deployed for the Gulf War in 1991 and in 1998 initiated the Anthrax Vaccine Immunization Program, calling for mandatory vaccination of all U.S. service members. By late 2001, roughly 2.1 million doses of AVA had been administered. Production of AVA was suspended in 1998 when the facility manufacturing the vaccine was closed for renovations, which were undertaken to meet regulatory requirements of the Food and Drug Administration (FDA).*

Concerns about the efficacy and safety of AVA, and about vaccine production, led Congress to direct the DoD to support an independent examination of AVA by the Institute of Medicine. In October 2000, the Institute of Medicine convened the Committee to Assess the Safety and Efficacy of the Anthrax Vaccine. The committee reviewed all available data, both published and unpub-

lished, and heard from representatives of DoD, FDA, and other federal agencies; from the vaccine manufacturer BioPort; from researchers studying the efficacy and safety of the vaccine; and from service members and others with concerns about the safety or efficacy of the vaccine. After the bioterrorism of fall 2001, the committee accelerated its original timetable for its review.

As indicated by evidence from studies in both humans and animals, the committee concluded that AVA, as licensed, is an effective vaccine to protect humans against anthrax, including inhalational anthrax. Moreover, because the vaccine exerts its protection via an antigen crucial to the action of the bacterium's toxins, AVA should be effective against anthrax toxicity from all known strains of B. anthracis, *as well as from any potential bioengineered strains.*

After examining data from numerous case reports and especially epidemiologic studies, the committee also concluded that AVA is reasonably safe. Within hours or days following vaccination, it is fairly common for recipients to experience some local events (e.g., redness, itching, swelling, or tenderness at the injection site), while a smaller number of vaccine recipients experience some systemic events (e.g., fever and malaise). But these immediate reactions, and the rates at which they occur, are comparable to those observed with other vaccines regularly administered to adults. The committee found no evidence that vaccine recipients face an increased risk of experiencing life-threatening or permanently disabling adverse events immediately after receiving AVA, when compared with the general population. Nor did it find any convincing evidence that vaccine recipients face elevated risk of developing adverse health effects over the longer term, although data are limited in this regard (as they are for all vaccines).

Regarding manufacture of AVA, the committee reviewed and evaluated the steps taken by BioPort to win FDA approval of its production process. With the newly validated manufacturing process being used in a renovated facility, AVA will be produced under strict controls according to current FDA requirements. The newly produced vaccine is expected to have greater assurance of consistency than the vaccine produced at the time of its original licensure.

It remains important to continue and improve monitoring efforts to detect any adverse health effects caused by AVA and other vaccines. Also needed are studies to establish a quantitative correlation of protective levels of antibodies in animals with antibody levels in humans after full immunization. Direct tests of the efficacy of AVA are neither feasible nor ethical in humans. However, corre-

lates of protection in animal models can be used to test the efficacy of AVA, as well as new vaccines against anthrax. The production, testing, and licensure of a new vaccine requiring fewer doses and producing fewer local reactions are needed.

Anthrax Vaccine Adsorbed[1] (AVA) was licensed in 1970. More than 2 million doses have been administered, and most of those doses have been given since 1998 to U.S. military personnel to protect them against possible exposure to anthrax spores used as biological weapons. The terrorist attacks of September 11, 2001, and the subsequent distribution through the U.S. mail of potent doses of anthrax spores drew new attention to the risks of anthrax exposure and to questions about the anthrax vaccine.

Until the 1990s, AVA had primarily been used by a small population with a risk of occupational exposure to anthrax (e.g., textile mill workers and veterinarians). In 1990, concerns that Iraq had biological weapons containing anthrax spores motivated the U.S. military to administer AVA to an estimated 150,000 service members deployed for the Gulf War. The existence of an Iraqi biological weapons program was confirmed in the mid-1990s (Henderson, 1999; Zilinskas, 1997), and in 1997 the Department of Defense (DoD) announced a plan to vaccinate all U.S. service members with the licensed anthrax vaccine. DoD's Anthrax Vaccine Immunization Program (AVIP) began in March 1998 with personnel scheduled for deployment to higher-risk areas (e.g., Korea and Southwest Asia). In 2000 a limited vaccine supply, the result of delays in federal approval for release of newly manufactured vaccine lots, began slowing plans to vaccinate all military personnel. As more service members were vaccinated under the mandatory AVIP, some raised concerns about the safety or the efficacy of AVA, and more than 400 personnel refused vaccination (Weiss, 2001). Some had also suggested a link between vaccination with AVA and illnesses in Gulf War veterans.

STUDY PROCESS AND INFORMATION SOURCES

Responding to the concerns about the anthrax vaccine and AVIP, the U.S. Congress directed DoD to enter into a contract with the National Research Council for a study of the vaccine's efficacy and safety.[2] In October 2000 the Institute of Medicine (IOM) convened the Committee to

[1] As of January 31, 2002, AVA will be manufactured under the name Biothrax.

[2] The study was called for in the conference report accompanying the 2000 DoD appropriations act P. L. No. 106-79 (1999).

Assess the Safety and Efficacy of the Anthrax Vaccine to carry out that study. Committee members were selected for their expertise in microbiology; vaccine research, development, manufacture, and evaluation; postmarketing surveillance of adverse events; regulatory and licensing procedures; epidemiology; biostatistics; immunology; and health surveillance.

The charge to the committee included consideration of the types and severity of adverse reactions, sex differences in adverse reactions, long-term health implications, the efficacy of AVA against inhalational exposure to all known anthrax strains, and the correlation of the safety and efficacy of the vaccine in animal models to its safety and efficacy in humans. The study was also to address the issue of validation of the manufacturing process, with consideration of discrepancies identified by the Food and Drug Administration (FDA) in February 1998, the definition of vaccine components, and identification of gaps in existing research. (See Appendix A for the Statement of Task.) The charge did not include evaluation of the DoD policy to vaccinate all service members, so the committee did not include an evaluation of the threat from biological warfare agents in its purview. Similarly, the committee was not asked to address the challenges in bioweapons vaccine development and procurement generally, which have recently been discussed in a statement from the Council of the Institute of Medicine (http://www.iom.edu/IOM/IOMHome.nsf/Pages/Vaccine+ Development) and in reports by the Gilmore Commission (http://www.rand.org/nsrd/terrpanel/) and DoD (http://www.defenselink.mil/pubs/Reporton BiologicalWarfareDefenseVaccineRDPrgras-July2001.pdf).

Since the terrorist attacks of September 11, 2001, and subsequent mail distribution of anthrax spores, interest in AVA has greatly increased. Consideration of the full range of topics concerning civilian use of the anthrax vaccine was beyond the purview of this report. However, some of the issues that the committee did address should also be of interest for civilians.

The committee held eight deliberative meetings plus four public workshops. At those workshops, the committee heard from representatives of DoD, FDA, and other federal agencies; from the manufacturer of AVA, BioPort; from researchers studying the efficacy and safety of the vaccine; and from service members and others with concerns about the safety or efficacy of the vaccine. The committee also commissioned a review of the available literature on adverse events associated with other vaccines routinely administered to adults.

The committee examined both published and unpublished data from studies of the safety and efficacy of AVA. The investigators involved in many of those studies presented their data and discussed their findings at committee workshops. In addition, several analyses of existing data were carried out at the committee's request.

ANTHRAX AND ANTHRAX VACCINE

Anthrax is caused by infection with *Bacillus anthracis*, a gram-positive, nonmotile, spore-forming organism (Brachman and Friedlander, 1999; Dixon et al., 1999). It is primarily a disease of wild and domestic animals. Historically, humans have contracted the disease through contact with infected animals or animal products, such as hair or hides, contaminated with anthrax spores. Depending on the site of infection, anthrax can occur in a cutaneous, gastrointestinal, or inhalational form. The disease had become extremely uncommon in any form in the United States until the bioterrorist incidents of the autumn of 2001 caused an outbreak of both cutaneous and inhalational cases of the disease. As of November 28, 2001, there had been 11 cases of inhalational anthrax, 5 of which were fatal, and 7 confirmed and 5 suspected cutaneous anthrax infections (CDC, 2001b). More than 30,000 people may have been exposed to anthrax spores (CDC, 2001a,b).

The virulence of *B. anthracis* derives from the production of a capsule and three toxin proteins: protective antigen (PA), edema factor (EF), and lethal factor (LF). To produce active toxins, PA must bind to cellular receptors and then to either EF or LF. AVA, the vaccine currently licensed for human use in the United States, is a cell-free filtrate containing PA as the principal immunogen. It is administered in six subcutaneous injections of 0.5 milliliters each. The first three doses are given 2 weeks apart, and the following doses are given 6, 12, and 18 months after administration of the first dose. Annual booster doses are required.

ANTHRAX VACCINE EFFICACY

The committee's observations and findings addressed the efficacy of immunization with the licensed vaccine, AVA, against inhalational anthrax and all known anthrax strains (see Chapter 3). Of particular concern is exposure to anthrax spores processed for use in biological weapons. The committee also examined what is known and what must still be established regarding the correlation of protection in animal models with immunity in humans.

It is important to note that efficacy is relative, not absolute. The degree of protection provided by a vaccine is determined by a variety of factors, which can include the size of the inoculum of exposure, the strain of the pathogen, and the host response. Even a vaccine considered highly effective may fail to protect some individuals under some circumstances.

Evaluating Efficacy of AVA

The efficacy of a PA-containing anthrax vaccine similar to AVA against anthrax infection was established by a randomized controlled field study of

textile mill workers (Brachman et al., 1962). Subsequent data from the Centers for Disease Control and Prevention (CDC) support the results of that study (FDA, 1985). The small number of inhalational cases in those studies provides insufficient information to establish the vaccine's efficacy against inhalational infection, but the data suggest that the vaccine has a protective effect.

Animal studies are essential for further investigation of the efficacy of AVA and other anthrax vaccines against inhalational disease because studies with humans are neither feasible nor ethical. Cases of inhalational anthrax are very rare, even where anthrax occurs naturally in the environment or as an occupational hazard. Moreover, human research subjects cannot be deliberately exposed to potentially lethal agents, such as anthrax spores, for no therapeutic reason and without the availability of a proven treatment.

Finding: Because additional clinical trials to test the efficacy of AVA in humans are not feasible and challenge trials with volunteers are unethical, by necessity animal models represent the only sources of the supplementary data needed to evaluate AVA's efficacy.

Animal models with pathological and immunological characteristics similar to those of humans could be considered the most appropriate ones for the evaluation of vaccine efficacy. The pathophysiology of anthrax in nonhuman primates, such as the macaque, most closely resembles the pathophysiology of anthrax in humans. Among the smaller and more available laboratory animals, rabbits most closely resemble nonhuman primates in terms of the pathology of anthrax and their response to the anthrax vaccine.

Finding: The macaque and the rabbit are adequate animal models for evaluation of the efficacy of AVA for the prevention of inhalational anthrax.

Efficacy of AVA Against All Known *B. anthracis* Strains

Several different *B. anthracis* strains are found in nature worldwide (Fellows et al., 2001; Keim et al., 2000), and analysis of tissue samples from victims of the release of anthrax spores from the Soviet biological weapons facility at Sverdlovsk in 1979 indicated the presence of several *B. anthracis* strains (Grinberg et al., 2001; Jackson et al., 1998). It is important to establish whether AVA can afford protection against the full range of naturally occurring or engineered *B. anthracis* strains.

Studies have shown that the protection that AVA affords guinea pigs differs by bacterial strain (Auerbach and Wright, 1955; Fellows et al., 2001; Ivins et al., 1994; Little and Knudson, 1986; Turnbull et al., 1986),

but AVA and a predecessor vaccine protected rabbits and monkeys against the numerous strains tested (Auerbach and Wright, 1955), including those that defeated the vaccine in guinea pigs (Fellows et al., 2001). No AVA-resistant strains have been demonstrated in nonhuman primates. Observational data from studies with humans also support the efficacy of AVA against a variety of strains, though exposure strains were not evaluated in the studies (Brachman et al., 1962; CDC, 1967–1971).

PA is the principal immunogen in AVA, and the efficacy of AVA against a broad spectrum of *B. anthracis* strains is consistent with the critical role of PA in the pathogenesis of anthrax (Bhatnagar and Batra, 2001; Cataldi et al., 1990; Smith and Keppie, 1954). As shown in Figure ES-1, PA must be competent to carry out multiple complicated tasks: it must bind to its receptor, form a heptamer, and bring EF and LF into the cell.

There is concern that natural mutations or bioengineered alterations of the PA component of anthrax could result in vaccine-resistant strains. Studies (Sellman et al., 2001; see also Mogridge et al., 2001) have shown, however, that a PA heptamer is deactivated by the presence of even a few mutant subunits. A deactivated heptamer is unlikely to be able to deliver EF and LF to the cytosol. The committee considers it improbable that a mutant PA that retains its function yet escapes the vaccine-elicited protective antibodies directed to the wild-type PA could be constructed at this time.

The likely difficulty of successfully altering PA is supported by evidence that the *B. anthracis* genome is highly conserved among strains isolated across a wide geographical area (Jackson, 2001; Keim et al., 1997) and that PA is also highly conserved (Jackson, 2001; Price et al., 1999). Because PA is critical to virulence and because its structure is so highly conserved, it appears likely that changing its structure would alter and thus eliminate its toxic action.

Finding: It is unlikely that either naturally occurring or anthrax strains with bioengineered protective antigen could both evade AVA and cause the toxicity associated with anthrax.

Establishing Animal Model Correlates of Anthrax Vaccine Efficacy

Several recent studies have used passive protection to demonstrate a relationship between levels of circulating anti-PA antibody and protection from challenge with anthrax spores (Barnard and Friedlander, 1999; Beedham et al., 2001; Little et al., 1997; McBride et al., 1998; Pitt et al., 2001; Reuveny et al., 2001).

Finding: The available data indicate that immunity to anthrax is associated with the presence of antibody to protective antigen.

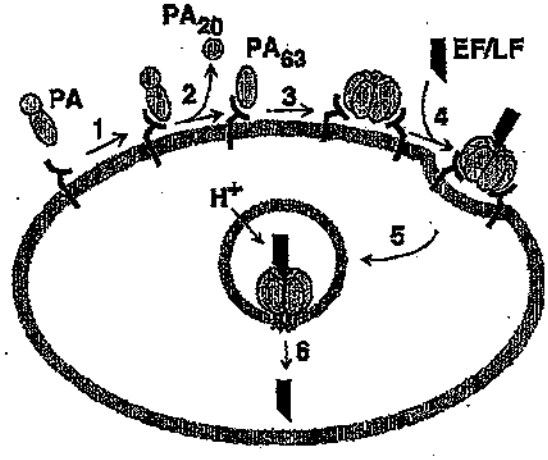


FIGURE ES-1 Model of anthrax toxin action. (1) PA binds to cellular receptor. (2–3) The protein is cleaved and activated to form a heptameric prepore. (4) LF, EF, or both bind to the heptamer, and the resulting complex is taken into an acidic compartment in the cell through endocytosis. (5–6) The acidic pH initiates the heptamer to pierce the membrane of the cell and translocate LF, EF, or both into the cytosol, where the toxins lead to damage. [Reprinted, with permission, from *Biochemistry* 38:10432–10441 (1999). Copyright 1999 by American Chemical Society.]

The information reviewed by the committee demonstrates that both humans and certain laboratory animals manifest the same disease after infection with the same anthrax organism and that both are protected by immunization with AVA, which elicits the production of antibodies to PA. This information establishes a *qualitative* correlation between protection in animal models and protection in humans. To move forward with research on the current anthrax vaccine or any new vaccines, however, a *quantitative* correlation of the protective levels of antibodies in animals with the antibody titers obtained after full immunization in humans is needed. Those correlates in animal models can then be used to test new vaccines for efficacy with confidence that the data from studies with animals will be predictive of the clinical results for immunized humans. The data from animal studies already developed suggest that serological correlates of human immunity can be developed in appropriate animal models. The committee commends this work and encourages its further development.

Recommendation: Additional passive protection studies with rabbits

and monkeys including the transfer of animal and human sera are urgently needed to quantify the protective levels of antibody in vivo against different challenge doses of anthrax spores.

Recommendation: Additional active protection studies should be conducted or supported to develop data that describe the relationship between immunity and both specific and functional quantitative antibody levels, including studies of

- **the relationship between the vaccine dose and the resulting level of antibody in the blood of test animals that protects the animals from challenge;**
- **the relationship between the level of antibody that protects animals from challenge and the level of antibody present in humans vaccinated by the regimen currently recommended for the licensed product; and**
- **the vaccine dose that results in a level of antibody in the blood of human volunteers similar to that in the blood of protected animals.**

Postexposure Use of Anthrax Vaccine

As a result of the inhalational exposure to anthrax spores from letters mailed in the autumn of 2001, questions about the postexposure efficacy of AVA have arisen. No data from studies with humans are available, but two papers provide information from studies with rhesus monkeys.

These limited data suggest that use of the vaccine in combination with an appropriate antibiotic for 30 days could provide excellent postexposure protection against inhalational anthrax. Although the additional benefit from receiving the vaccine after a prolonged period of antibiotic use is not proven, reliance on the vaccine alone after exposure is clearly insufficient, as some protection is needed during the time required for an immune response to develop. Additional studies on the postexposure use of AVA with antibiotics are needed.

Recommendation: DoD should pursue or support additional research with laboratory animals on the efficacy of AVA in combination with antibiotics administered following inhalational exposure to anthrax spores. Studies should focus on establishment of an appropriate duration for antibiotic prophylaxis after vaccine administration.

Conclusions Regarding Efficacy

A vaccine similar to AVA was shown to be effective against cutaneous anthrax in humans in the field trial supporting the original application for

licensure of AVA (Brachman et al., 1962). Although that study had too few cases to evaluate the vaccine's efficacy for the prevention of inhalational disease, the five inhalational cases observed during the trial occurred only among nonvaccinated or placebo recipients. Data from CDC on cases reported between 1962 and 1974 also indicated that the vaccine offered protection against the cutaneous form of the disease (FDA, 1985). Furthermore, laboratory experiments indicate that AVA provides effective protection against inhalational challenge in rabbits and macaques, the animal models in which the disease is most reflective of the disease in humans (Fellows et al., 2001; Ivins et al., 1996, 1998; Pitt et al., 2001). Because PA is critical to the virulence of *B. anthracis* and because PA's structure is so highly conserved, it appears likely that changing its structure would alter and thus eliminate its toxic action. Data from studies with animals suggest that AVA will offer protection against strains with PA-based toxicity. Finally, the available data indicate that immunity to anthrax is associated with the presence of antibodies to PA, such as those stimulated by the anthrax vaccine.

Finding: The committee finds that the available evidence from studies with humans and animals, coupled with reasonable assumptions of analogy, shows that AVA as licensed is an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by any known or plausible engineered strains of *B. anthracis*.

ANTHRAX VACCINE SAFETY

As with any pharmaceutical product or medical procedure, the use of vaccines carries a risk of adverse health effects that must be weighed against the expected health benefit. Expectations for the safety[3] of vaccines are especially high because, in contrast to therapeutic agents, which are given when a disease is known to be present (or at least suspected), vaccines are usually given to people who are healthy to protect them against a disease that they may not be exposed to in the future.

The committee evaluated case reports and epidemiologic studies providing information about the safety of the anthrax vaccine. Case reports can help to generate hypotheses about possible associations but are rarely sufficient by themselves to confirm such associations. Formal epidemiologic studies are usually needed to determine whether those adverse events iden-

[3]For this report, safety reflects expectations of relative freedom from harmful effects when a product is used prudently, considering the condition of the recipient and the health risk the product is directed against.

tified in case reports occur in exposed populations at a rate that exceeds the background rate in unexposed populations.

The case reports relating to AVA come primarily from the Vaccine Adverse Event Reporting System (VAERS), a passive surveillance system that collects reports on adverse events following the use of any vaccine licensed in the United States (see Chapter 5). A subset of the committee reviewed each of 120 VAERS reports on serious adverse events associated with AVA. The committee also heard testimony regarding adverse events following vaccination with AVA. These statements, some of which concerned cases reported to VAERS, added valuable insight into the conditions that some military personnel are experiencing.

In evaluating the epidemiologic studies of adverse events following receipt of AVA (see Chapter 6), the committee gave additional weight to those that (1) used active surveillance rather than self-reports of post-immunization events; (2) included sufficiently large numbers of subjects; (3) had clearly specified, objective criteria for the definition of adverse events; and (4) had sufficiently long postimmunization follow-up intervals to allow identification of later-onset events. Those studies that included a suitable unimmunized comparison group or in which evaluators were blinded to vaccination status were especially useful to the committee.

Conclusions Regarding AVA Vaccination and Adverse Events

Substantial data are now available from VAERS, epidemiologic studies with data from the Defense Medical Surveillance System (DMSS), and other epidemiologic studies for assessments of the health outcomes following vaccination with AVA. Immediate-onset health events are observable within hours or days following vaccination; later-onset events would be observable only months or years following vaccination.

Epidemiologic studies that have used either active surveillance (Brachman et al., 1962; Pittman, 2001b,c; Pittman et al., 1997, 2002, in press) or passive surveillance (Hoffman et al., submitted for publication; Pittman, 2001a; Pittman et al., 2001a,b; Wasserman, 2001) have consistently found local injection-site reactions, including redness, induration, edema, itching, or tenderness (see Table 6-1 for details). Systemic events, such as fever, malaise, and myalgia, are also associated with vaccination with AVA but are generally less common than injection-site reactions. The types of local and systemic reactions associated with AVA and the rates at which they were observed are comparable to those observed with other vaccines regularly administered to adults, such as diphtheria and tetanus toxoids and influenza vaccines (Treanor, 2001). Although these immediate-onset health effects can result in brief limitation of activities or the loss of time from work (Hoffman et al., submitted for publication; Wasserman,

2001), they are self-limited and result in no serious, permanent health impairments (AMSA, 2001a,b,c; Grabenstein, 2000; Lange et al., 2001a,b; Rehme, 2001; Rehme et al., 2002; Mason et al., 2001, submitted for publication; Sato, 2001a,b; Sato et al., 2001).

Finding: The data available from VAERS, DMSS, and epidemiologic studies indicate the following regarding immediate-onset health events following receipt of AVA:

- **Local events, especially redness, swelling, or nodules at the injection site, are associated with receipt of AVA, are similar to the events observed following receipt of other vaccines currently in use by adults, and are fairly common.**
- **Systemic events, such as fever, malaise, and myalgia, are associated with receipt of AVA, are similar to the events observed following receipt of other vaccines currently in use by adults but are much less common than local events.**
- **Immediate-onset health effects can be severe enough in some individuals to result in brief functional impairment, but these effects are self-limited and result in no permanent health impairments.**
- **There is no evidence that life-threatening or permanently disabling immediate-onset adverse events occur at higher rates in individuals who have received AVA than in the general population.**

Sex differences are seen in local injection-site reactions. Women are more likely than men to experience and report erythema, local tenderness, subcutaneous nodules, itching, and edema (Hoffman et al., submitted for publication; Pittman, 2001a,b; Pittman et al., 2001a,b, 2002; Wasserman, 2001). In addition, some systemic effects, including fever, headache, malaise, and chills, were sometimes more often reported by women than by men (Hoffman et al., submitted for publication; Pittman, 2001a; Pittman et al., 2001a,b), but rates of clinically observed systemic reactions generally did not differ substantially between men and women (Pittman, 2001b; Pittman et al., 2002). For female service members, reactions following vaccination against anthrax may be more likely to have an adverse effect on their ability to perform their duties (Hoffman et al., submitted for publication; Wasserman, 2001). Studies of other vaccines have also generally found higher rates of local reactions among women but similar rates of systemic reactions between men and women (Treanor, 2001). The factors that account for these sex differences are not known, but they could be a function of differences in muscle mass, differences in the doses per unit of body mass, physiologic factors, or differences in care-seeking behavior. Future studies of vaccination against anthrax should continue to analyze data for men and women separately.

Finding: The available data from both active and passive surveillance indicate that there are sex differences in local reactions following vaccination with AVA, as there are following administration of other vaccines. For female service members, reactions following vaccination with AVA can have a transient adverse impact on their ability to perform their duties. The factors that account for these sex differences are not known.

Recommendation: Future monitoring and study of health events following vaccination(s) with AVA (and other vaccines) should continue to include separate analyses of data for men and women.

Some of the data reviewed by the committee showed lot-to-lot differences in the reactogenicities of AVA doses (CDC, 1967–1971; Pittman, 2001a; Pittman et al., 2001a,b).

Unlike most vaccines, AVA is licensed for subcutaneous rather than intramuscular administration. The limited evidence from a small study that tested changes in the AVA dosing schedule and route of administration (Pittman, 2001b; Pittman et al., 2002) suggests that subcutaneous administration contributes to the local reactions but not systemic reactions associated with AVA. With other vaccines, subcutaneous administration is also associated with higher rates of local erythema or induration (Treanor, 2001), reactions commonly reported following the administration of AVA.

Finding: The currently licensed subcutaneous route of administration of AVA and the six-dose vaccination schedule appear to be associated with a higher incidence of immediate-onset, local effects than is intramuscular administration or a vaccination schedule with fewer doses of AVA. The frequencies of immediate-onset, systemic events were low and were not affected by the route of administration.

Recommendation: DoD should continue to support the efforts of CDC to study the reactogenicity and immunogenicity of an alternative route of AVA administration and of a reduced number of vaccine doses.

Some have expressed concerns about potential later-onset and chronic health effects resulting from AVA use. The available information regarding later-onset health effects is limited, as for all vaccines, but provides no convincing evidence of elevated risks of later-onset health events (AMSA, 2001a,b,c; Grabenstein, 2000; Lange et al., 2001a,b; Mason et al., 2001, submitted for publication; Peeler et al., 1958, 1965; Rehme, 2001; Rehme et al., 2002; Sato, 2001a,b; Sato et al., 2001; White et al., 1974). DMSS, which provides the best source of data for studying later-onset health effects, provides data on service personnel who have documented histories of vaccination with AVA and who have been observed for up to 3 years.

Although AVA has been administered to military personnel for more than 3 years, unreliable documentation of vaccinations before 1998 limits analysis of DMSS data for observation of potential vaccine-related health effects over longer periods.

Finding: The available data are limited but show no convincing evidence at this time that personnel who have received AVA have elevated risks of later-onset health events.

Recommendation: DoD should develop systems to enhance the capacity to monitor the occurrence of later-onset health conditions that might be associated with the receipt of any vaccine; the data reviewed by the committee do not suggest the need for special efforts of this sort for AVA.

The studies reviewed did not examine the use of AVA in children, the elderly, or individuals with chronic illnesses. In addition, information regarding the outcomes of pregnancy following use of the vaccine is limited. These limitations should be taken into account if AVA is considered for use in the general population.

ANTHRAX VACCINE MANUFACTURE

The committee was charged with addressing "validation of the manufacturing process focusing on, but not limited to, discrepancies identified by the Food and Drug Administration in February 1998." The committee could not directly validate the manufacturing process and did not wish to second-guess FDA's inspection and determination of validity. It was possible, however, to review and evaluate the steps by which BioPort worked to validate the AVA manufacturing process (see Chapter 7).

Documents that BioPort provided to the committee gave detailed information about findings from FDA inspections conducted since 1998, the company's responses to those findings, and FDA's evaluation of BioPort's progress. The committee paid special attention to materials on product characterization and process validation. It also considered the recent and increasing investments by BioPort and DoD in facility renovations and improvements in documentation of the manufacturing process, as well as the transfer, with approval from FDA's Center for Biologics Research (CBER), of filling operations to a contractor meeting Good Manufacturing Practices standards. The committee noted BioPort's access to technical support and assistance from CBER and DoD research and development resources. The results of these efforts were reflected in BioPort's reports of progress in correcting deficiencies previously noted by FDA, as reported at the committee's July 2001 meeting. This progress was confirmed by FDA.

On January 31, 2002, FDA approved BioPort's supplements to its Biologics License Application covering facility renovations, changes to the package label, and the contracted filling operations.

In evaluating BioPort's efforts to meet the manufacturing requirements for AVA, the committee noted FDA's changes and modernizations and improvements in the regulation of biologics, as well as the continuing effort at constructive criticism and response between the agency and the manufacturer. The committee also considered the history of the AVA manufacturer—in particular, the switch from a state-owned to a privately owned and operated interstate commercial venture—and the coincident changes in FDA oversight and validation requirements. Finally, the committee was mindful of the scientific and technical advances in vaccine manufacture and characterization that have occurred since the original licensure of the AVA product.

Finding: FDA's process of plant inspection and FDA's validation of the vaccine manufacturing process have changed and have become more stringent with time.

Finding: With high-priority efforts by the manufacturer and FDA, the manufacturing process for AVA has been validated so that vaccine manufactured postrenovation has been approved for release and distribution.

BioPort has responded to numerous specific citations from FDA regarding the manufacturing process and equipment and has now received FDA approval of its license supplements. In the committee's judgment, the cumulative effects of the changes in materials, equipment, and processes in response to FDA citations, as well as the changes in the regulatory climate and in scientific knowledge, are likely to result in greater assurance of consistency in the final AVA product.

Finding: AVA will now be produced by a newly validated manufacturing process under strict controls, according to current FDA requirements. As a result, the postrenovation product has greater assurance of consistency than that produced at the time of original licensure.

FUTURE NEEDS

Despite recent FDA approval of the license supplement for AVA manufacturing renovations, package insert, and contract filler, the committee is convinced that relying on AVA and the current specifications for its use is far from satisfactory. There is a need for research toward the development of a different and better anthrax vaccine, as well as a need for improvements in monitoring the safety of the current vaccine.

Future Use of AVA

Finding: Current events in both the military and civilian arenas highlight and confirm the importance of ensuring both the availability and the quality of the nation's anthrax vaccine.

With the deployment of U.S. troops to Afghanistan and surrounding areas and domestic bioterrorism incidents involving exposure to *B. anthracis* spores, vaccination against anthrax is likely to resume and possibly expand. This means that AVA is likely to be given to a much larger population than was anticipated at the time that the vaccine was licensed.

Meanwhile, the current supply of AVA is limited because of manufacturing difficulties, which have now been overcome. On the basis of information provided by BioPort and FDA, the committee notes that the AVA manufacturing process has been modified to incorporate more modern technology and procedures. These changes are expected to increase assurance of the consistency of the final product, which remains a relatively crude vaccine by current standards.

Although greater assurance of product consistency will occur, the levels of immunogenicity, safety, and stability of the postrenovation AVA product must be characterized. The committee emphasizes that the surveillance methods recommended below are the same as those that would be expected for any widely used vaccine and are not unique to AVA.

Finding: The AVA product produced in a renovated facility by a newly validated manufacturing process could differ from the prerenovation product in terms of its reactogenicity, immunogenicity, and stability. The information available to the committee suggests that AVA lots manufactured postrenovation may show less variation in reactogenicity because of greater consistency in the production process, and there is no a priori basis to believe that the postrenovation product will be more reactogenic or less immunogenic than the older vaccine.

Recommendation: As with all vaccines, AVA lots produced postrenovation should be monitored for immunogenicity and stability, and individuals receiving these lots should be monitored for possible acute or chronic adverse events of immediate or later onset.

Surveillance for Adverse Events

DoD has supported an independent civilian advisory panel called the Anthrax Vaccine Expert Committee (AVEC) to review each VAERS report associated with AVA.

The Future and AVEC

The committee found AVEC's expert scrutiny of VAERS reports for signals that might require further action to be an important component of surveillance for the safety of AVA. However, the value of such a review process may not be limited to AVA. Furthermore, the IOM committee is generally skeptical about attribution of causality, such as those that AVEC makes, from reports to a surveillance system like VAERS, especially given the potential for misclassification of reported events when considering them as possibly related or unrelated to vaccination. The committee emphasizes that a review of case reports to VAERS is appropriate only for the generation of hypotheses. More emphasis should therefore be placed on the use of AVEC-derived hypotheses to trigger additional analyses, such as those that can be performed with data from DMSS. Toward that end, AVEC and the Army Medical Surveillance Activity (the office responsible for DMSS) should maintain regular and frequent communication, with signals from the former leading to analyses by the latter. "Signals" are the earliest indication of a possible causal relationship between an exposure and a health event. Such signals can come from the anecdotal experiences of patients with an adverse event after the exposure or from preliminary analyses of data. A signal does not mean that a causal relationship exists, as there may be other explanations for the apparent association. Instead, a signal is merely an indication that further investigation is needed.

Although AVA appears to be associated with certain undesirable but self-limited or easily treated adverse events, the committee saw no indication from the currently available data of a need to continue special monitoring programs for AVA. Nevertheless, monitoring of vaccine safety in general and the safety of vaccines for use by members of the military in particular must be a priority. The committee observed several areas in which surveillance for the safety of vaccines in general and AVA in particular might be improved.

Finding: Given the concerns raised by some service members about the safety of the anthrax vaccine, the creation of AVEC was an appropriate complement to other resources in FDA, CDC, and DoD for the monitoring of vaccine safety concerns. The results of the extra monitoring did not indicate the existence of any sentinel events that were not detected in the existing FDA and CDC reviews. The committee finds no scientific reason for the continued operation of AVEC in its present form.

The IOM committee's observations about AVEC reflect no fault with the members of AVEC or its performance as that committee is constituted; rather, the IOM committee observes that AVEC was designed to pay extra

attention to safety concerns regarding the safety of AVA and that the data do not warrant the continuation of such exceptional attention. The resources supporting AVEC activities related to AVA alone could be more wisely invested in improved monitoring of the safety of vaccines in general.

Recommendation: DoD should disband AVEC in its current form and instead assist FDA and CDC in establishing an independent advisory committee charged with overseeing the entire process of evaluating vaccine safety. The proposed advisory committee can also assist on an ad hoc basis in the interpretation of potential signals detected in VAERS or other sources regarding the safety of any vaccine. The newly established FDA drug safety committee might be an appropriate model.

Should DoD choose to continue AVEC, the committee urges DoD to recommend a shift in AVEC's focus from making attributions of causality in individual cases to seeking any patterns or rate thresholds that have been crossed in terms of the serious adverse events reported to VAERS. AVEC could then develop criteria for signals from VAERS data for any vaccine that warrants additional follow-up and could in general further systematize its processes by developing standard operating procedures and a regular schedule for examination of aggregate VAERS data. Background rates of illnesses as well as the biological plausibility of hypothesized effects must be taken into consideration as part of the method used to identify signals of possible safety concerns.

Recommendation: If DoD chooses to continue AVEC, DoD should consider redefining the panel's role so that it serves as an independent advisory committee that responds on an ad hoc basis to specific requests to assist in the interpretation of potential signals detected by others (e.g., CDC and FDA) and reported to VAERS or other sources regarding the safety of all vaccines administered to service personnel rather than continuing the panel's current role of rereviewing each VAERS report related to AVA.

Additional Sources of Data on Adverse Events

Ensuring the best use and interpretation of VAERS reports requires complementary information from other sources that can be used to help analyze the signals that may be suggested by VAERS reports. One such resource is DMSS. DMSS can be used both to generate and test hypotheses. If VAERS raises a hypothesis, it can be further evaluated in DMSS. DMSS data can also be used to generate hypotheses (as in its quarterly screening reports); these then need to be evaluated in more detail within DMSS, including more detailed data analyses and efforts that might involve review

of medical records, for example. Formal testing of these hypotheses would require additional studies, however, in separate data sets.

Finding: DMSS is a unique and promising population-based resource for monitoring the emergence of both immediate-onset and later-onset (perhaps up to 5 years) health concerns among military personnel and for testing hypothesized associations between such health concerns and exposures resulting from military service, including vaccines.

Because DMSS is designed to record all medical encounters without depending on the decision of a patient or a physician to report a particular encounter, DMSS data may be cross-checked with the more open-ended but much less complete case reports collected through VAERS.

Recommendation: DoD should develop a capability for the effective use of DMSS to regularly test hypotheses that emerge from VAERS and other sources regarding vaccine-related adverse events.

Finding: DoD personnel have used DMSS to conduct valuable analyses in response to concerns about health effects that might be associated with vaccination with AVA. Yet DoD personnel working with DMSS data are necessarily limited in time and focus. DMSS data could therefore yield valuable insights in the hands of civilian researchers.

Recommendation: DoD should actively support and advance the development of DMSS data resources and the staffing of units that will allow the continuing rapid and careful analysis of these data, including but not limited to the proposed collaboration between CDC and the Army Medical Surveillance Activity.

Recommendation: DoD should investigate mechanisms that can be used to make DMSS data available to civilian researchers, as is done by civilian agencies, with appropriate controls and protections for privacy.

As discussed in Chapter 6, data on the later-onset adverse effects of vaccines are available for few, if any, vaccines. Although the committee found no data indicating that vaccination with AVA is associated with any later-onset adverse events or with any severe or lasting adverse events, some service members have had serious concerns about possible links between AVA and such adverse events. To make it possible to conduct studies of later-onset health concerns, DoD could take steps to improve access to data on the chronic or later-onset effects, if any, of vaccines in general.

Recommendation: DoD should carefully evaluate options for longer-term follow-up of the possible health effects of vaccination against

anthrax (and other service-related exposures). The committee recommends consideration of the following specific steps:

- Encourage participation in the Millennium Cohort Study[4] as part of a program to ensure adequate monitoring for any possible later-onset health effects that might be associated with vaccination with AVA or other service-related exposures.
- Collaborate with the Department of Veterans Affairs (VA) to monitor service members who receive medical care through VA facilities after separation from military service. Linking of data from DMSS to data from VA is a possible tool. Even though those who receive their medical care through VA may be an unrepresentative minority of all former military personnel, valid comparisons may be possible between those within that population who received a vaccine or other exposure and those who did not.
- Collaborate with VA to obtain fact-of-death information from the Beneficiary and Records Locator System and with the Social Security Administration to obtain death files. Data on the cause of death should be obtained from the National Death Index as needed.
- Ensure the long-term maintenance of DMSS and other relevant paper and electronic records so that retrospective studies will be feasible if health concerns are identified in the future.

New Anthrax Vaccine Development

Although AVA appears to be sufficiently safe and effective for use, it is far from optimal.

Finding: The current anthrax vaccine is difficult to standardize, is incompletely characterized, and is relatively reactogenic (probably even more so because it is administered subcutaneously), and the dose schedule is long and challenging. An anthrax vaccine free of these drawbacks is needed, and such improvements are feasible.

Initially, the committee urges that improvements to the currently licensed vaccine, AVA, be made as quickly as possible. The committee welcomes anticipated improvements in the assurance of lot-to-lot consis-

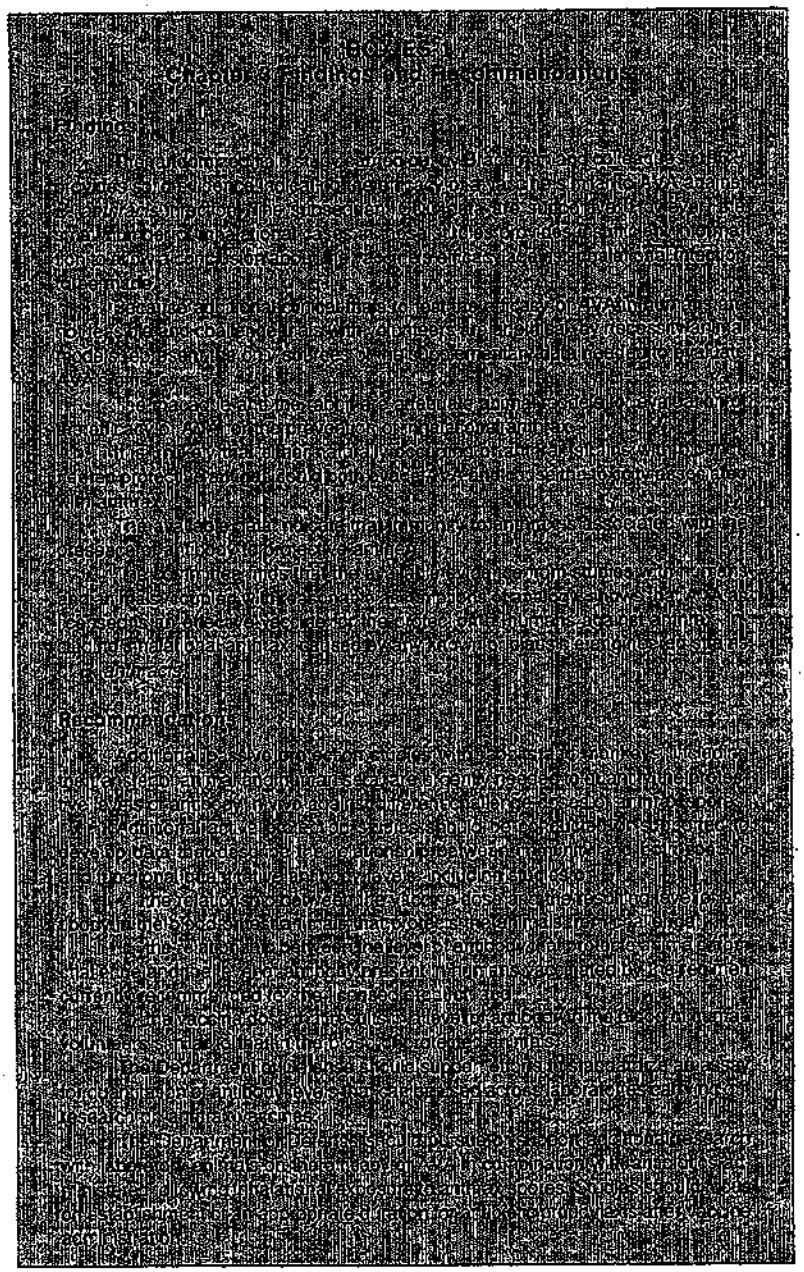
[4]The Millennium Cohort Study is a survey recommended by the U.S. Congress and sponsored by DoD. The study will monitor a total of 140,000 U.S. military personnel during and after their military service for up to 21 years to evaluate the health risks of military deployment, military occupations, and general military service (see http://www.millenniumcohort.org/about.html).

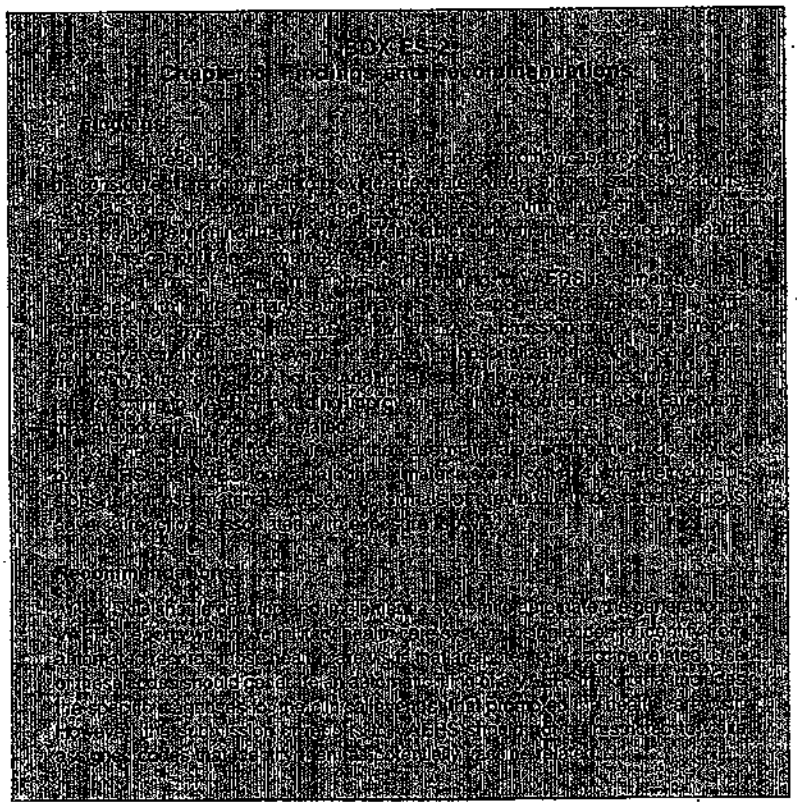
tency in the postrenovation vaccine. The committee also believes that it is likely that the rates of adverse events and the general acceptability of AVA will improve with a change in the route of administration (from the subcutaneous to the intramuscular route) and with a reduction in the total number of injections required and that such improvements would be desirable. Research to assess the effects of those changes in vaccine administration was under way as this report was being written.

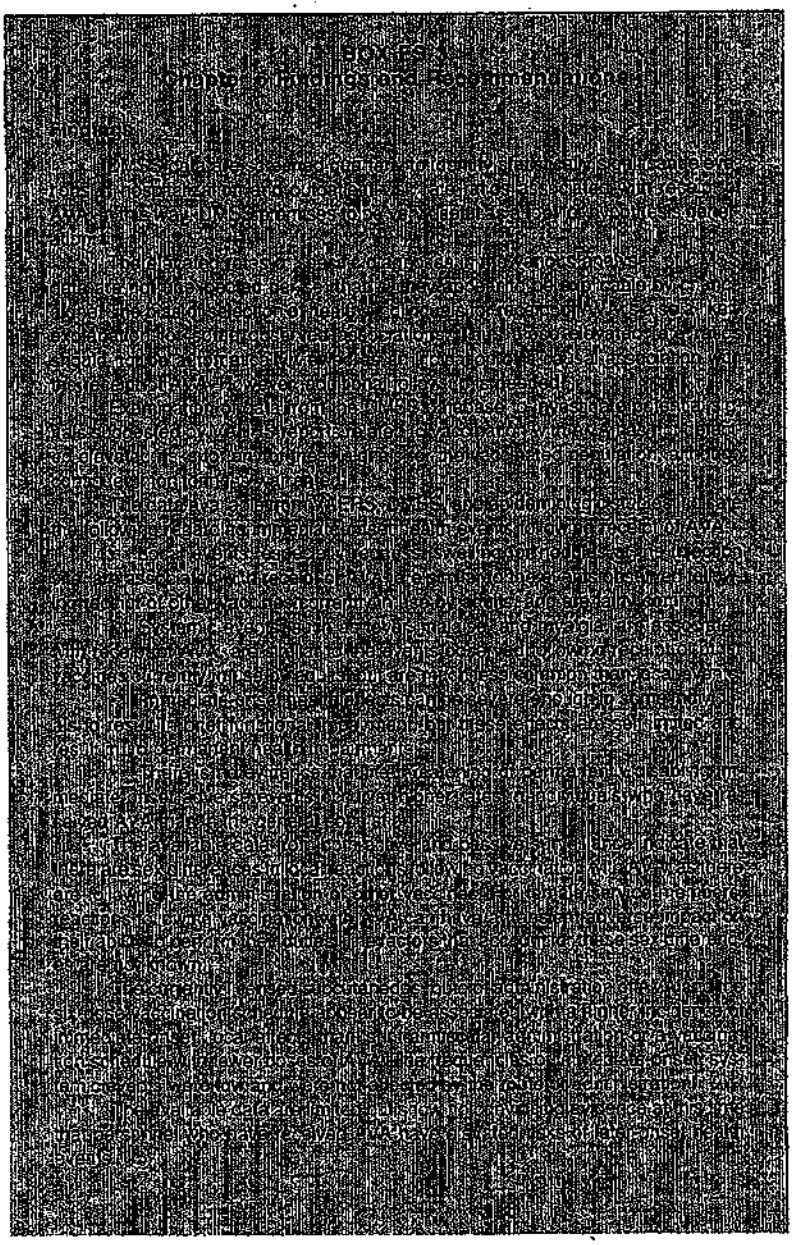
The committee concluded, however, that a new vaccine, developed according to more modern principles of vaccinology, is urgently needed. The committee did not comment on any particular new vaccine development program, and a review of research related to the development of a new vaccine was beyond its charge. The committee recognizes that research on new vaccines against anthrax is under way at DoD, the National Institutes of Health, and various university laboratories and strongly encourages continued and further support of work on promising new vaccines. Further research with AVA on topics such as correlates of immunity in animals, the components necessary to stimulate protective immunity, and the best way to administer the vaccine should aid in the development of new and improved vaccine products for protection against anthrax.

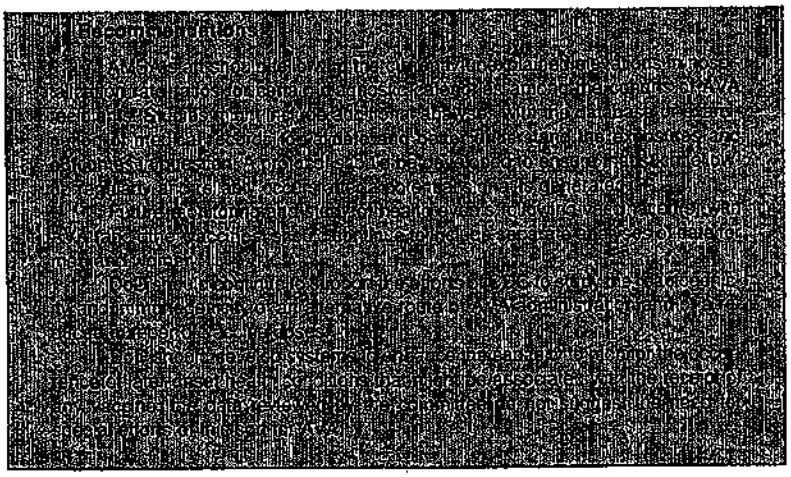
Recommendation: DoD should continue and further expedite its research efforts pertaining to anthrax disease, the *B. anthracis* organism, and vaccines against anthrax. Research related to anthrax should include, in particular, efforts such as the following:

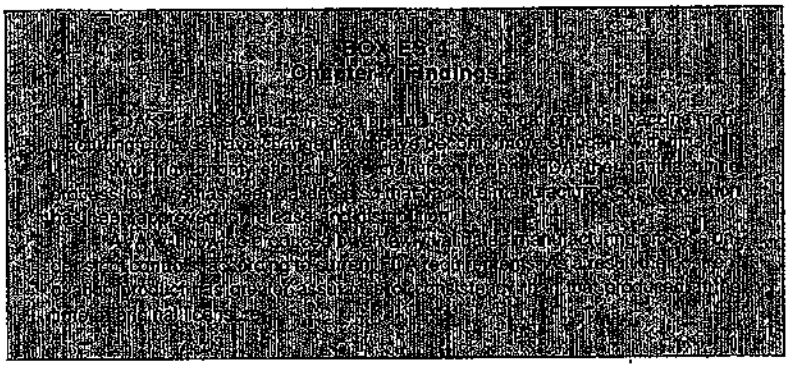
- **DoD should pursue and encourage research to develop an anthrax vaccine product that can be produced more consistently and that is less reactogenic than AVA;**
- **DoD should pursue and encourage research regarding the *B. anthracis* capsule;**
- **DoD should pursue and encourage research on the mechanisms of action of the anthrax toxins; such research could lead to the development of small-molecule inhibitors;**
- **DoD should pursue and encourage research to map the epitopes of the protective antigen that correlate with specific functional activities;**
- **DoD should pursue and encourage research to test the therapeutic potential of antitoxin proteins or antibodies; and**
- **DoD should pursue and encourage research into additional potential virulence factors in *B. anthracis*, and into other possible vaccine candidates.**

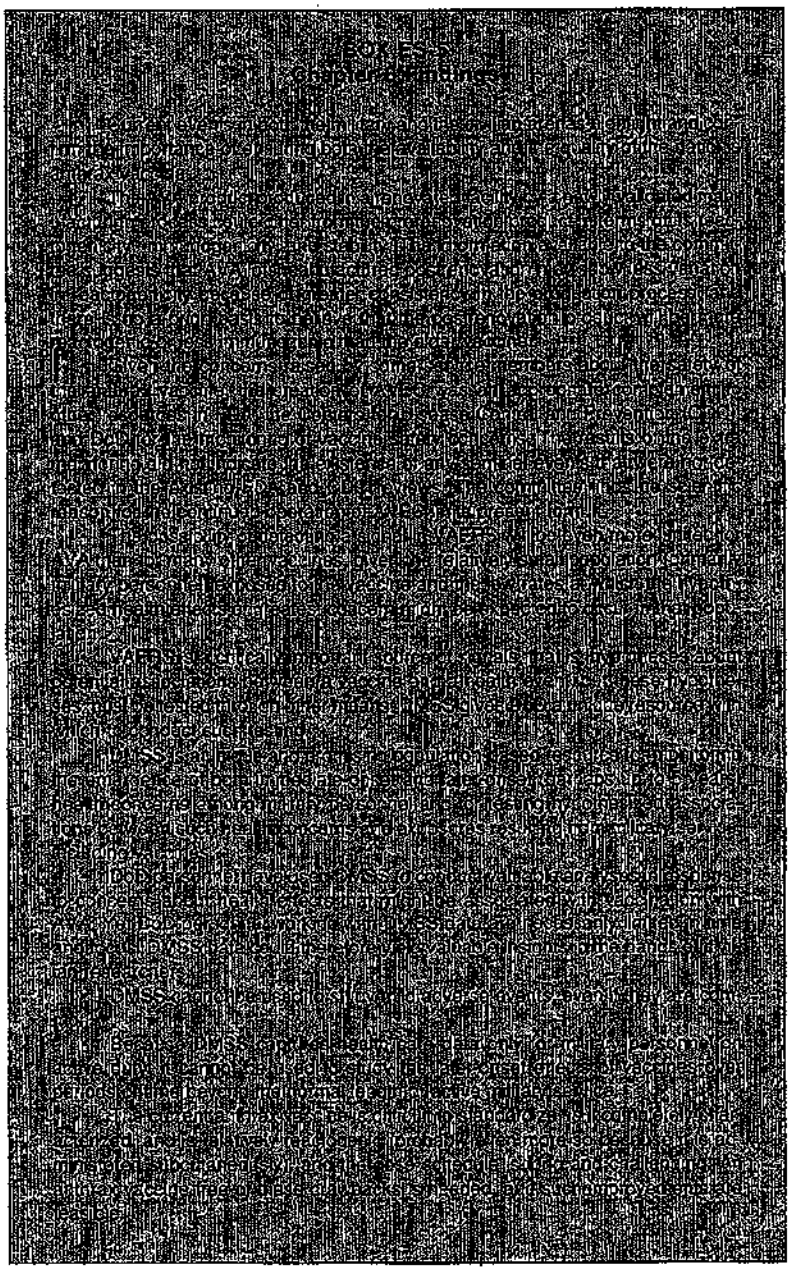


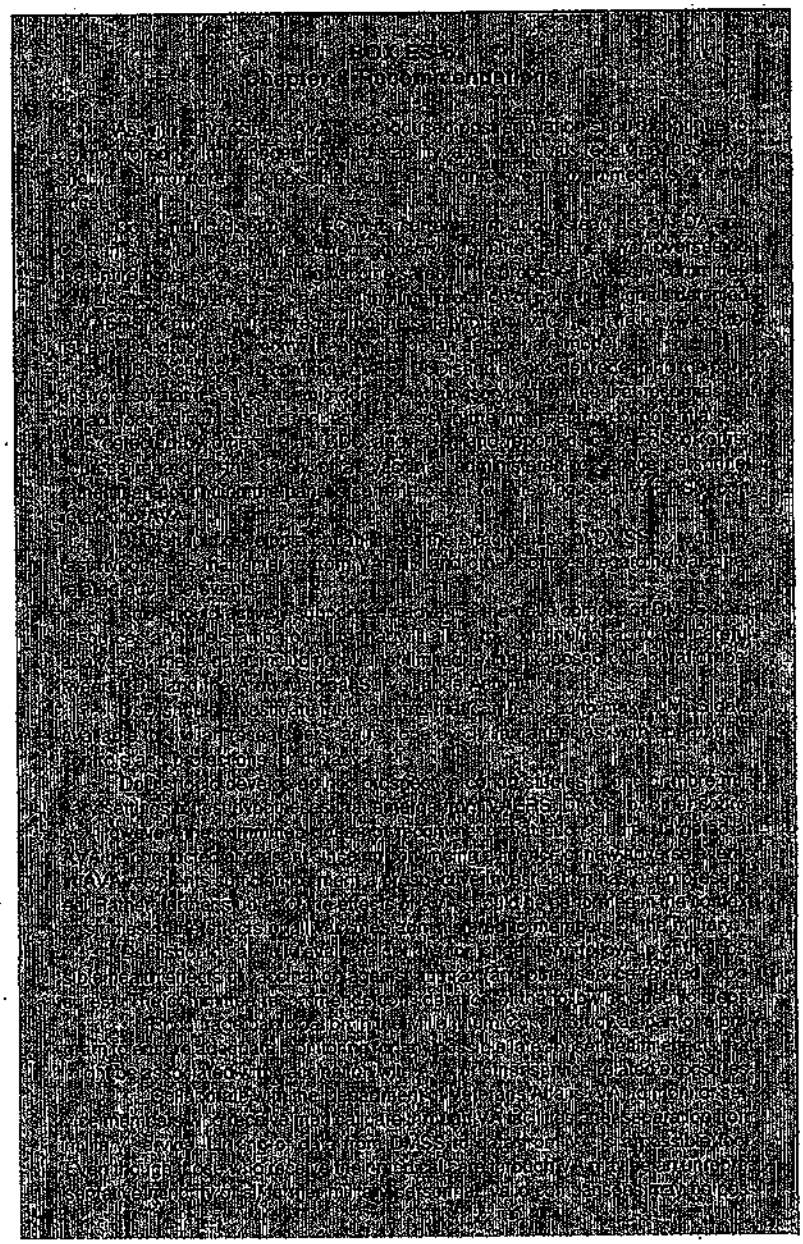


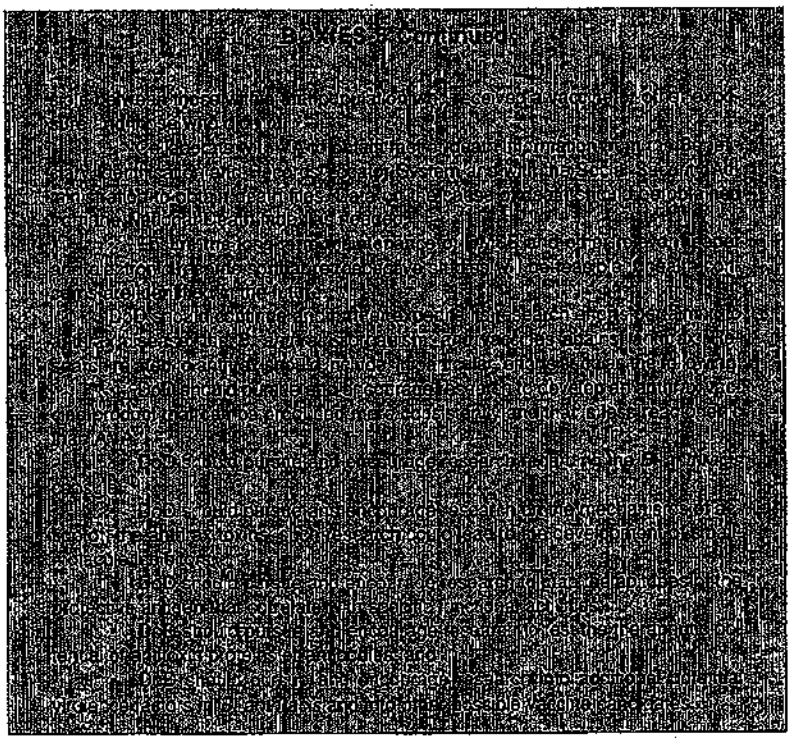



Recommendations


Box ES-1
Chapter 7 Findings







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Tab H

DEPARTMENT OF DEFENSE
ARMED FORCES EPIDEMIOLOGICAL BOARD
5109 LEESBURG PIKE
FALLS CHURCH VA 22041-3258

AFEB (15-1a) 2002-06 March 1, 2002

MEMORANDUM FOR The Assistant Secretary of Defense (Health Affairs)
The Surgeon General, Department of The Army
The Surgeon General, Department of The Navy
The Surgeon General, Department of The Air Force

SUBJECT: Vaccination Program to Protect Against Anthrax

1. During its Winter 2002 meeting, the Armed Forces Epidemiological Board (AFEB) was asked by the Assistant Secretary of Defense for Health Affairs to comment on the possible reintroduction of the Anthrax Vaccine Immunization Program (AVIP) to protect Armed Forces personnel, now that additional Food and Drug Administration (FDA) approved lots of the vaccine have become available. The Board has had a longstanding interest in force protection against biowarfare agents such as anthrax, and in recent years has issued a number of statements concerning use of the vaccine. These previous AFEB statements have supported the use of the vaccine when indicated to protect individuals being deployed to areas where analysis has determined that there is a credible risk of exposure to anthrax.

2. Since these statements were issued, a significant amount of new information has been collected based on the previous experience of the AVIP, which includes studies of short- and long-term safety and side effects associated with vaccination and both basic and applied research studies. The vaccine has also undergone intense scrutiny and review by several independent scientific bodies, including the Institute of Medicine of the National Academy of Sciences. The Board is cognizant of the issues associated with implementation of the total force anthrax immunization program including lack of consensus regarding the risk-benefit ratio, concerns about vaccine safety and efficacy, difficulties tracking vaccine receipt and delivery, and ultimately an inadequate supply of the vaccine that led to a slow-down of the AVIP.

3. The Board is impressed with the degree of diligence that has been given to addressing the concerns and sharing publicly the findings of research efforts, regardless of whether they were supportive of the program. We have seen no data that leads us to conclude that the vaccine is unsafe when administered according to the package insert. The range of reported side effects experienced by recipients of the anthrax vaccine are in line with previously published reports and compatible with similar vaccines. There are no convincing data demonstrating long-term adverse health impacts to recipients of anthrax vaccine, although additional studies are in progress. Data regarding efficacy, particularly against challenge with aerosolized anthrax spores, are less complete because they rely on

animal surrogates and very limited human studies, but there is no reason to believe that the vaccine does not offer valuable added protection to persons from any form of anthrax exposure.

4. The events of Autumn 2001 showed that the intentional use of anthrax can cause significant morbidity, mortality, and disruption of activities. This recent experience is likely to overcome some of the previous opposition to the program should a decision be reached to resume vaccination for personnel in settings where there is a significant risk of exposure to anthrax.

5. The Board recommends the following steps as a means of enhancing the anthrax immunization program:

- **DEVELOP ENHANCED PROGRAMS TO EDUCATE ALL ARMED FORCES PERSONNEL AND THE GENERAL PUBLIC ABOUT THE RISKS AND BENEFITS OF THE VACCINE AND THE REASONS FOR THE PROGRAM.**

- **MAINTAIN THE CURRENT VACCINE TRACKING SYSTEMS AND CONTINUE TO MONITOR FOR ACUTE AND LATENT VACCINE-RELATED MORBIDITY AMONG PERSONNEL WHO RECEIVE THIS VACCINE.**

- **DEVELOP A PROGRAM TO VALIDATE OR AUDIT THE CURRENT VACCINE TRACKING SYSTEMS SUCH THAT RECORDING ERRORS ARE MINIMIZED.**

- **ASSURE THAT MEASURES ARE IN PLACE SO THAT PERSONNEL IN WHOM THE VACCINE IS NOT INDICATED, ESPECIALLY WOMAN WHO ARE PREGNANT OR POTENTIALLY PREGNANT, DO NOT RECEIVE IT.**

- **ASSURE A STEADY AND UNINTERRUPTED SUPPLY OF LICENSED VACCINE TO MEET PROGRAM NEEDS AND MINIMIZE ANY FUTURE DISRUPTION OF PROGRAM ACTIVITIES AND CONTINUE EFFORTS TO DEVELOP ALTERNATE SOURCES FOR VACCINE PROCUREMENT.**

- **THE BOARD STRONGLY ENDORSES ONGOING EFFORTS TO DEVELOP NEW GENERATION ANTHRAX VACCINES THAT ARE POTENTIALLY LESS REACTOGENIC AND COULD REQUIRE LESS**

FREQUENT DOSING TO AFFORD PROTECTION. WE ALSO SUPPORT EFFORTS WITHIN DOD AND THE DEPARTMENT OF HEALTH AND HUMAN SERVICES TO EXPLORE ALTERNATIVE DOSING SCHEDULES AND ADMINISTRATION ROUTES TO MINIMIZE LOCALIZED REACTIONS WITH THE CURRENTLY AVAILABLE VACCINE. SUCH STUDIES WILL HOPEFULLY LEAD TO SIMPLER DOSING SCHEDULES THAT WILL MAKE THE VACCINE MORE ACCEPTABLE TO MILITARY AND OTHER AT RISK PERSONNEL WHILE REDUCING THE COMPLEX LOGISTICAL CHALLENGE OF ADMINISTERING THIS VACCINE TO SUCH A HIGHLY MOBILE POPULATION.

These activities should be part of the criteria used in making decisions about resumption of the anthrax immunization program.

6. The Board is pleased to continue to assist the DoD as it moves forward to develop policies regarding anthrax vaccination and other measures to protect Armed Forces personnel against the threat of biologic weapons of mass destruction.

FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD:

STEPHEN M. OSTROFF, M.D.
AFEB President

JAMES R. RIDDLE, DVM., MPH
Lt Col, USAF, BSC
AFEB Executive Secretary

CF:
Board Members and Consultants
USD (AT&L)
J4-MRD
USAMRMC
USAMRIID
SAAA-PPO
Library of Congress

(80)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

March 24, 2003,11:30 AM

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ellen P. Embrey, DASD, Force Health Protection and Readiness

SUBJECT: Pentagon Force Protection Agency (PFPA) Request for Priority in the Anthrax Vaccine Immunization Program

- The Pentagon Force Protection Agency requested that its Chemical, Biological, Radiological and Nuclear Directorate (CBRN) personnel receive priority in the Anthrax Vaccine Immunization Program (TAB C).

- The PFPA request included a three-tiered approach to vaccination. Tier 1 consists of approximately 128 employees of the Joint Operations Division (JOD), Hazard Response Division (HRD), and Lab Division (LD). Tiers 2 and 3 consist of administrative and support personnel that have limited potential risk for anthrax exposure inherent in their duties.

- The Joint Staff recommended that tier 1 personnel (128) be given priority for vaccination as an AVIP designated special mission unit (Priority 1). The Joint Staff further recommended that these personnel be provided with smallpox vaccination as an exception to policy. The Joint Staff recommended other tiers NOT be vaccinated at this time (TAB B).

- JOD personnel serve in capacities of liaisons to the response crisis center, building operation control center and incident command, and may have to travel through contaminated areas. The HRD may be tasked to collect concentrated air samples, collecting swabs from suspicious items, and respond to known biological events to ascertain areas of potential contamination. The LD provide hands-on manipulation of routine, suspicious and event-generated biological samples for agent identification.

RECOMMENDATION: ASD (HA) approve request by signing memorandum at TAB A.

COORDINATION: TAB D

Attachments:
As stated

Prepared by: Colonel David Adams, OASD (FHP&R), (b)(6), PCDOCS# 47128, 47168, 47345

THE ASSISTANT SECRETARY OF DEFENSE

1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

MEMORANDUM FOR DIRECTOR, JOINT STAFF
DIRECTOR, PENTAGON FORCE PROTECTION AGENCY

I approve your request to vaccinate certain personnel assigned to the Pentagon Force Protection Agency against anthrax and smallpox. Specifically, up to 128 personnel assigned duties in the Joint Operations Division, Hazard Response Division and Lab Division are approved to receive these vaccines. Execution of these vaccination programs are per previously published clinical and administrative guidelines and consistent with existing and approved Service implementation plans.

William Winkenwerder, Jr., MD

(b)(6),(b)(7)(E)

(b)(6),(b)(7)(E)

Coordination: Pentagon Force Protection Agency Request for Priority in the Anthrax Vaccine Immunization Program

DUSD (TSP&CP)	(b)(6)	Concur, 03/21/03
DATSD (CBD)		Concur, 03/21/03
DoD, OGC		_____
CoS, HA		_____
PDASD, HA		_____

Coordination: Pentagon Force Protection Agency Request for Priority in the Anthrax Vaccine Immunization Program

(b)(6)

DUSD (TSP&CP) ✓ 21 Mar 03

DATSD (CBD) _____

OGC _____

Coordination: Pentagon Force Protection Agency Request for Priority in the Anthrax Vaccine Immunization Program

DUSD (TSP&CP) _____

DATSD (CBD) (b)(6) concur 3/24/03

OGC _____

THE JOINT STAFF
WASHINGTON, DC

TAB B

Reply ZIP Code:
20318-0300

DJSM-0218-03
12 March 2003

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

Subject: Pentagon Force Protection Agency Request for Priority in the Anthrax Vaccine Immunization Program

1. The Pentagon Force Protection Agency (PFPA) has requested (Enclosure) that its Chemical, Biological, Radiological and Nuclear (CBRN) Directorate personnel receive priority in the Anthrax Vaccine Immunization Program (AVIP).

2. The PFPA request includes a three-tiered approach to vaccination. Tier 1 consists of approximately 128 employees of the Joint Operations Division, Hazard Response Division, and Lab Division. Tiers 2 and 3 consist of administrative and support personnel that have limited potential risk for anthrax exposure inherent in their duties.

3. Recommend that Tier 1 personnel be given priority for vaccination as an AVIP designated special mission unit (Priority 1). Also recommend that they be provided with smallpox vaccinations as an exception to policy. Approval of vaccinations for Tier 2 and 3 personnel is not recommended.

4. The Joint Staff point of contact for this action is (b)(6), (b)(6).

JAMES A. HAWKINS
Major General, USAF
Vice Director, Joint Staff

Enclosure

Copy to:
Director, Pentagon Force Protection Agency

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301

HEALTH AFFAIRS

To Dr. Whitecavender
for signature.
- Coordinator of
Request for Immunization for
Pentagon Force Protection Agency
operations personnel.

Joint staff recommendation
is at Tab B.

Draft.
3/19/03

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301

HEALTH AFFAIRS

I will include OJS request too.
Shared w/ them before original package. DM 3/27/03
JA

CAPT Adams —
Either include the JCS staff recommendation in the package or — preparatory — Coordinate w/ Dirs JCS Staff.
Tks
Dave T.

Trying to be consistent with Pres vaccine requests
D 3/27/03

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

March 17, 2003, 3:00 pm

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ellen P. Embrey, Deputy Assistant Secretary of Defense (Force Health Protection and Readiness)

SUBJECT: Pentagon Force Protection Agency (PFPA) Request for Priority in the Anthrax Vaccine Immunization Program

- The Pentagon Force Protection Agency requested that its Chemical, Biological, Radiological and Nuclear Directorate (CBRN) personnel receive priority in the Anthrax Vaccine Immunization Program. (TAB C).

- The PFPA request included a three-tiered approach to vaccination. Tier 1 consists of approximately 128 employees of the Joint Operations Division (JOD), Hazard Response Division (HRD), and Lab Division (LD). Tiers 2 and 3 consist of administrative and support personnel that have limited potential risk for anthrax exposure inherent in their duties.

- The Joint Staff recommended that tier 1 personnel (128) be given priority for vaccination as an AVIP designated special mission unit (Priority 1). The Joint Staff further recommended that these personnel be provided with smallpox vaccination as an exception to policy. The Joint Staff recommended other tiers NOT be vaccinated at this time. (TAB B).

- JOD personnel serve in capacities of liaisons to the response crisis center, building operation control center and incident command, and may have to travel through contaminated areas. The HRD may be tasked to collect concentrated air samples, collecting swabs from suspicious items, and respond to known biological events to ascertain areas of potential contamination. The LD provide hands-on manipulation of routine, suspicious and event-generated biological samples for agent identification.

RECOMMENDATION: ASD (HA) sign the coordination memorandum at TAB A.

COORDINATION: TAB D

Attachments:
As stated

Prepared by: Colonel David Adams, OASD (FHP&R), (b)(6)

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

MAR 2 0 2003

HEALTH AFFAIRS

MEMORANDUM FOR DEPUTY UNDER SECRETARY OF DEFENSE FOR
TECHNOLOGY SECURITY POLICY AND
COUNTERPROLIFERATION
DEPUTY ASSISTANT TO THE SECRETARY OF DEFENSE
FOR CHEMICAL BIOLOGICAL DEFENSE
GENERAL COUNSEL, DEPARTMENT OF DEFENSE

SUBJECT: Pentagon Force Protection Agency (PFPA) Request for Priority in the Anthrax Vaccine Immunization Program

The Pentagon Force Protection Agency requested that its Chemical, Biological, Radiological and Nuclear (CBRN) Directorate personnel receive priority in the Anthrax Vaccine Immunization Program.

Request your coordination on attached memorandum by COB, Mar 21, 2003.

William Winkenwerder, Jr., MD

Attachments:
As stated

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

March 24, 2003, 11:30 AM

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ellen P. Embrey, DASD, Force Health Protection and Readiness
(//s// 3-24-03 Colonel Rauch)

SUBJECT: Pentagon Force Protection Agency (PFPA) Request for Priority in the Anthrax Vaccine Immunization Program

- The Pentagon Force Protection Agency requested that its Chemical, Biological, Radiological and Nuclear Directorate (CBRN) personnel receive priority in the Anthrax Vaccine Immunization Program (TAB C).

- The PFPA request included a three-tiered approach to vaccination. Tier 1 consists of approximately 128 employees of the Joint Operations Division (JOD), Hazard Response Division (HRD), and Lab Division (LD). Tiers 2 and 3 consist of administrative and support personnel that have limited potential risk for anthrax exposure inherent in their duties.

- The Joint Staff recommended that tier 1 personnel (128) be given priority for vaccination as an AVIP designated special mission unit (Priority 1). The Joint Staff further recommended that these personnel be provided with smallpox vaccination as an exception to policy. The Joint Staff recommended other tiers NOT be vaccinated at this time (TAB B).

- JOD personnel serve in capacities of liaisons to the response crisis center, building operation control center and incident command, and may have to travel through contaminated areas. The HRD may be tasked to collect concentrated air samples, collecting swabs from suspicious items, and respond to known biological events to ascertain areas of potential contamination. The LD provides hands-on manipulation of routine, suspicious and event-generated biological samples for agent identification.

RECOMMENDATION: That the ASD (HA) sign memo at TAB A

COORDINATIONS: TAB D

ATTACHMENTS:
As stated

Prepared by: Col David Adams, OASD (HA)/FHP&R, (b)(6) PCDOCS# 47345, 47374

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

MAR 2 6 2003

MEMORANDUM FOR DIRECTOR, JOINT STAFF
DIRECTOR, PENTAGON FORCE PROTECTION AGENCY

I approve your request to vaccinate certain personnel assigned to the Pentagon Force Protection Agency against anthrax and smallpox. Specifically, up to 128 personnel assigned duties in the Joint Operations Division, Hazard Response Division and Lab Division are approved to receive these vaccines. Execution of these vaccination programs shall be consistent with previously published clinical and administrative guidelines, existing and approved Service implementation plans, and, in coordination with the WHS Office of General Counsel, applicable personnel procedures.

William Winkenwerder, Jr., MD

Pentagon Force Protection Agency Request for
Priority in the Anthrax Vaccine Immunization Program

COORDINATION

DUSD (TSP&CP)	(b)(6)	Concur, 03/21/03
DATSD (CBD)		Concur, 03/21/03
DoD, OGC		Concur as revised, 03/21/03
CoS (HA)		_____
PDASD (HA)		_____

Coordination: Pentagon Force Protection Agency Request for Priority in the Anthrax Vaccine Immunization Program

DUSD (TSP&CP) _____

DATSD (CBD) _____

OGC (b)(6) , as revised

3/21/03

****
*** TX REPORT ***
****

TRANSMISSION OK

TX/RX NO	1908
CONNECTION TEL	(b)(6)
SUBADDRESS	
CONNECTION ID	
ST. TIME	03/31 09:41
USAGE T	00'38
PGS. SENT	2
RESULT	OK

Deployments Health Support Directorate
5113 Leesburg Pike, Suite 901
Falls Church, Virginia 22041
(b)(6)
Fax: (b)(6)

FACSIMILE TRANSMITTAL SHEET 3/31/03 9:38:50 AM

TO: DIRECTOR, JOINT STAFF

FROM:
(b)(6)

ORGANIZATION:

FAX NUMBER:
(b)(6)

TOTAL NO. OF PAGES INCLUDING COVER: 2

PHONE NUMBER:
(b)(6)

SENDER'S PHONE NUMBER: (b)(6)

SUBJECT: REQUEST APPROVAL FOR VACCINATION

☐ URGENT ☐ FOR REVIEW ☐ PLEASE COMMENT ☐ PLEASE REPLY ☐ PLEASE RECYCLE

NOTES/COMMENTS:

PLEASE CONFIRM RECIEPT

****
*** TX REPORT ***
****

TRANSMISSION OK

TX/RX NO	1907	(b)(6)
CONNECTION TEL		
SUBADDRESS		
CONNECTION ID		
ST. TIME	03/31 09:43	
USAGE T	00'21	
PGS. SENT	2	
RESULT	OK	

Deployments Health Support Directorate
5113 Leesburg Pike, Suite 901
Falls Church, Virginia 22041
(b)(6)
Fax: (b)(6)

FACSIMILE TRANSMITTAL SHEET 3/31/03 9:37:58 AM

TO: DIRECTOR, PENTAGON FORCE PROTECTION AGENCY ***FROM:*** (b)(6)

ORGANIZATION:

FAX NUMBER: (b)(6)

TOTAL NO. OF PAGES INCLUDING COVER: 2

PHONE NUMBER: (b)(6)

SENDER'S PHONE NUMBER: (b)(6)

SUBJECT: REQUEST APPROVAL FOR VACCINATION

☐ URGENT ☐ FOR REVIEW ☐ PLEASE COMMENT ☐ PLEASE REPLY ☐ PLEASE RECYCLE

NOTES/COMMENTS:

PLEASE CONFIRM RECIEPT

Health Affairs

ROUTING AND TRANSMITTAL SHEET

TRICARE Management Activity

		Sign	Coord			Sign	Coord
3/26	ASD, HA BW	✓		Dir, TMA			
	PDASD, HA						
	DASD, C&PP			CMO			
	DASD, FHP&R			Dir, DHS			
	DASD, HB&FP			CFO			
	DASD, HPA			COO			
				Dir, TRICARE Operations/PEO			
	CIO, MHS			Dir, IMT&R			
3/21	OGC, DoD		✓	OGC, TMA			
	LA						
	CoS, HA		✓	Dir, A&M			
	Military Assistant			CoS, TMA			
	Dir, PI, HA			Dir, PI, TMA			
	Dir, P&S			Dir, Admin			
	Other (Specify)			Other (Specify)			

DMD (SKY) _____ Date: _____ **DMD (PNT)** A Date: 3/24/03

Date Received: 3/24/03 **Suspense Date:** _____

Subject: Pentagon Force Protection Agency (PFPA) Request for Priority in the Anthrax Vaccine Immunization Program

PCDOCS #: 47345, 47374 **OSD/P&R #:** _____

AO: COL Dave Adams **Office:** FHP&R **Phone #:** (b)(6)

NOTES: Orig. to Kotto for distro. A 3/24/03

TRICARE

TRICARE Management Activity

DOCUMENT MANAGEMENT DIVISION
ADMIN OFFICE

ACTION OFFICE DHS DATE 3-21-03 PCDOCS # 47374

ATTN:

The attached correspondence is returned for the following reason(s):

- ☑ **Distribution**
- ☐ **Coordination**
- ☐ **Revision**
- ☐ **Correct Signature Block**
- ☐ **Correct Envelope Size**
- ☐ **Correct Letterhead**
- ☐ **Provide Original/Supporting Documents**
- ☐ **Provide SD 391**
- ☑ **Retain for your Files**

Additional Comments:

Signed Response Scanned into PCDocs #47374

[Categorical Listing] [Numerical Listing]

(81)

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, D.C 20301-1200

HEALTH AFFAIRS

15 OCT 1999

MEMORANDUM FOR SURGEON GENERAL OF THE ARMY
SURGEON GENERAL OF THE NAVY
SURGEON GENERAL OF THE AIR FORCE

SUBJECT: : Policy for Reporting Adverse Events Associated with the Anthrax Vaccine

This memorandum establishes the Department of Defense (DoD) Anthrax Vaccine Immunization Program (AVIP) policy for reporting requirements on adverse events possibly related to the anthrax vaccine adsorbed (AVA).

Requirements for Generating a Vaccine Adverse Event Reporting System (VAERS) Form VAERS-1

For the purposes of reporting anthrax vaccine adverse events, a Form VAERS-1 (Attachment 1) must be completed and submitted using Service reporting procedures for those events resulting in a hospital admission or time lost from duty for greater than 24 hours or for those events suspected to have resulted from contamination of a vaccine lot. Further, health care providers are encouraged to report other adverse events that in the provider's professional judgment appear to be unexpected in nature or severity. In addition, the patient or a health care provider may submit a Form VAERS-1 directly to the Food and Drug Administration (FDA) for any possible adverse event. To obtain Form VAERS-1, contact the FDA at 1-800-822-7967 or visit the FDA web site www.fda.gov/cber/vaers/vaers.htm. Additional VAERS statistics are available from the National Technical Information Services (NTIS) at 1-800-553-6847.

A supplemental form (Attachment 2), specifically for use in connection with anthrax vaccine adverse event reporting, will be used by the Services' reportable disease project officers to verify completeness of and to classify each Form VAERS-1. The Services will submit a copy of the Form VAERS-1 and a supplemental form to the Army Medical Surveillance Activity (AMSA), U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM). The AMSA will serve as the central repository and will monitor all Form VAERS-1 submitted. The AMSA will coordinate the results of these reports directly with the DoD AVIP Agency, Office of the Army Surgeon General (OTSG), and the Services' Surgeons General.

Service Reporting Procedures

Army: All reports of anthrax vaccine adverse events are submitted by the chief of preventive medicine through the Army's automated reportable disease system to AMSA. These reports are consolidated daily into the Defense Medical Surveillance System (DMSS). In addition, a Form VAERS-1 is submitted to the chairman of the supporting medical treatment facility's (MTF) Pharmacy and Therapeutics Committee. Reports are submitted by the chairman, MTF Pharmacy and Therapeutics Committee, to the FDA's Vaccine Adverse Event Reporting System and copies of the Form VAERS-1 are provided to the reportable disease project officer at AMSA, DSN: 662-0471 or commercial: 202-782-0471.

Navy: All reports of anthrax vaccine adverse events are submitted by the preventive medicine

department or the senior medical officer through the Navy Disease Reporting System (NDRS) to the Navy Environmental Health Center (NEHC). These reports are consolidated monthly into the DMSS. In addition, a Form VAERS-1 is submitted by the health care provider to the FDA's Vaccine Adverse Event Reporting System and a copy to the reportable disease project officer at NEHC DSN: 864-5603 or commercial 757-462-5500. NEHC forwards a copy of the Form VAERS-1 and the supplemental form to AMSA.

Air Force: All reports of anthrax vaccine adverse events are submitted by the military health care provider to the Force Health Protection and Surveillance Branch, IERA/RSRH, 2513 Kennedy Circle, Brooks AFB, TX 78235-5123, DSN 240-3471 (commercial: 210-536-4371), FAX DSN 240-6841 (commercial: 210-536-6841). If the incident is life threatening or a death has occurred, the report will be made by telephone within 24 hours to IERA/RSRH. These reports are consolidated monthly into DMSS. A Form VAERS-1 is submitted to the FDA's Vaccine Adverse Event Reporting System and a copy to the Force Health Protection and Surveillance Branch. A copy of the Form VAERS-1 and supplemental form are sent to AMSA. Copies are also provided to the local Pharmacy and Therapeutic Committee, major command clinical points of contact, and the Air Force Medical Operations Agency (AFMOA).

Timeliness of Form VAERS-1 Reporting

A copy of Form VAERS-1 should be submitted to each Service's reportable disease project officer (AMSA, NEHC, IERA/RSRH) within seven days of the occurrence of the adverse event. The reportable disease project officer is responsible for verifying the completeness of the information on each report and completing an anthrax vaccine adverse event supplemental form (Attachment 2) prior to sending the report to AMSA. The reportable disease project officer has seven days from receipt to submit the copy of Form VAERS-1 and a completed supplemental form to AMSA so that consolidated DoD reporting can be provided to the AVIP Agency, OTSG.

Adverse events that are deemed life-threatening (such as anaphylaxis), result in death, or are suspected to be the result of contaminated lots must be reported telephonically to each Services' reportable disease project officer within 24 hours of the occurrence of the event. Each reportable disease project officer has an additional 24 hours to notify AMSA of the occurrence. Hard copy reports of the event should follow the initial telephonic report.

Classification of the Form VAERS-1

Each Service's reportable disease project officer is responsible for classifying Form VAERS-1 reports based on the information submitted and any other supplemental information necessary to complete a report and make a determination. The following classification system will be used to classify each report on the supplemental form:

Local Reactions:

Mild local reactions involve local erythema and induration of 1-2 cm diameter that may increase in size to 3-5 cm. Usual onset is within 24 hours and the reaction subsides by 48 hours. Reactions tend to increase in severity by the fifth injection, then decrease in severity with subsequent doses. Mild reactions may occur in up to 30 percent of recipients.

Moderate local reactions involve local erythema, induration, and pruritus involving an area more than 5 cm diameter. Subcutaneous nodules may occur at the injection site and persist for several weeks. Moderate reactions occur in up to 4 percent of recipients.

Large local reactions can consist of extensive edema from the site of injection extending past the elbow to possibly involving the forearm, in addition to local inflammatory reaction, focal rash, itching, and subcutaneous nodules. Large local reactions occur less frequently.

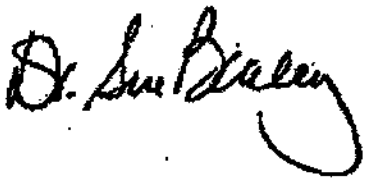
Systemic Reactions:

Systemic reactions usually are characterized by malaise, myalgia, arthralgia, and fatigue. The individual may have generalized rash and pruritis, dyspnea, and fever. Focal swelling and itching may appear at areas other than injection site. A simple headache may last a short duration and is treatable. Chills and fever are rare. Immediate reactions are suggestive of anaphylaxis. Systemic reactions rarely occur (< 0.2% injections).

Report to the Executive Agent of AVIP

AMSA is responsible for forwarding to the DoD AVIP Agency a weekly summary of the reported anthrax vaccine adverse events. This summary will compile the reports of anthrax vaccine adverse events submitted by each Service. The classification system maintains consistency of anthrax vaccine adverse event reporting within the DoD.

This policy provides guidance to support the Department's AVIP through improving vaccine adverse event reporting procedures of the Services' instruction "Immunization and Chemoprophylaxis" (AFJI 48-110, AR 40-62, BUMEDINST 6230.15, CG COMDTINST M6230.4E) of November 1, 1995. This policy is effective immediately and shall be included in all Service and Joint Staff plans and policies for the AVIP and for joint medical surveillance and force health protection



Dr. Sue Bailey

Attachments:
1. Form VAERS-1(FDA), Vaccine Adverse Event Reporting System
2. Anthrax Vaccine Adverse Event Supplemental Form

[Top]
Last update: 12/10/1999

(82)

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

ACTION MEMO

APR 3 2003

FOR: DEPUTY SECRETARY OF DEFENSE

FROM: William Winkenwerder, Jr., MD, ASD (Health Affairs)

SUBJECT: Department of Defense (DoD) Provision of Anthrax Vaccine for the Federal Bureau of Investigation (FBI)

- The Assistant Director, Counterterrorism Division of the FBI requested anthrax and smallpox vaccinations to support approximately 150 personnel.
- These personnel are integral to the FBI's mission responsible for federal law enforcement crisis response to weapons of mass destruction incidents involving U.S. interests.
- Originally requesting anthrax and smallpox, the FBI was successful in acquiring smallpox vaccine from the Department of Health and Human Services, the agreed upon source for this vaccine. However, DoD remains the primary source of anthrax vaccine for all interagency requests.
- An interagency agreement between DoD and the FBI is required and must be completed before the request can be supported.
- DoD Directive 6205.4, Immunization of Other Than U.S. Forces for Biological Weapons Defense, reserves to the Secretary of Defense the authority to approve the provision of vaccine to non-DoD entities.

RECOMMENDATION: That the DEPSECDEF sign the memorandum at TAB A.

COORDINATION: TAB B

Attachment:
As stated

Prepared by: Colonel David Adams, FHP&R, (b)(6) PCDOCS 47595, 47923

DEPUTY SECRETARY OF DEFENSE
1010 DEFENSE PENTAGON
WASHINGTON, DC 20301-1010

MEMORANDUM FOR DIRECTOR, FEDERAL BUREAU OF INVESTIGATIONS

SUBJECT: Request for Anthrax Vaccine

I approve your request for anthrax vaccination of approximately 150 FBI personnel who are assigned to national crisis response missions. This approval is subject to the terms of an interagency agreement addressing financial considerations and responsibility for any indemnification claim to the Department of Defense.

SUBJECT: Department of Defense (DoD) Provision of Anthrax Vaccine for Federal Bureau of Investigation (FBI)

COORDINATIONS

DASD (FHP&R)	(b)(6)	has seen 3/28/03
CoS (HA)		has seen 4/3/2003
PDASD (HA)		EW 4/3/2003
USD (P&R)	Dr. David S. C. Chu	David S. C. Chu 4 Apr 03

SUBJECT: Department of Defense (DoD) Provision of Anthrax Vaccine for Federal Bureau of Investigation (FBI)

COORDINATIONS

USD (P)	(b)(6)	Mar 21, 2003
USD (AT&L)		Mar 31, 2003
General Counsel		Mar 25, 2003
Director, Joint Staff		Mar 27, 2003

HA/TMA Document Profile

47595

Subject: DoD Provision of Anthrax Vaccine for the FB-CLOSED

Author: Col Adams
Date of Document: 3/28/2003
OSD # :
PR # :
Organization:
Department:
Assigned To: FHP&R
Prepared For: DEPSECCDEF
Suspense Date:
Coord Office(s):

Congressional Name:
Input By: DADAMS
Profiler's Directorate:
Response Signed By:
Dt Response Signed:
Doc Type: 102-03
Application: MS WORD
Previous Documents:
Related Documents: 47923

Notes:
4/8/03 CLOSED fwd to AO. VDK
On 4/7/03 rec'd comeback copy from P&R. Scanned and fwd to DMD/Sky5 for return to AO. (aas)
On 4/4/03 DMD/PNT rec'd signed pkg (from line) by PDASD(HA) and fwd to USD(P&R) for coord.(gjs)
On 4/3/03 fwd to ASD for sign. (aas)
On 4/2/03 rec'd coords and fwd pkg to HA CoS for review. (aas)
On 3/31/03 DMD/PNT fwd pkg to COL Adams for coord per CoS(HA).(gjs)

Beneficiary Info

Beneficiary Name:
Address 1:
Apartment #
Phone #
Email Address:
City:
State: **Zip**

History

Created: 3/28/2003 (b)(6)
Edited: 4/2/2003
Status: Available

Retention Schedule

Type:
Retention Days: 0

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☐ Secure Document
☐ Enable Content Searching

Health Affairs

ROUTING AND TRANSMITTAL SHEET

TRICARE Management Activity

	Sign	Coord		Sign	Coord
ASD, HA	✓		Dir, TMA		
PDASD, HA					
DASD, C&PP			CMO		
3/24/03 DASD, FHP&R		✓	Dir, DHS		
DASD, HB&FP			CFO		
DASD, HPA			COO		
			Dir, TRICARE Operations/PEO		
CIO, MHS			Dir, IMT&R		
OGC, DoD			OGC, TMA		
LA					
CoS, HA		✓	Dir, A&M		
Military Assistant			CoS, TMA		
Dir, PI, HA			Dir, PI, TMA		
Dir, P&S			Dir, Admin		
Other (Specify)			Other (Specify)		

DMD (SKY) _____ Date: _____ **DMD (PNT)** A Date: 3/28/03

Date Received: 3/28/03 **Suspense Date:** _____

Subject: DoD Provision of Anthrax Vaccine for the FBI

PCDOCS #: 47595, 47923 **OSD/P&R #:** _____

AO: Col Adams **Office:** FHP&R **Phone #:** (b)(6)

NOTES: Comeback copy to AO. A 4/7/03

TRICARE

TRICARE Management Activity

DOCUMENT MANAGEMENT DIVISION
ADMIN OFFICE

ACTION OFFICE FHP+R DATE 4/8/03 PCDOCS # 47595 47923

The attached correspondence is returned for the following reason(s):

- [x] Distribution
- [ ] Coordination
- [ ] Revision
- [ ] Correct Signature Block
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Closed

Additional Comments:

(83)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

ACTION MEMO

May 6, 2003 10:00 AM

FOR: ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

FROM: Ellen Embrey, DASD, (Force Health Protection and Readiness)

SUBJECT: Report to Congress on Separations as a Result of Refusing to Participate in the Anthrax Vaccine Immunization Program (AVIP).

- At TAB A is a draft Report to Congress on Separations as a Result of Refusing to Participate in the AVIP with a cover letter from Dr. Winkenwerder requesting coordination.
- Section 751 of the National Defense Authorization Act for Fiscal Year 2001 requires the Secretary of Defense to submit to Congress an annual written report on the number of members of the Armed Forces who have been separated as a result of refusing to participate in the AVIP.
- Coordinating offices will be given two weeks from the date of the coordinating letter to respond.

RECOMMENDATION: Sign letter at TAB A and forward for coordination.

COORDINATION: TAB B

Attachments:
As stated

Prepared by CDR Eugene de Lara, DHSD, (b)(6) PCDOCs# 17498

THE ASSISTANT SECRETARY OF DEFENSE

1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

MEMORANDUM FOR UNDER SECRETARY OF DEFENSE, PERSONNEL & READINESS
ASSISTANT SECRETARY OF DEFENSE, LEGISLATIVE AFFAIRS
GENERAL COUNSEL, DEPARTMENT OF DEFENSE
DIRECTOR, JOINT STAFF
DIRECTOR, MILITARY VACCINES OFFICE

SUBJECT: Report to Congress on Separations as a Result of Refusing to Participate in the Anthrax Vaccine Immunization Program (AVIP).

Section 751 of the National Defense Authorization Act for Fiscal Year 2001 requires the Secretary of Defense to submit to Congress an annual written report on the number of separations resulting from refusing to participate in the Anthrax Vaccine Immunization Program.

Request your coordination on the attached package no later than two weeks from the date of this memorandum.

My point of contact for this matter is CDR (b)(6) who may be reached at (b)(6) (b)(6). Coordinations may be faxed to (b)(6)

William Winkenwerder Jr., MD

Attachments:
As stated

DEPARTMENT OF DEFENSE
REPORT ON
SEPARATIONS THAT RESULT FROM A REFUSAL
TO PARTICIPATE IN THE ANTHRAX VACCINE
IMMUNIZATION PROGRAM
(January 1, 2002, through December 31, 2002)

Service	Separations	Component	Rank	Total
Army	0	Active	N/A	0
	0	Guard	N/A	0
	0	Reserve	N/A	0

Note: One reported separation occurred in the 2003 and will be reported in a subsequent report covering the 2003 timeframe.

Navy	0	Active	N/A	0
	0	Guard	N/A	0
	0	Reserve	N/A	0
Air Force	1	Active	E-4	1
	0	Guard	N/A	0
	0	Reserve	N/A	0
Marines	0	Active	N/A	0
	0	Guard	N/A	0
	0	Reserve	N/A	0

Services Total ----------→ 1

SUBJECT: Report to Congress on Separations as a Result of Refusing to Participate in the Anthrax Vaccine Immunization Program.

COORDINATION

	Concur	Non-concur	Comment
Under Secretary of Defense (P&R)	_____	_____	_____
Assistant Secretary of Defense (LA)	_____	_____	_____
DoD, (OGC)	_____	_____	_____
Director, Joint Staff	_____	_____	_____
Director, Military Vaccines Office	_____	_____	_____

(84)

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

MAY 28 2002

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (M&RA)
ASSISTANT SECRETARY OF THE NAVY (M&RA)
ASSISTANT SECRETARY OF THE AIR FORCE (M&RA)

SUBJECT: Support for an Accelerated Vaccine Planning Effort

REFERENCES: (a) DoD Directive 6205.3, "DoD Immunization Program for Biological Warfare Defense," November 26, 1993
(b) DoD Directive 5136.1, "Assistant Secretary of Defense for Health Affairs (ASD(HA))," May 27, 1994
(c) DoD Instruction 6205.2, "Immunization Requirements," October 9, 1986

Action is under way to increase interagency vaccine policy coordination to support development, production, distribution and use of vaccines for protection against biological warfare agents and other threats to public health. Within DoD, the Deputy Secretary of Defense is directing our support. In anticipation of the establishment of a more formal structure, we must immediately accelerate DoD planning and actions necessary to protect against such threats. Our initial efforts will focus on establishing a near-term contingency plan for responding to select disease outbreaks.

In order to accelerate our work, I am, under the authorities of references (a), (b), and (c), establishing a task force with the objective of submitting detailed contingency plans by October 1, 2002, with monthly interim reports to the USD(P&R). There are two immediate actions that require your assistance and support:

1. The Army, as Executive Agent for the DoD Immunization Program for Biological Warfare Defense, will have the lead for supporting the task force. This builds upon the excellent work of the Anthrax Vaccine Immunization Program (AVIP) Agency, which has already taken on broader vaccine program roles.

2. The task force will be established June 11, 2002 to develop detailed contingency plans for addressing select disease outbreaks. This task force will work full-time for four months to produce the required plans. I request that each Military Department identify appropriate military medical experts to participate on this task force. Please nominate one expert for each of the following: clinical medicine, preventive medicine, medical planning, and medical logistics by Monday, June 3, 2002. We will select one individual from each Service for participation in the task force.

This task force will work closely with representatives from the Department of Health and Human Services, and with other representatives from across the federal government. The Deputy Assistant Secretary of Defense (Force Health Protection and Readiness) will oversee the task force and report to me. I plan to work in close collaboration with the Assistant Secretary for Health, Department of Health and Human Services who has expressed a strong interest to establish joint collaboration now. The Under Secretary of Defense (Personnel & Readiness) has asked for an initial report within 4 weeks.

A meeting will be held on June 11, 2002 with the task force to further outline the requirements and expectations. My POC is COL Terry Rauch, (b)(6)

William Winkenwerder, Jr., M.D.

cc:
USD(P&R)
USD(AT&L)
JCS (J-4)
Surgeons General
Director, Administration & Management

(b)(6) **CON, OASD(HA)/TMA**

From: (b)(6)
Sent: Friday, May 24, 2002 7:52 AM
To: (b)(6)
Cc:
Subject: RE: Smallpox Task Force

looks okay to me. lets do it

-----Original Message-----
From: (b)(6) CIV, OASD(HA)/TMA
Sent: Thursday, May 23, 2002 1:21 PM
To: (b)(6)
Cc:
Subject: Smallpox Task Force

<< File: Support for Accelerated Vaccine Planning.doc >>

(b)(6)

I have made the suggested changes from OTSG to this memo (except for the ones recommending we establish an expanded AVIP office in this memo).

Pls chop quickly (by 1500) and return to me with an "Ok to sign."

Thanks, (b)(6)

(b)(6), CON, OASD(HA)/TMA

From: (b)(6), OASD(HA)
Sent: Friday, May 24, 2002 8:05 AM
To: (b)(6), ASD(HA)/TMA
Subject: RE: Smallpox Task Force

(b)(6) Sorry, got behind the power curve yesterday. This looks fine to me and Ms Embrey has also reviewed.

-----Original Message-----
From: (b)(6), CIV, OASD(HA)/TMA
Sent: Thursday, May 23, 2002 3:25 PM
To: (b)(6), OASD(HA)
Subject: RE: Smallpox Task Force

(b)(6) -- Any update?

-----Original Message-----
From: (b)(6), CIV, OASD(HA)/TMA
Sent: Thursday, May 23, 2002 1:21 PM
To: (b)(6)
Cc:
Subject: Smallpox Task Force

<< File: Support for Accelerated Vaccine Planning.doc >>

(b)(6)

I have made the suggested changes from OTSG to this memo (except for the ones recommending we establish an expanded AVIP office in this memo).

Pls chop quickly (by 1500) and return to me with an "Ok to sign."

Thanks, (b)(6)

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301

HEALTH AFFAIRS

To Dr. Winkenwerder
for signature.

Ms. Embrey did it this
a Friday.
What a task master!

Fran T.
5/28/02

CMAT Control #
2001103-0000033

(85)

HEALTH AFFAIRS

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON. D.C.

OCT 15 1999

MEMORANDUM FOR SURGEON GENERAL OF THE ARMY
SURGEON GENERAL OF THE NAVY
SURGEON GENERAL OF THE AIR FORCE

SUBJECT: Policy for Reporting Adverse Events Associated with the Anthrax Vaccine

This memorandum establishes the Department of Defense (DoD) Anthrax Vaccine Immunization Program (AVIP) policy for reporting requirements on adverse events possibly related to the anthrax vaccine adsorbed (AVA).

Requirements for Generating a Vaccine Adverse Event Reporting System (VAERS) Form VAERS-1

For the purposes of reporting anthrax vaccine adverse events, a Form VAERS-1 Attachment 1) must be completed and submitted using Service reporting procedures for ose events resulting in a hospital admission or time lost from duty for greater than 24 hours or for those events suspected to have resulted from contamination of a vaccine lot. Further, health care providers are encouraged to report other adverse events that in the provider's professional judgment appear to be unexpected in nature or severity. In addition, the patient or a health care provider may submit a Form VAERS-1 directly to the Food and Drug Administration (FDA) for any possible adverse event. To obtain Form VAERS-1, contact the FDA at I-800-822-7967 or visit the FDA web site **www.fda.gov/cber/vaers/vaers.htm**. Additional VAERS statistics are available from the National Technical Information Services (NTIS) at I-800-553-6847.

A supplemental form (Attachment 2), specifically for use in connection with anthrax vaccine adverse event reporting, will be used by the Services' reportable disease project officers to verify completeness of and to classify each Form VAERS-1. The Services will submit a copy of the Form VAERS-1 and a supplemental form to the Army Medical Surveillance Activity (AMSA), US. Army Center for Health Promotion and Preventive Medicine (USACHPPM). The AMSA will serve as the central repository and monitor all Form VAERS-1 submitted. The AMSA will coordinate the results of these reports directly with the DoD AVIP Agency, Office of the Army Surgeon General (OTSG) and the Services' Surgeon General.

Services Reporting Procedures

Army All reports of anthrax vaccine adverse events are submitted by the chief of preventive medicine through the Army's automated reportable disease system to AMSA. These reports are consolidated daily into the Defense Medical Surveillance System (DMSS). In addition, a Form VAERS-1 is submitted to the chairman of the supporting medical treatment facility's (MTF) Pharmacy and Therapeutics Committee. Reports are submitted by the chairman, MTF Pharmacy and Therapeutics Committee, to the FDA's Vaccine Adverse Event Reporting System and copies of the Form VAERS-1 is provided to the reportable disease project officer at AMSA, DSN: 662-0471 or commercial: 202-782-0471.

Navy: All reports of anthrax vaccine adverse events are submitted by the preventive medicine department or the senior medical officer through the Navy Disease Reporting System (NDRS) to the Navy Environmental Health Center (NEHC). These reports are consolidated monthly into the DMSS. In addition, a Form VAERS-1 is submitted by the health care provider to the FDA's Vaccine Adverse Event Reporting System and a copy to the reportable disease project officer at NEHC DSN: 8645603 or commercial 757-462-5500. NEHC forwards a copy of the Form VAERS-1 and the supplemental form to AMSA.

Air Force : All reports of anthrax vaccine adverse reactions are submitted by the military health care provider to the Force Health Protection and Surveillance Branch, IERA/RSRH, 2513 Kennedy Circle, Brooks AFB, TX 782355123, DSN 240-3471 (commercial:210-536-4371), FAX DSN 240-6841 (commercial: 210-536-6841). If the incident is life threatening or a death has occurred, the report will be made by telephone within 24 hours to IERA/RSRH. These reports are consolidated monthly into DMSS. A Form VAERS-1 is submitted to the FDA's Vaccine Adverse Event Reporting System and a copy to the Force Health Protection and Surveillance Branch. A copy of the Form VAERS-1 and supplemental form are sent to AMSA. Copies are also provided to the local Pharmacy and Therapeutic Committee, major command clinical points of contact and the Air Force Medical Operations Agency (AFMOA).

Timeliness of Form VAERS-1 Reporting

A copy of Form VAERS-1 should be submitted to each Services' reportable disease project officer (AMSA, NEHC, IERA/RSRH) within seven days of the occurrence of the adverse event. The reportable disease project officer is responsible for verifying the completeness of the information on each report and completing an anthrax vaccine adverse event supplemental form (Attachment 2) prior to sending the report to AMSA. The reportable disease project officer has seven days from receipt to submit the copy of Form VAERS-1 and a completed supplemental form to AMSA so that consolidated DoD reporting can be provided to the AVIP Agency, OTSG.

Adverse events that are deemed life-threatening (such as anaphylaxis), result in death, or are suspected to be the result of contaminated lots must be reported telephonically to each Services' reportable disease project officer within 24 hours of the occurrence of the event. Each reportable disease project officer has an additional 24 hours to notify AMSA of the occurrence. Hard copy reports of the event should follow the initial telephonic report.

Classification of the Form VAERS-1

Each Services' reportable disease project officer is responsible for classifying Form VAERS-1 reports based on the information submitted and any other supplemental information necessary to complete a report and make a determination. The following classification system will be used to classify each report on the supplemental form:

Local Reactions:

Mild local reactions involve local erythema and induration of 1-2 cm in diameter that may increase in size to 3-5 cm. Usual onset is within 24 hours and the reaction subsides by 48 hours. Reactions tend to increase in severity by the fifth injection, then decrease in severity with subsequent doses. Mild reactions may occur in up to 30 percent of recipients.

Moderate local reactions involve local erythema, induration, and pruritus involving an area more than 5 cm diameter. Subcutaneous nodules may occur at the injection site and persist for several weeks. Moderate reactions occur in up to 4 percent of recipients.

Large local reactions can consist of extensive edema from the site of injection extending past the elbow to possibly involving the forearm, in addition to local inflammatory reaction, focal rash, itching, and subcutaneous nodules. Large local reactions occur less frequently.

Systemic Reactions:

Systemic reactions usually are characterized by malaise, myalgia, arthralgia, and fatigue. The individual may have generalized rash and pruritis, dyspnea, and fever. Focal swelling and itching may appear at areas other than injection site. A simple headache may last a short duration and is treatable. Chills and fever are rare. Immediate reactions are suggestive of anaphylaxis. Systemic reactions rarely occur (greater than 0.2% injections).

Report to the Executive Agent of AVIP

AMSA is responsible for forwarding to the DoD AVIP Agency a weekly summary of the reported anthrax vaccine adverse events. This summary will compile the reports of anthrax vaccine adverse events submitted by each Service. The classification system maintains consistency of anthrax vaccine adverse event reporting within the DoD.

This policy provides guidance to support the Departments AVIP through improving vaccine adverse event reporting procedures of the Services' instruction "Immunization and Chemoprophylaxis" (AFJI48-110; AR 40-562; BUMEDINST 6230.15; CG COMDTINST M6230.4E) of November 1, 1995. This policy is effective immediately and shall be included in all Service and Joint Staff plans and policies for the AVIP and for joint medical surveillance and force health protection.

Dr. Sue Bailey

VACCINE ADVERSE EVENT REPORTING SYSTEM

VAERS

24 Hour Toll Free Information 1-800-822-7967
P.O. Box 1100, Rockville, MD 20849-1100
PATIENT IDENTITY KEPT CONFIDENTIAL

For CDC/FDA Use Only
VAERS Number _____
Date Received _____

Patient Name:	Vaccine administered by (Name):	Form completed by (Name):
Last First M.I. Address City State Zip Telephone no. (___)	Responsible Physician Facility Name/Address City State Zip Telephone no. (___)	Relation to Patient ☐ Vaccine Provider ☐ Patient/Parent ☐ Manufacturer ☐ Other Address *(if different from patient or provider)* City State Zip Telephone no. (___)

1. State	2. County where administered	3. Date of birth (mm dd yy)	4. Patient age	5. Sex ☐M ☐F	6. Date form completed (mm dd yy)

7. Describe adverse events(s) (symptoms, signs, time course) and treatment, if any

8. Check all appropriate:
- ☐ Patient died (date mm dd yy)
- ☐ Life threatening illness
- ☐ Required emergency room/doctor visit
- ☐ Required hospitalization (_____days)
- ☐ Resulted in prolongation of hospitalization
- ☐ Resulted in permanent disability
- ☐ None of the above

9. Patient recovered ☐YES ☐NO ☐UNKNOWN

10. Date of vaccination (mm dd yy) Time _____ AM PM

11. Adverse event onset (mm dd yy) Time _____ AM PM

12. Relevant diagnostic tests/laboratory data

13. Enter all vaccines given on date listed in no. 10

	Vaccine (type)	Manufacturer	Lot number	Route/Site	No. Previous Doses
a.					
b.					
c.					
d.					

14. Any other vaccinations within 4 weeks prior to the date listed in no. 10

	Vaccine (type)	Manufacturer	Lot number	Route/Site	No. Previous doses	Date given
a.						
b.						

15. Vaccinated at:
☐ Private doctor's office/hospital ☐ Military clinic/hospital
☐ Public health clinic/hospital ☐ Other/unknown

16. Vaccine purchased with:
☐ Private funds ☐ Military funds
☐ Public funds ☐ Other/unknown

17. Other medications

18. Illness at time of vaccination (specify)

19. Pre-existing physician-diagnosed allergies, birth defects, medial conditions(specify)

20. Have you reported this adverse event previously? ☐ No ☐ To health department ☐ To doctor ☐ To manufacturer

Only for children 5 and under

22. *Birth weight* _____ lb. _____ oz.

23. *No. of brother and sisters*

21. Adverse event following prior vaccination (check all applicable, specify)

	Adverse Event	Onset Age	Type Vaccine	Dose no. in series
☐ In patient				
☐ In brother or sister				

Only for reports submitted by manufacturer/immunization project

24. *Mfr./imm. proj. report no.*

25. *Date received by mfr./imm.proj.*

26. *15 day report?* ☐ Yes ☐ No

27. *Report type* ☐ Initial ☐ Follow-Up

Health care providers and manufacturers are required by law (42 USC 300aa-25) to report reactions to vaccines listed in the Table of Reportable Events Following Immunization. Reports for reactions to other vaccines are voluntary except when required as a condition of immunization grant awards.

Form VAERS-1(FDA)

"Fold in thirds, tape & mail-DO NOT STAPLE FORM"

NO POSTAGE NECESSARY IF MAILED IN THE UNITED STATES OR APO/FPO

BUSINESS REPLY MAIL

FIRST-CLASS MAIL PERMIT NO. 1695 ROCKVILLE, MD

POSTAGE WILL BE PAID BY ADDRESSEE

VAERS
P.O. Box 1100
Rockville MD 20649-1 100

DIRECTIONS FOR COMPLETING FORM

(Additional pages may be attached if more space is needed)

GENERAL

Use a separate form for each patient. Complete the form to the best of your abilities. Items 3, 4, 7, 6, 10, 11, and 13 are considered essential and should be completed whenever possible. Parents/Guardians may need to consult the facility where the vaccine was administered for some of the information (such as manufacturer, lot number or laboratory data.)

Refer to the Reportable Events Table (RET) for events mandated for reporting by law. Reporting for other serious events felt to be related but not on the RET is encouraged.

Health care providers other than the vaccine administrator (VA) treating a patient for a suspected adverse event should notify the VA and provide the information about the adverse event to allow the VA to complete the form to meet the VA's legal responsibility.

These data will be used to increase understanding of adverse events following vaccination and will become part of CDC Privacy Act System 09-20-0136, "Epidemiologic Studies and Surveillance of Disease Problems". Information identifying the person who received the vaccine orthat person's legal representativewill not be made available tothe public, but may be available to the vaccinee or legal representative.

Postage will be paid by addressee. Forms may be photocopied (must be front & back on same sheet).

SPECIFIC INSTRUCTIONS

Form Completed By: To be used by parents/guardians, vaccine manufacturers/distributors. vaccine administrators, and/or the person completing the form on behalf of the patient or the health professional who administered the vaccine.

Item 7: Describe the suspected adverse event. Such things as temperature, local and general signs and symptoms, time course. duration of symptoms diagnosis, treatment and recovery should be noted.

Item 9: Check "YES' if the patient's health condition is the same as it was prior to the vaccine, "NO" if the patient has not returned to the pre-vaccination state of health, or "UNKNOWN" if the patient's condition is not known.

Item 10: Give dates and times as specifically as you can remember. If you do not know the exact time, please

Item 11: indicate "AM" or "PM" when possible if this information is known. If more than one adverse event. give the onset date and time for the most serious event.

Item 12: Include "negative" or "normal" results of any relevant tests performed as well as abnormal findings.

Item 13: List ONLY those vaccines given on the day listed in Item 10.

Item 14: List any other vaccines that the patient received within 4 weeks prior to the date listed in Item 10.

Item 16: This section refers to how the person who gave the vaccine purchased it, not to the patient's insurance.

Item 17: List any prescription or non-prescription medications the patient was taking when the vaccine(s) was given.

Item 16: List any short term illnesses the patient had on the date the vaccine(s) was given (i.e., cold, flu, ear infection).

Item 19: List any pre-existing physician-diagnosed allergies, birth defects, medical conditions (including developmental and/or neurologic disorders) for the patient.

Item 21: List any suspected adverse events the patient, or the patient's brothers or sisters, may have had to previous vaccinations. If more than one brother or sister, or if the patient has reacted to more than one priorvaccine. use additional pages to explain completely. For the onset age of a patient, provide the age in months if less than two years old.

Item 26: This space is for manufacturers' use only.

SSN of recipient: _____ Date of adverse event: _____

Service: 0 USA 0 USN 0 USAF Date of vaccination: _____
0 USMC 0 Other

Location (facility) of adverse event: _____
_____

Meets criteria for required reporting: O Yes 0 No

Patient hospitalized: O Yes 0 No

Patient on quarters > 24hrs: O Yes 0 No

Classification of reaction:
0 Mild local reaction
0 Moderate local reaction
0 Large local reaction
0 Systemic reaction

Suspected lot contamination: 0 Yes 0 No If yes, lot number: _____

Form submitted by: 0 AMSA 0 NEIIC 0 IERA/RSRH

Date form submitted to AMSA: _____

Comments:

_____
_____
_____
_____
_____
_____
_____
_____

(86)

HEALTH AFFAIRS

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON. D.C.

SEP 11 1998

MEMORANDUM FOR SECRETARY OF THE ARMY
SECRETARY OF THE NAVY
SECRETARY OF THE AIR FORCE

SUBJECT: Policy for Deviation from Anthrax Vaccine Immunization Schedule

Full immunization with Anthrax Vaccine Adsorbed requires six doses administered over 18 months to complete the primary series. Doses are to be administered at 0, 2, and 4 weeks, 6 months, 12 months, and 18 months (where the first dose is given at "week 0"). Yearly boosters are administered thereafter to maintain immunity. This schedule is the only regimen shown to protect humans against anthrax and is the schedule approved by the Food and Drug Administration.

At its April 15, 1998 meeting, the Infectious Diseases Control Subcommittee of the Armed Forces Epidemiological Board (AFEB) reviewed the data available on this issue and made recommendations based on this data. This DoD policy is based upon the AFEB recommendations. In addition, the Advisory Committee on Immunization Practices (ACIP), U.S. Public Health Service (*MMWR* Vol. 43, No. RR-I, Jan. 28, 1994) does not generally recommend reinstitution of the entire series of a vaccine because of an interruption in the immunization schedule. For the anthrax vaccine! this approach is supported by unpublished data in humans that shows a robust antibody response to the anthrax vaccine one to two years after a partially completed primary series. However, because the consequences of inhalation anthrax are severe and the correlation between serum anthrax antibody titers and protection in humans is uncertain, the policy outlined in this memorandum reflects a more conservative approach to dealing with an interruption of the anthrax vaccine immunization schedule than the ACIP recommendation (Le., restart the primary immunization series with the first dose if only one dose in the primary series has been administered and more than two years have elapsed).

Based on the findings cited above, the Department of Defense policy shall be to adhere to the published immunization schedule. Deviation from this schedule should be the exception rather than the rule and be documented by bonafide reasons such as pregnancy, active infection, etc. Although the effect of specific deviations from this schedule on the efficacy of the vaccine is unknown, in general, the greater the deviation the less certain the protective effect in humans.

Doses of the vaccine should not be administered on a compressed or accelerated schedule (for example, shorter intervals between doses or more doses than required) For an individual who is late for or has missed a dose in the standard immunization schedule, the following procedures shall be followed:

- If only one dose in the primary series has been administered and more than two years have elapsed, restart the primary immunization series with the first dose.

- If one dose in the primary series has been administered but less than two years have elapsed or two or more doses have been administered, the

primary series does not need to be restarted. Resume the primary series with administration of the next dose in the series. Administer subsequent doses of vaccine at intervals based on the date the last dose was given, not when it was originally scheduled.

. If an annual booster has not been administered on time, administer the booster dose at the earliest possible date, adjusting the subsequent booster schedule accordingly. Once the primary series of six doses is complete, the primary series is never repeated.

This policy is effective immediately and should be included in Service and Joint Staff plans and policies for the Departments Anthrax Vaccine Immunization Program.

Dr. Sue Bailey

cc:
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force
Director of the Joint Staff

HA Policy 98-045

(87)

HEALTH AFFAIRS

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, D.C.

MAR 10 2000

MEMORANDUM FOR SECRETARY OF THE ARMY
SECRETARY OF THE NAVY
SECRETARY OF THE AIR FORCE

SUBJECT: Policy on Adherence to the Anthrax Vaccine Immunization Schedule and Medical Exemptions to Anthrax Vaccination

This memorandum is intended to provide policy guidance on the following medical issues: compliance with FDA-approved vaccine guidelines on the scheduling and administration of anthrax vaccine; the medical exemptions to anthrax vaccination; and the reporting of adverse events associated with the anthrax vaccine.

Dosage Schedule.

The Commissioner of the Food and Drug Administration (FDA) recently expressed concern over reports that some members of the Armed Forces in both Active and Reserve components are receiving their anthrax vaccine doses substantially later than called for by the schedule approved by the Food and Drug Administration (FDA), as described in the vaccine manufacturer's package insert. As stated clearly in all Anthrax Vaccine Immunization Program (AVIP) policies, full immunization requires six doses administered at 0, 2, and 4 weeks, and at 6, 12, and 18 months, to complete the primary series. This schedule is the only schedule approved by the FDA at this time.

All reasonable steps should be taken to ensure that shots are given on or as close as possible to the recommended schedule. As stated in my memorandum of September 11, 1998 (HA Policy No. **98-045**), doses of the vaccine should not be administered on a compressed or accelerated schedule (for example, shorter intervals between doses or more doses than required).

Continued senior leadership attention is necessary to assure proper implementation of the program. Administration of the vaccination schedule at the unit command level requires, at a minimum, notification to the recipient of the date, time, and location for the next scheduled shot, the availability of the next shot at the proper time, and implementation of a procedure to recall the patient if he or she does not appear as scheduled. Higher command levels should monitor and provide appropriate follow-up to ensure compliance. Accurate documentation in both individual medical records and Service-specific automated immunization tracking systems will greatly aid this effort. Attention should be directed to those units having a significant percentage of the second and third doses being administered more than seven days late, and the fourth, fifth, or sixth doses being given more than 30 days late.

To ensure uniformity of practice, in cases in which a dose is received beyond the scheduled date, administration of the next shot in the series should be based on the interval of time between doses, as indicated on the FDA-approved schedule. The approved dosing intervals are: two weeks between doses 1 and 2; two weeks between doses 2 and 3; five months between doses 3 and 4; six months between doses 4 and 5; and six months between doses 5 and 6. For example, if dose 3 is received six weeks

, after dose 2 (rather than the normally scheduled two weeks), dose 4 should be given five months after dose 3. There are no data to support reduced immune effectiveness of the vaccine if doses are given later than the scheduled time but doses given too early may result in reduce immune responses.

Medical Exemptions.

The granting of medical exemptions is a medical function that can only be performed by a privileged health care provider. Such individual exemptions should be applied only when medically warranted, with the overall health and welfare of the patient clearly in mind. The granting of medical exemptions should be based on potential benefits versus risks and should always take into consideration the immediate threat assessment.

Temporary medical exemptions are warranted in the five situations listed below.

1. Immunosuppressive Therapy. Individuals receiving systemic corticosteroid therapy, other immunosuppressive drug therapies, or radiation therapy, may be in a state of temporary immunodeficiency. Because of potential suppression of the immune response, these individuals should be deferred from receiving the anthrax vaccine until immune function returns, as determined by the attending physician.
2. Acute Illnesses. Serious acute diseases or acute injuries may be potentially aggravated by anthrax vaccination or can lead to more severe side effects with immunization. This includes any acute febrile illnesses. Vaccinations may resume, as determined by the attending physician.
3. Post-surgery. Post-surgical situations may warrant temporary vaccination deferment in order to ensure full recovery through convalescence. The timeframe when vaccinations may resume following a surgical procedure will be again be determined by the patient's attending physician.
4. Pregnancy. Anthrax vaccine should be deferred until after pregnancy. Because anthrax immunization is largely based on occupational risk, vaccination should resume with full assumption of duties following pregnancy, unless a longer post-partum interval is medically indicated, and be in accordance with current DoD and Service policies.
5. Other Conditions. In situations where a medical condition is in the process of being evaluated or treated, a temporary deferral of anthrax vaccination may be warranted. This would include significant vaccine-associated reactions that are being evaluated. The timeframe for deferral will be determined by the attending physician, and in accordance with current DoD and Service policies.

Situations warranting a permanent medical exemption include: severe reaction to a previous anthrax vaccination, where it has been determined that further vaccination will seriously endanger the health status of the patient; and Human Immunodeficiency Virus (HIV) infection and other chronic immunodeficiencies, where the immune response may be unpredictable and such individuals would not be deployed to a high threat area.

If an individual's case is complex or not readily definable, an allergist/immunologist, or other appropriate medical specialist, should be consulted before any exemption is granted. If a permanent deferment from further immunizations is indicated, appropriate DoD and Service policies will be pursued for the granting of such exemptions. Medical records will be accurately and appropriately annotated pertaining to any temporary or permanent exemptions. Health care providers will periodically review exemptions, to assure that they continue to be valid.

Adverse Events.

As provided in HA Policy No. 99-031, Policy for Repotting Adverse Events Associated with the Anthrax Vaccine, 15 October 1999, any serious adverse reaction temporally associated with receipt of a dose of anthrax vaccine should be immediately evaluated by a privileged health care provider and any specialists, if indicated. The clinical practice

guidelines available on the AVIP web site (www.anthrax.osd.mil). can also be consulted.

Vaccine Adverse Event Reporting System (VAERS) reports shall be filed using Service reporting procedures for those events resulting in hospital admission or lost duty time or work greater than 24 hours or from those events suspected to have resulted from contamination of a vaccine lot. Further, health care providers are encouraged to report other adverse events that in the provider's professional judgment appears to be unexpected in nature or severity. In other situations in which the patient wishes to submit a Form VAERS-1 report, the health care provider will assist the patient in completion of the reporting form. VAERS-1 form reports may be obtained by accessing the AVIP web site or by calling the FDA at I-800-822-7967.

These policies are effective immediately and should be communicated to appropriate commanders, health care providers, and others involved in the implementation of the AVIP.

Dr. Sue Bailey

cc:
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force
Director of the Joint Staff

Office of the Assistant Secretary of Defense

Washington DC 20301-1200

Health Affairs

Facsimile Cover Sheet

To: Bob Menig/Gen Vesser
Organization: OSAGWI
Phone: (b)(6)
Fax:

From: (b)(6) DVM, MPVM
Organization: OASD/HA(Clinical Services)
Program Director, Health Sciences
Phone: (b)(6) email (b)(6) @ha.osd.mil
Fax:

Date: December 17, 1999
Pages including this cover page:

General Vesser: Attached is a copy of the signed minutes from the last NCB Working Group, November 17, 1999. Dr. (b)(6)

DoD NCB Medical Defense Working Group
MINUTES OF MEETING

Date: November 17, 1999
Time: 11:00 p.m. - 12:30 p.m.

Subject: See Attached Agenda.

Attendees: MG Claypool, RADM Mayo, (RET LTG) Vesser, Mr. Casciotti, CAPT Maguire, COL Huycke, Dr. Clawson, Mr. Kuhn, LTC Thompson, LTC Pierson, LTC Ross, Dr. Cirone

MG Claypool made opening remarks. The purpose of this meeting was to discuss the agenda items, i.e., issues related to PB, INDs, and related field training. His first question was to reaffirm the need for the group. Is there purpose to continue on a regular basis? The consensus was positive. General Claypool noted that he will retire soon and this would be his last meeting. His replacement has not been identified. He will recommend that RADM Cowan or Mr. Richards chair this meeting until his replacement is announced.

The first item on the agenda was to discuss the status of the policy on PB. MG Claypool noted that this was somewhere in progress to the SECDEF for signature. If or when it will be signed is unknown. Since this has not been signed, members are not at liberty to disseminate the draft. Mr. Casciotti suggested that it might be appropriate to write another memo on INDs. If the SECDEF concurs and signs that memo, Dr. Bailey could reference it and send a memo on PB.

The next item on the agenda was a presentation about the status of the PB protocol by LTC Pierson. LTC Pierson was representing MG Parker. He provided briefing charts (attached). He discussed the history of the PB protocol. He stated that this recognizes that military operations occur across a spectrum of threats with voluntary to mandatory participation. The protocol provides a mechanism to inform service members of information required by Executive Order 13139 and changes to FDA regulations (21 CFR 50.23. It will be a challenge for implementation because of self-administration and logistical tracking requirements. The protocol has had a series of revisions in the past six months based on various institutional reviews. Training requirements of the Executive Order are included in the protocol to include: the basis for a Presidential determination that informed consent is not feasible; means for tracking use and side effects; benefits and risks of the investigational drug; and a statement that the drug is not approved. The outstanding issues to complete the protocol include: describing the record keeping system which must be capable of tracking from supplier to individual; plans for dissemination of information; recording use of drug in the medical record; daily census of individual use of PB; post-deployment screening; and collection of case report forms.

Discussion followed. Mr. Casciotti asked if it will be two protocols, one with and one without informed consent. The answer to the question is No. There is only one protocol which describes conditions under which PB administration would be under voluntary or mandatory conditions. He asked about the informed consent process in the field environment. LTC Pierson felt that the education process needed to be in advance –

perhaps at deployment. Personnel sign that they have been briefed. The Informed consent part comes when the command determines that PB should be distributed or taken. In some deployments, it may be know in advance that a threat exists and personnel may be given PB tabs at deployment after the educational brief. Personnel will sign that they have the tablets and the taking of the tablet is the consent. There needs to be a daily consus of who took what at the unit level and this forwarded for recordkeeping purposes. Personnel will be told that they cannot be ordered to take the PB unless the President approved a waiver of informed consent. This will be staffed and presented to the IRB and FDA. The FDA would have to sign off. Dr. Cirone asked if this plan would meet the requirements of the EO and Section 1107. Both LTC Pierson and Mr. Casciotti believed that it would or that it could be properly argued that it satisfies the requirements. It was noted that in time the PIC could be used for tracking. RADM Mayo noted that the record keeping could be just like the anthrax vaccine. The distribution of the PB tablet would be like the vaccine. It could be recorded and tracked in the same manner with the same adverse reaction data recorded. LTG (Ret) Vesser noted that the training aspect will be difficult in that some units will train and others have a full training schedule and this may not be at the top of their list of training priorities. Other discussion continued finally noting that the HSRRB will be given the protocol in January 2000. After review and comment, it will go to the Joint Staff for review and comment or approval by the CINCs. Then back to the HSRRB before going to the FDA. MG Claypool suggested that a proof of concept would be great if possible – e.g., use this in a training exercise to test the system.

The next item on the agenda was the briefing on the regulatory status of PB by Dr. Clawson. His briefing charts are attached. He noted the history of the process since 1994. He stated that the sponsor plan was presented to the FDA with a plan for two studies – one in guinea pigs to correlate RBC AChE, PB blood levels, tissue Ache inhibition, and extent of recovery of a physiologically relevant response in diaphragm muscle. This would include the study of recovery of guinea pig RBC AChE inhibition in vitro. Th other study would be exposure to soman of human RBCs removed from volunteers given PB. This plan was presented to the FDA. FDA requested: Add a lethality arm to the guinea pig study (concurred); add a second species (agreed to add the rat); consider the use of rhesus (unresolved); provide justification of cross-species similarities (submitted). The Animal Use Committee approved the guinea pig study protocol in August 1999. The pilot studies are underway and the estimated completion date is the 4th quarter FY00. The rat study protocol is in preparation with an estimated start date of 1st quarter FY00. The estimated completion date is 1st quarter FY01. The clinical study protocol is in preparation with an estimated start date of 2nd quarter FY00 and an estimated completion date of 3rd quarter FY00. The unresolved issue is the requirement for a primate study. Dr. Clawson noted that they are looking at a new manufacturer (ICN). The new formulation will require a bioequivalence study before approved by the FDA. Estimated start date is 4th quarter FY00 with a resubmit target date of 4th quarter FY01 for the NDA.

Discussion followed. USAMMDA expects to hear from the FDA before the new year about the need for the primate study. If required to do this, the study would be expected to start next summer with a completion date of one year from the start. A significant concern is the approval of the Animal Use Committee and the availability of rhesus monkeys.

The next topic was the DRAFT DoD Directive on use of PB. MG Claypool noted that the draft is in Dr. Bailey's office for signature of the coordination document. Once signed, it will be hand carried to staff offices with a suspense of January 15, 2000.

The last item on the agenda was a discussion of the training requirements of the Section 1107 and the EO 13139. Copies of the Section 1107, Section 13139, and the Interim Final Rule by the FDA on the waiver of informed consent were presented to the members. Also a draft statement for possible use to provide the Services information for manuals, training classes and pamphlets. Dr. Cirone will work with the Army SG staff to see what and how to prepare and distribute information required for training.

MG Claypool asked for closing remarks. Mr. Casciotti asked about the POC for the FDA that was discussed with Mr. Oliver – also about the status of the BioPort review. MG Claypool noted that Mr. Oliver will work with JPO and he wants a lot by lot report of anthrax vaccine status. MG Claypool indicated that we have enough anthrax vaccine to last until March. If the new lots are approved, we will have enough for August. The need to have the production facility approved and restart production is at a critical stage. He noted that there is also a concern about potency test results. General Claypool also noted that four members of congress wrote the FDA about concerns about BioPort and the anthrax program. FDA is concerned about the letter.

MG Claypool closed the meeting reiterating the next action. Summary: MG Claypool directed that there be continuing meetings of the NCB Medical Defense Working Group. The USAMRMC will continue to work the PB protocol and the PB NDA. Dr. Cirone will work the training issue. The DoD Directive on INDs will be staffed. If needed, a memo on IND use will be prepared for the SECDEF signature followed by a memo from Dr. Bailey on use of PB.

Robert G. Claypool, MG, MC, USA
Chairman, NCB Medical Defense Working Group

Attachments
As stated

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

CMAT Control #
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89

22 Dec 1999

Honorable John W. Warner
Chairman, Committee on Armed Services
United States Senate
Washington, DC 20510-6050

Dear Mr. Chairman:

I am pleased to forward this Report in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill. The Department of Defense (DoD) has funded a study directed to develop and validate an assay to test for the presence of squalene antibodies.

There is no evidence to support the allegations that squalene was used as a component in vaccines administered to Gulf War veterans. In its investigations of illnesses among Gulf War veterans, the Senate Special Investigations Unit (SIU) found no credible information indicating that vaccines used during the Gulf War contained squalene. The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant. The DoD funded study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and can be detected in human serum.

Our commitment to civilian and Federal researchers and to Gulf War veterans is to support and fund high quality research. This is best assured when all decisions on research funding are based on a process of rigorous, competitive, and independent peer review of all research proposals.

Sincerely,

Dr. Sue Bailey

cc:
Honorable Carl Levin
Ranking Democrat

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

22 DEC 1999

Honorable Tim Hutchinson
Chairman, Subcommittee on Personnel
Committee on Armed Services
United States Senate
Washington, DC 20510-6050

Dear Mr. Chairman:

I am pleased to forward this Report in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill. The Department of Defense (DoD) has funded a study directed to develop and validate an assay to test for the presence of squalene antibodies.

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Sincerely,

Dr. Sue Bailey

cc:
Honorable Max Cleland
Ranking Democrat

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

Honorable Floyd D. Spence
Chairman, Committee on Armed Services
House of Representatives
Washington, DC 20515-6035

22 DEC 1999

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Sincerely,

Dr. Sue Bailey

Dr. Sue Bailey

cc:
Honorable Ike Skelton
Ranking Democrat

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

22 DEC 1999

Honorable Steve Buyer
Chairman, Subcommittee on Military Personnel
Committee on Armed Services
House of Representatives
Washington, DC 20515-6035

Dear Mr. Chairman:

I am pleased to forward this Report in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill. The Department of Defense (DoD) has funded a study directed to develop and validate an assay to test for the presence of squalene antibodies.

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Sincerely,

Dr. Sue Bailey

Dr. Sue Bailey

cc:
Honorable Neil Abercrombie
Ranking Democrat

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

22 DEC 1999

Honorable Ted Stevens
Chairman, Committee on Appropriations
United States Senate
Washington, DC 20510-6025

Dear Mr. Chairman:

I am pleased to forward this Report in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill. The Department of Defense (DoD) has funded a study directed to develop and validate an assay to test for the presence of squalene antibodies.

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Sincerely,

Dr. Sue Bailey

Dr. Sue Bailey

cc:
Honorable Robert C. Byrd
Ranking Democrat

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

22 DEC 1999

Honorable Ted Stevens
Chairman, Subcommittee on Defense
Committee on Appropriations
United States Senate
Washington, DC 20510-6028

Dear Mr. Chairman:

I am pleased to forward this Report in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill. The Department of Defense (DoD) has funded a study directed to develop and validate an assay to test for the presence of squalene antibodies.

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Sincerely,

Dr. Sue Bailey

Dr. Sue Bailey

cc:
Honorable Daniel K. Inouye
Ranking Democrat

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

27 DEC 1999

Honorable C. W. Bill Young
Chairman, Committee on Appropriations
House of Representatives
Washington, DC 20515-6015

Dear Mr. Chairman:

I am pleased to forward this Report in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill. The Department of Defense (DoD) has funded a study directed to develop and validate an assay to test for the presence of squalene antibodies.

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Sincerely,

Dr. Sue Bailey

Dr. Sue Bailey

cc:
Honorable David R. Obey
Ranking Democrat

THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

22 SEP 1999

Honorable Jerry Lewis
Chairman, Subcommittee on Defense
Committee on Appropriations
House of Representatives
Washington, DC 20515-6018

Dear Mr. Chairman:

I am pleased to forward this Report in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill. The Department of Defense (DoD) has funded a study directed to develop and validate an assay to test for the presence of squalene antibodies.

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Sincerely,

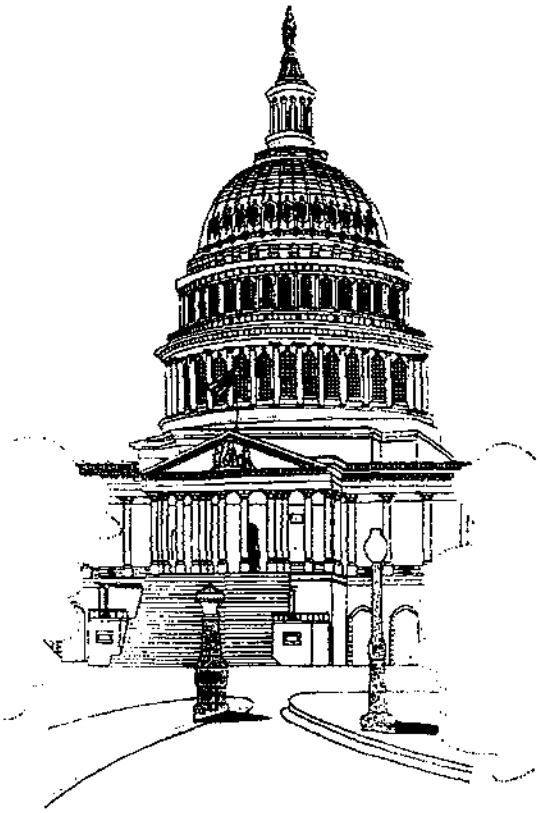
Dr. Sue Bailey

Dr. Sue Bailey

cc:
Honorable John P. Murtha
Ranking Democrat

REPORT TO CONGRESS

GULF WAR ILLNESS



Development and Validation of an Assay to Test for the Presence of Squalene Antibodies

Executive Summary

This Report has been prepared in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill:

> The Committee concurs with the findings of a recent GAO report on squalene antibodies and is concerned by the Department's reluctance to test for squalene antibodies since squalene is a potential contributing factor in illnesses of veterans of the Persian Gulf War. The Secretary of Defense is directed to develop and/or validate the assay to test for the presence of squalene antibodies. A report detailing the proposals to carry out this requirement shall be submitted to the Committee by January 1, 2000.

A May 1999 *Vanity Fair* article, "The Pentagon's Toxic Secret," alleged that the Department of Defense possibly used "an illicit and secret anthrax vaccine" on its own soldiers.[31] According to a Vanity Fair news release, "the licensed formula for...anthrax vaccine may have been altered, without formal FDA approval, to contain an experimental, and potentially dangerous, additive," squalene, that reportedly "causes incurable diseases in lab animals and may be the cause of some cases of Gulf War syndrome." The *Vanity Fair* article went on to suggest that the modified anthrax vaccine "may be part of the stockpile now being administered in the wake of the DoD's December 1997 decision to immunize 2.4 million people in the armed services against anthrax." A NewsWatch Associate editor presented an opposing review of the allegations entitled "Vanity Scare" in May 1999.[32]

On March 29, 1999, Congressman Jack Metcalf announced the release of a General Accounting Office (GAO) report, which he had requested, regarding squalene antibodies in veterans suffering from Gulf War illnesses. The GAO Report, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" (GAO/NSIAD-99-5) recommended that DoD "conduct research designed to replicate or dispute the unpublished independent research results that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans."[33]

In its investigations of illnesses among Gulf War veterans, the Senate Special Investigations Unit (SIU) found no credible information indicating that vaccines used during the Gulf War contained squalene.[38] In its report, the SIU stated that according to the Food and Drug Administration (FDA), squalene can be contained in a vaccine due to two different processes: 1) as an adjuvant, which is an agent to enhance the immune response; or 2) in minute quantities in vaccines manufactured using eggs, since eggs are rich in squalene and cholesterol. The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant.

To investigate the squalene hypothesis, a scientifically proven test for squalene antibodies is needed to assess whether Gulf War veterans have antibodies to squalene. In response to a DoD solicitation for research on illnesses among Gulf War veterans, a DoD investigator and nationally recognized expert on antibodies to cholesterol and other lipids submitted a research proposal to determine the feasibility of developing a test for antibodies to squalene.

The funded research project to determine whether antibodies to squalene exist has five main objectives:

1) Development and validation of an ELISA assay for antibodies to squalene.
2) Evaluation and potential development of other assays for antibodies to squalene.

3) Development of a positive control antibody to squalene.
4) Production of the positive control antibody to squalene for use in the assays.
5) Testing of normal human serum for antibodies to squalene by ELISA and other methods.

The DoD funded study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and can be detected in human serum.

Background

Squalene is a relatively simple, linear hydrocarbon. It is a naturally occurring molecule in the human metabolic process that synthesizes cholesterol.[1] Squalene is present in human sebum and cell wall structures. Squalene is also a component of shark liver oil, some vegetable oils, and plant and animal cell membranes.[2] It is licensed by the FDA as a dietary supplement in the United States and is listed in the *Physicians' Desk Reference*. Squalene is used commercially in the cosmetic industry and in sunscreen products.[3]

Epidemiological studies of breast and pancreatic cancer in several Mediterranean populations have demonstrated that increased dietary intake of olive oil is associated with a small decreased risk or no increased risk of cancer, despite a higher proportion of overall lipid intake. Experimental animal model studies of high dietary fat and cancer also indicate that olive oil has either no effect or a protective effect on the prevention of a variety of chemically induced tumors. As a working hypothesis, it is proposed that the high squalene content of olive oil, as compared to other human foods, is a major factor in the cancer risk-reducing effect of olive oil. Experiments in vitro and in animal models suggest a tumor-inhibiting role for squalene.[4] In addition, studies using squalene in combination with low-dose pravastatin have demonstrated combination therapy significantly reduces total cholesterol and LDL cholesterol and increases HDL cholesterol to a greater extent than either drug alone.[5]

Squalene is one of several components of adjuvant formulations in a variety of vaccines.[6] One common formulation is MF59. MF59 is a safe, practical, and potent adjuvant for use with human vaccines.[7] Toxicology studies in animal models and Phase I-III studies in humans have demonstrated the safety of MF59 with HSV, HIV, and influenza vaccines.[7-17] Hilhers, et al, concluded that reactogenicity and stability but not adjuvanticity of synthetic sulfolipo-polysaccharide/squalane/water formulations depended on the molecular weight of synthetic sulfolipo-polysaccharide and that synthetic sulfolipo-cyclodextrin/squalane/water is a promising non-mineral oil adjuvant as it combines strong adjuvanticity (i.e. better than the mineral oil-based adjuvant presently applied) with low reactogenicity and good stability.[18]

However, Lorentzen has reported that the cholesterol precursor squalene (C30H50), through nonspecific activation of the immune system, can precipitate arthritis in rats. Using arthritis-prone rat strains to search for disease-triggering factors among molecules which initially induce innate defense reactions rather than specific immune responses, Lorentzen reported on the potential for endogenous lipids to precipitate arthritis.[19] In addition, there is evidence that in some instances squalene has a negative effect on the nervous system.[20-21]

Pamela B. Asa, Ph.D., an unaffiliated molecular biologist from Memphis, Tennessee and Yan Cao, M.D. and Robert F. Garry, Ph.D., from Tulane University, New Orleans, Louisiana have theorized that illnesses afflicting veterans of the Gulf War are an atypical connective tissue disease (an autoimmune disease) resulting from use of the vaccine adjuvant, squalene.[22-23] These investigators have reportedly developed an immunoassay for detecting anti-squalene antibodies and used the assay to test blood serum samples from various patient and control groups.

To investigate this hypothesis, DoD has funded a scientific program which will answer several major questions. Initially, the research staff will determine if antibodies to squalene exist and if an assay can be developed to detect and quantify these antibodies. In addition, an animal model will be used to induce anti-squalene antibodies to use as positive controls to characterize anti-squalene antibodies in

humans. If a positive antibody response to squalene can be induced in mice, then normal human serum can be tested for possible antibodies to squalene. Next, the research program will focus on qualitative detection of squalene and development of a chemical assay. Finally, the research program will examine the biological implications of antibodies to squalene.

Discussion

Pamela B. Asa, who has worked in the area of rheumatology and silicone-gel breast implants, presented a theory in 1995 of "human adjuvant disease" and its possible link to Persian Gulf War (PGW) Veterans' Illnesses. She theorized that silicone adjuvant (an agent added to a vaccine to increase antigenic response) was responsible for PGW veterans developing "human adjuvant disease."[24] A scientific review prepared by an independent non-governmental medical expert on September 13, 1995 of Dr. Asa's "Report on Gulf War Syndrome" found the basic hypothesis and supporting evidence presented was based on a series of erroneous assumptions and unsupported conjectures.[25] A similar review by the Medical, Chemical and Biological Defense Research Program found the basic hypothesis and supporting evidence presented by Dr. Asa were flawed or inaccurate.[26] Available information also strongly argues against Dr. Asa's hypothesis:

> All vaccines used during the Gulf War have a long history of safety and all, except BotTox that was used under an Investigational New Drug (IND), were licensed by the FDA at the time of the Gulf War.
>
> Since the standard immunization series is given to individuals in basic and advanced training, only a relatively small number of additional vaccines were given during deployment to the Persian Gulf, and the previous use of these vaccines has not resulted in problems similar to those reported by GW veterans.
>
> All vaccine lots are individually licensed for safety and efficacy. The vaccines used, therefore, are unlikely to be contaminated or of low quality.
>
> The only adjuvant used in the vaccines given to Gulf War personnel was alum. Alum is an FDA-approved adjuvant with a long history of safety. It has been given to millions of people worldwide without significant problems. No experimental adjuvants were used by the military.
>
> There are no reports of alum causing human adjuvant disease or any other chronic disease.
>
> There are no reports of chronic inflammatory responses at the sites of immunization with vaccines containing alum as would be expected if human adjuvant disease were to occur.
>
> Several recent studies have failed to show any association between silicone-gel implants and increased incidence of connective tissue disease. There is little supporting evidence, other than anecdotal reports, that silicone-gel implants cause an increase in connective tissue diseases or human adjuvant disease.

Dr. Asa's current work focuses on the presence of antibodies to squalene in a cohort of 142 Gulf War-era veterans or military employees. She theorizes that "Gulf War Syndrome" manifests a spectrum of signs and symptoms similar to that of other atypical connective tissue diseases and that most "Gulf War Syndrome" patients have serum antibodies to squalene, an immunological adjuvant. The study protocol attributes the hypotheses to findings in one (1) patient from a NIH-sponsored trial using squalene as an adjuvant.[22] The findings of the current unpublished work apparently originate from samples collected under this protocol. It is unknown if informed consent was obtained from individuals submitting samples for testing or if an Institutional Review Board (IRB) reviewed and approved the research protocol. Review of the draft manuscript indicates the basic hypothesis and supporting evidence presented as flawed or inaccurate. The findings from the study must be interpreted with caution as flawed methodology including biased sample selection and potential cofounders weaken any potential association. The following information also strongly argues against the current hypothesis:

> If in fact antibodies to squalene are present in Gulf War veterans, the clinical significance of finding these antibodies in humans is unknown. Squalene is normally present in humans as part of the body's production of

cholesterol. In addition, it is found in human sebum (skin oils) and plant and animal cell membranes. Antibodies to cholesterol in humans are common.

There may be alternative explanations for the reported laboratory findings, including: detection of naturally occurring squalene; cross-reaction with compounds similar to squalene; elevated levels of squalene due to a known or unknown disease process causing human illnesses, or; laboratory error or contaminant.

If in fact anti-squalene antibodies are present in the blood of Gulf War-era veterans, this is not sufficient to establish an association of squalene or squalene antibodies with any illness(es) among Gulf War veterans.

The assay for anti-squalene antibodies, which independent researchers at Tulane University developed, has not been validated at other laboratories nor have their findings been subjected to minimal peer review through publication in the scientific literature.

The only adjuvant used in the vaccines given to Gulf War personnel was alum. Alum is an FDA-approved adjuvant with a long history of safety. It has been given to millions of people worldwide without significant problems. No experimental adjuvants were used by the military.

The anthrax vaccine given to service members during the Gulf War and subsequently did not and does not contain squalene.

The Army Surgeon General has verified that the anthrax vaccine was never produced at any alternate production facilities in the U.S. during the Gulf War, and anthrax vaccine production at the Michigan Biologic Products Institute (MBPI, now BioPort) never contained squalene. Stanford Research Institute, International has recently completed verification testing for squalene on 6 lots of anthrax vaccine and verified that no squalene was detectable in any of the vials.

There are no data demonstrating increased rates of autoantibodies in ill Gulf War veterans.

Unfortunately, we cannot be sure that the theorists actually detected antibodies to a synthetic squalene adjuvant in the veterans they tested. They reportedly used a variation of a previously described assay.[27] This technique was used to claim findings of the first evidence from a blinded study of the existence of a laboratory marker that correlates with the severity of local and systemic complications in silicone breast implant recipients. The assay in question detects antibodies, not to silicone, but to a synthetic polymer whose characteristics have not been fully described. In subsequent letters to the editor, many noted the methodological flaws in the study, argued that since the antibody is not against silicone, there was no reason to suppose the implants had anything to do with the symptoms or antipolymer antibody assay test results, and noted that the investigators had reported similar high seroactivity in fibromyalgia patients.[28] A Committee named by the Institute of Medicine (IOM) recently reported that a careful study of all the evidence indicates that women with silicone breast implants are no more likely to develop chronic disease than women without the implants. The IOM Committee did not address antipolymer antibodies; however, they stated that "The clinical significance of a recently described antipolymer antibody test is unclear, although the polymer in question is not silicone or silicon containing, and it is extremely unlikely that it measures an antisilicone antibody."[29]

Dr. Garry and Tulane University reportedly received a U.S. patent in 1997 for an assay that could detect antibodies to polymers, of which squalene is one. In a letter from Dr. Garry to DoD, Re: Anti-Squalene Antibodies, dated May 7, 1999, Dr. Garry informed DoD that Tulane University Medical Center had applied for a patent on the use of anti-squalene antibodies in assessing Gulf War Syndrome. Dr. Garry also informed DoD that Tulane was the sole owner of the intellectual property provided in the letter of May 7, and that DoD should share the data only with those who have a specific need to know. In this letter, Dr. Garry reviewed the specifics of the anti-squalene antibody assay, or ASA Assay, that measures the binding of serum immunoglobulins to squalene.

The Office of the Army Surgeon General (OTSG) requested an update in early May 1999 on investigations, tests, and projects to investigate allegations regarding squalene in the anthrax vaccine and plans for developing an assay for squalene antibodies.[30] In the update, the Army stated that all lots of the anthrax vaccine released by DoD would be tested and that current testing to date by Stanford Research Institute, International confirmed that no squalene was detectable in any of the vials. The FDA is doing additional testing. Dr. Garry provided the manuscript outlining the details of his proposed assay to OTSG for review. It was the opinion of COL Alving and Dr. Matyas that there were "dozens of important technical and theoretical flaws" in the assay-many described by COL Alving as "fatal flaws." Dr. Garry had informed COL Alving and Dr. Matyas that, "even in the absence of peer-reviewed scientific validation, the patent rights to the technology for measuring antibodies to squalene had been exclusively licensed by Tulane University for commercial development by a company called, Autoimmune Technologies, L.L.C." Dr. Garry was unaware of the scientific literature that exists on antibodies to cholesterol. When informed of the antibodies to cholesterol by COL Alving, Dr. Garry "agreed that the purported antibodies that he observed might well represent antibodies that react with cholesterol."

Excerpts of the GAO report entitled, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" stated that independent researchers had developed a test based on a Western blot assay and had detected antibodies to squalene in the blood of sick Gulf War veterans. If the description of the test described in the GAO report is accurate, there are some technical points that would seem to invalidate such a test:

> Squalene is a non-charged long chain hydrocarbon that would not be expected to migrate on a gel such as required in a Western blot assay.
>
> Because squalene lacks charge, it would not be expected to transfer to nitrocellulose as is done in a Western blot assay

On March 29, 1999, Congressman Jack Metcalf (Washington) announced the release of a GAO report, which he had requested, regarding squalene antibodies in veterans suffering from Gulf War illnesses. The GAO Report, "Gulf War Illnesses: Questions about the Presence of Squalene Antibodies in Veterans Can be Resolved" (GAO/NSIAD-99-5) recommended that DoD "conduct research designed to replicate or dispute the independent research results that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans."[33] The GAO did not comment on the ethical conduct of the research including a requirement for informed consent and IRB review of the protocol. The GAO did note that Chiron and Ribi ImmunoChem reported that their squalene adjuvant formulation had been tested on over 9,000 and 1,000 human subjects, respectively.

The clinical significance of finding antibodies to squalene is unknown. Squalene is normally present in humans as part of the body's production of cholesterol. It is found in human sebum (skin oils) and plant and animal cell membranes. The scientific work that has been done on squalene's role in human health and disease notes the positive effects of dietary squalene on cancer prevention and cholesterol regulation and the safety and efficacy of squalene as a vaccine adjuvant. There may be alternative explanations for the reported laboratory findings, including: detection of antibodies to cholesterol;[34-37] detection of antibodies to naturally occurring squalene; cross-reaction with compounds similar to squalene; elevated levels of squalene due to a known or unknown disease process causing human illnesses, or; laboratory error or contaminant.

The assay for anti-squalene antibodies developed by independent researchers at Tulane University has not been minimally validated through publication in the scientific literature. The investigators have

reportedly submitted a manuscript to a peer-reviewed medical journal; to date, however, this effort apparently has not been successful.

Since the Gulf War, squalene has been a component of vaccines undergoing testing by the Walter Reed Army Institute of Research (WRAIR). Volunteers received the vaccines in well-controlled studies that followed FDA regulations. Squalene is one of several components of the adjuvants found in each of two vaccine products undergoing testing by WRAIR. Pharmaceutical grade squalene is used to produce the oil emulsion used in these vaccine products. The exact compositions of the adjuvant in these vaccines are proprietary and belong to DoD Cooperative Research and Development Agreement (CRDA) partners. Development, evaluation, and FDA approval for the use of these adjuvant systems has been conducted by DoD CRDA partners and WRAIR. The two vaccines are investigational products for the prevention of malaria and human immunodeficiency virus (HIV) infection. Information on the study on the HIV vaccine has not yet been published and is considered proprietary information. Information on the study involving the malaria vaccine has been published in the scientific literature.[39]

Prior to its use in humans, the vaccines containing the emulsion underwent extensive FDA-mandated Good Laboratory Practices repeat dose toxicology studies involving rodents, rabbits, guinea pigs and nonhuman primates. The details of these studies (four volumes) were filed with the FDA as part of the IND application. The studies revealed anticipated inflammatory responses surrounding the site of injection. No gross changes were observed. No laboratory abnormalities were found.

Conclusion

Allegations of an ongoing conspiracy by the media and others is troubling. Squalene is not a foreign substance. It is normally present in the human body in large quantities because it is a precursor to the biosynthesis of cholesterol in the liver. The DoD funded study should provide adequate scientific evidence to resolve the issue of whether squalene antibodies exist and if they can be detected in human serum. Since squalene is being used as an adjuvant in some newer generation vaccines, this question becomes of interest not only to the military but also to the general public. Previously, these investigators were able to demonstrate antibodies to cholesterol. Squalene may not be immunogenic by itself, but under certain circumstances antibodies to the compound may arise. Although antibodies to cholesterol and possibly squalene occur naturally, this does not necessarily mean they have an adverse effect.

This research proposal was submitted in response to a competitive solicitation for proposals. The proposal was peer reviewed independent of the Department, by the American Institute of Biological Sciences, and received a high scientific merit score. Programmatic review was accomplished by the Department and the Research Working Group of the Persian Gulf Veterans Coordinating Board. Based on the results of this research, further studies can be pursued, if appropriate, to look at the existence of these antibodies in Gulf War veterans and their correlation to disease.

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The Military Immunization Information Source

Vaccines are important tools that help protect the health of the men and women who serve their nation in uniform. The disease threat may spread person-to-person in recruit training. It may be a disease acquired by consuming contaminated food or water or from the bite of an infected mosquito during deployments. The threat may be the hostile use of a biological warfare agent. Vaccines provide a safe and effective means of countering the threats to personal health and military readiness.

This site provides access to current immunization program information for the Department of Defense (DoD) and the Military Services. Since DoD immunization programs are built on the foundation of national standards of immunization practice, the site provides links to other governmental and non-governmental sites dedicated to vaccines, immunization practices, and vaccine safety.

What's New

> What's New
> Military Indications for Vaccines
> Department of Defense Immunization Information
> Joint Staff & Unified Commands Immunization Information
> Military Services Immunization Information
> Military Immunization Training
> Link to Department of Health & Human Services
> Other Sources of Immunization Information
> Care of Reserve Component Members with Immunization Adverse Reactions

ASD (Health Affairs) issued a policy for the use of **varicella** (chickenpox) vaccine. The memorandum directs use of the vaccine for military accessions and health care workers who are susceptible to infection with varicella-zoster virus. Serologic screening is the preferred method to establish susceptibility to infection. Children will be immunized according to **ACIP** recommendations. HA Policy 99-034, November 22, 1999.

ASD (Health Affairs) issued a policy for the use of **inactivated poliovirus vaccine.** The memorandum directed adoption of the all inactivated poliovirus vaccine **(IPV)** schedule for the immunization of children against poliomyelitis within the Military Health System and outlined the need to transition to IPV for immunizing recruits, officer accessions, and travelers. HA Policy 99-029, October 22, 1999.

ASD (Health Affairs) issued a policy for the use of **Lyme disease vaccine.** Lyme disease vaccine will be provided to beneficiaries of the Military Health System in accordance with the recommendations of the Advisory Committee on Immunization Practices (ACIP), Centers for Disease Control and Prevention (CDC). Lyme disease vaccine is not recommended as a routine vaccine for military service members, but the vaccine should be considered for occupational groups of military members and/or **DoD** civilian employees whose duties result in frequent or prolonged exposure to tick-infested habitats in areas of high or moderate risk for Lyme disease. HA Policy 99-030, October 28, 1999.

ASD (Health Affairs) issued a policy for **reporting adverse events associated with the anthrax vaccine.** A Vaccine Adverse Event Reporting System (VAERS) Form VAERS-1 must be completed and submitted using Service reporting procedures for those events resulting in a hospital admission or time lost from duty for greater than 24 hours or for those events suspected to have resulted from contamination of a vaccine lot. Health care providers are encouraged to report other adverse events that in the provider's professional judgment appear to be unexpected in nature or severity. In addition, the patient or a health care provider may submit a Form VAERS-1 directly to the Food and Drug Administration (FDA) for any possible adverse event. HA Policy 99-031, October 15, 1999.

Wyeth Lederle Vaccines voluntarily has withdrawn from the market its rotavirus vaccine RotaShield(The manufacturer has requested the immediate return of all doses of the vaccine. The company's press release can be accessed at the web address below. **www.ahp.com/releases/wa 101599. htm**

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Military Indications for Vaccines

Vaccines Typically Administered to U.S. Military Personnel, 1999 (U.S. Army, U.S. Navy, U.S. Marine Corps, U.S. Air Force, U.S. Coast Guard)

Timing	Vaccine	Routine Schedule for Basic Immunity
Recruits and officer accessions (Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 15)	Adenovirus 4 & 7 . ** Diphtheria Hepatitis A * Influenza Measles Meningococcal disease . Mumps * Poliovirus Rubella Tetanus Varicella . Yellow Fever .	Single dose Every 10 years Two doses Annual Single dose Single dose Single dose Single dose Single dose Every 10 years Two doses One dose
Routine during career (active duty & reserve component) (Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 14 & 18)	Diphtheria Influenza Tetanus	Every 10 years Annual Every 10 years
Alert forces and forces deploying or traveling to high risk areas . Vaccine administered if not previously immunized or if booster dose needed) (Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 17)	Anthrax Cholera . ** Hepatitis A Hepatitis B . Japanese encephalitis Meningococcal disease Plague *** Poliovirus Rabies * Typhoid Yellow fever	Six-dose series Two doses Two doses Three doses Three doses Single dose Three doses One dose Three doses One to two doses Single dose
Individualized according to occupational or personal needs	Haemophilus influenzae type b Hepatitis B Lyme disease Meningococcal disease Pneumococcal disease Rabies Varicella	Single dose Three doses Three doses Single dose Single dose Three doses Two doses

. Vaccination policy varies among Military Services.
. * Booster doses may be required at annual or other intervals to sustain immunity.
*** Vaccine seldom used and/or supply is limited.
Primary Source: Air Force Joint Instruction 48-I **10/United** States Army Regulation **40-562/Navy** Bureau of Medicine 8 Surgery Instruction 6230.1 **5/Coast** Guard Commandant Instruction **M6230.4E**. Immunizations & Chemoprophylaxis. Washington, DC, November 1, 1995.

Vaccines and Toxoids

(Note: All paragraph notations [i.e.: Paragraph **28**] reference the Joint Instruction on "Immunizations and Chemoorophylaxis", PDF format)

Adenovirus **Types 4 and 7 Vaccine**
Military Indication. In military recruit populations, for prevention of febrile respiratory diseases and disease outbreaks that is acquired through person-to-person transmission of these specific adenovirus types. The vaccine is no longer available.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 28

Anthrax Vaccine
Military Indication. For prevention of anthrax, primarily inhalation anthrax, after exposure to spores of the bacteria Bacillus ***anthracis*** as a biological warfare or bioterrorism agent. Inhalation anthrax is almost uniformly fatal once symptoms develop.

DoD Anthrax Vaccine Immunization Prooram

DoD Policy
Policy for Reporting Adverse Events Associated with the Anthrax Vaccine (HA Policy 99-031, October 15, 1999)
Policy for Deviation from Anthrax Vaccine Immunization Schedule (HA Policy 98-45, September 11, 1998)

CDC Recommendations
MMWR 1999;48:69-74, Bioterrorism Alleging Use of Anthrax and Interim Guidelines for Management -- United States, 1998

Cholera Vaccine
Military Indication. None at present. Cholera vaccine may be required to meet the international travel requirements of a few nations.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 29
ACIP Recommendations
MMWR 1988;37:617-18,623-24, Cholera Vaccine

***Haemophilus influenzae* B (Hib) Vaccine**
Military Indication. None at present. For prevention of invasive Hib infection in adults at increased risk of infection because of immunological or other host defense abnormalities per ACIP recommendations.

ACIP Recommendations
MMWR 1985;34:201, Polysaccharide Vaccine for Prevention of H. influenzae Type b

Hepatitis A Vaccine
Military Indication. For prevention of hepatitis A, an acute infection of the liver, that is acquired by consuming food or water contaminated with hepatitis A virus during deployment or travel to areas with poor food, water, and sewage sanitation. Hepatitis A is endemic worldwide.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 30

ACIP Recommendations
MMWR 1996;45(RR-15), Prevention of Hepatitis A Through Active or Passive Immunization

Hepatitis B Vaccine
Military Indication. For prevention of hepatitis B, a potentially chronic infection of the liver, that is acquired through percutaneous, sexual, and other permucosal exposure to blood and body fluids from persons infected with hepatitis B virus. Hepatitis B infections occur worldwide, and some persons maintain a chronic carrier state.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 31
ACIP Recommendations
MMWR 1995;44:574-5, Update: Recommendations to Prevent Hepatitis B Virus Transmission
MMWR 1991;40(RR-14), Hepatitis B Virus: A Comprehensive Strategy for Eliminating Transmission in the United States Through Universal Childhood Vaccination// Appendix A: Postexposure Prophylaxis for Hepatitis B

Influenza Vaccine
Military Indication. For prevention of influenza A and B, acute febrile respiratory viral infections, that can cause epidemics within military populations, especially under conditions of crowding, such as recruit training, aboard ship, extended air transport, or certain deployment settings. Influenza A has the potential for pandemic spread.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 32
ACIP Recommendations
MMWR 1999;48(RR-4), Prevention and Control of Influenza

Japanese Encephalitis Vaccine
Military Indication. For prevention of Japanese encephalitis, a mosquito-borne viral disease, during deployments and travel to endemic areas in Eastern Asia and the western Pacific Islands. Japanese encephalitis virus causes an acute infection of the brain, spinal cord, and meninges with high rates of complications, chronic disability, and death.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 33
ACIP Recommendations
MMWR 1993;42(RR-1), Inactivated Japanese Encephalitis Virus Vaccine

Lyme Disease Vaccine
Military Indication. No specific military indication.
Lyme disease vaccine should be considered in conjunction with other measures for the prevention of Lyme disease in persons who reside, work, or recreate in areas that have a high or moderate risk for ticks infected with Borrelia burgdorferi and who engage in activities that result in frequent or prolonged exposure to tick infested habitat.

DoD Policy
Policy for the Use of Lyme Disease Vaccine (HA Policy 99-030, October 28, 1999)

ACIP Recommendations
MMWR 1999;48(RR-7), Recommendations for Use of Lyme Disease Vaccine // Appendix Methods Used for Creating a National Lyme Disease Risk Map

Measles, Mumps, and Rubella **(MMR) Vaccine**
Military Indication. For prevention of measles, mumps, and rubella primarily by boosting immunity acquired from childhood vaccination. The three acute viral infections are spread by the respiratory route or person-to-person contact. In military recruit populations, measles can cause disease outbreaks. Rubella usually causes a mild infection, but infection during the first trimester of pregnancy puts the fetus at high risk of congenital rubella syndrome. Young adults may experience more severe complications from mumps infection. All three diseases occur worldwide primarily among children.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 34
ACIP Recommendations
MMWR 1998;47(RR-8). Measles, Mumps, and Rubella-Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome and Control of Mumps

Meningococcal Vaccine
Military Indication. For the prevention of meningitis and other systemic infection caused by the bacteria Neisseria meningitidis, serogroups A, C, W-l 35, and Y. No vaccine against Group B meningococci, another common pathogen, is currently licensed in the United States. Recruits and other military populations living in conditions of crowding are at increased risk for meningococcal infection; historically, outbreaks have occurred in recruit populations. Meningococcal vaccine may be indicated for deployment and travel to areas with highly endemic meningococcal disease.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 35
ACIP Recommendations
MMWR 1999;48(05): 104, Change in Recommendation for Meninococcal Vaccine for' Travelers
MMWR 1997;46(RR-05). Control and Prevention of Meninococcal Disease //Control and Prevention of Serogroup C Meninctococcal Disease: Evaluation and Management of Suspected Outbreaks

Plague Vaccine
Military Indication. None at present. A licensed vaccine is not available currently. Plague has been identified as a potential biological warfare agent.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 36
ACIP Recommendations
MMWR 1996;45(RR-14). Prevention of Plague

Pneumococcal Vaccine
Military Indication. None at present. For prevention of pneumococcal disease in adults at increased risk of systemic infection or severe disease per ACIP recommendations. Persons at increased risk include those with functional or anatomic asplenia, chronic cardiovascular disease, chronic pulmonary disease, chronic liver disease; or immunological or other host defense abnormalities.

ACIP Recommendations
MMWR 1997;46(RR-8). Prevention of Pneumococcal Disease

Poliomyelitis Vaccine
Military Indication. For prevention of poliomyelitis primarily by boosting immunity acquired from childhood vaccination. Polio is acquired through person-to-person transmission through the fecal-oral route. Persons deploying or traveling to areas with poor sanitation are at increased risk, although international immunization efforts have decreased polio incidence worldwide.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 37

DoD Policy
Policy for the Use of Inactivated Poliovirus Vaccine (HA Policy 99-029. October 22, 1999)

ACIP Recommendations
MMWR 1999;48:590. Revised Recommendations for Routine Poliomyelitis Vaccination
MMWR 1997;46(RR-3). Poliomyelitis Prevention in the United States

Rabies Vaccine
Military Indication. For prevention of rabies after the bite of an animal suspected to be infected with rabies virus. Vaccine is given in conjunction with wound care and the

administration of human rabies immune globulin (HRIG). For pre-exposure immunization of persons occupationally at risk of exposure to rabid animals (e.g., animal handlers and certain laboratory, wildlife management, and security personnel) and persons assigned long-term to regions with endemic rabies, especially in dogs and cats.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 38
ACIP Recommendations
MMWR 1999;48(RR-1), Human Rabies Prevention - United States, 1999

Smallpox Vaccine
Military Indication. None at present. In 1979, the World Health Organization Global certified the global eradication of naturally occurring smallpox. Smallpox has been identified as a potential biological warfare agent.

Joint Instruction on 'Immunizations and Chemoprophylaxis" Paragraph 39
ACIP Recommendations
MMWR 1991;40(RR-14), Vaccinia (Smallpox) Vaccine

Tetanus-Diphtheria **(Td) Toxoids**
Military Indication. For prevention of tetanus and diphtheria primarily by boosting immunity acquired from childhood vaccination. Tetanus is an acute illness caused by an exotoxin of Clostridium tetani, a bacteria that grows at the site of wounds contaminated with its spores. C. tetani spores are ubiquitous in the environment worldwide. Diphtheria is an acute disease caused by a cytotoxin of the bacteria Corynebacterium diphtheriae. Diphtheria occurs worldwide.

Joint instruction on 'Immunizations and Chemoprophylaxis" Paragraph 40
ACIP Recommendations
MMWR 1991;40(RR-10), Diphtheria, Tetanus, and Pertussis: Recommendations for Vaccine Use and Other Preventive Measures

Typhoid Vaccine
Military Indication. For prevention typhoid fever, a systemic bacterial disease, acquired by consuming food or water contaminated with Salmonella typhi during deployment or travel to typhoid endemic areas and other areas with poor sanitation.

Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 41
ACIP Recommendations
MMWR 1994;(RR14), Typhoid Immunization

Varicella Vaccine
Military Indication. For prevention of varicella (chickenpox) among susceptible military members, especially recruits and other trainees, living in military environments conducive to person-to-person spread of respiratory diseases (such as barracks and ships). Although varicella is a common childhood viral disease, adults experience a more severe illness and have higher rates of complications and death.

Joint Instruction on 'Immunizations and Chemoprophylaxis" Paragraph 42
DoD Policy for the Use of Varicella (Chickenpox) Vaccine (HA Policy 99-034, November 22, 1999)
ACIP Recommendations
MMWR 1999;48(RR-06), Prevention of Varicella Updated Recommendations
MMWR 1996;45(RR-11), Prevention of Varicella // Summary of Recommendations for Varicella Vaccination // Appendix

Yellow Fever Vaccine
Military Indication. For prevention of yellow fever, a mosquito-borne viral disease, and to meet international health requirements during deployment or travel to yellow fever endemic areas.

Joint Instruction on 'Immunizations and Chemoprophylaxis" Paragraph 43

ACIP Recommendations
MMWR 1990;39(RR-6), Yellow Fever Vaccine

General Recommendations and Other Vaccines

General Recommendations
Joint Instruction on "Immunizations and Chemoprophylaxis" Section B
ACIP Recommendations
MMWR 1994;43(RR-1), General Recommendations on Immunization
Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Adolescents
ACIP Recommendations
MMWR 1996;45(RR-13), Immunization of Adolescents Recommendations of the Advisory Committee on Immunization Practices, the American Academy of Pediatrics, the American Academy of Family Physicians, and the American Medical Association

Vaccine Side Effects and Adverse Reactions
Joint Instruction on "Immunizations and Chemoprophylaxis" Paragraph 12
ACIP Recommendations
MMWR 1996;45(RR-12), Vaccine Side Effects, Adverse Reactions, Contraindications, and Precautions Recommendations of the ACIP

Health Care Workers
ACIP Recommendations
MMWR 1997;46(RR-18), Immunization of Health-Care Workers: Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infection Control Practices Advisory Committee (HICPAC)

BCG Vaccine
ACIP Recommendations
MMWR 1996;45(RR-4), The Role of BCG Vaccine in the Prevention and Control of Tuberculosis in the United States A Joint Statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices

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- Joint Chiefs of Staff Memorandum, Deployment Health Surveillance and Readiness-The Joint Chiefs of Staff (JCS) provide direction to the operational commanders and forces charged with carrying out assigned missions worldwide. This memorandum (MCM-251-98, December 4, 1998) provides procedures for assessing health readiness and conducting health surveillance in support of JCS and unified commands deployments. Enclosure A provides general guidance on immunizations required for individual deployment health readiness.

- U.S. European Command-The Command Surgeon provides preventive medicine guidance, including immunizations, for U.S. military operations and exercises in the EUCOM area of responsibility, which includes 89 countries and territories extending from the North Cape of Norway, through the waters of the Baltic and Mediterranean seas, most of Europe, parts of the Middle East, to the Cape of Good Hope in South Africa.

- U.S. Central Command-The Command Surgeon provides preventive medicine guidance, including immunizations, for U.S. military operations in the CENTCOM area of responsibility, which includes 25 nations, ranging from Egypt in the West to Pakistan in the East, from Kazakhstan in the North to Kenya and the Horn of Africa in the South, and the waters of the Red Sea, Arabian Gulf, and the Western portions of the Indian Ocean.

- Other Unified Commands-The three other major geographic unified commands currently do not post on a webpage the requirements for immunizations and other preventive medicine measures for their areas of responsibility. The following links point to the unified command's home page.

U.S.Pacific Command
U.S. Atlantic Command
U.S. Southern Command

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- Care of Reserve Component Members with Immunization Adverse Reactions

- DoD Instruction 6205.2. "Immunization Requirements"-This instruction provides policies on immunizations for all members of the U.S. military, civilian employees of the Department of Defense, and eligible beneficiaries of the Military Health System. It requires programs to prevent illness from diseases that are preventable through immunization. The current instruction, dated October 1986, is being updated.

- DoD Directive 6205.3, "DoD Immunization Proaram for Biological Warfare Defense"-This 1993 directive establishes policy and provides guidance for immunization to protect U.S. personnel against biological warfare threats and for the development and acquisition of vaccines for biological warfare defense.

- DoD Anthrax Vaccine Immunization Proaram-Secretary of Defense William Cohen approved a plan to vaccinate the entire force with anthrax vaccine beginning in 1998 to counter the threat that anthrax will be used as a biological warfare agent against U.S. forces.

Assistant *Secretary of Defense for Health Affairs Immunization Policies and Announcements*

- Policy for the Use of Varicella (Chickenpox) Vaccine (HA Policy 99-034, November 22, 1999)
- Policy for the Use of Inactivated Poliovirus Vaccine (HA Policy 99-029, October 29 9 9 1
- Policy for the Use of Lyme Disease Vaccine (HA Policy 99-030, October 28, 1999)
- Policy for Reporting Adverse Events Associated with the Anthrax Vaccine (HA Policy 99-031, October 15, 1999)
- Policy for Deviation from Anthrax Vaccine Immunization Schedule (HA Policy 98-45, September 11, 1998)
- Policy on Use and Interchangeability of Licensed Adult Hepatitis A Vaccines (HA Policy 98-23, February 27, 1998)
- Policy for Use of Hepatitis A Virus (HAV) Vaccine and Immune Globulin (IG) (HA Policy 96-054, August 12, 1996)
  This policy was amended by Amendment to ASD(HA) Policy 96-054, "Policy for Use of Hepatitis A Virus (HAV) Vaccine and Immune Globulin" (HA Policy 97-047, May 5, 1997)
- Hepatitis B Immunization Policy for Department of Defense Medical and Dental Personnel (HA Policy 97-06, October 3, 1996)
- Recommendations Regarding the Use of the Newly Licensed Hepatitis A Vaccine in Military Personnel (HA Policy 95-004, April 19, 1995)

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Military Services Immunization Information

- Joint Instruction on "immunizations and Chemoprophylaxis"-This joint Air Force, Army, Navy, and Coast Guard publication (AFJI 48-110, AR 40-562, **BUMEDINST** 6230.15, CG **COMDTINST M6230.4E)** provides the requirements for the Armed Forces Immunizations Program, establishes principles, procedures, policies, and responsibilities for the immunizations program, and implements pertinent Department of Defense directives and international health regulations and requirements. While the publication applies primarily to the uniformed members of the four departments, it provides guidance on immunizations for selected Federal employees and family members eligible for care within the Military Health System.

- Army Immunization Information-The U.S. Army Center for Health Promotion and Preventive Medicine, Directorate of Clinical Preventive Medicine, creates policy and guidance on the control of diseases, including vaccine-preventable diseases, and injuries relevant to military populations and **DoD** beneficiaries.

- Naw and Marine Corps Immunization Information-The Navy Environmental Health Center maintains this **webpage** to provide the information regarding Department of Defense, Department of the Navy (Navy and Marine Corps), and national immunization policies and practice.

- Air Force Immunization Information-The Department of Public Health, U.S. Air Force School of Aerospace Medicine maintains this **webpage** to provide the information regarding Department of the Air Force immunization policies and practices and to provide links to other immunization resources.

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Military Immunization Tracking

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- Immunization Tracking in the Individual Health Record. The primary record keeping system for immunizations is Standard Form (SF) 601, Health Record-Immunization Record, which is part of the individual's permanent outpatient health record. The International Certificate of Vaccinations (Department of Health and Human Services Form PHS-731) supplements the SF-601. Section G of the instruction "Immunizations and Chemoprophylaxis" outlines record keeping requirements.

- Immunization Tracking in PHCA-The Preventive Health Care Application (PHCA) is a computerized health maintenance system, including an immunization tracking system, for the Military Health System. PHCA, which is currently being installed and tested at military medical facilities, will serve as a standard solution for health care providers to deliver and track clinical preventive services.

- Immunization Tracking in DEERS

- Army Immunization Tracking in MEDPROS-The Medical Protection System (MEDPROS) was designed to track the administration of vaccinations, particularly the anthrax vaccine. MEDPROS is a module with the Army's Medical Occupational Data System (MODS).

- Navy/Marine Corps Immunization Tracking in SAMS-Naval Medical Information Management Center (NMIMC) supports the Immunization Tracking System to capture immunization data using the SNAP-Automated Medical System (SAMS) software project.

- Air Force Immunization Tracking in ASIMS—The Aeromedical Information Management System (ASIMS) is a collection of user-developed software modules that help manage base-level Aeromedical Services programs, including the Military Immunization Tracking System (MITS).

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THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1200

20 July 195

MEMORANDUM FOR SECRETARY OF THE ARMY
SECRETARY OF THE NAVY
SECRETARY OF THE AIR FORCE

SUBJECT: Ensuring Reserve Component Have Full Access to Department of Defense (DoD) Military Treatment Facilities (MTF) for Treatment and Evaluation of Adverse Events from DoD Directed Immunizations

Title 10, United States Code for the Armed Forces directs that members of the Reserve components who incur or aggravate any injury, illness, or disease while performing active duty for less than 30 days, or inactive duty training are entitled to medical care appropriate for the treatment of the injury, illness or disease. Adverse reactions from DOD-directed immunizations are line of duty illnesses. Therefore, when a member of the Reserve component presents for treatment at an MTF, expressing a belief that the condition for which treatment is sought is related to receiving an immunization during a period of duty, the member must be examine and provided necessary medical care.

Once treatment has been rendered or the individual's emergent condition is stabilized, a Line of Duty and/or Notice of Eligibility will t determined as soon as possible. No treatment beyond that justified to. stabilize the condition or emergency is authorized until Service ...ction is validated. Reserve component members should seek medical attention with their personal healthcare providers for injuries, illness or disease unrelated to duty.

Healthcare providers must submit a Vaccine Adverse Event Reporting System (VAERS-1) form for vaccine reactions that result in a hospital admission, loss of duty for greater than 24 hours, or suspected to have resulted from the contamination of the vaccine. The DoD and Food and Drug Administration encourage health care providers and individuals to report to VAERS any clinically significant adverse event occurring after the administration of any vaccine licensed in the United States. Reports to VAERS may be made in writing or by calling 1-800-822-7967. Reporting instructions are available on the Internet at http://www.fda.gov/cber/vaers.htm.

Providing MTF access to members of the Reserve components who may have health problems resulting from DoD-directed immunizations is our responsibility and an important way to keep trust with this large portion of the Total Force.

Dr. Sue Bailey

cc:
JSD (P&R)
ASD (RA)
Vice Chief of Staff, Army
Director, Joint Chief of Staff
Commandant, USCG HQ

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CMAT Control #
2002217-0000024

Desert Storm Battle Registry
P.O. Box 77381
Washington, DC 20013
Tel: 540-477-2923
Fax: 540-477-2941

Dear Mike Kilpatrick

August 2nd 2002

What is being done to contact past Gulf War Anthrax Vaccine recipients for FDA / CBER to comply with FDA's "follow up of a investigational drug" requirement?

We would like the classified portions of the Anthrax data on the OSAGWI internal servers be declassified and released to our organization for review.

Sincerely
Kirt P. Love
Director, DSBR

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

Mr. Kirt Love
Desert Storm Battle Registry
P.O. Box 77381
Washington, D.C. 20013

Dear Mr. Love:

In our last meeting you delivered a letter with questions regarding anthrax vaccine information.

The anthrax vaccine is fully licensed and approved by the Food and Drug Administration (FDA) and has been since 1970. The FDA determined that the anthrax vaccine as used by DoD in the anthrax vaccine immunization program is an approved drug being used in accordance with its approved label. The Department of Defense's use of anthrax vaccine for pre-exposure prevention using six doses over 18 months is consistent with the Food and Drug Administration-licensed use of the vaccine. Because it is an FDA approved vaccine, there is no follow-up requirement.

You also asked about classified anthrax data on OSAGWI internal servers. All medically relevant Gulf War information was declassified by the Services. This information would have been included in that declassification effort and is available to the public on *GulfLINK*. If you have specific documents you would like declassified you should contact the Department of Defense Directorate for Freedom of Information and review at (703) 697-1 160.

If you have any other questions about the anthrax vaccine or the anthrax vaccination program, we suggest you contact AVIP at (877) 4388222. Thank you for the opportunity to address your concern

Sincerely,

Michael E. Kilpatrick, M.D.
Deputy Director
Deployment Health Support

Desert Storm Justice Foundation, Inc.

Dear Mike Kilpatrick

Sept 20th, 2002

Listed below are the following questions the D.S.J.F. would like for Deployment Health Support directorate to answer for us:

1. Is DOD using a newer NBC Detector since the Persian Gulf War? If so, what is the model #, manufacturer (s), and specifications for NBC detection and warranty, if any.

2. Is Deployment Link now using official shot records for our troops, who in future deployments have already received or will receive the Anthrax Vaccine and other experimental drugs?

3. Has DOD obtained a newer version of MOPP Suits and NBC mask since the Gulf War? if so, will these suits and mask protect our future troops against "Dusty Mustard," which our past NBC equipment lacked the capability to protect against?

4. If the above listed equipment is a newer version than what was used in the Persian Gulf War, then what are the manufactured warranties on the above purchased materials?

Sincerely,

Paul D. Lyons, SSG.
USA Retired
President, D.S.J.F.
http://www.dsjf.org

(2)

Desert Storm Battle Registry
P.O. Box 77381
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Dear
To Whom It May Concern:

I would like to address several issues on behalf of the Gulf War Veterans as well as the present day and future soldiers that could be deployed to a region that unknown risks may arise.

1. During redeployment of the Gulf Troops some of the equipment that was utilized in country received special cleaning to decontaminate the equipment. However, this was not the case for all units except for their vehicles and the weapons that were turned in to the arms supply. Many personnel, (specifically the soldiers that did not live in the barracks,) did not turn in their personal equipment such as sleeping bags, NBC gear, etc for decontamination and this was not requested by the unit Commanders. What policies/procedures are now in place to ensure that the families of the troops are not exposed to biological and chemical contaminates from cleaning this equipment, or from contact with this equipment. Are any procedures being implemented to assist the families in recognizing the symptoms for contact exposure to these contaminants?

2. What policies have been implemented to protect service members from the volatile combination of carcinogens that were known to be present during Desert Shield and Desert Storm? Such as The CARC Paint that was used openly around and by the troops for painting their vehicles. The fuel for the space heaters required to keep the soldiers warm at night. The smoke, fumes and chemicals from the oil well fires, burning vehicles etc.

3. There have been eleven years pass since Desert Shield and Desert Storm, and numerous studies have been completed concerning the chemicals and biological agents that the soldiers were exposed to during their deployment. What is now known about the dormancy of the biological agents that were present and what is now known about the half-life of both the chemicals and biological agents in the area? What is the immediate risk to the soldiers that are to be deployed to the area in the near future from these hazards?

4. For future deployments, will the units be issued updated, new NBC gear? What measures are being taken to ensure that the equipment being issued to the soldiers will offer adequate protection to prevent the known health problems of their predecessors?

5. There has been eleven years pass since many of the soldiers returned from the Gulf region and there have been numerous studies concerning the exposures and the effects to date what data is available to the vets and their families about the exposures that cause health problems?

Sincerely
Leslie D. Stevenson
Leslie D. Stevenson
State Commander
DSBR,

(3)

Desert Storm Battle Registry
P.O. Box 77381
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September 14, 2002

Dear Mrs. Ellen Embrey:

What were the OSHA, or environmental health standards in place during Desert Shield and Storm and the clean up efforts immediately following?
I know that since that time more has been done to inform local units of hazardous materials, and the proper way to handle and use them, but I would like to know what was in place at that time. I ask this because I was not deployed, and by the time things from the desert were arriving back, I was pregnant, and tasked to clean the NBC gear (masks, M8 alarms, MOPP suit), tents, sleeping bags, etc. Not once was I ever briefed on what I was using, the known affects on my unborn child, or given any indication that any of the cleaning products being harmful, carcinogenic, or toxic in any form, nor was I given the option not to use them. Some of the cleaners I know I used at that time were TSP- trisodium phosphate (decon of NBC equipment), and Trich- Trichlorofloroethane (electronics), Break free (weapons), and denatured alcohol.
I do not want to know about those specific cleaners. I am asking what system, and specific regulations were in place during that time that should have been followed, and what specific changes have been made to those policies to insure the safety of our troops today.

What policies are in place to ensure that non-deployed troops are not exposed to battlefield hazards such as depleted uranium dust, or chemicals and biologicals (if used in theater of operations) due to cleaning and servicing returning equipment? What is the disclosure policy to those troops that they may be working with, or inadvertently exposed to those agents? What is being done to insure that the troops know and understand the symptoms that may indicate inadvertent exposure?

What research is being done, or has been done on the actual persistence rates of the chemicals and biologicals Sadam was known to have at the time of Desert Storm? I am not asking about the assumed rates, I am asking specifically about any data from the samples actually collected at that time.
I would also like to know what, if anything, has been done about sampling that environment recently. I ask this specifically due to the fact that I believe that we are destined to once again have troops in that theater, and I am concerned about not only anything new that Sadam may use, but anything that may be left over from the first time that troops should be prepared for.

If the EPA regulates emissions from Diesel engines, and all other engines as a matter of public safety and health, what is being done to change the IOM statement that the smoke from the burning oil wells, space heaters, etc. did not cause, contribute, or significantly impact veterans health issues? I ask this specifically due to the following excerpt from the EPA website http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=29060

"This assessment examined information regarding the possible health hazards associated with exposure to diesel engine exhaust (DE), which is a mixture of gases and particles. The assessment concludes that long-term (i.e., chronic) inhalation exposure is likely to pose a lung cancer hazard to humans, as well as damage the lung in other ways depending on exposure. Short-term (i.e., acute) exposures can cause irritation and inflammatory symptoms of a transient nature, these being highly variable across the population. The assessment also indicates that evidence for exacerbation of existing allergies and asthma symptoms is emerging. The assessment recognizes that DE emissions, as a mixture of many constituents, also contribute to ambient concentrations of several criteria air pollutants including nitrogen oxides and fine particles, as well as other air toxics. The assessment's health hazard conclusions are based on exposure to exhaust from diesel engines built prior to the mid-1990s."
I also ask due to the large number of veterans that have breathing problems since returning.

I also ask in light of the recent findings of the EPA released through the Associated press, which states the following:
WASHINGTON (Sept. 3) - Diesel exhausts from large trucks and other sources probably cause lung cancer, the Environmental Protection Agency concluded Tuesday in a report that buttresses a push to reduce truck emissions through stricter requirements for cleaner diesel fuel.

The EPA report concludes that uncertainties remain about long-term health effects of exposure to diesel exhausts. It said, however, that studies involving both tests on animals and occupational exposure suggest strong evidence of a cancer risk to humans.

"Overall, the evidence for a potential cancer hazard to humans resulting from chronic inhalation exposure to (diesel emissions) is persuasive," said the health impact report released by the EPA.

The report mirrors conclusions made previously in documents from various world health agencies and studies in California and is particularly significant because the EPA is the federal agency that regulates diesel emissions under the Clean Air Act.

I am also interested in any data that may be available on any military regulation of exposures of this kind.

Sincerely,

Tonia A. Goertz

Tonia S. Goertz
Minnesota State Commander - DSBR
PO Box 73
Lake Benton, MN 56149

(4)

Desert Storm Battle Registry
P.O. Box 77381
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Dear Ellen Embrey

Will the United States use pyridostigmine bromide (PB) for nerve gas protection if we invade Iraq?

If no, why?. What has changed since the Gulf war that makes this a reasonable decision?

If yes, why? What peer reviewed scientific studies support this decision.

Has the DoD changed its policy on the usefulness of PB?

Why?

James R Moss

Sincerely
James Moss
Member, DSBR

Desert Storm Battle Registry
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(5)

To Whom It May Concern:

SUBJECT: NSO Representation & Gulf War Related Issues

It is imperative that the DSBR be permitted to participate in any and all future NSO briefings by the Department of Veterans Affairs and the Department of Defense. No other organization is in tune with the primary concerns of the Gulf War Community. To exclude the DSBR from representing the concerns of its constituents before the DOD/DVA/DHSD only raises questions of whether or not these agencies are truly interested in providing adequate answers to sick Gulf War Veterans.

There are several questions, which beg answering. These include:

1) **Of the approximately 675,000 military personnel, who served during Operations Desert Shield/Storm, how many have been medically discharged?** Secondly, how many of those now no longer on active duty have been awarded service-connected disabilities as a direct result of service in the gulf. How many of the 675,000 have passed away?

2) **What measures have been put in place to ensure that the VAER's program is available to all deploying personnel to any and all areas of operations?** Adverse vaccine reporting should not effect how the individual soldiers are treated. Commanders should ensure that any negative reports be sent forward.

3) **If there were no NBC incidents resulting from the destruction of the nine nuclear reactors and numerous bio-chemical bunkers then why haven't all the documents been made available under the Freedom of Information Act?**

4) **All future pre-deployment blood samples drawn should be stored with SSN# so that any sick veteran in the future can request a sample of their blood to prove that any injury due to vaccination or NBC incidents can determine their health consequences from their service.** Blood is already being stored for research purposes. Why not make it available to the soldier they are drawing the blood from?

5) **Informed Consent should not be discarded for the sake of National Security.** The Anthrax vaccine is an experimental vaccine. Russia has developed a super strain of anthrax and we do not know if our vaccine is capable of protection. Soldiers should not be used as guinea pigs.

6) **Squalene of a synthetic nature found in gulf war veteran's blood needs to be addressed as a crime and an immediate investigation should be conducted as to how this adjuvant was used to increase the efficiency of the vaccine/s.** As to date no real answer has been given that would satisfy veterans who have this synthetic squalene in their blood.

7) **Why has the DOD/DVA failed to administer SPECT exams to sick gulf war veterans and returning deployed active duty personnel suffering from neurological problems?** Instead soldiers and veterans are screened and diagnosed with somatoform disorders.

Sincerely,

Dannie Wolf

Dannie Wolf
Oklahoma State Commander,
DSBR/AVJF

Desert Storm Battle Registry
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(6)

To: DHSD

Sep 19, 2002

1. Medical personnel of all specialties are in short supply for all services. This is both a Homeland Security and Veterans support issue. What is status of training of VA personnel on radiation, chemical and biological protocols?
2. In a Thursday, September 19, 2002; Page A01 article, the Washington Post reports "The Bush administration has abandoned an international effort to strengthen the Biological Weapons Convention against germ warfare, advising its allies that the United States wants to delay further discussions until 2006." Have sufficient Force Health Protection measures, to include antidotes, been implemented to support our troops in the event of a conflict where chemical (I.E. VX nerve agent or mustard agent) and/or biological (I.E. anthrax or botulinum toxin) weapons are used?
3. Has the Veterans' Appeals Control and Locator System (VACOLS) and subset Gulf War Veterans Information System (GWVIS), consolidation of existing VA, BVA, VHA, and VBA information systems into a single source of information about Gulf War veterans, including health and disability matters been completed?
4. What Comprehensive Clinical Evaluation Program and VA Gulf War Health Examination Registry data fields were not incorporated into the new VACOLS relational database?
5. The 2000 Census reported that approximately 350,000 gulf war veterans were drawing a disability. Is this data inline with the number of individual records in the Gulf War Veterans Information System (GWVIS) database?
6. What is your position on the "planned destruction" of the original DoD's Comprehensive Clinical Evaluation Program and the VA's Gulf War Health Examination Registry data?
7. Why is the CCEP and PGR data not being sent to NARA for archive?
8. When will the GWVIS database be accessible to researchers and what agency will control access to it?
9. The 2000 Census reported that approximately 350,000 gulf war veterans were drawing disability pay. What is the breakdown of diagnoses and disability percentages?
10. What is the current number of gulf war veterans receiving social security?
11. What is the status of Project DoD-94, the study "Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. Gulf War Veterans"?
12. Why are only 100,000 records being examined in project DoD-94, if the 2000 Census reports that approximately 350,000 gulf war veterans are drawing some form of disability?

13. VA physicians are not currently using the VBA/VHA Clinical Practice Guidelines. Has a training plan been formulated to correct this?

14. Are the Guidelines for Disability Examinations In Gulf War Veterans being utilized for mandated follow-up VBA C&P disability exams?

15. Is there a mechanism in place where a claim of increased disability is automatically entered into the system if a follow-up VBA C&P disability exam shows that the veteran has gotten worse?

16. Veterans are assigned to a Primary Care Manager Team based on their most significant diagnosis, however many gulf war vets have multiple comorbid diagnoses. What mechanism is in place for the teams within the hospital and between hospitals to share information about treatment protocols that have been found to benefit veterans but have not been the results of a study?

17. Do the various services provide the same information on pre-discharge programs? What are the common denominators between the services, to include type of information provided (I.E. education and VA benefits) and effectiveness of various NSO presentations?

18. Are Deployment Health Assessment Protocols being followed for pre and post deployment Afghanistan and Persian Gulf veterans?

19. At what level is the deployment surveillance database shared between the component services?

Sincerely

CDR David W Seipel
USN TDRL
GA State Commander
DSBR

Desert Storm Battle Registry
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(7)

Dear Mike Kilpatrick

[1] Since this announcement (Contracts/Procurements June 2002) The U.S. Army Medical Research and Material Command is soliciting proposals for original research on service members who served in the Southeast Asia theater of operations during the Persian Gulf War on possible health effects of exposure to low levels of hazardous chemicals and the individual susceptibility of humans to such exposure under environmentally controlled conditions.

- [a] What organization or facility will do this project?
- [b] When will this begin?
- [c] How do you plan to contact participates for this study?

[2] For Operations Desert Shield and Desert Storm, the Army and the Air Force directed that one-page health summary forms be prepared at the time of mobilization. These "abbreviated health records" were to be sent with deploying soldiers and airmen in place of full individual health records. As part of an initiative to identify and facilitate veterans' access to their Gulf War inpatient records, staff from the special assistant's office searched through records at the National Personnel Records Center in St. Louis - permanent storage site for all records of hospitalizations in military medical facilities. The team located more than 25,000 inpatient records of deployed Gulf War servicemembers and entered the information into a database.

Veterans can call OSAGWI at (800) 497-6261 for a database search and assistance in obtaining copies of their records.

- [a] when will I get my records for treatment at the 85th Evac Hospital for Jan 90 Saudi Arabia ?

Defense Occupational and Environmental Health Readiness System
- Industrial Hygiene

- [a] I request the titles of all documents (memorandums, notices, regulations) which have come into existence or modified since 30 May 91 to 2001 under DOEHR subject.

Sincerely

VenusVal Hammack

VenusVal Hammack,
State Commander, Massachutes
Administrator, DSBR

(8)

5011 Ruthie Cove
Memphis, TN 38127

Desert Storm Battle Registry
P.O. Box 77381
Washington, DC 20013
Tel: 540-477-2923
Fax: 540-477-2941

Dear Mike Kilpatrick,

This will a very hard letter to write knowing that fellow veterans are sick or have lost their life after the Gulf War of 1991 do no protection during the war. We required information from your DOD and the VA. Should we go back to these areas for war are we (USA) not putting our young men in danger, again? Are we "FORGOTTEN WARRIORS"? During Gulf War, We had the Warriors Cry for our country. But now, We cry for our self and future warriors!

Have you read the Address at Fall Congressional / Coalition Leadership Breakfast by Dr. Doug Rokke. 325 Russell Senate Office Building, U.S. Senate ,Washington D.C. on November 10, 2000. If you should read this. Just use the Internet and type in Dr. Doug Rokke and you will find great information on the Bauer's Team: Preparing Medical Personnel for War.

I have lost dear friends after coming home from the Gulf War. One warriors required a hearth and lung transplant and other one needed the same. Both of these men were non-smoker with one being a postman , the other a farmer. One member served in (2) two Wars the other in (3) wars. Both of these soldiers never requested help from the VA until after the Gulf War. Both veterans did not get treatment from the VA; because they were not service. What a great lost to this country but a great lost to their families.

Please, understand that I am not finding fault in you. Just the system that will not find answers to the problems and will not answers to our question; that we may find answers for our self.

I will not stop looking for answers for all our Gulf War Vets and future Vets of Gulf Wars. At present time, I am talking to (2) two Congressmen about not getting answers. How they can help Gulf War with many of their problems. And I hope to stop this in becoming another Agent Orange for this country.

Thank you for you time in these matters from all DSBR State Commanders.

Sincerely
Phillip W. Nelson, Sr.
State Commander of Tennessee
DSBR

Desert Storm Battle Registry
P.O. Box 77381
Washington, DC 20013
Tel: 540-477-2923
Fax: 540-477-2941

(9)

Dear Capt.. Michael E. Kilpatrick
DHSD
Office of the Assistant Secretary of Defense
For Health Affairs
Four Skyline Plaza
5113 Leesburg Pike Suite 901
Falls Church , VA 22041

Capt. Kilpatrick:

I would like to have you address certain concerns I have in regards to Deployment Health of the past, current and future troops and personnel.

Leishmaniasis, as you well know, is endemic to the Persian Gulf Theatre and is listed by CENTCOM and Walter Reed as one of 13 deadly infectious diseases that pose a known threat to those deployed to the region, as of January 1991.

At a press conference January 12, 2001, by the Rand Corporation and Bernard Rostker, they stated that because of the threat of insect borne Infectious Diseases, Leishmaniasis in particular, that there was an overuse of pesticide and insecticides, but that the incident rate of these infections was at a minimum because of their use and because of the winter season in the region. You also were recently quoted in an article dated 8 August, 2002 in the Atlanta Journal-Constitution that troops use "battle dress uniform", treated with insect repellent, but acknowledge that "troops aren't going to wear long sleeves when it's really hot" You also are quoted that " the government also conducts frequent medical risk assessments of the environments where soldiers are working, testing for example, to see if sand flies are in the vicinity".
Please elaborate on the forms of "medical risk assessment".

What form of testing is being applied to identify these infections? You know that the viscerotropic form of Leishmaniasis is not to culture biopsy material, it can be achieved through PCR, because the DoD/VA have not been able to develop a species specific sero test; it is a genetically mutated strain of the disease, that starts cutaneously, then turns to attack the internal organs and other soft tissues, particularly to the victims genetic predispositions.

What is the status of said species-specific sero- testing?

Has a skin prick test been successfully developed for use on those displaying symptoms in the field that the DoD/VA have been jointly researching?

What information has been compiled about familial genetics in regards to the "tropism " of the form of Leishmaniasis that the DoD/VA have been working on for years? And how could this research be performed without families in turn being infected prior to said research?

It is reported that only 19 cutaneous cases and 12 visceral cases were reported and treated in returning Gulf War Veterans. In a declassified document from Operations Support Directorate dated Oct.1990, Subject: Special Telegraphic Report of Selected Conditions (RCS MED 16 (RA)) It states that a 30 year old active duty soldier was air vac'd and treated for visceral Leishmaniasis. It also states within this document that the 60 known courses of treatment for visceral Leishmaniasis had already been exhausted.

That is 3x the numbers reported nearly three months before Operation Desert Storm was even initiated. Why and how are the numbers so conflicting? Did you just stop testing as to not truly reflect the infection rate?

Why have you not added my husband to those numbers when he has not only a verified diagnosis, but has an adjudicated Department of Veterans Affairs claim that grants service-connection to Leishmaniasis?

And furthermore, why has the CCEP protocol for DoD dated June 1994 not been followed through with those thousands that display the symptomology?

Why are the recommendations stated in the "Adequacy of the VA Persian Gulf Registry and Uniform case Assessment Protocol, Findings and recommendations for Immediate Actions" #13 and #14 not been acted upon?

What of the recommendations offered are being utilized from the "Health Consequences of Service During the Persian Gulf War: Recommendations for research and Information Systems"?

What true medical surveillance is taking place?

I feel this is gross medical negligence on the part of the DoD and the Veterans Administration, and because of a lack of action on your part, millions are at risk of transmission and infection through blood products, person to person and to offspring and have been for over twelve years!

The incident rate of infection is underreported because of a lack of testing and identification, and there is a falsehood perpetuated that the only vector is the sandfly. You have failed to warn those at risk about the dangers of transmission from person to person, transplacental and genetic damage to offspring. You have also failed to inform those at risk about the cycle of reproduction of the sandfly that was noted to reproduce not only in standing water, which most from our culture would recognize, but that they are not only nocturnal feeders, but they lay their eggs in the soft, moist crevices of the sand bags used at the base of every tent used for our precious military personnel; hence incubators with waiting meals to feed upon. There was a medical directive that was not disseminated to the troops to sweep and clean these areas of their quarters to help prevent insect bites and subsequent transmission. You also failed to warn them that dogs, camels, goats, sand gerbils and lizards are also known vectors.
A similar situation looms large over our nation in regards West Nile Virus, as now verified by a transmission from blood transfusion and blood products to organ donation transplantation and subsequent deaths.

As you should also be aware, this form of Leishmaniasis can not only lay dormant and in remission for many years, as documented in a case that was diagnosed and treated at Walter Reed in 2000, it can lay dormant without symptoms present for up to 43 years. It is also Pentastam resistant, which is the known classic treatment for visceral Leishmaniasis.
But of course, as you also know, this is no classic visceral Leishmaniasis; it is viscerotropic: Ever turning, ever changing, ever mutating. Its only known treatment has been an infusion treatment of Amphotericin B with Lipid Complex to reduce toxic side effects and permanent damage to the renal system. It also has a very high rate of reincidence even after such treatment. For a three-week course of treatment, the costs exceed $100,000. for hospitalization and follow up: a very expensive treatment to save the lives of those that have served this country honorably who have answered the call.

Is this possibly another policy to cut costs?

Or is it to limit the threat of panic most certain to occur with the public of which you serve, when they find out that not only was there a blood ban on donations from returning Gulf War Veterans, contracted individuals and journalists from the American Red Cross and Military Blood Banks, but that it was lifted to soon as of Jan.,1, 1993?

You most certainly are aware of the epidemic of Leishmaniasis currently in Kabul with over 280,000 confirmed cases in the indigenous population and its threat to those currently deployed to that region of the world, but that there are current out breaks in India, Palestine and Brazil. Will Dr. Steven Beverly of Harvard/ Washington University of St. Louis funded by the DoD deal with these situations through a newly developed vaccine? Or just insecticide soaked clothing that residually will cause Central nervous system damage by it over exposure, again?

There are of course, vaccines currently available, but not FDA approved; during the Iran –Iraqi war, the Iranians did not vaccinate their +300,000 troops for Anthrax exposure, but they did for Leishmaniasis.

Here in the United States, it is also known that Leishmaniasis has infected canines in over 21 states; the media reported erroneous information that the infection was most likely transmitted either by Gulf War Veterans themselves or by animals(pets) acquired and brought back to the States by military personnel. You and I know this is not possible: military personnel, let alone civilians cannot enter this country with "pets" in tow.
So how would this be scientifically or physically possible? Why would this infection be used to villanize our returning heroes, if the only said vector is the "sandfly"?

I wait in earnest for your response to these questions, for I now have verification that my husband's infection was subsequently transmitted to me sexually, and in turn, I not only suffered a miscarriage, but our following live births of our two children also have titers for Leishmaniasis, verified through PCR on October 4, 2000, through help and information from the Bill and Melinda Gates Foundation and testing through the Federal University of Rio de Janeiro, Brazil and funded through humanitarian research dollars.

I have never been out of this country and my children certainly have not been to Saudi Arabia. Detroit and Flint, Michigan are not known for their tropical climate or conditions,
My family continues to suffer from permanent effects to the Central Nervous System and Immune System, and both children are profoundly affected by this disease and other exposures that my husband incurred during his service in the Gulf War including , but not limited, to uninformed consent of vaccines, PB, low-level nerve agents ie: sarin and his verified infection by Leishmaniasis which was never diagnosed or treated by DoD and VA protocol or health systems allowing the infection to ravage his body and provide the opportunity for others to become infected for over 8 years, before being identified , diagnosed and treated by the civilian health care system through Medicaid and Medicare.

Sincerely
Janyce E. Brown
Michigan State Commander
DSBR,
5051 Winston Drive
Swartz Creek, Michigan 48473-1224
(b)(6)

(10)

Desert Storm Battle Registry
P.O. Box 77381
Washington, DC 20013
Tel: 540-477-2923
Fax: 540-477-2941

Dear Mike Kilpatrick

Sept 20th 2002

Veterans of Washington State, are not being informed of Project Shad nor receiving needed healthcare or testing for possible exposure to biological/chemical agents during the 60's.

On Dec. 1, 2000, Thomas L. Garthwaite, Under Secretary for Health, Veterans Affairs, put out a Fact Sheet recommending that VA medical Centers need to provide evaluations to eligible veterans who may have been exposed to hazardous material during "Project Shad".
It also goes on to state, that it is encouraged that copies of the Information letter, (IL 10-2000-012) be provided to Primary Care Teams and outpatient clinics, including community-based outpatient clinics, as well as Vet Centers.

After 2 yrs, VA Doctors, Primary Care Teams and outpatient clinics in Washington State no nothing about Project Shad. VA employees are not being informed and if their not informed, they can't inform Veterans.

Most of the VA employees I've spoke with at American Lake, Seattle & Spokane VAMC's, haven't heard of Project shad. Employees can't answer questions or provide information to project shad veterans seeking care & testing, because they've never heard of it.

MD's, PA's, Nurses, Admitting clerks, Receptionists, VAMCs Directors office, Patient Advocates, VA Infectious Disease depts., Lab services, Pharmacies and Eye clinics have never heard of Project Shad, yet the current plan to inform veterans by the DVA is by word of mouth.
I urge you to put forth a plan to Inform & seek out Veterans during the sixties, of the possibility of exposure to biological agents.
It could easily cost the lives of many veterans by delaying the care we urge each other to provide to our pets, but withhold from our Veterans & their families.

Sincerely

Allan R. Opie

Allan Opie
Wa. State Commander
DSBR,
(b)(6)
161 Bunch RD
Wauconda, WA. 98859

Desert Storm Battle Registry
P.O. Box 77381
Washington, DC 20013
Tel: 540-477-2923
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(11)

Dear Ellen Embrey

I would recommend that a study be done of Gulf War veterans who received anthrax vaccine, along with a matched control group who had not received vaccine—possibly taken from people who enrolled in the military after the Gulf War, and whose vaccination status is known.

There are approximately 400 (former)Fort Bragg soldiers whose vaccination status, dates of vaccinations and number of doses are known. Dr. Philip Pittman has just published a paper discussing results learned when this cohort of soldiers was given booster doses of anthrax and botulinum toxoid vaccine.

Here is the reference:

Pittman PR, Hack D, Mangiafico J, Gibbs P, McKee KT, Friedlander AM, Sjogren MH.

Antibody response to a delayed booster dose of anthrax vaccine and botulinum toxoid.
Vaccine. 2002 May 15;20(16):2107-15.
PMID: 11972980

Studying this cohort will resolve the entire question of whether anthrax vaccine contributed to Gulf War Illnesses.

Sincerely your,

Meryl Nass, MD
(b)(6)

Desert Storm Battle Registry
P.O. Box 77381
Washington, DC 20013
Tel: 540-477-2923
Fax: 540-477-2941

(12)

Dear Mike Kilpatrick

The following information is critical to requiring answers that directly impact many veterans, family members and the general population. Ask why Plum Island was designated a Bio-Level 5 facility and why mycoplasma was developed there for biological warfare purposes. The main reason for this question is because the DoD has downplayed the significance of this particular pathogen. This makes absolutely no sense because the Department of the Army funded the Patent that Dr. Shyh-Lo holds titled "Pathogenic Mycoplasma" back in 1986. The Uniformed Services University Health Services also taught this in their syllabus until 1993-94. Then there were the vaccine trials conducted at Huntsville Prison in Texas years prior to the Gulf War. Then comes the Gulf War and many veterans who have been fortunate enough to get tested, are positive for mycoplasma fermentans incognitus strain. This is a horrendous cover-up and it is obscure to many physicians in the private sector. The sheer knowledge that this organism was weaponized and that many of us suffer from its effects warrants criminal negligence on the part of the DoD for their refusal to acknowledge its existence and provide treatments. This presents a double-edged sword as well, because we were either exposed to it during the Gulf War (because we supplied Iraq with it) and it was also used in experimental vaccines that many of us received. They must answer to biological exposures...something they have continually downplayed and avoided at all costs. Now is the time to hammer them and demand the truths. Below is an excerpt from Patricia Doyle, PhD, who has done extensive research on Plum Island, Fort Dietrich and some of their nasty secret experimentations.

Plum Island, The History...03/20/00

by Patricia Doyle
I have documented that in 1970, just one year after Nixon ended the US biowar offensive research program, 10 million dollars was granted by the US Gov't. to Plum Island for the purpose of establishing a mycoplasma for use in germ war research department. It was illegal to work with mycoplasma in the Continental U.S. and this was the reason that the early work did not take place at Ft. Derrick. Plum Island had two very good reasons for winning the new mycoplasma research dept. First of all, it is technically an island; secondly, Plum Island was a biowar research facility. So, in order to commence mycoplasma research, Plum Island was designated a biolevel 5 facility and a 5-year project began.

In 1975, Plum Island's mycoplasma research was doing so well, the Govt. continued to maintain funding for that department. In the 1980's a young scientist, who had completed his graduate research at Cornel, was hired to head the mycoplasma biowar research project. This scientist was Dr. Jawad Al Aubaidi. When it was evident that hostilities would break out in the Persian Gulf, Dr. Aubaidi went home to his native Iraq and was appointed to head the mycoplasma research project at the Univ. of Baghdad.

One of Dr. Aubaidi's projects was filling payloads of scud missiles with mycoplasma strains. In 1995, Dr. Aubaidi was murdered by the Israelis. His demise, or, neutralization was made to look like an accident. I have much more information on Plum Island, and a recent update regarding the ongoing encephalitis research at that facility. I have also found out that Plum Island scientists were testing Japanese Family of encephalitis vaccine on HUMAN VOLUNTEERS. Dr. Peter Mason and Dr. R.E. Shope both of Plum Island worked on the encephalitis vaccine project with Dr. Monath of OraVax Co. Dr. Shope and Dr. Jerry Hauer (Hauer-Feb. 1999-Nov.99- Mayor's Office of Emergency Management) worked together and are on a committee for bioterrorism preparedness.

March 1999 OraVax Co. was on the brink of financial disaster. Their stocks were bottomed out due to a vaccine they wanted to showcase did not work. March 1999, power outage at Plum Island. I suspect the West Nile Virus, as well as Malaria and some other Arboviruses escaped Plum Island. Dr. Jerry Hauer was hired by the FBI due to his "excellent and timely" handling of the WNV outbreak in N.Y. Dr. Thomas P.C.

Monath and OraVax have recently had their stocks triple in value. OraVax is ready to market chimerivax for use against West Nile Virus. Dr. Shope was hired by Univ. of Texas Galveston. I have a lot more on Shope. 3 previous accidents at Yale alone. Last one, 1994, Sabin virus broke loose. Faulty test tube? Sabin virus is a mild hemoreghic fever in the Ebola and marburg family.
Bio accident 1978, Plum Island, Foot and Mouth Disease. I have further discovered that Plum Island has projects whereby they infect ticks with agents of brucella toxins. Another, infecting ticks with African Swine Fever. I have also learned that Plum Island had CURED a young Connecticut girl of LYME DISEASE at the Plum Island IN HOUSE HOSPITAL. So, the bioweaponeers do have the antidote. Too bad, the rest of the population is not being accorded the cure.
I have a friend meeting with a former member of the Mossad. I am hoping to find out WHY DR. JAWAD AL AUBAIDI was murdered. I also would like to know why a top-secret biowar research facility would hire scientists from nations that are not friendly to the US. I am now tracing some scientists from China. I am curious about Dr. Lo, who patented the mycoplasma incognitus strain. Aren't you just a bit curious? Don't you want to know how many Russians, Red Chinese, North Koreans, Vietnamese; Cubans etal are heading up our biowar research projects? What is the connection between the Gulf War Illness, our veterans and Plum Island, Dr. Aubaidi, the US Govt. and the Mossad? Must be something to die for? Just like Dr. Aubaidi.

Sincerely,
Bob Jones

From: Edward J. Bryan
Researcher for Gulf War Illnesses
Health Care Liaison (VA / BU) 1995-2001
685 Broadway St. # 74
Malden, Massachusetts. 02148
Tel.# 1-781-321-3161

(13)

To: The Honorable Donald Rumsfeld
Secretary Of Defense
1000 Defense Pentagon
Washington, D.C. 20301

September 20, 2002.

Re: Michael E. Kilpatrick, MD
Director, Deployment Health Support

Dear Secretary Rumsfeld,

There are still many issues left unresolved and the research that was done on a (**Partial Investigation**), by only talking to a small number of veterans, and taking random samples. Your office did say in 1999, they would conduct epidemiological studies, that never happened. There are long term health concerns that are not being addressed.

The veterans only want to be treated medically, and acknowledged for our service and to our country. However, the U.S. Government turned a blind eye on this 250 million dollar study. The claims are rising as we speak and the death rate is out of control.

There are several concerns I have to address,

1). Oil Well Fires: There was very little done, all the pictures show the toxic smoke plume going down wind, over the troops, for 1,500 miles or more. The oil came down with the rain and was very intense. The smoke was above the threshold limit value (TLV), for the February 1991 through November 1991 time frake. Dhahran had 2-3 miles of Visibility in smoke and haze. Out of 10 sampling sites, 3 worked, some of the time. Again this was only a partial investigation. At the gulf war Confconfference from January 24-26, 2001. It was said by this office that the (Bombing Campaign) was going to be reissued,that never happened. All that came from the January 24-26, 2001, meeting was reports of stress and anxiety. The conference was reporting more neurological disorders.

2). Pesticide Exposures: The troops applied this daily to their uniforms and their own bodies. This is an on going issue at IOM. We found a (Peer Reviewed) book on Recognition and Management of Pesticide Poisonings, E.P.A. 735-R-98-003 March 1999 and Military Nerve Agent Book FM-8-285. These books tell the story and tell the answers. We didn't have this book on September 7, 2002. at the IOM Hearing, Dr. Soxs will have to look at this again.

3). Carbon Monoxide Exposure: There is no report of the CDC Conference, from February 28, - March 2, 1999, and no study to date. What are the Doctors doing ?

4). Nerve Agent Exposures: According to the Health Conference at the Mark Center from January 24-26, 2001, there are real exposures that could be medically identified from current medicine. This is the conference that our government wants to hear from. Why aren't the Medical Professionals reporting the health concerns to your office ? There should be oversight coming from your immediate office at the pentagon, your sub-offices elect not to report findings that relate to health matters.

5). The (**Milk Factory**). The baby bottle factory was a major issue in 1991 and still is to date September 20, 2002. Mr. Walpole, and Mr. Fox of the (CIA), told me that they were ready to release this information about (**The Milk Factory**) in November 1999. Well I brought this complaint to L.T.G. Vesser and your office several times and still there is no reply. How long do the veterans have to wait ?

6). DOD / VA / and Civilian Doctors are still observing patients and at times speaking for them. When is this going to stop. Doctors only know of basic medicine and the Doctors treating gulf war veterans need to be greatly educated, even with todays protocol.

7). When is the U.S. Government going to start washing the lungs of the World Trade Center (**Rescue Workers**) ?

8). What does Gulf War Illnesses and West Nile Virus (WNV) have in common, they both are ignored.

9). Gulf War 1 VS. Gulf War 2

Retired L.T.G. Vesser's statement made on Sept. 3, 1999. at

(OSWAGI) on Gulf War Illnesses about this National Problem states,

He States that with his experience the (1991 Gulf war) was,

" The most toxic battlefield since W.W. 1 ".

On October 11, 2000. Maj. Gen. Randall L. West at a hearing states that:

" That the winds blew from North to South ".

And with the ill winds came the smoke, chemicals, etc, down over the troops. This must be the fog of war, everyone is talking about.

An article in Newsweek September 16, 2002.

On guard, A year later states on, pg. 40, Chemical Plants and other Hazardous Materials: This is a THOUSAND-POINTS-OF-VUL-nerability risk that has remained largely below the radar. As a result, industry lobbyists and infighting among a multitude of government agencies trying to defend their turf have combined to hold Ridge's office and the Environmental Protection Agency at bay-meaning no new regulations to enhance chemical-plant safety and the security of the thousands of daily shipments of hazardous materials. One blown-up plant, truck or train, and the press will be calling for the scalps of those who let it happen. No wonder why so many people have diseases, When will you tell your workers that these Chemical Exposures are Hazardous to their Health. Your Gas Station Attendants, Diesel Truck Drivers, Asphalt Plant Workers, White House Workers, All Military Personnel, U.S. Firefighters, Factory workers, U.S. Homes, etc.

Desert Storm Veterans and U.S. Firefighters have the same Chronic Health Condition, Car Accidents and Heart Attacks.

[redacted]

Science Magazine June 3, 2002. John Feussner says,

" It was quite a Toxic Soup " and yes a

dozen of Medical Panels have poured over the evidence and hearings.

Edward J. Bryan says,

" Now we know, Where the DOD / VA cut their time short, on, the reporting of the health effects, of the different toxins used in the gulf war ".

Just look at the numbers, they just don't add up, the (TLV-TWA) time weight average, (STEL-TLV) short term exposure limit, (TLV-C) and Ceiling limits, with the toxic exposures. Every chemical has a (TLV) threshold limit values. All the Environmental Exposures have to be looked at and adjusted by there mean values. This is something the U.S. Government will not do. What are the Doctors getting paid to do ? Over 250 Million Dollars was spent on these Studies and only Stress and Aniexty so far ? This tells the American Public, when we go to war with IRAQ Again, the troops will come back with even more diseases, Gulf War 2 , this will only prove that the U.S. Government doesn't have any lessons learned. When will we know the truth.

Mr. Edward J. Bryan

685 Broadway St. # 74
Malden, Massachusetts. 02148
Tel.# 1-781-321-3161

C.C. House Oversight Committee
C.C. Senate Oversight Committee

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Mr. Paul Lyons
President
Desert Storm Justice Foundation, Inc.
P.O. Box 42879
Indianapolis, Indiana 46242-0879

Dear Mr. Lyons:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. Many of the questions posed fall outside the purview of our office. We have forwarded those questions to the appropriate agencies for a direct response to you.

During the meeting, Mr. Love asked that we schedule a follow-on meeting and that we allow sufficient time for you to coordinate arrangements for other participants. Based on the current calendar, any day during the week of December 9-13 is available. If this presents a challenge and you would prefer to meet in January, please let me know. At this time, we are unable to project an available block of time in January. We should be able to do so in mid-December.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Commander David W. Seipel (U.S. Navy, Ret.)
Georgia State Commander
Desert Storm Battle Registry
300 Treetop Drive
Bremen, Georgia 30110-4420

Dear Commander Seipel:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. The majority of the questions you provided us dealt with Department of Veterans Affairs issues. We have forwarded those questions to their public affairs office and are requesting that they respond to you directly. Your question regarding the number of veterans receiving social security has been forwarded to the Social Security Administration.

During the meeting, you asked if there were other ways you could bring questions to our office. As in the past, we are happy to accept questions presented at meetings. I encourage you to also make use of our contact center — the toll-free number is (800) 497-6261. The office is staffed Monday through Friday, from 9 a.m. to 9 p.m. (Eastern Standard Time) — those who answer the phones are all veterans. We can also be reached via e-mail. The URL is: *http://www.gulflink.osd.mil/gulf_message_form.html.* If you have an inquiry that requires immediate action, I recommend contacting us by telephone.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Mr. Dannie Wolf
Oklahoma State Commander
Desert Storm Battle Registry
3908 N.W. Santa Fe Avenue
Lawton, Oklahoma 73505-3720

Dear Mr. Wolf:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. Many of the questions posed fall outside the purview of our office. We have forwarded those questions to the appropriate agencies for a direct response to you.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Ms. Tonia S. Goetz
Minnesota State Commander
Desert Storm Battle Registry
P.O. Box 73
Lake Benton, Minnesota 56149

Dear Ms. Goetz:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. Many of the questions posed fall outside the purview of our office. We have forwarded those questions to the appropriate agencies for a direct response to you.

In the meeting, one of the participants asked if there were other ways the attendees could bring questions to DoD. As in the past, we are happy to accept questions presented at meetings. I encourage you to also make use of our contact center — the toll-free telephone number is (800) 497-6261. The office is staffed Monday through Friday, from 9 a.m. to 9 p.m. (Eastern Standard Time) — those who answer the phones are all veterans. We can also be reached via e-mail. The URL is: *http://www.gulflink.osd.mil/gulf_message_form.html.* If you have an inquiry that requires immediate action, I recommend contacting us by telephone.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Mr. Phillip W. Nelson Sr.
Tennessee State Commander
Desert Storm Battle Registry
5011 Ruthie Cove
Memphis, Tennessee 38127

Dear Mr. Nelson:

Thank you for your letter expressing your concerns on both the welfare of Gulf War veterans and the servicemembers who could be called upon to deploy in future conflicts. We share your concerns and are working with the services to ensure the force health protection policies are both in place and complied with.

Enclosed are the responses and some fact sheets providing the information to questions that your group submitted at the September 20, 2002, meeting. We provided copies directly to all the attendees. Many of the questions posed at the meeting fall outside the purview of our office. We have forwarded those questions to the appropriate agencies for a response. They will respond to you directly.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Ms. Janyce E. Brown
Michigan State Commander
Desert Storm Battle Registry
5051 Winston Drive
Swartz Creek, Michigan 48473-1224

Dear Ms. Brown:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. Many of the questions posed fall outside the purview of our office. We have forwarded those questions to the appropriate agencies for a direct response to you.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Mr. Allan Opie
Washington State Commander
Desert Storm Battle Registry
161 Bunch Road
Wauconda, Washington 98859

Dear Mr. Opie:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. Many of the questions posed fall outside the purview of our office. The majority of the questions you provided us dealt with Department of Veterans Affairs issues. We have forwarded those questions to their public affairs office and are requesting that they respond to you directly.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Ms. Meryl Nass, M.D.
124 Wardtown Road
Freeport, Maine 04032

Dear Dr. Nass:

Enclosed are some fact sheets and responses to questions submitted by you and your counterparts at our September 20, 2002, meeting. We are providing responses directly to all of the participants. Also, a number of the posed questions fall outside our purview. We have forwarded the questions to the appropriate subject-matter experts for a response, and we asked that they respond directly to each inquirer.

We appreciate your comments and recommendations on possibly conducting an anthrax vaccine study. Currently, there are no plans for this effort. This decision is based on work completed by the National Academy of Sciences' Institute of Medicine (IOM) earlier this year. After performing a comprehensive analysis and review of data, the IOM reported in March 2002: "The committee observes that no data that indicate the need for the continuation of special monitoring programs for AVA have emerged, but it recognizes the real concerns for service members ordered to take the vaccines."

On another note, in the past we have forwarded copies of the Research Working Group's annual report to Congress. I have enclosed a copy of the March 2002 report for your use and reference.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

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5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Mr. Edward J. Bryan
685 Broadway Street #74
Malden, Massachusetts 02148

Dear Mr. Bryan:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002 meeting. We provided copies directly to all the attendees. A number of questions posed fall outside the purview of our office. We forwarded those questions to the respective agencies for a response. We also requested that they contact the veteran directly.

I appreciated your phone call on the day before the meeting. With that input, I was able to provide your areas of concern to Dr. Kilpatrick. This was most helpful, as you had only a short period of time to present your issues during the meeting.

Thank you for the opportunity to address your concerns. I hope the information is useful to you. If you need any further information or if we can be of any further assistance, please let me know.

Sincerely,

Barbara A. Goodno

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Mr. James Moss, Ph.D.
Desert Storm Battle Registry
1508 N.W. 35th Way
Gainesville, Florida 32605

Dear Dr. Moss:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. Many of the questions posed fall outside the purview of our office. We have forwarded those questions to the appropriate agencies for a direct response to you.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Mr. Kirt Love
Desert Storm Battle Registry
P.O. Box 77381
Washington, D.C. 20013

Dear Mr. Love:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. Many of the questions posed fall outside the purview of our office. We have forwarded those questions to the appropriate agencies for a direct response to you.

During the meeting, you asked that we schedule a follow-on meeting and that we allow sufficient time for you to coordinate arrangements for other participants. Based on the current calendar, any day during the week of December 9-13 is available. If this presents a challenge and you would prefer to meet in January, please let me know. At this time, we are unable to project an available block of time in January. We should be able to do so in mid-December.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Mr. Bob Jones
C/O Desert Storm Battle Registry
Desert Storm Battle Registry
P.O. Box 77381
Washington, D.C. 20013

Dear Mr. Jones:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. Many of the questions posed fall outside the purview of our office. We have forwarded those questions to the appropriate agencies for a direct response to you.

We are providing this response via Mr. Love's address, as we do not have a direct address for you.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

DEPARTMENT OF DEFENSE
5113 LEESBURG PIKE, SUITE 901
FALLS CHURCH, VIRGINIA 22041-3226

DEPLOYMENT
HEALTH SUPPORT

NOV 13 2002

Ms. VenusVal Hammack
Desert Storm Battle Registry
P.O. Box 77381
Washington, D.C. 20013

Dear Ms. Hammack:

Enclosed are the responses and some fact sheets that provide the information to questions submitted by you and your associates at our September 20, 2002, meeting. We provided copies directly to all of the attendees. Many of the questions posed fall outside the purview of our office. We have forwarded those questions to the appropriate agencies for a direct response to you.

During the meeting, you asked when you would receive your records of treatment at the 85th Evacuation Hospital during your deployment for the Gulf War. We have forwarded a request to the National Personnel Records Center in Saint Louis, Missouri, on your behalf to have a copy of your medical records mailed to you.

Thank you for the opportunity to address your concerns. If you need any further information or if we can be of any further assistance, please contact us.

Sincerely,

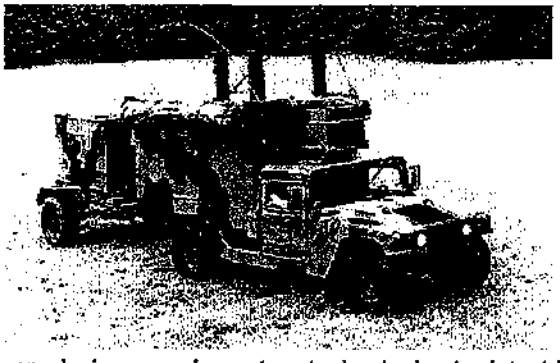
Barbara A. Goodno

Barbara A. Goodno
Program Director, Public Affairs and Outreach

Enclosures

Edgewood Area - Aberdeen Proving Ground, Maryland 21010-5424
U.S. Army Soldier and Biological Chemical Command

Biological Integrated Detection System (BIDS)



BIDS Components:

- Vehicle (M1097 HMMWV)
- Shelter (S-788)
- Generator (PU-801)
- Bio Detection Suite

Description: The BIDS consists of a shelter (S-788 Lightweight Multipurpose Shelter) mounted on a dedicated vehicle (M1097 Heavy High Mobility Multipurpose Wheeled Vehicle (HMMWV)) and equipped with a biological detection suite employing complementary technologies to detect large area biological attacks. The system includes a trailer-mounted 15-kw generator (PU-801) to provide electrical power. The BIDS Biological Detection Suite links aerodynamic particle sizing, bioluminescence/fluorescence, flow cytometry, mass spectrometry, and immunoassay technologies in a complementary, layered manner to increase detection confidence. To fill the urgent need for a biological detection system, yet field mature technologies, the BIDS has an evolutionary acquisition strategy. Initially, a non-developmental item (NDI) BIDS (M31), consisting of primarily off-the-shelf instrumentation, provided a limited manual detection/identification capability. This was being followed by a pre-planned product improvement (P3I) BIDS (M31A1) with an expanded and semi-automated detection/identification capability. Current integration of the Joint Biological Point Detection System (JBPDS) will provide a fully automated, objective BIDS (M31E2) with broad-spectrum biological detection/identification capability.

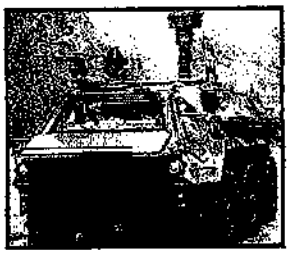
Use: The number of countries pursuing an offensive biological warfare program continues to increase. The priority of the U.S. Army's Biological Defense Program is to limit the effects of large area biological warfare attacks. As a U.S. Army corps level asset, the BIDS will mitigate the effects of large area biological warfare attacks during all phases of a campaign. Individual BIDS systems are strategically employed throughout the Corps area to create a sensor array/network. The BIDS network will be used for warning and confirming that a biological attack has occurred, will provide presumptive identification of the biological agent being used, and will produce a safely configured sample for later laboratory analysis. The BIDS is C130 aircraft transportable, has roll-on/roll-off capability, and can operate in a dismounted role separate from its dedicated Heavy HMMWV.

Status: The BIDS was developed and produced at the U.S. Army Soldier and Biological Chemical Command, Aberdeen Proving Ground, Maryland. The NDI BIDS was fielded during FY96 and FY97. The P3I BIDS fielding was completed in February 2000.

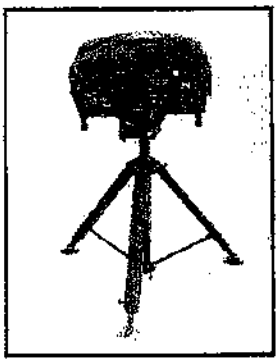
For additional information, please contact Director, Edgewood Chemical Biological Center, ATTN: AMSSB-REN-CW, Aberdeen Proving Ground, MD 21010-5424. The System Manager can also be reached by telephone at (410) 436-5541 or DSN 584-5541.

Rev. 10-23-01

M21 Automatic Chemical Agent Alarm



Description: The M21 Alarm is the first standoff chemical agent detector approved for fielding to the soldier. It detects both nerve and blister agents at line-of-sight distances up to 5 kilometers. In a stationary position, the M21 Alarm automatically scans a 60 degree arc. It is a passive infrared (IR) device that will react both audibly by horn and visually by illuminating either a blister or nerve light.



Mission: Identify nerve and blister agent vapors up to a 5-kilometer (km) distance

User: U.S. Army and U.S. Marine Corps

Capabilities:

- First fielded standoff chemical detector
- Allows commanders to identify and maneuver around contaminated areas
- Range is 5-km line-of-sight
- Uses passive infrared detection
- Increases the effectiveness of the Fox Reconnaissance System

For additional information, please contact Program Director-Detection, ATTN: AMSSB-PM-RNN-D, Aberdeen Proving Ground, MD 21010 - 5424. The Program Director can also be contacted by E-mail, by telephone at (410) 436-6587 or DSN 584-6587, or by fax to (410) 436-8929.

For additional information, please contact Director, Edgewood CB Center, ATTN: AMSSB-REN-ED, Aberdeen Proving Ground, MD 21010-5424. The System Manager can also be contacted by telephone at (410) 436-5626 or DSN 584-5626.

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Edgewood CB Center

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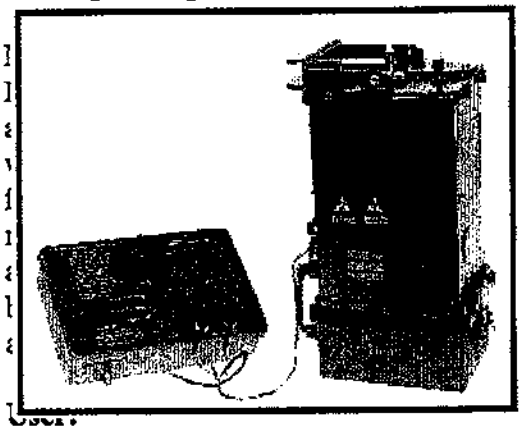
M22 Automatic Chemical Agent Alarm

Description: The M22 is an "off-the-shelf" automatic chemical agent alarm system capable of detecting and identifying standard blister and nerve agents. The M22 system is man-portable, operates independently after system start-up, and provides an audible and visual alarm. The M22 system also provides communications interface for automatic battlefield warning and reporting.



User:
U.S. Army, U.S. Navy, U.S. Air Force, and U.S. Marine Corps.

Capabilities:

- Area warning
- Collective Protection Equipment (CPE) monitoring
- Operation on and in vehicles
- Compatible with MICAD

Improvements over the M8A1 Automatic Chemical Agent Alarm System:

- Provides simultaneous detection and warning of nerve and blister agents
- Significantly more sensitive than M8A1
- Operates in a collective protection environment
- Much less response to interference

For information on Wipe Test Requirements, please click here.

For information on fielding and new equipment training, please click here.

For additional information, please contact Program Director-Detection, ATTN: AMSSB-PM-RNN-D, Aberdeen Proving Ground, MD 21010 - 5424. The Program Director can also be contacted by E-mail, by telephone at (410) 436-6587 or DSN 584-6587, or by fax to (410) 436-8929.

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Non-Developmental Item

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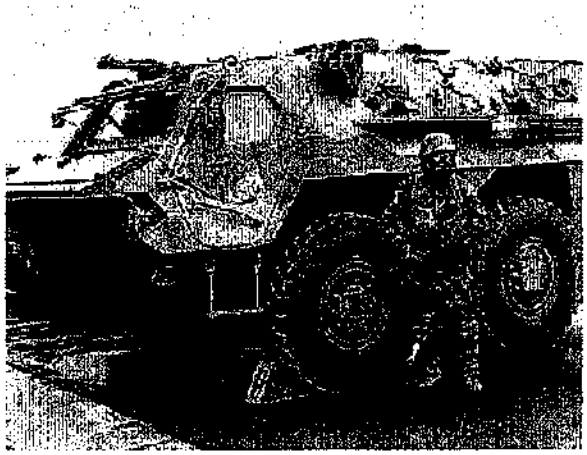
Joint Service General Purpose Mask (JSGPM)



Description: The JSGPM is designed to replace the M40/M42/MCU-2/P series masks. It will significantly reduce mission degradation and will be compatible with future equipment and soldier systems. The JSGPM will improve visual field-of-view and increase a soldier's abilityto perform mission essential tasks because physiological burdens, such as breathing resistance, will be reduced. A key feature of the mask will be reduced weight and bulk. The mask will be developed through a performance specification sponsored by the joint services.

Mission: Provide face, eye, and respiratory protection from battlefield concentrations of CB agents, toxins, toxic industrial materials and radioactive particulate matter.

User: All services - replaces current M40/M42 and MCU-2/P series protective masks.

Target Capabilities:

- Improved protection, including selected toxic industrial chemicals
- Improved field of view
- Lower breathing resistance
- Reduced weight/bulk
- Improved compatibility with sighting and targeting devices
- Significantly lower Total Ownership Cost (TOC)

Goal: 50% improvement over the existing M40 and MCU-2/P series

protective masks.

Major Accomplishments Last 12 months:

- Awarded Program Definition Risk Reduction (PDRR) Contract to Avon Rubber and Plastics, Cadillac, MI, on 30 Mar 00. Key partners include Avon Technical Products, Wiltshire, England, SAIC, Abingdon, MD, and Guild Associates, Inc., Columbus, OH.
- Conducted Concept Review on 6-8 Sep 00.
- Conducted Configuration Baseline Review on 22 May 01.
- Conducted Prototype Production Readiness Review on 14-15 Aug 01.

Plans for FY02:

- Approve TEMP Nov 01.
- Approve JALSP Nov 01.
- Conduct EDT Nov 01-Feb02.
- Conduct Interim Milestone B on 28 Mar 02.

For additional information, please contact the Program Director-Respiratory Protection, ATTN: AMSSB-PM-RNN-P, Aberdeen Proving Ground, MD 21010-5424. The Program Director can also be contacted by E-mail, by telephone at (410) 436-1776 or DSN 584-1776, or by fax to (410) 436-1383.

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Response To Questions From September 20, 2002 Meeting

NBC equipment and protective gear:
You can find a listing and descriptions of nuclear, biological and chemical detection equipment in the Army's inventory at: http://www.sbccom.army.mil/products/nbc.htm Samples of the information papers are attached. You can obtain more information on this issue by contacting the Headquarters' Public Affairs Office at:

E-mail: *public.affairs@sbccom.apgea.army.mil*

Headquarters' Address:

Commander
U.S. Army Soldier & Biological Chemical Command
ATTN: AMSSB-PA
5183 Blackhawk Road, Bldg. E5101, Rm. 225
Aberdeen Proving Ground, MD 21010-5424

Documenting immunizations, including the FDA approved Anthrax vaccine:

- DoD policies require the documentation of all immunizations given to service members. For deployments, the JCS requires immunizations to be recorded on the abbreviated medical record (DD Form 2766), supplemented as necessary by the pocket immunization record (PHS 731) and service-specific forms.
- The individual services have fielded electronic immunization tracking systems:
  - The Army uses its Medical Protection System (MEDPROS) to electronically record immunizations of its service members.
  - The Navy uses its Shipboard Automated Medical System (SAMS) to electronically record immunizations of its service members, then forwards this information through the Naval Medical Information Management Center (NMIMC) to the Defense Eligibility Enrollment Reporting System (DEERS).
  - The Air Force uses its Complete Immunizations Tracking Application (AF-CITA) to record immunizations given at both medical facilities and field locations, and indicates good success with all component members.
- There are initiatives to combine or link the data from these systems for both personal and population health purposes through DEERS, the Composite Health Care System (CHCS II) and the Theater Medical Information Program (TMIP).

Possible exposure of personnel and families to contaminated equipment
There has been no evidence that non-deployed military members or deployed members' families were exposed to biological and chemical contaminants from contact with equipment returning from the Gulf War.

CARC Paint
Military regulations and standard operating procedures require conformance to, and compliance with, public law and national consensus standards for the hazard communication program (HAZCOM). DoD Instruction 6050.5, the Department of Defense Hazard Communication Program, outlines responsibilities and procedures for a comprehensive hazard communication program that includes training for DoD personnel in potential occupational health hazards. Department of Defense personnel are to be informed of safe work practices and are to be trained in the selection, use, and availability of personal protective equipment (PPE) to prevent injuries and illnesses. It states that it is the Department of Defense policy to protect personnel from the adverse effects of workplace hazardous materials and waste, to reduce chemically related injuries and illnesses, and to establish and maintain a standardized hazardous materials information system. Each service and component is required to establish and maintain hazard communication programs that conform to the requirements of DoD Instruction 6050.5 and comply with the Occupational Safety and Health Administration (OSHA) hazard communication requirements.

Dormancy of biological and chemical agents in the Persian Gulf region
The Department of Defense subject matter experts have completed extensive research on the various biological and chemical agents that are believed to be in the inventory of potential adversaries in the region. They have good data on the dormancy of these agents. The U.S. Army Center for Health Promotion and Preventive Medicine (CHPPM) is responsible for and will conduct the appropriate monitoring and testing in the areas our servicemembers will be deployed.

What data is available to veterans and family members on studies concerning exposures and effects.
All the information we have concerning possible exposures to veterans of the Gulf War are posted on the GulfLINK web page to include associated government funded research.

OSHA standards in place in Desert Shield/Storm
OSHA standards do not apply to a combat theater. Manufacturers place warnings on the materials and liquids used to clean equipment that warn an individual of the dangers of exposure without proper equipment or improper use of these materials. It is the responsibility of the unit officers and NCO's to ensure their service members know, understand and follow these safety precautions.

Policies to ensure non-deployed service members are not exposed to battlefield contaminants
There is no indication that non-deployed servicemembers or family members were exposed to harmful battlefield contaminants. If there is any indication that deployed personnel and their equipment were exposed to chemical or biological weapons, the appropriate decontamination procedures will be accomplished. Additionally, personnel will be provided medical treatment and the follow-on health care and monitoring based on the type of exposure.

Samplings currently being conducted in Persian Gulf Region
The U.S. Army Center for Health Promotion and Preventive Medicine is responsible for conducting environmental surveillance. An information paper on their program is enclosed. You can obtain more information by visiting their web site at: http://chppm-www.apgea.army.mil/desp/pages/despinfo.htm

Smoke from burning oil wells, space heaters etc. and veterans' health
We have found no evidence to change the findings of our oil well paper nor the Institutes of Medicine findings that oil well fires did not cause, contribute or significantly impact veterans long-term health.

Military regulations related to environmental exposures
DoDD 6490.2, DoDI 6490.3 and JCSMCM-0006-02 are Department of Defense Regulations that relate to environmental exposures.

VAERS
The Assistant Secretary of Defense (Health Affairs) and all of the service Surgeons General have emphasized the importance of following the policy already in place for reporting vaccine adverse events. When adverse events occur at the treatment facility, medical care providers must ensure that the report is forwarded. When an adverse event occurs after the patient has departed the treatment facility, it is up to that individual to ensure the information gets reported. When administering vaccinations, medical care providers should be briefing the recipient on what to expect and what they should do if there is an adverse event.

Storage of pre-deployment blood samples
Pre-deployment blood samples are stored in such a manner that an individual's specimen can be retrieved for testing if necessary. If a servicemember's health is believed to have been impacted adversely by a deployment, the sample is available to medical care providers to assist in that servicemember's diagnosis and treatment.

Squalene
The Department of Defense has looked into the issue of squalene and, unless new information is discovered, believes it has been adequately addressed. DoD has funded research on this topic and studies are still underway.

Release of documents in reference to the destruction of nuclear reactors and bio-chemical bunkers under the Freedom of Information Act (FOIA)
FOIA provides exemptions on the release of information based on a variety of reasons. If there are documents that relate to the incidents referred to above, the information that falls into an exemption category would not be released. That would be the only reason all the documents related to the incidents referred to would not have been released.

Policy on use of Pyridostigmine Bromide and other Investigational New Drugs

- Public Law 105-261, the Strom Thurmond National Defense Authorization Act For Fiscal Year 1999, amended section 1107 of title 10, United States Code by specifying that only the President may waive the requirement for informed consent to administer an investigational new drug (IND) or drug unapproved for its applied use to a member of the armed forces. The law further specifies the conditions under which the President may grant such a waiver and that the Secretary of Defense is the only official who may request such a waiver. When a waiver is granted by the President, the Secretary must notify the chairman and ranking minority members of the four congressional committees most concerned with defense. The President may grant a waiver only if he/she determines, in writing, that obtaining consent is not feasible, is contrary to the best interests of the member, or is not in the interests of national security.

- Executive Order 13139, 30 September 1999, spells out the manner in which the above requirements will be executed. The Order indicates the steps by which the Secretary will develop a waiver request for the President, perform the necessary congressional and public notifications, and monitor the adherence to the provisions of the order and other regulations. The Order also spells out requirements for training and informing military personnel and commanders about the use of the investigational drug.

- In making determination to waive the informed consent requirement, the President must apply the standards set forth by relevant FDA regulations (21 CFR 50.23). This includes 1) Service member is confronted by a life-threatening situation, 2) no FDA approved alternative method exists, 3) and the SECDEF has determined that waiver is in the best interest of the forces at risk.

- DoD Directive 6200.2, August 1, 2000 establishes policy and assigns responsibility for carrying out the requirements of the law and the Executive Order.

- DoD scientists are developing research protocols for various IND products, such as Pyridostigmine Bromide (PB).

Desert Storm Battle Registry attendance at Deployment Health Support Directorate Roundtables

The Desert Storm Battle Registry is a group of concerned veterans. As we have stated on numerous occasions, our office will communicate on a routine basis with servicemembers, veterans, their families and the public. The veterans and military service roundtable meeting is an opportunity for Department of Defense representatives to meet with organizations that officially represent their millions of members. Mr. Love and Mr. Lyons have been informed about the criteria the Desert Storm Battle Registry must meet in order to be invited to monthly roundtables with the recognized veteran and military organization representatives.

How many Gulf War veterans were medically discharged? Died?
We were not able to determine how many Gulf War veterans were medically discharged. Information provided by the Social Security Administration identified 9113 Gulf War veterans have died.

SPECT
Medical care providers will recommend a SPECT scan if clinically indicated. They are not done routinely because the utility of SPECT scans is still the subject of research. Until indications for SPECT scans are clearer, routine use of this procedure as a screening test, which involves exposing the patient to radiation, should only be done as part of an approved research study where participants give their informed consent.

Are sufficient force health protection measures in place
The Department of Defense believes that the force health protection policy, training and protective measures in place are sufficient to protect our service members.

Planned destruction of CCEP and Gulf War Registry original evaluation documents
We are not aware of any plan to destroy original CCEP or Gulf War Registry evaluation records. CCEP evaluation records are already being archived at NARA.

U.S. Army Medical Research and Material Command research solicitation
Contact the U.S. Army Medical Research and Material Command Public Affairs Office MCMR-PA at (301) 619-2736 for information on their research program.

The request on providing all the document titles associated with DOEHR must be submitted under the Freedom of Information Act (FOIA) to the Department of Defense FOIA office. Their address is:

Directorate of Freedom of Information Act and Security Review
Room 2C757
1157 Defense Pentagon
Washington, D.C. 20301-1155

Has Dr. Kilpatrick read Doug Rokke's address at the Fall Congressional/Coalition Leadership Breakfast
Dr. Kilpatrick has not read Doug Rokke's address at the Fall Congressional/Coalition Leadership breakfast. Our organization was not aware that he had addressed that forum and has not received a copy of text of the address.

SHAD
All the information we have available on SHAD is posted to our DeploymentLINK. You can find the information at:
http://deploymentlink.osd.mil/current_issues/shad/shad_intro.shtml

Recommendation to conduct a study of Gulf War veterans who received anthrax vaccine versus control group that did not
We will forward this recommendation to the research working group.

Leishmaniasis

DoD-funded research into diagnostic methods and treatment for leishmaniasis continues today as it has for decades. Please refer to the Medsearch web site for research projects funded since the Gulf War. Military researchers' work in this area is a modest, but important, part of global research efforts directed against the various forms of leishmanial disease which threaten large portions of the world's population outside the United States. Military interest in leishmaniasis has historically reflected concerns about this threat to deployed US forces. Unfortunately, standards for the diagnosis and treatment of leishmaniasis have not changed dramatically since 1991. Research into the development of a serological test for leishmanial infection has so far failed to yield a new, practicable test. In the absence of such a test, laboratory confirmation of the diagnosis depends upon either microscopic examination of biopsy material or a positive culture of a biopsied lesion or organ. Walter Reed Army Institute of Research investigators have found that an investigational test using PCR methodology has shown great promise in diagnosing cutaneous disease. In underdeveloped parts of the world without sophisticated medical care, the diagnosis of cutaneous leishmaniasis is often made on clinical grounds, without the use of supplementary testing. The principal treatments used around the world for the more serious forms of leishmaniasis consist of pentavalent antimony and Amphotericin B. The latter has recently been approved by the FDA for treatment of visceral leishmaniasis. Research into new treatments, including possible oral and topical medications, has identified several new, promising drugs.

Plum Island and mycoplasma development for biological warfare purposes

There was no program to develop mycoplasma as a biological weapon. The history of Plum Island in New York includes information that the U.S. Army Chemical Corps had been planning an animal disease research laboratory there in the early 1950's. At the completion of all construction work on May 26, 1954, the Chemical Corps' Plum Island new facility was officially deactivated, without ever having been used. The United States Department of Agriculture (USDA) was designated to receive the transfer of Plum Island in 1952, about the time when the Chemical Corps was initiating the laboratory building process. On July 1, 1954, the Army officially transferred the property of Plum Island to the USDA. The new Animal Disease Laboratory building 101 compound was dedicated on Sept. 26, 1956. All of the buildings renovated by the Chemical Corps in 1952-54 were occupied by the new Plum Island Animal Disease Center (PIADC). In October 1991, all operation and maintenance activities were privatized, transferring to a contractor (under USDA supervision) all personnel involved in these activities. Currently the operations and maintenance of the PIADC are conducted through a contract with LB&B Associates, Inc., headquartered in Columbia, Md.

Pesticide Exposures

The Department of Defense has instituted changes in training and the use of pesticides. Pesticides use and misuse have not been ruled out as possible causes of some of the symptoms and illnesses experienced by some Gulf War veterans. Research continues.

CDC Conference report on Carbon Monoxide Exposure
The Centers for Disease Control (CDC) have information on carbon monoxide exposure on their web site at: *http://www.cdc.gov/nceh/airpollution/carbonmonoxide/default.htm*

Nerve Agent Exposures
The Department of Defense has acknowledged that some Gulf War veterans were possibly exposed to low levels of chemical agents and that it is not clear what the long-term health implications are for this possible exposure. Research continues in this area.

Milk Factory
This issue was looked into before and there was no evidence to indicate that any further investigation was necessary.

Patient Treatment by DoD, VA and Civilian Doctors
We recognize that the Department of Defense could have done better in handling the illnesses experienced by Gulf War veterans. An effort has been made to better educate and sensitize our medical care providers to the problems Gulf War veterans have experienced. As a result the following actions have occurred.

- The National Defense Authorization Act for Fiscal Year 1999 authorized the Secretary of Defense to "...establish a center devoted to a longitudinal study to evaluate data on the health conditions of members of the Armed Forces upon their return from deployment on military operations for the purposes of ensuring the rapid identification of any trends in diseases, illnesses, or injuries...."

- The goal of the three DoD centers is "...to improve our ability to identify, treat, and minimize or eliminate the short- and long-term adverse effects of military service on the physical and mental health of veterans."

- The Deployment Health Research Center has been directly engaged with the VA in the IOM-recommended Millennium Cohort Study to evaluate whether deployment-related exposures are associated with post-deployment health outcomes. It also manages the national DoD Birth Defects Registry.

- The Deployment Health Clinical Center has been a leading proponent for the development of post-deployment health evaluation and management clinical practice guidelines, which have recently been implemented throughout the DoD and VA health systems.

- The Deployment Health Surveillance Center is the DoD proponent for the identification of and response to medical threats associated with deployments and, most recently, acts of terrorism.

Rescue Workers
The Centers for Disease Control (CDC) are looking into health issues concerning the rescue workers and personnel who worked in buildings in the vicinity of the World Trade Center at the time of the attack. You can obtain information on this issue from the CDC web site at: *http://www.cdc.gov/niosh/emres01.html*

West Nile Virus

According to the Centers for Disease Control West Nile virus is spread by the bite of an infected mosquito, and can infect people, horses, many types of birds, and some other animals. Most people who become infected with West Nile virus will have either no symptoms or only mild ones. However, on rare occasions, West Nile virus infection can result in severe and sometimes fatal illnesses. There is no evidence to suggest that West Nile virus can be spread from person to person or from animal to person except as recently occurred in this country through blood transfusion or organ transplantation. If you would like more information on West Nile Virus, visit the CDC web site at the following address: *http://www.cdc.gov/ncidod/dvbid/westnile/qa/overview.htm*

Several of the attendees at the meeting asked questions concerning Department of Veterans Affairs issues to include benefits, service-connected disabilities, VA training VACOLS, GWVIS availability to researchers, benefits and health care associated with SHAD, and veteran studies. All of these questions have been referred to the Department of Veterans Affairs for response.

DEPARTMENT OF DEFENSE
ARMED FORCES EPIDEMIOLOGICAL BOARD
5109 LEESBURG PIKE
FALLS CHURCH, VA 22041-3258

REPLY TO
ATTENTION OF

AFEB

AUG 12 2002

MEMORANDUM FOR

The Assistant Secretary of Defense (Health Affairs)
The Surgeon General, Department of The Army
The Surgeon General, Department of The Navy
The Surgeon General, Department of The Air Force

SUBJECT: Therapeutics Against Biowarfare Agents - 2002-09

1. References:

a. Memorandum, OASD(HA)/FHP&R, 13 March 2002, Therapeutics Against Biowarfare Agents.

b. Memorandum, AFEB 00-09, 3 Aug 2000, Antibiotics Against Biowarfare Agents.

c. Department of Defense Directive 6205.3, "Use Of Investigational New Drugs For Force Health Protection," dated August 1, 2000.

2. The Armed Forces Epidemiological Board (AFEB) annually provides recommendations to the Assistant Secretary of Defense for Health Affairs and the DoD Executive Agent on vaccines and immunization protocols necessary to enhance protection against validated biological warfare threat agents. On March 13, 2002 the AFEB was requested as part of this requirement to also review existing Joint Operational Requirement Documents, progress on specific efforts to obtain new indications for existing therapeutics, and acquisition status of biologics (treatment and prophylaxis) against the current prioritized list of biowarfare agents and finally, to make recommendations on the current status of requirements and suggested priorities.

3. On 21 and 22 May 2002 the AFEB met to consider the biological threat agents designated by the Chairman of the Joint Chiefs of Staff. The Board received briefings on the current intelligence based biological warfare threat, the Medical Biological Defense Research Program, the Joint Vaccine Acquisition Program, and a Medical Requirements Review from the Joint Service Integration Group of the Chemical and Biological (CB) Defense Program. The Board noted that the current intelligence based biological warfare threat list had not been formally validated by the Chairman of the Joint Chiefs of Staff.

4. The AFEB has previously made recommendations on the most appropriate antibiotics to be used for treatment and prevention of illnesses from biowarfare agents. Some of the antibiotics recommended were not labeled for these indications, thus potentially requiring their use as an investigational new drug (IND) under a protocol which would require written informed consent. Upon making these recommendations, the Board felt that the labeling status should not be a determining factor if there was a clear best option based on other criteria. However, the Board does recognize that it may not be feasible from an operational, logistical, or combat readiness point of view to use drugs under an IND status and the preference is for use of an approved and labeled product whenever possible.

5. To assist with review of the available products, either approved or labeled, as an IND with or without a protocol, or under research and development, the Board worked with the Military Services and produced a matrix listing available vaccines and therapeutics. The recommendations on vaccines, antibiotics and therapeutics are based on this rank ordered matrix. From this review and cognizant of the questions posed to the Board, the Board makes the following findings and recommendations:

a. NO JOINT OPERATIONAL REQUIREMENT DOCUMENTS CURRENTLY EXIST WITH THE GOAL OF OBTAINING NEEDED NEW INDICATIONS FOR EXISTING THERAPEUTICS FOR TREATMENT OR PROPHYLAXIS AGAINST BIOWARFARE AGENTS.

b. OTHER THAN FOR ANTHRAX, LITTLE TO NO PROGRESS HAS BEEN MADE IN OBTAINING NEW INDICATIONS FOR EXISTING THERAPEUTICS.

c. THE ACQUISITION STATUS OF BIOLOGICS (FOR TREATMENT OR PROPHYLAXIS) AGAINST THE CURRENT PRIORITIZED LIST OF BIOWARFARE AGENTS IS FOCUSED EXCLUSIVELY ON VACCINES, WITH TIMELINES FOR AVAILABLE APPROVED AND LABELED PRODUCTS PROJECTED SEVERAL YEARS IN THE FUTURE.

d. THE DOD SHOULD VIGOROUSLY PURSUE EFFORTS TO DEVELOP FDA APPROVED VACCINES AGAINST THE VALIDATED BIOWARFARE AGENTS.

e. RECOGNIZING THE EXTENDED GAP IN THE AVAILABILITY OF APPROVED VACCINES AGAINST BIOWARFARE AGENTS, THE DOD SHOULD INITIATE IMMEDIATE DEVELOPMENT OF JOINT OPERATIONAL REQUIREMENT DOCUMENTS TO: 1) OBTAIN NEW INDICATIONS FOR EXISTING THERAPEUTICS FOR TREATMENT OR PROPHYLAXIS AGAINST BIOWARFARE AGENTS, 2) DEVELOP NEEDED IND APPLICATIONS, 3) DEVELOP NEEDED TREATMENT PROTOCOLS, AND 4) FUND THE RESEARCH NEEDED TO SUPPORT

AFEB (15-1a) 2002-09
SUBJECT: Therapeutics Against Biowarfare Agents

FDA APPROVAL OF DRUGS AND BIOLOGICS FOR THE BIOWARFARE INDICATIONS PREVIOUSLY RECOMMENDED BY THE AFEB.

6. The above recommendations were unanimously approved.

FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD:

STEPHEN M. OSTROFF, M.D.
AFEB, President

JAMES R. RIDDLE, D.V.M., M.P.H.
Colonel, USAF, BSC
AFEB Executive Secretary

3 Encls
1. DoDD 6200.2/6205.3 (Force Health Protection) - Vaccine, Therapeutics, and Prophylaxis
2. Memorandum, OASD(HA)/FHP&R, 13 March 2002, Therapeutics Against Biowarfare Agents
3. Memorandum, AFEB 00-09, 3 Aug 2000, Antibiotics Against Biowarfare Agents.

CF:
Board Members and Consultants (w/o Encls)
USAMRMC (w/o Encls)
USAMRIID (w/o Encls)
USD(AT&L) (w/o Encls)
Joint Vaccine Acquisition Program (w/o Encls)
J4-MRD (w/o Encls)
DASG-HCF (w/o Encls)
JSIG (w/o Encls)
DATSD(CBD) (w/o Encls)
AMEDD(C&S) (w/o Encls)

DoDD 6200.2/6205.3 (Force Health Protection) - Vaccine, Therapeutics, and Prophylaxis[1,2]
(AFEB May 2002 Working Papers)

DISEASE ***Anthrax***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) - Treatment	COMMENTS
FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)	**Anthrax Vaccine** (Preexposure) Bioport vaccine (licensed) 0.5 mL SC @ 0, 2, 4 wk, 6, 12, 18 mo then annual boosters	**ciprofloxacin** (Px) 500 mg PO bid x 60 days **doxycycline** (Px) 100 mg PO bid x 60 days **Penicillin V Potassium** (Px) 500 mg q 6 h x 60 days	**ciprofloxacin** (Rx) 400 mg IV q 12 h initially then by mouth x 60 days (adult) 15 mg/kg/dose NTE 500mg/dose q12hr x 60 days (pediatric) **doxycycline** (Rx) 200 mg IV, then 100 mg IV q 12 h **Penicillin** (Rx) 4 million units IV q 4 h	In an experimental study of monkeys, injection with the anthrax vaccine at 0 and 2 weeks offered complete protection against aerosol anthrax challenge at 8 and 38 weeks and 88% effectiveness at 100 weeks. Anthrax vaccine may cause soreness, redness, itching, swelling, and nodules at the injection site. About 30% of men and 60% of women report these local reactions. For both genders, between 1% and 5% report reactions of 1 to 5 inches in diameter. Serious events, such as those requiring hospitalization, are rare; once per 200,000 doses. Ciprofloxacin and doxycycline prepositioned for deployed forces. PenVK for sensitive organisms only. Once sensitivity data is available then consider switching children to penicillin or amoxicillin. Combined antibiotic regimen may be more effective for treatment. Per AFEB 00-09, first choice for treatment is ciprofloxacin and second choice is doxycycline. Per AFEB 00-09, first choice for post-exposure prophylaxis is ciprofloxacin and second choice is doxycycline.
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)	**Anthrax Vaccine** (Rx/Px) FDA accepted DoD BB-IND #1081/Contingency Use Protocol for volunteer anthrax vaccination Rx/Px SC @ 0, 2, 4 wk *in* combination with approved and labeled antibiotics			If unvaccinated, begin initial doses of vaccine under FDA accepted DoD IND/Protocol Implementation guide available for vaccine use IND post exposure w/ antibiotics. CDC has IND to conduct study to investigate reduced dose and IM administration of vaccine. DoD (AVIP) to conduct follow-up reduced dose/IM administration of vaccine under BioPort BB-IND #7281.
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				JVAP May 2002 projects next generation Anthrax Vaccine baseline IND stockpile quantities obtained FY06. Potential alternates for Rx: gentamicin, erythromycin, and chloramphenicol. CDC treatment protocol for use of Anthrax Human Immune Globulin (AIG).

[1] USAMMA-HHS reciprocal support agreement for access to the National Pharmaceutical Stockpile.

[2] Rank ordered matrix with recommended interventions listed in order of optimal choice.

DISEASE ***Botulinum Toxins***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) - Treatment	COMMENTS
FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				Skin test for hypersensitivity before equine antitoxin administration. CDC has limited quantities of trivalent equine antitoxin for serotypes A, B, E. A, B is licensed by Connaught; and E is a CDC IND Product. CDC trivalent equine antitoxin (CDC IND #6750), A,B, E.
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)	**Pentavalent Toxoid** (Preexposure) FDA Accepted DoD BB-IND #3723/Laboratory Use Protocol for pentavalent toxoid (scrotypes A – E), 0.5 ml deep SC @ 0, 2 & 12 wk, then yearly boosters DoD IRB Approved Contingency Use Protocol to be submitted to BB-IND #3723,CDC#161 (06/02) (CDC BB-IND #161: SIP program administered under this IND)		**Heptavalent Equine Despeciated Antitoxin** (Rx) FDA accepted DoD BB-IND #7451/ Treatment Use Protocol for heptavalent equine despeciated antitoxin for serotypes A-G: 1 vial (10 mL) IV **Botulinum Immune Globulin (First Flight)** (Rx) FDA accepted DoD BB-IND #3703/ Treatment Use Protocol for Botulinum Immune Globulin (BIG), $F(ab')_2$, Heptavalent, Equine **Whole IgG (Human) Pentavalent** (Rx) FDA accepted DoD BB-IND #1332/ Treatment Use Protocol for Botulism Immune Globulin Pentavalent (Human) (A-E)	
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)	**Pentavalent Toxoid** (Preexposure) DoD pentavalent toxoid Contingency Use Protocol awaiting DoD IRB approval (06/02); will be submitted to FDA under BB-IND 3723		**Heptavalent Equine Despeciated Antitoxin** (Rx) **Botulinum Immune Globulin (First Flight)** (Rx) **Whole IgG (Human)** (Rx) DoD IND #7451,3703,1332/ Umbrella Emergency Use Protocol awaiting DoD IRB approval. (06/02); will be submitted to FDA under new IND	JVAP May 2002 projects rBotulinum Bi-valent (AB) IND stockpile quantities obtained FY06.

DISEASE ***Plague***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) - Treatment	COMMENTS
FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)			**gentamicin** (Rx) **doxycycline** (Rx) 200 mg IV then 100 mg IV bid, until clinically improved then 100mg PO bid for total of 10-14 d **doxycycline** (Rx) 100 mg PO q 12 h x 5-7 d continued at least 2 d after afebrile **Streptomycin** (Rx) 2 grams daily in 2 divided doses IM. A minimum of 10 days of therapy is recommended **Tetracycline** (Rx) 1-2 grams divided in two or four equal doses continued at least 2 d after afebrile	Greer inactivated vaccine (FDA licensed) is no longer available. Gentamicin - Approved indication, no dosage information provided. Standard dose in subjects with serious infections and normal renal function is 3mg/kg/day in 3 divided doses (q8h). Doxycycline is not the recommended treatment.
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)		**doxycycline** (Px) 100 mg PO bid x 7 d or duration of exposure **ciprofloxacin** (Px) 500 mg PO bid x 7 d **Tetracycline** (Px) 500 mg PO qid x 7 d	**gentamicin** (Rx) 5mg/kg or IV once daily x 10 - 14 d **ciprofloxacin** (Rx) 400mg IV q 12 h until clinically improved then 750 mg PO bid for total of 10 –14 d **doxycycline** (Rx) 200 mg IV, then 100 mg IV bid, until clinically improved then 100mg PO bid for total of 10-14 d. **Tetracycline** (Rx) 1-2 grams divided in two or four equal doses continued at least 2 d after afebrile.	Per AFEB 00-09, first choice is gentamicin and second choice is ciprofloxacin. Per AFEB 00-09, first choice for post-exposure prophylaxis is doxycycline and second choice is ciprofloxacin. Chloramphenicol for plague meningitis. 25 mg/kg IV, then 15 mg/kg qid x 14 d Alternate Rx: trimethoprim-sulfamethoxazole JVAP May 2002 projects plague vaccine IND stockpile quantities obtained FY08.

DISEASE ***Ricin Toxin***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) - Treatment	COMMENTS
FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				Inhalation: supportive therapy G-I : gastric lavage, superactivated charcoal, cathartics. IND #6181 withdrawn 8/12/96.
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				JVAP May 2002 lists Ricin vaccine in tech base and projects ricin vaccine IND stockpile quantities obtained FY08.

DISEASE ***Encephalitis Viruses***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) – Treatment	COMMENTS
FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				Supportive therapy: analgesics and anticonvulsants prn.
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)	**VEE Live Attenuated Vaccine** (Preexposure) FDA Accepted DoD BB-IND #142/ Laboratory Use Protocol for VEE TC-83 live attenuated vaccine: 0.5 mL SC x1 dose **VEE Inactivated Vaccine** (Preexposure) FDA Accepted DoD BB-IND #914/ Laboratory Use Protocol for VEE C-84 vaccine: (formalin inactivated TC-83), 0.5 mL SC for up to 3 doses **EEE Inactivated Vaccine** (Preexposure) FDA Accepted DoD BB-IND #266/ Laboratory Use Protocol for EEE inactivated vaccine: 0.5 mL SC at 0 & 28 d **WEE Inactivated Vaccine** (Preexposure) FDA Accepted DoD BB-IND #2013/ Laboratory Use Protocol for WEE inactivated vaccine:0.5 mL SC at 0, 7, and 28 d			VEE vaccine manufactured in 1965. Live, attenuated vaccine, with significant side effects. 25%-35% or recipients require 2-3 days bed rest. Time to develop immunity – 8 weeks. Must be given prior to EEE or WEE (if administered subsequent, antibody response decreases from 81% to 67%). VEE TC-83 reactogenic in 20%. No seroconversion in 20%. Only effective against subtypes 1A, 1B, and 1C. VEE C-84 vaccine used for non-responders to VEE TC-83. WEE vaccine manufactured in 1991. Antibody response is poor, requires 3-dose primary (one month) and 3-4 boosters (one month apart). Primary series antibody response in 29%, 66% after four boosts. Time to develop immunity – six months. EEE manufactured in 1989. Antibody response is poor, requires 3-dose primary (one month) and 1-2 boosters (one month apart). Primary series yields antibody response in 77%; 5%-10% of non-responders after boosts. Time to immunity – 3 months. EEE and WEE inactivated vaccines are poorly immunogenic. Multiple immunizations are required.
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				Multivalent VEE vaccine advanced development funded through FY04.

DISEASE ***Tularemia***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) - Treatment	COMMENTS
Tularemia FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)			**Streptomycin (Rx)** 1-2 grams daily IM in divided doses x 7-14 days until patient is afebrile for 5-7 days **doxycycline (Rx)** 100 mg PO q 12 h x 5-7 d continued at least 2 d after afebrile **doxycycline (Rx)** 200 mg IV, then 100 mg IV q 12 h **Tetracycline (Rx)** 1-2 grams divided in two or four equal doses continued at least 2 d after afebrile	Streptomycin is not the recommended treatment, is in limited supply and may be difficult to obtain.
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)	**Live attenuated vaccine** (Preexposure) FDA Accepted DoD BB-IND #157/ Laboratory Use Protocol for live attenuated vaccine: single 0.1ml dose by scarification			Vaccine manufactured in 1964. Vaccine cannot be used because of FDA "clinical hold". FDA requires study report of 35 years of clinical trials. FDA unlikely to review new protocols.
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)		**ciprofloxacin (Px)** 500 mg PO q 12 h for 14 d **doxycycline (Px)** 100 mg PO bid x 14 d **Tetracycline (Px)** 500 mg PO qid x 14 d	**gentamicin (Rx)** 3-5 mg/kg/d IV x 10-14 d **ciprofloxacin (Rx)** 400 mg IV q 12h until improved, then 500 mg PO q 12 h for total of 10 - 14 d **ciprofloxacin (Rx)** 750 mg PO q 12 h for 10 - 14 d	Per AFEB 00-09, the first choice for treatment is gentamicin and second choice is ciprofloxacin. Per AFEB 00-09, first choice for post-exposure prophylaxis is ciprofloxacin and second choice is doxycycline. JVAP May 2002 projects tularemia vaccine IND stockpile quantities obtained FY05.

DISEASE ***Smallpox***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) – Treatment	COMMENTS
FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)	**Dryvax** (Preexposure) Dryvax (1:1) CDC BB-IND#9829/ Contingency Use Protocol for vaccination in response to act of Bioterrorism Dryvax (1:1) CDC BB-IND#9829/ Laboratory Use Protocol **TSI (Salk) Vaccine** (Preexposure) TSI (Salk) Vaccine DoD BB-IND #4984/ No Protocol			
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)	**Dryvax** (Preexposure) **Dynport Vaccine** (Preexposure) DoD JVAP IND. **Acambis/Acambis-Baxter** (Preexposure) CDC/DHHS IND. **Dryvax** (Postexposure) Dryvax (1:1) DoD IND/ Contingency Use Protocol awaiting DoD IRB approval (06/02); will be submitted to FDA under new IND		**VIG (Vaccinia Immune Globulin)** (Rx) FDA Accepted DoD BB-IND #8429/ Treatment Use Protocol for disseminated vaccinia for laboratory workers: VIG 0.3-0.6 ml/kg infusion Treatment/Emergency Use Protocol for VIG to treat deployable forces for disseminated vaccinia awaiting DoD IRB approval (06/02); will be submitted to FDA under BB-IND #8429 **Cidofovir 5 mg/kg infusion** (Rx) Cidofovir Treatment/Emergency Use Protocol for smallpox treatment awaiting DoD IRB approval (06/02); will be submitted to FDA under new IND Cidofovir Treatment/Emergency Use Protocol for disseminated vaccinia treatment to be submitted to the USAMRIID Human Use Committee (06/02); will be submitted to DoD IRB; will submit under previous cidofovir IND	Dryvax - Wyeth calf lymph vaccinia vaccine 100 dose vials undiluted: 1 dose by scarification. Greater than 97% take after one dose within 14 days of administration. Contraindications include pregnancy, history of eczema or the presence of active skin diseases, and immunodeficiency. Potential complications include encephalitis and generalized vaccina. It is estimated up to one death (up to five deaths per million in unvaccinated adults) and 74 complications occur per million vaccinations in the general population. Dryvax is effective up to 4 days post exposure. Pre and post exposure vaccination recommended if > 3 years since last vaccine JVAP May 2002 projects Vaccinia, Cell Culture Derived vaccine IND stockpile quantities obtained FY03.

DISEASE ***Staphylococcus Enterotoxins***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) – Treatment	COMMENTS
FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				Ventilatory support for inhalation exposure.
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				JVAP May 2002 projects Staphyloccal Enterotoxin Vaccine IND stockpile quantities obtained FY09.

DISEASE ***Marburg/Ebola***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) - Treatment	COMMENTS
FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				Aggressive supportive care and management of hypotension very important. Human antibody used with apparent beneficial effect in uncontrolled human trials.
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				AHF Candid #1 vaccine (x-protection for BHF) (IND) RVF inactivated vaccine (TSG IND 365) TSG IND 4307 Live attenuated MP 12 vaccine Ribavirin (CCHF/Lassa/KHF) (TSG IND #16666 30 mg/kg IV initial dose; then 16 mg/kg IV q 6 h x 4 d; then 8 mg/kg IV q 8 h x 6 d
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)				Passive antibody for AHF, BHF, Lassa fever, and CCHF. JVAP May 2002 lists Marburg and Ebola vaccine in tech base and projects IND product obtained in FY09 and FY12 for Marburg and Ebola respectively.

DISEASE ***Q Fever***	VACCINE/TOXOID (Rx/Px) Preexposure (Rx) - Treatment (Px) - Postexposure Prophylaxis	CHEMOPROPHYLAXIS (Px) (Px) - Postexposure Prophylaxis	CHEMOTHERAPY (Rx) (Rx) - Treatment	COMMENTS
FDA Approved & Labeled Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)			**doxycycline** (Rx) 100 mg PO q 12 h x 5-7 d continued at least 2 d after afebrile **doxycycline** (Rx) IV 100mg IV q12h **Tetracycline** (Rx) 1-2 grams divided in two or four equal doses continued at least 2 d after afebrile	Per AFEB 00-09, the first choice for treatment is doxycycline.
DoD IRB Approved and/or FDA Accepted IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)	**Inactivated Whole Cell Vaccine** (Preexposure) FDA Accepted DoD BB-IND #610/ Laboratory Use Protocol for Inactivated Whole Cell Vaccine: Single 0.5 ml s.c. injection; SIP protocol			Q-Fever vaccine manufactured in 1970. Significant side effects if administered inappropriately; sterile abscesses if prior exposure/skin testing required prior to vaccination. Time to develop immunity – 5 weeks.
No IND/Protocol Preexposure Treatment (Rx) Postexposure Prophylaxis (Px)		**doxycycline** (Px) 100 mg PO bid x 5 d (start 8-12 d post-exposure) **Tetracycline** (Px) 500 mg PO qid x 5 d (start 8-12 d post-exposure)		Per AFEB 00-09, first choice for post-exposure prophylaxis is doxycycline.

Department of Defense

DIRECTIVE

NUMBER 6200.2

August 1, 2000

ASD(HA)

SUBJECT: Use of Investigational New Drugs for Force Health Protection

References: (a) Section 1107 of title 10, United States Code
(b) Executive Order 13139, "Improving Health Protection of Military Personnel Participating in Particular Military Operations," September 30, 1999
(c) Title 21, Code of Federal Regulations, Parts 50, 56, 312, Subpart I of Part 314, Subpart G of Part 601, current edition
(d) House Report No. 105-736, Conference Report to Accompany Proposed Strom Thurmond National Defense Authorization Act for Fiscal Year 1999, page 685
(e) through (f), see enclosure 1

1. PURPOSE

This Directive:

1.1. Establishes policy and assigns responsibility for compliance with references (a) through (c) for the use of investigational new drugs for force health protection.

1.2. Designates the Secretary of the Army as the DoD Executive Agent for the use of investigational new drugs for force health protection.

2. APPLICABILITY AND SCOPE

This Directive:

2.1. Applies to the Office of the Secretary of Defense, the Military Departments, the Chairman of the Joint Chiefs of Staff, the Combatant Commands, the Office of the

Inspector General of the Department of Defense, the Defense Agencies, the DoD Field Activities and all other organizational entities within the Department of Defense (hereafter referred to collectively as "the DoD Components").

2.2. Applies to all uses of investigational new drugs by the Department of Defense for force health protection.

2.3. Does not apply to actions by DoD healthcare providers that are within standard medical practice in the United States and are not subject to FDA regulations at reference (c).

3. DEFINITIONS

3.1. Force Health Protection. An organized program of healthcare preventive or therapeutic treatment, or preparations for such treatment, designed to meet the actual, anticipated, or potential needs of a group of military personnel in relation to military missions.

3.2. Investigational New Drug (IND). A drug or biological product subject to the FDA regulations at 21 CFR Part 312 (reference (c)), including:

3.2.1. A drug not approved or a biological product not licensed by the FDA.

3.2.2. A drug unapproved for its applied use.

3.3. Drug Unapproved for Its Applied Use. A drug or biological product administered for a use not described in the labeling of the drug or biological product approved by the FDA (referred to in subsection (g)(2) of reference (a)), and for which FDA requirements of use authorization and prior informed consent (referred to in subsections (d)(4) and (f)(1) of reference (a)) are applicable, but not including uses to which those requirements are inapplicable based on standard medical practice in the United States (referred to in reference (d)).

3.4. Particular Military Operations. A military operation or specific military mission or function, which involves any chemical, biological, or radiological warfare or endemic disease threats.

4. POLICY

It is DoD policy that:

4.1. Force Health Protection. Personnel carrying out military operations shall be provided the best possible force health protection, including safe and effective medical countermeasures to chemical, biological or radiological warfare and endemic disease threats.

4.1.1. DoD Components shall make preferential use of products approved by the FDA for general commercial marketing, when available, to provide the needed medical countermeasure.

4.1.2. When no FDA-approved product is available to meet a foreseeable threat, the Secretary of the Army, as Executive Agent, shall carry out appropriate research and development program activities directed toward obtaining general commercial marketing approval by the FDA of safe and effective medical countermeasures. Such activities shall include use of special FDA rules at 21 CFR subpart I of part 312 and subpart G of part 601 (reference (c)) for the approval of new drugs and biological products for use against lethal or permanently disabling toxic substances when efficacy studies in humans cannot be conducted ethically.

4.1.3. When, at the time of the need for a force health protection countermeasure against a particular threat, no safe and effective FDA-approved drug or biological product is available, DoD Components may request approval of the Secretary of Defense to use an IND. Such requests must be justified based on the available evidence of the safety and efficacy of the drug and the nature and degree of the threat to personnel.

4.1.4. When using INDs for force health protection, DoD Components shall comply with 10 U.S.C. 1107, E.O. 13139, and applicable FDA regulations (references (a) through(c)).

4.2. Approval by the Secretary of Defense to Use INDs. Use of an IND for force health protection requires approval of the Secretary of Defense.

4.2.1. A Commander of a Combatant Command shall submit a request through the Chairman of the Joint Chiefs of Staff (CJCS), coordinated with the ASD(HA), the USD(Policy), Secretary of the Army as Executive Agent, and DoD General Counsel. Such a request must document a confirmed, high threat for which

the use of an IND is needed, consideration of the risks and benefits of use of the IND, and compliance with the requirements of this Directive.

4.2.2. The Secretary of the Army, as Executive Agent, in concert with the Commander of the Combatant Command involved and the ASD(HA), shall develop a specific treatment protocol for use of the IND. The protocol shall comply with 21 CFR Part 312 (reference (c)). The protocol shall be approved by the Army Surgeon General's Human Subjects Research Review Board (HSRRB), a duly constituted Institutional Review Board under 21 CFR Part 56 (reference (c)), prior to submission to the FDA for review under 21 CFR Part 312 (reference (c)). Unless the Secretary requests a waiver by the President, the protocol will provide for, consistent with 21 CFR Part 50 (reference (c)), the prior informed consent of members receiving the IND. If the request for use of the IND also includes a request for waiver of informed consent, the requirements of sections 4.3. through 4.8., below, shall also apply.

4.3. Requests By the Secretary of Defense to the President for a Waiver of Informed Consent. Under 10 U.S.C. 1107 (reference (a)), only the President may grant a waiver of informed consent to use an IND for force health protection in connection with members' participation in particular military operations and only the Secretary of Defense may request that the President grant such a waiver.

4.3.1. Grounds for Request. The Secretary shall request a waiver only upon a determination that obtaining informed consent:

4.3.1.1. Is not feasible.

4.3.1.2. Is contrary to the best interests of the member.

4.3.1.3. Is not in the interests of national security.

4.4. Standards and Criteria for Requesting a Waiver of Informed Consent. In making a determination referred to in section 4.3.1.1. or 4.3.1.2., above, the Secretary shall apply, and in making a determination referred to in section 4.3.1.3., above, the Secretary will consider, the standards and criteria set forth in 21 CFR 50.23(d) (reference (c)). Those standards and criteria are:

4.4.1. The extent and strength of evidence of the safety and effectiveness of the IND in relation to the medical risk that could be encountered during the military operation supports the drug's administration under an IND.

4.4.2. The military operation presents a substantial risk that military personnel may be subject to a chemical, biological, nuclear, or other exposure likely to produce death or serious or life-threatening injury or illness.

4.4.3. There is no available satisfactory alternative therapeutic or preventive treatment in relation to the intended use of the investigational new drug.

4.4.4. Conditioning use of the IND on the voluntary participation of each member could significantly risk the safety and health of any individual member who would decline its use, the safety of other military personnel, and the accomplishment of the military mission.

4.4.5. A duly constituted institutional review board (IRB) established and operated in accordance with the requirements of section 4.5., below, has reviewed and approved the IND protocol and the administration of the IND without informed consent.

4.4.6. The risks and benefits of using the IND are evaluated with consideration of:

4.4.6.1. The context in which the IND will be administered, e.g., the setting or whether it will be self-administered or it will be administered by a health professional.

4.4.6.2. The nature of the disease or condition for which the preventive or therapeutic treatment is intended.

4.4.6.3. Conditions that could alter the intended effects of the IND, to the extent any such data are available.

4.4.7. Applicable logistical record keeping systems are capable of tracking and will be used to track movement of the IND from supplier to the individual recipient.

4.4.8. Each member involved in the military operation will be given, prior to the administration of the investigational new drug, a specific written information sheet (including information required by section 4.8.1.) concerning the IND, the risks and benefits of its use, potential side effects, and other pertinent information about the appropriate use of the product.

4.4.9. Medical records of members involved in the military operation will

accurately document the receipt by members of the notification required by section 4.4.8., above.

4.4.10. Medical records of members involved in the military operation will accurately document the receipt by members of any IND in accordance with FDA regulations, including 21 CFR part 312 (reference (c)).

4.4.11. The protocol provides for adequate follow-up to assess whether there are beneficial or adverse health consequences that result from the use of the investigational product.

4.4.12. The Secretary of the Army, as Executive Agent, is pursuing drug development, including a timeline, and marketing approval, in accordance with FDA regulations, with due diligence.

4.4.13. The IND protocol may proceed subject to review by the FDA under reference (c) and a decision by the President on the informed consent waiver request.

4.4.14. Applicable DoD Components will provide training to the appropriate medical personnel and potential recipients on the specific IND to be administered prior to its use.

4.4.15. The Commander of the Combatant Command concerned has stated and justified the time period for which the waiver is needed, not to exceed one year, unless separately renewed under these standards and criteria.

4.4.16. DoD Components will report to the FDA and to the President any changed circumstances relating to these standards and criteria (including the time period referred to in section 4.4.15., above) that otherwise might affect the determination to use an IND without informed consent.

4.4.17. The Secretary of the Army, as Executive Agent, shall provide the public notice referred to in section 4.7.3., below.

4.4.18. Use of the IND without informed consent otherwise conforms with applicable law and DoD policy.

4.5. Institutional Review Board Approval. An Institutional Review Board (IRB), compliant with 21 CFR Part 56 (reference (c)), shall approve every protocol for the use of an IND for force health protection. The Army Human Subjects Research Review

Board (HSRRB), under the Surgeon General of the Army, is designated as the IRB responsible for purposes of IRB activities under this Directive.

4.5.1. In any case in which a protocol proposes to include a waiver of informed consent, the following additional requirements shall be applicable to the HSRRB review and approval of the protocol.

4.5.1.1. The HSRRB must include at least three non-affiliated members who shall not be employees or officers of the Federal Government (other than for purposes of membership on the HSRRB) and shall be required to obtain any necessary security clearances. The HSRRB shall review the proposed IND protocol at a convened meeting at which a majority of the members are present including at least one member whose primary concerns are in nonscientific areas and, if feasible, including a majority of the non-affiliated members.

4.5.1.2. Minutes of the HSRRB meeting(s) at which the proposed protocol was discussed shall be provided to the Secretary of Defense and the FDA. The minutes shall be in sufficient detail to show attendance, actions taken, the votes taken (including number of members voting for, against, or abstaining), the reasons for requiring changes in or disapproving any portion of the protocol, and a written summary of the discussion of controversial issues and their resolution.

4.5.2. The HSRRB must review and approve:

4.5.3.1. The information sheet required by sections 4.4.8., above, and 4.8.1., below.

4.5.3.2. The adequacy of the plan to disseminate information, including distribution of the information sheet to potential recipients, on the investigational product (e.g., in forms other than written).

4.5.3.3. The adequacy of the information and plans for its dissemination to healthcare providers, including potential side effects, contraindications, potential interactions, and other pertinent considerations.

4.5.3.4. An informed consent form as required by FDA regulations at 21 CFR part 50 (reference (c)) in those circumstances in which the protocol includes informed consent by some or all personnel involved.

4.6. Content of Request by the Secretary of Defense to the President. A request by the Secretary to the President for a waiver of informed consent shall be developed

in consultation with the FDA. Upon submission by the Secretary of the waiver request to the President, a copy of the request shall be provided to the Commissioner of FDA. The content of the request shall at a minimum include:

4.6.1. A full description of the threat, including the potential for exposure. If the threat is a chemical, biological, or radiological weapon, the waiver request shall contain an analysis of the probability that the weapon will be used, the method or methods of delivery, and the likely magnitude of its affect on the exposed individuals.

4.6.2. Documentation of compliance with the requirements of the FDA regulations at 21 CFR 50.23(d) (reference (c)). If the request is based on the grounds identified in sections 4.1.1. or 4.1.2., the documentation will include a statement that certifies and a written justification that documents that each of the criteria and standards set forth in 21 CFR 50.23(d) (reference (c)) (which also appear at section 4.4., above) have been met. If the Secretary finds it highly impracticable to certify that all such criteria and standards have been fully met because doing so would significantly impair the Department of Defense's ability to carry out the particular military mission, the Secretary will provide to the President a written justification that documents which criteria and standards have or have not been met, explains the reasons for not meeting those which have not been met, and provides additional justification why a waiver should be granted solely on the grounds identified in section 4.1.3., above.

4.6.3. Any additional information pertinent to the Secretary's determination, including the minutes of the HSRRB meetings at which the IND use was considered.

4.7. Action Required After Waiver of Informed Consent. Following a waiver of informed consent by the President, DoD Components shall ensure proper implementation.

4.7.1. Monitoring

4.7.1.1. DoD Components responsible for implementation shall conduct an ongoing review and monitoring to assess adherence to the standards and criteria under 21 CFR 50.23(d) (reference (c)) and adhere to any periodic reporting requirements specified by the President at the time of the waiver approval. The Secretary shall provide to the President any required reports, with a copy to the FDA Commissioner.

4.7.1.2. The DoD Inspector General shall conduct an ongoing review and monitoring to assess adherence to the standards and criteria under 21 CFR 50.23(d) (reference (c)).

4.7.2. Congressional Notification. The Secretary shall, as soon as practicable, make the Congressional notifications required by 10 U.S.C. 1107(f)(3)(B) (reference (a)).

4.7.3. Public Notification. The Secretary shall, as soon as practicable and consistent with classification requirements, issue a public notice in the Federal Register describing each waiver of informed consent determination and a summary of the most current scientific information on the products used, as well as other information the President determines is appropriate.

4.7.4. Changed Circumstances. The Secretary shall notify the President and the FDA Commissioner if the threat countered by the IND changes significantly or if significant new information on the IND is received.

4.7.5. Termination of Waiver. A waiver expires at the end of one year (or an alternative time not to exceed one year specified by the President) or upon notification by the Secretary to the President that the particular military operation creating the need for the use of the IND has ended, whichever is earlier.

4.7.6. Request for Renewal. A request by the Secretary for a renewal by the President of a waiver must meet the same criteria as the original request and shall include any new information available relevant to the standards and criteria under 21 CFR 50.23(d) (reference (c)).

4.8. Training and Risk Communication

4.8.1. Notice Requirement for IND Use. When using an IND for force health protection, DoD Components shall provide prior notice to personnel receiving the drug or biological product of the following:

4.8.1.1. That it is an IND (including specific information on whether it is approved by FDA and/or whether it is unapproved for its applied use).

4.8.1.2. The reasons the IND is being used.

4.8.1.3. Information regarding the possible side effects of the IND,

including any known side effects possible as a result of interaction of the IND with other drugs or treatments being administered to such personnel.

4.8.1.4. Other information as required to be disclosed by the FDA.

4.8.2. Information to Povidiers for IND Use. DoD Components shall ensure that healthcare providers who administer the IND or who are likely to treat members who receive the IND receive the information identified in sections 4.8.1.3. and 4.8.1.4., above.

4.8.3. Record Keeping on Use of IND and Notice Requirement. DoD Components shall ensure that medical records of personnel who receive an IND accurately document the receipt of the IND and the notice required by section 4.8.1., above.

4.8.4. Ongoing Training and Health Risk Communication DoD Components shall provide ongoing training and health risk communication on the requirements of using an IND in support of a military operation to all military personnel, including those in leadership positions, during chemical and biological warfare defense training and other training, as appropriate. This ongoing training and health risk communication shall include general information about 10 U.S.C. 1107, E.O. 13139, and 21 CFR 50.23(d) (references (a) through (c)).

4.8.5. Special Additional Training and Health Risk Communication When Informed Consent Is Waived

4.8.5.1. If the President grants a waiver of informed consent, DoD Components shall provide training to all military personnel conducting the waiver protocol and health risk communication to all military personnel receiving the specific investigational drug to be administered prior to its use.

4.8.5.2. The Secretary shall submit the training and health risk communication plans as part of the IND protocol submission to the FDA and the reviewing IRB. Training and health risk communication shall include at a minimum:

4.8.5.2.1. The basis for any determination by the President that informed consent is not or may not be feasible.

4.8.5.2.2. The means for tracking use and adverse effects of the investigational drug.

4.8.5.2.3. The benefits and risks of using the investigational drug.

4.8.5.2.4. A statement that the investigational drug is not approved (or not approved for the intended use).

4.8.5.3. DoD Components shall keep operational commanders informed of the overall requirements of successful protocol execution and their role, with the support of medical personnel, in ensuring successful execution of the protocol.

4.9. INDs for Non-military Personnel. In any case in which an IND is used for force health protection for military personnel and subject to the same health risk are Emergency-Essential civilian employees (reference (e)) and contractor personnel performing essential contractor services (reference (f)) in conjunction with the military mission, the IND shall be available for protection of these non-military personnel under the same terms and conditions, except that the authority to waive informed consent under references (a) through (c) is inapplicable to these personnel.

5. RESPONSIBILITIES

5.1. The Assistant Secretary of Defense (Health Affairs), under the Under Secretary of Defense (Personnel and Readiness), shall have primary responsibility for policy under this Directive, is authorized to issue Instructions for implementation of, and grant exceptions otherwise authorized by law to, this Directive, and shall monitor implementation of this Directive and any implementing Instructions.

5.2. The Secretary of the Army shall serve as Executive Agent for the execution of policy under this Directive and any implementing Instructions.

5.3. The Secretaries of the Military Departments shall implement requirements of this Directive, any implementing Instructions issued by the ASD(HA), and requirements established by the Secretary of the Army, as Executive Agent. In implementing an IND protocol, the Secretaries of the Military Departments shall strictly comply with requirements of the protocol.

5.4. The Chairman of the Joint Chiefs of Staff shall coordinate and direct activities of the Commanders of the Combatant Commands in the implementation of this Directive.

5.5. The Commanders of the Combatant Commands shall validate confirmed, high threats for which an IND is needed for force health protection, develop in coordination with the Executive Agent IND protocols which will comply with requirements of this Directive, any implementing Instructions issued by the ASD(HA), and requirements established by the Executive Agent, execute IND protocols in strict compliance with their requirements, and implement other requirements of this Directive, any implementing Instructions, and requirements established by the Executive Agent.

6. EFFECTIVE DATE

This Directive is effective immediately.

Rudy de Leon
Deputy Secretary of Defense

Enclosures - 1
E1. References, continued

E1. ENCLOSURE 1

REFERENCES, continued

(e) DoD Directive 1404.10, "Emergency-Essential (E-E) DoD U.S. Citizen Civilian Employees," April 10, 1992

(f) DoD Instruction 3020.37, "Continuation of Essential DoD Contractor Services During Crises," November 6, 1990

Department of Defense

DIRECTIVE

NUMBER 6205.3

November 26, 1993

ASD(NS&CP)

SUBJECT: DoD Immunization Program for Biological Warfare Defense

References: (a) Title 10, United States Code
(b) DoD Instruction 6205.2, "Immunization Requirements," October 9, 1986
(c) AR 40-562/NAVMEDCOMINST 6230.3/AFR 161-13/CG COMDTINST M6230.4D, "Immunizations and Chemoprophylaxis," November 7, 1988
(d) DoD Directive 5136.1, "Assistant Secretary of Defense for Health Affairs," December 2, 1992
(e) through (g), see enclosure 1

1. PURPOSE

This Directive:

1.1. Establishes policy, assigns responsibilities, and prescribes procedures for members of the Department of Defense against validated biological warfare threats, and prioritization of research, development, testing, acquisition, and stockpiling of biological defense vaccines under reference (a).

1.2. Provides vaccination guidance that focuses exclusively on defense against biological warfare threats and complements immunization requirements for naturally occurring endemic disease threats outlined in references (b) and (c).

1.3. Addresses peacetime and contingency requirements for immunization against biological warfare threats against U.S. personnel.

1.4. Designates the Secretary of the Army as the "DoD Executive Agent" for the

DoD Immunization Program for Biological Warfare Defense.

1.5. Provides direction on levels of acquisition and stockpiling of biological defense vaccines and prioritizes research and development efforts in defending against current and emerging biological warfare threats.

2. APPLICABILITY AND SCOPE

This Directive applies to:

2.1. The Office of the Secretary of Defense, the Military Departments (including their National Guards), the Chairman of the Joint Chiefs of Staff, the Unified Commands, and the Defense Agencies (hereafter referred to collectively as "the DoD Components"). The term "Military Services," as used herein, refers to the Army, the Navy, the Air Force, and the Marine Corps.

2.2. Essential DoD civilian personnel, and personnel of other Federal Departments, when assigned as part of the U.S. Armed Forces.

3. DEFINITIONS

Terms used in this Directive are defined in enclosure 2.

4. POLICY

It is DoD policy that:

4.1. For immunization, the following personnel, subject to special exceptions approved by the Chairman of the Joint Chiefs of Staff, should be immunized against validated biological warfare threat agents, for which suitable vaccines are available, in sufficient time to develop immunity before deployment to high-threat areas:

4.1.1. Personnel assigned to high-threat areas.

4.1.2. Personnel predesignated for immediate contingency deployment (crisis response).

4.1.3. Personnel identified and scheduled for deployment on an imminent or ongoing contingency operation to a high-threat area.

4.2. For vaccine research, development, testing, evaluation, acquisition, and stockpiling, efforts for the improvement of existing vaccines and the development of new vaccines against all validated biological warfare threat agents shall be integrated and prioritized. The Department of Defense shall develop a capability to acquire and stockpile adequate quantities of vaccines to protect the programmed force against all validated biological warfare threats.

5. RESPONSIBILITIES

5.1. The Under Secretary of Defense for Acquisition and Technology shall ensure the coordination and integration of the DoD Immunization Program for Biological Warfare Defense with all acquisition-related elements of the DoD Biological Defense Program.

5.2. The Under Secretary of Defense for Policy shall review all facets of the DoD Immunization Program for Biological Warfare Defense to ensure that it is consistent with DoD policy and is adequately integrated into overall DoD biological defense policies.

5.3. The Assistant Secretary of Defense for Health Affairs shall:

5.3.1. Serve as the advisor to the Secretary of Defense as in DoD Directive 5136.1 (reference (d)) on the DoD Immunization Program for Biological Warfare Defense.

5.3.2. In consultation with the DoD Executive Agent, the Secretaries of the Military Departments, and the Chair of the Armed Forces Epidemiological Board, identify vaccines available to protect against biological threat agents designated by the Chairman of the Joint Chiefs of Staff and recommend appropriate immunization protocols.

5.3.3. Issue instructions to the Military Departments and the other appropriate DoD Components on the immunization of DoD personnel, under the guidelines of this Directive, and monitor and evaluate the implementation of those instructions.

5.4. The Secretary of the Army, as the DoD Executive Agent for the Immunization Program for Biological Warfare Defense, shall:

5.4.1. Besides those responsibilities in the Deputy Secretary of Defense Memorandum and the Joint Service Agreement (references (e) and (f)), do the following to enhance the DoD Immunization Program for Biological Warfare Defense, and report annually through the Assistant Secretary of Defense for Health Affairs (ASD(HA)) to the Secretary of Defense the capability to carryout those policies:

5.4.1.1. Vaccine Research and Development

5.4.1.1.1. Priorities developed in coordination with the ASD(HA), the Chairman of the Joint Chiefs of Staff, and the Secretaries of the Military Departments shall include the development of vaccines against validated biological warfare threat agents for which none exist, improvement of vaccines that are unacceptable in the time they take to produce immunity or in the level of immunity they produce or are inadequate because of the number of doses required to achieve immunity, assessment of the effectiveness of vaccines against biological warfare threat agents in their likely modes of use (e.g., aerosols), and development of multivalent vaccines that will produce protective immunity after a single vaccination. Vaccines must be either licensed by the Food and Drug Administration (FDA) or have been designated, under FDA requirements, "for use as investigational new drugs (INDs)," as in 21 CFR 50 (reference (g)).

5.4.1.2. Vaccine Acquistion and Stockpiling

5.4.1.2.1. Develop and maintain a DoD capability to acquire and stockpile adequate quantities of vaccines to protect the programmed force against all validated biological warfare threat agents for which suitable vaccines exist.

5.4.1.2.1. On an annual basis, provide information and recommendations, in coordination with the Secretaries of the Military Departments and the Chair of the Armed Forces Epidemiological Board, to the ASD(HA) on vaccines to acquire and appropriate immunization schedules that include reimmunization required to develop and maintain protective immunity. Those recommendations should include, but not be limited to the following:

5.4.1.2.1.1. All relevant data on the effectiveness of each vaccine against the corresponding biological warfare threat agent.

5.4.1.2.1.2. The expected type, frequency, and severity of vaccine-associated adverse reactions.

5.4.2. Serve as the focal point for the submission of information from the Services, as specified by subsection 5.5., below, and monitor the Services' implementation of the DoD Immunization Program for Biological Warfare Defense. Recommend appropriate changes and improvements to the Secretary of Defense through the ASD(HA), and the Secretaries of the Military Departments. Report to the Secretary of Defense annually on the Immunization Program for Biological Warfare Defense.

5.4.3. The Executive Agent Acquisition Executive (AE) shall plan, program, and budget for biological defense. The AE shall coordinate directly with the ASD(HA), the Under Secretary of Defense for Policy, the Under Secretary of Defense for Acquisition, the Secretaries of the Departments, and other offices as required to ensure program integration.

5.5. The Secretaries of the Military Departments shall:

5.5.1. Implement, monitor, evaluate, and document the DoD Immunization Program for Biological Warfare Defense in their Department and establish procedures for coordinating and reporting the following information to the Executive Agent:

5.5.1.1. The identification, reporting, and epidemiologic evaluation of vaccine-associated adverse reactions, in accordance with FDA requirements.

5.5.1.2. The collection and forwarding of data required by the Executive Agent needed to meet requirements of the FDA for products that are the INDs.

5.5.2. Transmit the instructions of the ASD(HA) about the immunization program for biological warfare defense to subordinate units.

5.5.3. Program and budget for the required vaccinations for members of their Department and provide the DoD Executive Agent with projected program requirements.

5.6. The Chairman of the Joint Chiefs of Staff, in consultation with the Commanders of the Unified Commands; the Chiefs of the Military Services; and the Director, Defense Intelligence Agency (DIA), annually and as required, shall validate and prioritize the biological warfare threats to DoD personnel and forward that list to the DoD Executive Agent through the ASD(HA).

5.7. The Commanders of the Unified Commands, annually and as required, shall

provide the Chairman of the Joint Chiefs of Staff with their assessment of the biological warfare threats to their theaters.

5.8. The Chair of the Armed Forces Epidemiological Board, in consultation with the DoD Executive Agent and the Secretaries of the Military Departments, annually and as required, shall identify to the ASD(HA) vaccines available to protect against validated biological warfare threat agents, and recommend appropriate immunization protocols.

6. PROCEDURES

The DoD Immunization Program for Biological Warfare Defense shall be conducted, as follows:

6.1. The Commanders of the Unified Commands, annually and as required, shall provide the Chairman of the Joint Chiefs of Staff with their assessment of the biological warfare threats to their theater.

6.2. The Chairman of the Joint Chiefs of Staff, in consultation with the Commanders of the Unified Commands; the Chiefs of the Military Services; and the Director, DIA, annually, shall validate and prioritize the biological warfare threats to DoD personnel and forward them to the DoD Executive Agent through the ASD(HA).

6.3. Within 30 days of receiving the validated and prioritized biological warfare threat list from the Chairman of the Joint Chiefs of Staff, the DoD Executive Agent shall, in consultation with the Secretaries of the Military Departments and the Chair of the Armed Forces Epidemiology Board, provide recommendations to the ASD(HA) on vaccines and immunization protocols necessary to enhance protection against validated biological warfare threat agents.

6.4. Within 30 days of receiving the coordinated recommendations of the DoD Executive Agent, the ASD(HA) shall direct the Secretaries of the Military Departments to begin immunization of the specified DoD personnel against specific biological warfare threat agents.

6.5. For biological threats for which the only available vaccine is an ND, it shall be administered under 21 CFR 50 and 312 (reference (g)) and the established ND protocol and/or other applicable legal procedures.

7. INFORMATION REQUIREMENTS

The annual reporting requirements in section 5., above, have been assigned Report Control Symbol DD-POL(A) 1921.

8. EFFECTIVE DATE AND IMPLEMENTATION

This Directive is effective immediately. The Secretaries of the Military Departments shall forward one copy of implementing documents to the Assistant Secretary of Defense for Health Affairs within 120 days.

William J. Perry
Deputy Secretary of Defense

Enclosures - 2

1. References
2. Definitions

E1. ENCLOSURE 1

REFERENCES, continued

(e) Deputy Secretary of Defense Memorandum, "Biological Warfare Defense Program," August 26, 1991

(f) Joint Service Agreement, "Joint Service Coordination of Chemical Warfare and Chemical-Biological Defense Requirements, Research, Development, and Acquisition," July 5, 1984

(g) Title 21, Code of Federal Regulations, Parts 50, "Informed Consent of Human Subjects," and 312, "Investigational New Drug Application," current edition

E2. ENCLOSURE 2

DEFINITIONS

E2.1.1. Biological Warfare Agent. A microorganism or biological toxin intended to cause disease, injury, or death in humans.

E2.1.2. Biological Warfare Threat. A biological materiel planned to be deployed to produce casualties in humans.

E2.1.3. High-Threat Area. A geographic area in the proximity of a nation or nations considered to pose a potential biological threat to DoD personnel by the Chairman of the Joint Chiefs of Staff in consultation with the Commanders in Chief of the Unified Commands and the Director, DIA.

E2.1.4. Immunity. The capacity to resist the effects of exposure to a specific biological agent or toxin.

E2.1.5. Immunization. The process of rendering an individual immune. Immunization refers to "the administration of a vaccine to stimulate the immune system to produce an immune response (active immunization)." That process may require weeks to months and administration of multiple doses of vaccine.

E2.1.6. Programmed Force. The DoD active and Reserve force approved by the Secretary of Defense in the Future Years Defense Program.

E2.1.7. Vaccination. The administration of a vaccine to an individual for inducing immunity.

E2.1.8. Vaccine. A preparation that contains one or more components of a biological agent or toxin, and induces an immune response against that agent when administered to an individual.

E2.1.9. Validated Biological Warfare Threat Agent. A biological warfare agent that is validated as a threat to DoD personnel by the Chairman of the Joint Chiefs of Staff, in consultation with the Commanders of the Unified and Specified Commands; the Chiefs of the Military Services; and the Director, DIA.

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON DC 20301-1200

HEALTH AFFAIRS

MAR 13 2001

MEMORANDUM FOR EXECUTIVE SECRETARY, ARMED FORCES EPIDEMIOLOGICAL BOARD

SUBJECT: Therapeutics Against Biowarfare Agents

The Armed Forces Epidemiological Board (AFEB) annually provides recommendations to the DoD Executive Agent on vaccines and immunization protocols necessary to enhance protection against validated biological warfare threat agents. In August of 2000, the AFEB provided the Department with a list of recommended antibiotics against biowarfare agents, as requested by the Office of the Assistant Secretary of Defense for Health Affairs. Although approved for use by the Food and Drug Administration, many of the recommended antibiotics were not labeled for the specific use recommended by the AFEB.

In this regard, I would like the AFEB to review existing Joint Operational Requirement Documents, progress on specific efforts to obtain new indications for existing therapeutics, and acquisition status of biologics (treatment and prophylaxis) against the current prioritized list of biowarfare agents and make recommendations to this office on the current status of requirements and suggested priorities. As part of the AFEB deliberations, I would expect the Board to receive briefings from the Joint Staff (Joint Service Integration Group) on existing joint requirements and the Joint Program Office on acquisition status and efforts to obtain new indications for existing therapeutics.

I request that the Board address this issue at the May AFEB meeting in concert with the periodic review of the threat list.

Ellen P. Embrey
Deputy Assistant Secretary of Defense
(Force Health Protection and Readiness)

Attachments
As stated

DEPARTMENT OF DEFENSE
ARMED FORCES EPIDEMIOLOGICAL BOARD
5109 LEESBURG PIKE
FALLS CHURCH VA 22041-3258

AFEB (15-1a) 00-9

03 August 2000

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)
THE SURGEON GENERAL, DEPARTMENT OF THE ARMY
THE SURGEON GENERAL, DEPARTMENT OF THE NAVY
THE SURGEON GENERAL, DEPARTMENT OF THE AIR FORCE

SUBJECT: Antibiotics Against Biowarfare Agents

1. On March 13, 2000 the Deputy Assistant Secretary of Defense for Health Operations Policy requested that the Armed Forces Epidemiological Board, in consultation with the Centers for Disease Control and Prevention (CDC), provide recommendations on the most appropriate FDA approved antibiotics to be used for treatment of the primary bacterial and rickettsial agents on the biowarfare threat list. Specifically, recommendations were requested for treatment of the organisms which cause anthrax, plague, tularemia, brucellosis, glanders, and Q fever.

2. The selection of antibiotics to prevent and treat illness from biowarfare agents has received considerable recent attention. In December 1999, a Medical Biological Defense Material (MBDM) policy meeting was held at Fort Detrick, Maryland to develop a list of preferred antibiotics for post-exposure prophylaxis. A triservice field manual "Treatment of Biological Warfare Agent Casualties," which includes antibiotic recommendations, has recently been finalized. CDC is developing a civilian pharmaceutical stockpile for prevention and treatment of illness due to large-scale bioterrorism and has also addressed the issue. Beginning in 1999, the Journal of the American Medical Association (JAMA) has begun publishing a series of articles on biological warfare agents, including treatment and prophylaxis, based on the recommendations of a Working Group on Civilian Biodefense constituted by The Johns Hopkins School of Public Health. During the May 2000 AFEB meeting, the Board heard a presentation on this topic by LtCol George Christopher from the US Army Medical Institute of Infectious Diseases, who led the effort to develop the triservice field manual, and discussed the issues with the Board and the Disease Control Subcommittee.

3. In developing the list of recommended agents, the Board reviewed the above materials and considered the following issues:

- Efficacy of the drugs against the threat agents based on peer-reviewed publications and other data sources
- Potential for antimicrobial resistance (natural and bioengineered)
- Side effects profiles of the alternative antimicrobial agents
- Ease of administration (especially dosing frequency)
- Broadness of spectrum (how many agents would be covered)
- Interactions with other drugs or products which may be used simultaneously
- Cost (including potential changes in cost as patents lapse)
- Shelf life

4. Two additional issues were also considered. Although the major group in which these drugs would be used is front-line active duty personnel, there may also be dependents (including pregnant women and children) in some high-risk settings in whom the recommended therapies are contraindicated. And while all of the therapeutics discussed is FDA licensed, they are often not labeled for the prophylaxis and treatment of biowarfare agents. Such off-label use will require that potential recipients provide informed consent to be given the medication under an established protocol. However, the Board felt that labeling status should not be the determining factor if there was a clear best option based on the other criteria.

5. The Board made the following comments and recommendations:

a. **FOR THESE SIX THREAT AGENTS, ANTIBIOTIC ALTERNATIVES ARE LIMITED FOR BOTH PROPHYLAXIS AND TREATMENT. THE MAJOR ANTIBIOTICS UNDER CONSIDERATION BASED ON BROADNESS OF SPECTRUM AND EFFICACY ARE THE FLUOROQUINOLONES (SPECIFICALLY CIPROFLOXACIN) AND TETRACYCLINES (SPECIFICALLY DOXYCYCLINE). WHEN SUBJECT MATTER EXPERTS CONSIDERED THE CRITERIA ABOVE, THERE WAS LITTLE TO DIFFERENTIATE THESE TWO CLASSES IN TERMS OF A CLEAR BEST ALTERNATIVE. DOXYCYCLINE APPEARS TO HAVE A BROADER SPECTRUM, IN THAT IT IS CONSIDERED AN ALTERNATIVE FOR ALL SIX THREAT AGENTS, AND IS CONSIDERABLY LESS EXPENSIVE THAN ANY OF THE FLUOROQUINOLONES. HOWEVER, IT WAS CONSIDERED TO HAVE A GREATER INCIDENCE OF SIDE EFFECTS, AND WAS CONSIDERED MORE HARMFUL IN PREGNANT WOMEN AND CHILDREN. THESE DRUGS WERE FELT TO BE ROUGHLY EQUIVALENT WITH RESPECT TO THE OTHER CRITERIA (SHELF LIFE, EASE OF ADMINISTRATION, POTENTIAL FOR RESISTANCE, AND DRUG INTERACTIONS). REGARDLESS OF WHICH DRUG IS SELECTED AS THE FIRST CHOICE FOR ANY OF THESE DISEASES, THE OTHER MUST ALSO BE AVAILABLE AS A BACK-UP.**

b. **THE MDBM POLICY GROUP (WHICH ADDRESSED <u>ONLY POST-EXPOSURE PROPHYLAXIS</u>) SELECTED CIPROFLOXACIN AS THE DRUG OF CHOICE FOR ANTHRAX AND TULAREMIA WITH DOXYCYCLINE AS THE BACKUP, WHILE DOXYCYCLINE WAS THE FIRST CHOICE FOR PLAGUE WITH CIPROFLOXACIN AS THE BACKUP. DOXYCYCLINE (COMBINED WITH RIFAMPICIN FOR BRUCELLOSIS) WAS CONSIDERED THE FIRST LINE PROPHYLACTIC AGENT FOR GLANDERS, BRUCELLOSIS, AND Q FEVER. THE BOARD SUPPORTS THESE CHOICES.**

c. FOR THERAPY, CIPROFLOXACIN IS ALSO THE DRUG OF CHOICE FOR ANTHRAX WITH DOXYCYCLINE AS THE BACKUP. FOR BOTH PLAGUE AND TULAREMIA, STREPTOMYCIN IS CONSIDERED THE TRADITIONAL THERAPEUTIC DRUG OF CHOICE, BUT BECAUSE OF THE ROUTE (INTRAMUSCULAR) AND FREQUENCY OF ADMINISTRATION, AND LIMITED SUPPLY, THIS DRUG POSES SIGNIFICANT LOGISTICAL CHALLENGES FOR LARGE SCALE USE IN COMPARISON TO OTHER AMINOGLYCOSIDES (SPECIFICALLY GENTAMICIN). THE BOARD RECOMMENDS THE SELECTION OF THIS DRUG FOR TREATMENT WITH CIPROFLOXACIN AS A THERAPEUTIC ALTERNATIVE. FOR Q FEVER AND BRUCELLOSIS THE THERAPEUTIC CHOICE IS DOXYCYCLINE (WITH RIFAMPICIN ADDED FOR BRUCELLOSIS) WHILE FOR GLANDERS THERAPY WOULD INCLUDE CEFTAZIDIME AND RIMETHOPRIM/ SULFAMETHOXAZOLE. SPECIFIC RECOMMENDATIONS ARE INCLUDED IN THE ATTACHED TABLE.

d. IT IS OUR UNDERSTANDING THAT THE MANUFACTURERS OF CIPROFLOXACIN ARE ENGAGED IN DISCUSSIONS WITH FDA TO DETERMINE THE REQUIREMENTS FOR CHANGING THE LABELING TO INCLUDE PROPHYLACTIC USE AGAINST THE MAJOR BIOWARFARE THREAT AGENTS. SHOULD A LABEL CHANGE OCCUR, IT WOULD BE AN ADDED INCENTIVE TO SELECT THIS DRUG OVER DOXYCYCLINE TO BECAUSE OF THE OFF-LABEL USE ISSUE. OF NOTE, NEWER FLUOROQUINOLONES HAVE THE ADVANTAGE OF ONCE DAILY ADMINISTRATION. ALTHOUGH DOSING FREQUENCY IS MORE OF AN ISSUE IN CIVILIAN SETTINGS, THE ADDED EASE OF ADMINISTRATION WOULD BE A STRONG CONSIDERATION FOR SELECTION OF ONE OF THESE AGENTS (I.E. LEVOFLOXACIN) IF BIOEQUIVALENCY AGAINST THE THREAT AGENTS COULD BE DETERMINED AND THE COST WAS NOT SIGNIFICANTLY DIFFERENT.

e. SPECIFIC RECOMMENDATIONS*:

	POST-EXPOSURE PROPHYLAXIS		THERAPY	
Threat Agent	**1st Choice**	**2nd Choice**	**1st Choice**	**2nd Choice**
Anthrax	**Ciprofloxacin**	**Doxycycline**	**Ciprofloxacin**	**Doxycycline**
Plague	**Doxycycline**	**Ciprofloxacin**	**Gentamicin**	**Ciprofloxacin**
Tularemia	**Ciprofloxacin**	**Doxycycline**	**Gentamicin**	**Ciprofloxacin**
Glanders	**Doxycycline**		**Ceftazidime TMP/Sulfa**	
Brucellosis	**Doxycycline Rifampicin**		**Doxycycline Rifampicin**	
Q fever	**Doxycycline**		**Doxycycline**	

***Dosage and duration as per MBDM guidance**

6. The above comments and recommendations were unanimously approved by the Board.

7. The above comments and recommendations have been reviewed by the appropriate representatives from the CDC who also concur.

FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD:

F. MARC LAFORCE, M.D.
AFEB President

BENEDICT M. DINIEGA
Colonel, USA, MC
AFEB Executive Secretary

2 Encls
1. Question to Board
2. MBDM Recommendations

AFEB (15-1a) 00-9 03 August 2000
SUBJECT: Antibiotics Against Biowarfare Agents

Copies Furnished:
Board Members
DASG-ZH
OASD(HA)/HOP, Prog. Dir.,
Prev. Med. & Surveillance
AFMOS/SGOP
DASG-HS-PM
HQ, USMC, PMO,CAPT Kenneth W. Schor
Dep. Dir. Occup. Hlth. & Prev. Med. Div, BUMED-DN
CDR, WRAIR
CDR, USACHPPM, ATTN: MCHB-DC-C
CDR, USAMRMC
Navy Env. Health Center
Dir, Med Resources, Plans & Policy Div. (N931)
CDR Mark Tedesco, USPHS
COL Andrew S. Warde,
BvetMed Msc MRCVA
Lcol Maureen Fensom, CFMS

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

MAR 13 2000

MEMORANDUM FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD

SUBJECT: Antibiotics Against Biowarfare Agents

The Armed Forces Epidemiological Board (AFEB) has been very helpful in the review and prioritization of biological threat agents facing our Armed Forces. In our continuing efforts to ensure that the most effective medical therapies are readily available for the military, we additionally require a review of antimicrobial drugs.

In light of the need for the Department of Defense to maintain a high level of readiness and to maintain adequate stockpiles of specific antibiotics, I request that the Armed Forces Epidemiological Board conduct a review of antibiotics approved by the Food and Drug Administration that may prove useful against certain infectious biological warfare agents. This review should involve appropriate consultation with Centers for Disease Control and Prevention (CDC) staff, as they will have very similar concerns regarding what is needed for the domestically-oriented national pharmaceutical stockpile for medical response to terrorism.

I ask the AFEB to provide recommendations to this office on the most appropriate antibiotics that would be indicated for the treatment of the primary bacterial and rickettsial agents on the biowarfare threat list. Of greatest concerns are the infectious agents causing anthrax, plague, tularemia, brucellosis, glanders, and Q fever. The recommendations should describe any precautions or contraindications associated with the administration of any antibiotics.

I request that you address this issue at your next AFEB meeting in May in concert with your periodic review of the threat list and provide your results within 60 days of your meeting.

J. Jarrett Clinton

RADM J. Jarrett Clinton, MD, MPH, USPHS
Deputy Assistant Secretary of Defense
(Health Operations Policy)

Medical Biological Defense Material (MBDM) Policy Meeting
1000-1200, 01 DEC 99
USAMRIID
Fort Detrick, MD

1. Attendees: See Annex A

2. Introductory Comments:

- Antibiotics have already been fielded for use as post exposure prophylaxis against Biologica Warfare (BW) agents (i.e. Desert Shield, Desert Storm, Desert Thunder).
- Antibiotics are expensive, but the Army has shown their willingness to support this cost. OTSG has programmed $4M into the FY02-05 POM in support of Force Packages 1 & 2 and Forward Deployed (370,000 personnel).
- Issuing antibiotics to Servicemembers for use as post exposure prophylaxis for BW agents is generally interpreted as an "Off Label" Use – not FDA approved and thus a complex and sensitive legal issue. MMWR (Feb 99) is not FDA Policy. "Off Label" doe not equate "Inappropriate" but ASD(HA) will not currently promulgate Policy promoting "Off Label" use.

At the Service level, we do write policy and doctrine: Draft FM 8-284 addresses and outlines the use of antibiotics as a prophylaxis with vaccine as a treatment.

We discussed the potential for abuse but it is regarded as negligible in the face of a BW threat.

After defining and reviewing ANNEX B, Doxy and Cipro were the recommended contenders for use as the primary drug.

Issues:

- Taking Doxy and Cipro simultaneously increases side effects.
- Doxy may have more severe side effects (photosynthesis and GI tract upset) than Cipro.
- With 2 of 3 of the lethal BW agents, use of Cipro is advantageous over Doxy.
- Cipro may work well enough on remainder agents.
- If anthrax is major concern – Cipro is preferred with a theater reserve of Doxy.

If we recommend one drug, access to second drug must be available – we will have to maintain a contingency stockpile within the medical system, at the very least. The contingency drug stockpile is maintained to address the issue of Servicemembers who do not respond to the primary drug prophylaxis – who, for one reason or another, become ill from exposure to either the primary prophylactic antibiotic or the BW agent. This drug would be stockpiled within the medical system to allow for administration on a physician's advice.

There is no label recommendation for prophylaxis of these agents. There is little or no animal or human data for the use of any drug for prophylaxis.

Currently, only Chemical Casualty Treatment Sets are fielded. Maintenance of these sets is the responsibility of the individual units, with some supplemental support from OTSG. There is a proposal circulating within the logistics community for the Potency & Dated (Ps &Ds) in the Chemical Casualty Treatment Sets to be centrally managed within the DRBs under MDEP HSCB.

AMEDDC&S, DCDD defines the doctrine which defines the type, severity, and number of casualties and the treatment necessary. Strong consideration should be given to fielding a BW agent treatment capability.

3. MEDICAL RECOMMENDATION:

Ciprofloxacin is recommended as the primary drug
2 tabs / day X 30 days X 370K Servicemembers
Doxycyline is recommended as a contingency backup
2 tabs / day X 30 days X 370K Servicemembers X 25% (Contingency Factor)

4. Logistical Supportability:

Cipro

Per Bayer, the current FSS price for Ciprofloxacin is $179.96 for the individually sealed product.

tabs/day	days	# soldiers		total tablets
2	30	370,314		22,218,840
# packages of 100 required:				222,188
7-year shelf life; buy 1/7 ea. yr:				31,741
Price per package(w/ addition of PV CRR (1.3%)			$	182.30
Total cost per year (constant 00)			$	5,786,420.76

Doxy

The Prime Vendor price for Doxycycline, 100mg, 100s individually Sealed is $9.30 (WRAMC PV cost).

tabs/day	days	# soldiers		total tablets
2	30	370,314		22,218,840
Contingency - need 25%				5,554,710
# packages of 100 required:				55,547
2-year shelf life; buy 1/2 ea. yr:				27,774
Price per package: (w/ addition of PV CCR (1.3%)			$	9.42
Total cost per year (constant 00)			$	261,626.84

The surge capacity is relatively robust for either Doxy or Cipro but greater for Doxy.

5. Follow-on Actions:

a. LTC Scott, DCDD, will introduce this issue to MPSP on 7 Dec 99 for Principal Signature in Feb 00.

b. LtCol Christopher, USAMRIID, will draft the detailed technical medical analysis (ANNEX B) for recommendations to decide which drug will be used as prophylaxis for post exposure to BW agents. A preliminary report will be prepared for DCDD for the MPSP meeting 7 Dec 99.

c. USAMMA will provide an estimate of storage, shelf life extension, maintenance/sustainment etc. (i.e. an analysis of the total logistical sustainability of this proposal).

d. Issues regarding the definition of "Credible Evidence" of exposure will be addressed separately:

- What is the accepted hierarchy of information?
- How do we define the criteria for administration of a post exposure prophylactic?
- What is a "credible exposure?"
- Is there precedent in this from PB?

ANNEX A

NAME	ORGANIZATION	PHONE	EMAIL
(b)(6)	OTSG	(b)(6)	
	USAMRIID		
	USAMMA		
	USAMMA		
	RAM IV		
	USAMRIID		
	OTSG/Sherikon, Inc.		
	USAMRIID		
	USAMRIID		
	USAMRIID		
	USAMRIID		
	AMEDDC&S(DCDD)		

Medical Biological Defense Material (MBDM) Policy Meeting
1000-1200, 01 DEC 99
USAMRIID
Fort Detrick, MD

ANNEX B

Best Medical Advice: (only addressing post exposure prophylaxis, not in personnel)

AGENT	ANTIBIOTIC	ROUTE	TIME	COMMENTS
Anthrax	#1 - Ciprofloxacin	500mg po bid	30 days	adjunct to vaccination
	#2 - Doxycycline	100mg po bid		doxy resistant strains Also Considered: Penicillin, tetracycline Off label for both drugs
Plague	#1 – Doxycycline	100mg po bid	1 wk	off label, is for therapy (recommended by CDC)
	#2 – Cipro	500mg po bid	1 wk	off label Also considered: Tetracycline, Chloramphenicol
Tularemia	#2 – Doxy	100mg po bid	2 wk	relapses w/ Doxy treatment
	#3 – Tetra #1 – Cipro	500mg	4 wk	off label
Glanders/ Melioidosis	#1 – Doxy TMP-SMX	100mg po bid treatment recommendations only Combination therapy – for acute sepsis	2 wk	in vitro, off label
Brucellosis	#1 – Doxy	200mg po /day	6 wk	full course of therapy advised
	#1 – Rifampin #2 - Ofloxacin	600-900 mg po /day		combined therapy
Q Fever	#1 – Doxy	100mg po bid	5 days beginning day 8 through 12	
	Tetracycline considered (based on treatment)	500mg po bid	5 days,8-12 days post exposure	
Cholera	recommended not considering this agent for chemoprophylaxis			

MEMORANDUM FOR DEPUTY ASSISTANT SECRETARY OF DEFENSE (FHP&R)

SUBJECT: Deployment Health Support Directorate (DHSD) Weekly Activity Report, 1-5 July 2002

Investigations and Analysis Division (IAD)

- **Center for Military History.** Members of DHSD unit locations team briefed BG John S. Brown, Chief of History, US Army and Commander, US Army Center of Military History (CMH), and selected members of his staff on 27 June 2002, at Ft McNair, Washington, DC. COL Sulka presented an overview of the directorate and its expanded force health protection missions with emphasis on DHSD's individual assignments and unit location team efforts. CMH is responsible for the appropriate use of history throughout the US Army. This mission requires that CMH record the official history of the Army in both peace and war, and advise the Army Staff on relevant historical matters, contributing essential background information for decision making, staff actions, command information programs, and public statements by Army officials. Among those in attendance were Dr. Jeffrey Clark, Chief Historian of the US Army; Dr. Richard A. Gorell, Chief, Field Programs; Dr. Richard A. Stewart, Chief of Histories Division; and Mr. Tom Whitsett, DHSD. Discussions centered on policy and practices of operational record keeping, disposition and archiving of those records-- issues that the health and the historian communities share. DHSD has worked with this command in the past in attempting to leverage its resources and influence to help determine unit locations in documenting or assessing potential group environmental exposures and to reconstruct health related operational events of the Gulf War. BG Brown appreciated the update and offered to assist in any matter pertaining to the DHSD mission (POC (b)(6) (b)(6)).

- **CJTF180 Theater-wide Occupational and Environmental Health Surveillance (OEHS) Plan Development.** A member of DHSD attended the kick-off meeting for the development of a campaign plan to implement occupational environmental health surveillance requirements for the Afghanistan Theater of Operations (CJTF180). The meeting was held at USACHPPM on 26 June 2002. The purpose of the plan is to address the USCENTCOM Deputy Commander's desire to implement a theater-wide occupational and environmental health surveillance plan in accordance with the Joint Staff memorandum MCM-0006-02, "Updated Procedures for Deployment Health Surveillance and Readiness," dated 1 February 2002. Meeting members drafted an outline for the plan that USACHPPM personnel will complete. USACHPPM will circulate a draft version to meeting attendees for review and comment by 11 July. A final version is expected by September (POC (b)(6) (b)(6)).

- **Defense Information Systems Agency (DISA).** Members of DHSD visited the Defense Information Systems Agency (DISA) readiness reporting group located in Falls Church, VA. COL Sulka presented a brief overview of the directorate and its efforts in the areas of unit locations and individual assignments. The purpose of the meeting was to determine if current readiness reporting systems would provide the detailed information required to track

the duration of a deployment until return, for both units and individuals from their home station. They indicated that, within DoD, the Status of Resources and Training System (SORTS) is a key information management system which provides the Joint Staff with access to common information on the identification, location, resources, and readiness of all U.S. Forces units worldwide. DHSD received a SORTS demonstration showing the utility of the system and how it interfaces with the Joint Operations Planning and Execution System (JOPES). An additional meeting of the two organizations will occur in the near future to discuss operational command and control systems, combat service support systems, and their potential to provide the level of granularity and report frequency, to meet the needs of the military health system (POC (b)(6)).

Public Affairs (PA)

- **"Veterans Right to Know" Legislation Generates Media Interest.** PA received two calls as a result of a Congressional action 27 June 2002. Larry Wheeler – Gannett, and Eliot Kleinberg – *Palm Beach Post*, asked for a response to legislation (sponsored by Senators Cleland, Nelson and McCain) that compels DoD to declassify all information on all post World War II chemical, biological and nuclear tests. PA explained that as a result of the topic being outside of DHSD's scope, it could not comment on the legislation. Both reporters asked for more information on Project SHAD. PA provided them with the DeploymentLINK URL and the VA's Helpline toll-free telephone number. DHSD expects balanced coverage, though it anticipates harsh words from Senator Nelson. Earlier this week he told a South Florida *Sun Sentinal* reporter that he had pushed for an inquiry, yet received few answers (POC (b)(6)).

- **VSO/MSO Monthly Roundtable Meeting (June (2002).** DHSD met with 11 military and veterans' service and Interagency representatives 27 June 2002. Attendees received briefings on Reserve Component mobilizations from ESGR, a report on the recently completed Interagency Symposium on Research on Military Women and Veterans from LTC Ritchie (HA), as well as an update on the on-going GAO review of the DoD Deployment Health Surveillance Program. Meeting notes and briefing slides were sent to those representatives unable to attend the meeting due to other commitments (POC (b)(6)).

- **Anthrax Vaccine Announcement Made Today.** In support of Health Affairs, the PA team implemented the rollout plan coordinated earlier in the year:

  * Coordinated teleconference for Dr. Winkenwerder and 18 third-party subject-matter experts.

  * Notified by phone 28 service organization and Interagency representatives of the pending announcement. Provided copies of the announcement via fax and e-mail.

  * Monitored the announcement and later conducted a Nexis search. Two *AP* stories, one national and one international, were posted by 6 p.m. Forwarded the information to Marianne Coates, HA External Affairs. Later in the evening, the *AP* piece was rewritten and tailored for about 10 different audiences. The only story was a short piece written by

AFP. Network coverage was most notably absent. *ABC*'s World *News Tonight* spoke of it for approximately 10 seconds. No other networks addressed the issue.

* Created draft banner document and posted to DeploymentLINK 1 July 2002.

* Delivered information packages to VSO/MSO and interagency representatives on Tuesday, 2 July by courier or mail (POC (b)(6)).

- **Navy Congressional Liaison Office Millington, Tennessee SHAD Query.** PA provided confirmation from the SHAD team to the Congressional Liaison POC Mr. Smith, that the veteran about whom he was calling had been on-board the USS Granville Hall during one of the tests. PA also informed him that the veteran could file his claim with the VA and if there were to be a question, the VA would contact DHSD and we would, in turn, provide written confirmation (POC Ms. Goodno, 703-578-8552).

- **Non-Commissioned Officers Association Conference.** An outreach team will meet at the NCOA's 41st national conference in Denver, Colorado, with approximately 500 delegates from more than 150 chapters. In addition to deployment health-related information materials, the team will also offer information associated with the recent anthrax vaccine announcement. The AVIP team provided copies of the DoD press release, the 28 June policy, and the "Myths and Facts" document for distribution (POC (b)(6) (b)(6)

- **SHAD.** Via Marianne Coates, PA received a request for information from LTC Fairlamb at the State Department. LTC Fairlamb is gathering information for LTG Cosumano's upcoming visit to the Marshall Islands. He requested a background paper and talking points; coordination is under way (POC (b)(6) .

Deployment Health Support Directorate Upcoming Travel and Events:

July

4-7	Non-Commissioned Officers Association 41st Annual Convention, Denver, CO. Lisa Gates and Bernard Hayes to exhibit.
15	DHS Brief to Representative Murtha's Staff, 0900, Location TBD.
24-25	Visit to Ft. Drum, NY.
25	VSO/MSO Meeting, 1100, Pentagon.

August

9-16	Fifth Annual Force Health Protection and Second Annual DoD Population Health and Health Promotion Conferences, Baltimore, MD. Mrs. Morris, MAJ Robinson, Tom Whitsett, Tom Stewart, and Jeff Prather to speak. DHS display to be provided.
10-13	Air Force Sergeants Association International Convention, Jacksonville, FL. DHS display to be provided.
14	ASBREM Secretariat Committee Meeting, 1300-1500, 1777 Kent St., 15th Floor Conference Room. Dr. Kilpatrick to attend.
18-22	Enlisted Association of the National Guard of the United States, Niagara Falls, NY. DHS display to be provided.
19-24	Purple Heart National Convention, South Portland, ME. DHS display to be provided.
23-27	American Legion 84th National Convention, Charlotte, NC.
23-29	Veterans of Foreign Wars 103rd National Convention, Nashville, TN. DHS display to be provided.

September

7-9	National Guard Association of the United States, Long Beach, CA. DHS display to be provided.
9-11 (T)	First Annual Deployment Health Conference, Risk Communication and Terrorism: New Approaches for Clinical Practice, Hilton Alexandria Mark Center, Alexandria, VA.
12	VSO/MSO Meeting, 1100.
13	WRAMC Special Care Program, 0900-1200, Small Conf. Rm., Sky 4.
16-18	Air Force Association Aerospace Technology Exposition, Marriott Wardman Park Hotel, Washington, DC. DHS display to be provided.

(b)(6)
08/06/2002 09:15 AM

To: (b)(6) @OSAGWI
cc:

Subject: DHSD's Weekly Activity Report

2b please

---------- Forwarded by (b)(6) OSAGWI on 08/06/2002 10:18 AM ----------

To: (b)(6) @ha.osd.mil
cc: (bcc: (b)(6) /OSAGWI)

Subject: DHSD's Weekly Activity Report
Document is set for Permanent Archival

Attached, please find the Deployment Health Support Directorate Weekly Activity Report.

FHP&R WAR 07.03.02

Deployment Health Support Directorate

(b)(6)
Chief, Case Management Assignment Team
Deployment Health Support Directorate
(b)(6)

CMAT Control # 2002225-0000009 (95)

(b)(6) CIV, OASD/HA

From: (b)(6) CIV, OASD/HA
Sent: Wednesday, November 04, 1998 3:35 PM
To: (b)(6) LtCol, OASD/HA
Subject: FW: Tasker for the SOB -- Informed Consent

From: (b)(6) CIV, OASD/HA
Sent: Wednesday, November 04, 1998 2:52 PM
To: (b)(6) CAPT, OASD/HA
Subject: FW: Tasker for the SOB -- Informed Consent

From: (b)(6) CIV, OASD/HA
Sent: Monday, November 02, 1998 2:02 PM
To: (b)(6)
Cc:
Subject: Tasker for the SOB -- Informed Consent

The Special Oversight Board(SOB) -- not my acronym -- has requested testimony by HA at a meeting in mid November. I have been asked to prepare a short information sheet to respond to the question "Describe current policy regarding informed consent and experimental drugs and vaccines." I have taken the paper prepared by GC and attached -- however, I have made a few pen changes to make it current. I deleted the last sentence in the first paragraph. "The FDA should not forclose needed Presidential options to respond to a military or civilian emergency." I have changed Comment three to say " The FDA and DoD are working together" rather than "should work together". Also I eleminated "could" in the last sentence to now read "FDA and DoD best assist the President in carrying out these responsibilities by working together ... Let me know if these changes are OK. If so, you have your info sheet. (b)(6

SOB Testimony paper IC (fda35a...

Describe current policy regarding informed consent and experimental drugs and vaccines.

1. There are very few FDA-approved drugs and vaccines that will protect against the deadly threats of chemical and biological weapons. For the foreseeable future, the United States will continue to need to rely on "investigational new drugs" for medical defense in both military and civilian terrorist contexts.

The United States today faces the monumental challenge of establishing quickly a credible medical defense against chemical and biological weapons in contexts of both military operations and civilian terrorist response. For most chemical and biological threat agents -- such as soman, smallpox, plague, tularemia, botulinum and other toxins, and bioengineered substances -- there are not yet available effective, FDA-approved prevention or treatment products. Research, development, and production of such products will take many years, even with FDA's commendable new animal efficacy rule. In the meantime, the best medical judgments available will demand the use of some products classified by the FDA as "investigational" -- a term which encompasses a wide range of circumstances from pharmacologic agents that are early in the research cycle to those which are approved drugs but used for different clinical indications in everyday medical practice. In general, "investigational" products may only be used under FDA rules designed to regulate well-controlled clinical studies -- rules that are simply not feasible in the context of a chemical or biological battlefield or a domestic mass casualty terrorism incident. DoD believes the President must be given a range of options -- including the feasible use of "investigational" products -- for providing credible medical protection against chemical and biological weapons.

2. In the military context, the Joint Chiefs of Staff and the Chairman of the Joint Chiefs of Staff have determined that the preservation of authority to uniformly use an investigational new drug if force health protection requirements so dictate is militarily imperative.

When an investigational product is the only means available to protect against a lethal chemical or biological weapon, the lives of individual members, the safety of their comrades who rely on them, and the success of the military mission require uniform use of the medical protection. Further, the nation would demand that military commanders do all in their power and authority to employ prudent medical countermeasures in the face of a biologic and chemical threat. The consequences of an action which leads to foregoing availability of a needed investigational new drug will lead to an unacceptable military operational setting in which the lives of personnel and the accomplishment of mission are jeopardized. The authority to direct usage of medical countermeasures and waive informed consent is limited to cases in which, based on the nature of the threat, the evidence of safety and efficacy, and the absence of an available satisfactory alternative therapy, use of the investigational product is clearly in the best interest of the individual service member. Retention of such authority is essential in support of Force Health Protection.

3. Congress has adopted authority for the President to waive informed consent for the use of investigational drugs in military operations. FDA and DoD are working together to establish

standards and criteria that will help the President determine when informed consent is not feasible or contrary to the best interests of the members involved.

The National Defense Authorization Act for Fiscal Year 1999, on which Congress has now completed action, includes a provision (section 731), sponsored by Senator Byrd, which establishes the controlling policy. The Byrd Amendment provides that the President and only the President can waive informed consent for military operations. To do so, the President must determine in writing in relation to "a particular military operation" that obtaining consent "is not feasible," or "is contrary to the best interest of" the military personnel involved, or "is not in the interests of national security." If the President's determination is based on the "not feasible" ground or the "best interest" ground (the grounds currently in the FDA law and regulation), "the President shall apply the standards and criteria that are set forth in the relevant FDA regulations for a waiver." If the President's determination is based on the "national security" ground, it is independent of FDA regulations. FDA and DoD best assist the President in carrying out these responsibilities by working together to establish "standards and criteria" for determining that informed consent is not feasible or contrary to the best interest of military personnel.

4. Secretary Cohen's current program of immunizing the military against anthrax includes an effective system of education, computerized record keeping, adverse event reporting, medical surveillance, and senior military and civilian leadership and oversight. This program provides the foundation for effective implementation of other chemical and biological defense actions, including those involving investigational new drugs.

Secretary Cohen's Anthrax Vaccine Immunization Program (AVIP) has addressed previous criticisms of DoD and provides a foundation for managing medical defense initiatives, including those requiring the use of "investigational new drugs." Key features include the distribution to all personnel of information papers on the benefits and risks of the vaccine and information sessions in which personnel can ask questions. Accurate computerized records are maintained in a centralized data base. Between March 10, 1998, and September 22, 1998, 75,191 military personnel received immunizations. Of these, 47,788 have completed the initial three shots of the series, and of these, 5,983 have received their fourth shot. Adverse events are reported in the information system and are independently reviewed by a board of civilian experts. Of the 182,705 shots given, there have been seven reports submitted to the FDA and Center for Disease Control and Prevention's Vaccine Adverse Event Reporting System of reactions following the administration of the anthrax immunization. Six of these were minor. One service member had a more severe illness that began shortly after receiving the third dose of vaccine. He has recovered and returned to duty. AVIP also provides the necessary information on who received shots, what side effects occurred and, if there were exposure, how effective was the vaccine. Detailed implementation plans were developed, approved by senior leadership, and are being executed with strict oversight, control, management, and accountability. Additional requirements would pertain to use of investigational drugs and vaccines -- which would be committed to by DoD and agreed to by FDA under the specific protocol involved -- but the foundation for effective implementation has now been established.

CMAT Control #
2002106-0000010 (96)

Deployment Health Support
Trip Report

A. Event: American College of Physicians-American Society of Internal Medicine (ACP-ASIM) Annual Session

B. Dates: 10-14 Apr 02

C. Location: Philadelphia, Pennsylvania

D. Event Point of Contact: (b)(6)
Telephone Number:
E-mail Address: (b)(6)

E. DHS Attendees: Dr. Kilpatrick

F. Assets Used: N/A

G. Individuals Contacted:

H. Purpose: The ACP-ASIM Annual Session is a national educational meeting for internists. The goal of Annual Session is to provide practical medical knowledge for improving patient care.

I. Discussion: Some 5200 internal medicine specialists from across the US and overseas attended this annual meeting. Of the 14 sessions I attended (90-120 minutes each), 7 were directly or partially relevant to the focus of DHSD.

BIOTERRORISM: (Dr Richard Wenzel) Anthrax, smallpox, plague, glanders, tularemia and botulism were discussed. An excellent description, appropriate for physicians, of the activity of the anthrax protective antigen, edema factor and lethal factor was illustrated. Post-exposure antibiotic treatments were described. Complications of smallpox vaccination, from prior data, were discussed as complications for a decision to reinstitute vaccination. Operation White Coat was mentioned in the tularemia presentation. The ACP-ASIM Bioterrorism Resource Center at http://acponline.org/bioterro/?hp was referenced.

PSYCHOLOGICAL EFFECTS OF TERRORISM: (LtCol Engel) Anxiety/depression rates are higher in patients with a greater number of physical symptoms. If a medical diagnosis for physical symptoms is not clear at the first visit, only 15% of patients obtain an explanatory diagnosis with further work-up. "If you have to prove you are ill, you can't get well." (Norman Hadler) Physicians should let patients have their own view of why they are ill. Proof of illness cause is a high test, plausibility of illness cause is a low test and "stress" is a word to avoid because of its unpredictable lay meanings. Healthcare is service and technology. The patient-provider collaboration is necessary, goals should be negotiated and monitoring and follow-up are necessary. (Only 20 people attended this session).

OCCUPATIONAL ASTHMA and ALLERGIES IN THE WORKPLACE: (Dr David Bernstein) Occupational etiologies occur in 5-20% of asthmatics. Latency periods up to 2 years indicate an immunologic pathway from exposure to proteins, chemical haptens or chemicals. No latency indicates reactive airway dysfunction syndrome (RADS). Proof for compensation is difficult. Some asthmatics develop work aggravated asthma. Management starts with stopping exposure, then treating symptoms. Sick building syndrome does not have evidence based data, symptoms are heterogeneous and increasing ventilation results in symptom improvement.

SYMPTOM SYNDROMES: (Dr Dan Clauw) Fibromyalgia, chronic fatigue, multiple chemical sensitivity, somatoform disorders, Gulf War illnesses and other chronic pain disorders by CDC into a single entity called Chronic Multisymptom Illnesses (CMI). There is no evidence for many suspected etiologies (mycoplasma, mononucleosis, Chiari malformation of the spine, etc). Genetics may play a role. Triggers are numerous (infection, physical trauma, psychological stress/distress, hormone alterations, drugs, vaccines, and catastrophic events [not natural disasters]). In symptomatic individuals, the centers in the brain that process pain have a "volume control" problem (lower threshold). Animal research shows genetics and early life events (trauma) permanently change the way adults respond to stress. Individual control and family support result in less stress (animal work). Treating CMI today is similar to treating hypertension 50 years ago. Education, validate symptoms, emphasize they are non-destructive, can't be cured by can be managed, focus on wellness and function not illness or pain, patient takes an active role in treatment. Treatment includes various drugs, but exercise (useful to describe it as a drug for its physiological effects) and cognitive behavioral treatment are important. (About 900 attended this session).

CHEMICAL AND ENVIRONMENTAL WEAPONS: (David Moore) Basically this was a summary of the Army's USARMRICD handbook on chemical agents. No threat or clinical focus was presented. Important points stressed were (1) protect yourself in treating these casualties, (2) flush with lots of soap and water, and (3) protect the treatment facility.

VACCINES: The FRONT-LINE DEFENSE AGAINST BIOTERRORISM: (Dr Gregory Poland) Discussed anthrax, smallpox and plague vaccines. For anthrax vaccine stated if the Protective Antigen is genetically altered, it won't couple with edema factor or lethal factor to produce toxins. It is not recommended for pregnant women, but fetal defects have not been shown to be caused by any non-live agent vaccine. Women to be vaccinated should be asked if they are pregnant. If they respond "no", the vaccine should be given, without other testing. The concerns raised about the anthrax vaccine were due to lack of information (particularly by those giving the shots), misinformation and disinformation, Gulf War illnesses (something is to blame), fear and the media and Congress. He closed with a quote from Einstein "Only two things are certain - the universe and human stupidity, and I'm not sure about the universe."

IRRITABLE BOWEL SYNDROME: (Dr Suzanne Rose) Dr Clauw had suggested this diagnosis was a part of Chronic Multisymptom Illnesses. Dr Rose validated that IBS patients who seek care have greater psychosocial disturbances than those who do not seek care. After

discussing all differential diagnoses, Dr Rose concluded by saying patient education, an ongoing patient-physician relationship, minimal diagnostic studies, setting realistic treatment goals and setting the patient's responsibilities are parts of optimal treatment.

Each of these presentations should be on the ACP-ASIM website (http://www.acponline.org/)

J. Deliverables: Trip Report

K. Recommendations: Use appropriate materials from this meeting to develop communication materials for DHS outreach.

L. Follow-up actions: N/A

M. Prepared by: Michael E. Kilpatrick, MD

Kari Atkinson [redacted]

To: (b)(6)

cc:

Subject: Trip Report
Document is set for Permanent Archival

All:

Attached is the trip report from the American College of Physicians-American Society of Internal Medicine (ACP-ASIM) Annual Session.

ACP-ASIM Annual Session 10-14 Ap

(b)(6) Please CMAT

(b)(6)
Operations Manager
Deployment Health Support Directorate

(b)(6)
04/04/2002 02:37 PM

To: (b)(6) @OSAGWI
cc:

Subject: anthrax article

2b please

---------- Forwarded by (b)(6) OSAGWI on 04/04/2002 02:40 PM ----------

(b)(6)
03/14/2002 10:31 AM

To: (b)(6)
cc:

Subject: anthrax article

(b)(6) –

Attached is the draft piece. It has been seen by (b)(6) and incorporates his edits.

Regards
(b)(6)

---------- Forwarded by (b)(6) OSAGWI on 03/14/2002 09:51 AM ----------

anthrax article for ASD(HA)

(b)(6)
Public Affairs Specialist
Deployment Health Support Directorate
(b)(6)

(b)(6)
Deputy for Public Affairs and Outreach
Deployment Health Support Directorate
(b)(6)

(b)(6)
Chief, Case Management Assignment Team
Deployment Health Support Directorate
(b)(6)

Protecting the Force: The Anthrax Vaccine

By William Winkenwerder, Jr., M.D., M.B.A.

The attacks that launched our nation into war with terrorism last September 11th also made us all aware that terrorists will do anything within their power to achieve their ends. The fact that terrorist organizations, and the rogue nations that support them, can gain access to chemical and biological weapons means that we must be prepared to face threats to our force from risks beyond flying bullets or artillery fire. As the Assistant Secretary of Defense for Health Affairs, your health and safety is my personal responsibility. For that reason, I have ordered the anthrax vaccine to be issued to our service members, starting with those we believe to be at greatest risk of biological attack.

Some of you may have heard that the vaccine is unsafe, or ineffective. Instead of listening to rumors, I hope you'll check what doctors and researchers have to say. For example, the Institute of Medicine is a national organization whose only function is to advance scientific knowledge to improve human health. Following a two-year research effort, this past March the Institute released their findings. The researchers found the anthrax vaccine to be safe and effective against all the ways people get anthrax infections, including inhalational anthrax. In fact, the evidence showed that the vaccine is effective against anthrax caused by all known or plausible engineered strains of the disease.

Additionally, researchers found no evidence that people face an increased risk of experiencing life-threatening or disabling adverse events immediately after receiving the anthrax vaccine compared with the general population not receiving the vaccine. Nor did they find any convincing evidence that people face elevated risk of adverse health effects over the longer term. You can read their summary of the report for yourself on the Internet, at *http://www.iom.edu/iom/iomhome.nsf/WFiles/Anthrax-4-pagerFINAL/$file/Anthrax-4-pagerFINAL.pdf*

In the next few weeks, you'll be hearing more about the program from leaders in your chain of command and members of your medical community. They will tell you what we know about the vaccine and what you can expect. They will let you know that local reactions to this vaccine are not uncommon. The typical reactions include soreness, redness, itching, swelling, and lumps at the injection site. The types and frequency of these reactions are similar to those we see with other common vaccines, such as the tetanus and influenza vaccines. During the discussions with your leaders and health care providers, I encourage you to ask questions. You are your own best health advocate.

We in the Department of Defense have no doubt that the threat of an enemy using anthrax as a weapon against us is very real. Anthrax is the top choice of biological weapons. The disease is almost always fatal if not treated early, and the odorless, colorless spores could be spread on the battlefield without warning.

At least seven of our potential adversaries have worked to develop an offensive biological warfare capability using anthrax. One of them, Iraq, has admitted to producing and weaponizing anthrax. Civilian experts have told us the threat is real. Congress considers it real. And the intelligence community says it's real. Knowing that our enemies will use whatever means they have to pursue their ends, I believe we have an obligation to use every means available to protect you. That includes our best intelligence, detection equipment, protective gear, and a safe, effective, FDA approved vaccine. We owe you that protection.

CMAT # 1998233-E000001

OFFICE OF THE SECRETARY OF DEFENSE
1000 DEFENSE PENTAGON
WASHINGTON, DC 20301-1000

SPECIAL ASSISTANT
FOR
GULF WAR ILLNESSES

OCT 0 9 1998

(b)(6)

Dear (b)(6)

Thank you for providing me with your insights on the response to your previous e-mail. In your e-mail, you point out that the use of the word "SOME" (your emphasis) meant that there were veterans who are sick because of the anthrax vaccine. Allow me to restate for clarity, as the original sentence was grammatically incorrect: Neither we in the DoD nor other outside agencies such as the Institute of Medicine or the Presidential Advisory Committee on Gulf War Veterans' Illnesses, have found any evidence that this vaccine is linked to those symptoms we have seen in **any** of our sick Gulf War veterans. (Emphasis added for clarity).

Your next point is also a grammatical one. In the response to you, a hyphenated word was being used as an adjective, "vaccine-preventable," and was modifying the noun "disease." The words were incorrectly quoted without the hyphenation in your message to give a completely different meaning than the one intended. Your use of the partial quote, "But we are distressed when a service member becomes very ill or dies from a vaccine-" without completing the entire sentence "...vaccine-preventable disease during the course of their military service or when a military unit's effectiveness is compromised by high rates of a vaccine-preventable disease" is contextually inappropriate. I hope the meaning is now clearer.

The article you quote that appeared in the Navy Times was based upon a Food and Drug Administration (FDA) inspection at the vaccine manufacturing plant. The manufacturer is not a government agency. The FDA inspects and approves all drugs and vaccines that are released for use to the public, including use by the military. The article you cite indicates that the FDA is doing their job to ensure the purity and efficacy of the anthrax vaccine manufacturing process to protect public health.

Civilians have for more than 25 years used the anthrax vaccine. Veterinarians (one trained and authorized to treat animals medically) as well as many of the people who work within the livestock industry have received the anthrax vaccination. Although there may be different strains of anthrax, "wild" (naturally occurring) or those developed as a biological warfare agent by this nation's enemies, the disease is still anthrax. Vaccination is the safest way to protect our military forces. The threat is very real as inhalation of anthrax has a 99 percent lethality rate. Service members who have taken the entire six-shot series are fully protected against naturally occurring anthrax, and will most likely survive other strains of anthrax well.

102-19.6.2

The anthrax vaccine does not contain living bacteria, but is made of certain components taken from dead bacteria. In this respect it is similar to diphtheria-pertussis-tetanus vaccinations (DPT) that American children receive before entering school. There is no evidence that the anthrax vaccine is associated with any chronic or permanent local or systemic effects.

In your recent e-mail and in your previous e-mail, you expressed concern about a soldier who reported that he was threatened by his first sergeant with the administration of the anthrax vaccine by force. I understand your concern about this issue. The decision has been made to protect our military forces from anthrax infection from terrorist fallout or enemy attack. Troops will be informed about this program and the vaccine. Those with questions will have them answered. If an active duty member then refuses the anthrax vaccination, the officer in charge will give the member a direct order to be vaccinated. Further refusal will be dealt with legally, not by force. Members of the Armed Forces understand the basic tenet of obeying lawful orders. In addition to a sense of duty, military personnel are members of a team. Ensuring the good order and discipline, as well as the combat capabilities, of the team are key responsibilities of the unit's leadership. Lawful orders are not negotiable, as all service members understand.

Your e-mail further addressed a urine test being used to determine contamination levels. You may be referring to a recent announcement concerning medical follow-up testing for Gulf War service members who may have been exposed to depleted uranium. A uranium level urine test can be administered to detect trace uranium levels. This urine test does not address the other types of exposure that you mentioned.

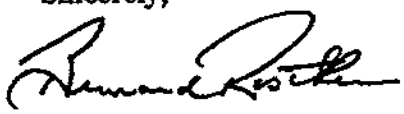
Finally, you requested additional information about the number of Gulf War veterans who have died since the Desert Shield/Storm. We know the number of service members who have died because we compared the social security numbers of the service members who participated in Desert Shield/Storm with the social security numbers kept in the Social Security Administration's death records. We do not have the additional information for which you asked -- state, age, illness, symptoms, causes of death, etc. We do not have autopsies, nor do we have urine samples from these people.

During the Gulf War, 372 deaths occurred among service members in the Gulf region: 148 occurred as the direct result of combat, 193 resulted from injuries not incurred in battle, and 30 resulted from illness. Of the 30 illness deaths, none was from cancer, one was from infectious disease, two were from cardiovascular causes, 21 were initially described as unexpected/undefined, and six others died from miscellaneous causes. Of the 21 unexpected deaths, autopsies were performed on 18 of the deceased. Findings at autopsy were: 13 had serious heart disease; one died of pulmonary embolism from venous thrombosis in the leg; one from ethanol toxicity and aspiration pneumonia; one from unintentional drug overdose; one from gangrene of the bowel due to mesenteric volvulus; and, one from a ruptured cerebral aneurysm. This information comes from an article written by Writer, DeFraites, and Brundage published in the Journal of the American Medical Association, January 10, 1996, Vol. 275, No. 2.

The Departments of Defense, Veterans Affairs, and Health and Human Services are sponsoring additional research into mortality of Gulf War veterans that may address some of the information you now seek. These studies are currently underway, so we cannot report their findings. The only definitive study we have, is an early study by Dr. Kang, which can be ordered from the New England Journal of Medicine web site at (http://www.nejm.org/content/1996/0335/0020/1498.asp).

Thank you for contacting us, I hope this letter has addressed your concerns.

Sincerely,



Bernard Rostker

CONGRESSIONAL or SPECIAL CORRESPONDENCE

Office of Special Assistant for Gulf War Illnesses
Internal Routing/Tasking Sheet

CMAT: 8233-6001

Date: 10/2/96

Coord/ Routing	Position/Organization		Action	Info	Comments
	Special Assistant	(SA)			
	Deputy Special Assistant	(DSA)			
	Executive Assistant to SA	(EA)			
	Executive Assistant to DSA	(EADSA)			
	☐ Director, Investigation & Analysis _____ (IAD) ☐ DepDir _____ ☐ MED _____ ☐ VDM _____ ☐ C/B _____ ☐ ENV _____ ☐ PAG _____				
	Dir Public Affairs & Outreach	(PA)			
	Dir Legislative Outreach	(LA)			
	Dir Quick Reaction Team	(QR)			
1	Dir Medical-Health & Benefits Collab	(MHB)	GWI		after changes. Drop Mail
	Legal Advisor	(LGL)			
	Writers Group	(WG)			
2	PM, Gulf War Illnesses Support	(PM)	*	9/10	
	Editorial Review ☐ AMB _____ ☐ Editors _____	(ER)			
	CMAT	(CMAT)			
	Action Management Call 845-8369 ☐ COMEBACK COPY TO: _____ ☐ GET CMAT NUMBER WHEN SIGNED & SENT ☐ READING FILE ☐ CHRON FILE				

SUSPENSE:

Prepare reply for signature of:

☐ SA/GWI ☐ SD ☐ DSD ☐ DepSA/GWI

Sign
Send

☐ Congress ☐ SOB ☐ FOIA ☐ OSD ☐ WBM ☐ VSO/MSO
☐ Ltr to SA ☐ IR ☐ E-Mail ☐ OGA ☐ Other ☐ Veteran

KEYWORDS:

(99)

CMAT Control #
1998343-0000031

To:	Through:	From:
Special Oversight Board for Department of Defense Investigations of Gulf War Chemical and Biological Incidents (Meeting) Senate Hart Building, Rm. SH-216 2nd St. and Constitution Ave, NE Washington, D.C., 20510	Mr. Roger Kaplan Deputy Executive Director 1401 Wilson Blvd., Suite 401 Arlington, VA, 22209 (703) 696-9470 Fax (703) 696-4062	Joe P. Poe, Jr., USA (Ret.) Founder and President Unified Veterans of America, Inc. 197 Jonesboro Rd, Dunn, NC, 28334 (910) 892- 6967 Fax (910) 892- 5066 Date: November 10, 1998

MILITARY BACKGROUND INFORMATION

Name: Joe P. Poe, Jr. (b)(6) SSG(P) United States Army (Ret.) 28 Jun 1972 - 01 Jul 1992.
MOS': 91A - Combat Medic, 91B - Senior Combat Medic, 91D - Surgical Specialist, Additional - 11B.
Additional Skill Identifiers: Level 3 NCO, "P"- Paratrooper, "X"- Drill Sergeant. (91D3PX)
Security Clearances: Basic ENTNAC; SECRET; TS - Need to Know
Combat Assignments: Panama "Operation Just Cause", 18 Dec 89 - 10 Jan 90; Saudi Arabia and Iraq - "Operation Desert Shield" and "Operation Desert Storm", 11 Aug 90 - 27 Mar 91.
Assignments: C/ 326th Med. Bn, 101st Airborne Division; 121st Evac. Hosp., 8th Army; B/ 307th Med. Bn, 82nd Airborne Division; Company's B,C, & D/ 7th Bn., 2nd Training Brigade, Ft. Jackson, SC (TRADOC); Company C, and HHC, 307th Med. Bn., 82nd Airborne Division; 5th MASH, 44th Med. Bde., 1st Corps Spt. Command, XVIII Airborne Corps.
Primary Duties: Airborne Medic; Airborne Surgical Specialist; Airborne Surgical Section Sgt.; Drill Sergeant; Airborne Ambulance Platoon Sgt.; Surgical Platoon Sgt.; Forward Surgical Team - Tm. Sgt; Forward Surgical Element - Acting 1SG.
Additional Duties: Nuclear Accident Incident Control Party; Company & Battalion (S-3)Chemical, Biological, Radiological- NCO; Company & Battalion (S-3) Nuclear, Biological, Chemical- NCO; Company & Battalion (S-1) Re Enlistment NCO; Company & Battalion (S-3) Air Movements Operations NCO; Company & Battalion (S-3) Hazardous Materials Handling NCO; Company & Battalion (S-3) Plans Operations & Training NCO; Company & Battalion (S-3) OPFOR Instructor & NCOIC; Company, Battalion & Division- Expert Field Medical Badge- Instructor & NCOIC; Company- Survival Escape Resistance and Evasion- Instructor; Company & Battalion -Rifle Marksmanship - Instructor; Battalion- Area Studies NCO; Company, Battalion & Brigade- Bayonet Instructor; Jump Master.
Military Training: BCT; AIT; Basic Airborne; OR Tech.; Jungle Operations Training Course; Cold Weather Training; Race Relations; Advanced Airborne; Air Movements; Junior Leadership; XVIII Airborne Corps Non Commissioned Officers Academy; Drill Sergeants Academy; Advanced NCO Educational System: Canadian Airborne; CBR School; NBC Refresher Course; Re Enlistment; Hazardous Materials Handling; First Sergeants Administrative Course; Rappel Master Certified.
Awards, Decorations, Badges: Bronze Star Medal, Meritorious Service Medal, Army Commendation Medal (4OLC), Army Achievement Medal (4OLC), Good Conduct Medal (Silver Clasp), National Defense Service Medal (2 Bronze Stars), South West Asia Service Medal (2 Bronze Stars), Armed Forces Expeditionary Medal (1 Bronze Star), NCO Development Ribbon (Level 3), Army Service Ribbon, Overseas Service Medal, Saudi Service Medal, Kuwati Liberation Medal, Meritorious Unit Commendation, Expert Marksman Badge (M-16), Expert Field Medical Badge, Master Parachutist Wings, Drill Sergeant Badge, Canadian Jump Wings.
Further information: If needed, can be obtained from my Official Military Personnel File.

Current Status: 100% Permanently and Totally Disabled, with Aid and Attendance, Service Connected, Persian Gulf War, "Undiagnosed". Multiple systemic disorders, multiple neuropathy, organic brain disorders, adrenal tumor (benign), atypical seizures, sense-neural vision-hearing loss, stomach tube fed.

/---PUBLIC STATEMENT, & SUBMISSION of SUPPORTING EVIDENTIARY DOCUMENTS by:---/
JOE P. POE, JR., SSG, USA, (Ret.)

1. Respectfully, to members of the Board, all present, and for the record, I publicly protest the dual role of, Mr. Bernard Rostker, recently nominated by the President of the United States, and approved by the Senate as the new, Under Secretary of the Army, while he simultaneously serves as the, Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses. His demonstrated ability to swerve and vacillate regarding verified reports and documents from professional military leaders, and published material from medical doctors, and researchers, has been clearly established since his appointment on 12 November 1996. Whether by design of appointment, or personal desire, Mr. Rostker has clearly ignored professional input from outside his office. Evidence of his ability to "spin" the facts and effectuate "his" office's policy of damage control, will be presented by speakers present other than myself. As a veteran and concerned citizen, I believe this dual role will present an extreme conflict of interest. And serves only to bury data collected by his personnel, deeper into the abyss of "policy" control, and making he is so well adept to, through his vast experience with RAND, and other "policy" predictors and implementers.

2. Though not related directly to the purposes of this Board (Case Incidents Reports), the following *significantly verifies the ongoing tactics of appeasement, misinformation, and credibility problems with* the Rostker led team, as they "Leave No Stone Unturned". A matter with which the current Special Oversight Board, must clearly be aware of, and hopefully act upon, in a timely and positive manner. Due to the need for brevity, I will cite 4 specific areas. Supporting documented evidence is provided.

On Monday, 26 May 1998, at 1000 hours, myself and veterans named in the documentation met with two members of the Mr. Rostker's team, for almost 4 hours. The purpose was to again seek, and establish a real working relationship with DoD, VA and the veteran community. The DoD, OSADSDGWI personnel we met with were; Michael E. Kilpatrick, Captain, Medical Corps, *USN, Director, Medical & Health Benefits Collaboration; and, Joe Gordon, Col., USMC, (Ret.),* Director of Public Affairs. Our requests, statements, and proposals were received openly. We were asked to assist their office as well, in an effort to maintain open and continuing dialogue. This meeting was initiated by veterans seeking answers / treatment to "GWI", and a hopeful establishment of non confrontational credibility, between DoD, VA, and Veterans. This transpired approximately 6 months ago. We left the table with cautious optimism, this caution has proven itself warranted. We cooperated, and subsequently were appeased, ignored, and ultimately given conflicting or inaccurate information. We did not request or propose to climb the whole mountain, we strongly sought reciprocal efforts toward jointly breaching the foothills. This has not occurred.

It is important to note, that the organization I represent, Unified Veterans of America, Inc., is a non profit, Veterans advocacy organization dedicated to the strength of this great nation, and the well being of our veteran population and their families, past, present, and future. We stand fast in lawful and peaceful resolve to domestic inadequacies for all veterans and military personnel in uniform. We strongly support and defend the Constitution of the United States of America.

We are a Member Organization of; the National Vietnam & Gulf War Veterans Coalition, the National Gulf War Resource Center, and the Operation Desert Shield - Storm Association.

Additionally, many within our organization are members in good standing with; the American Legion, the Veterans of Foreign Wars, the Disabled American Veterans, various Civic and Community organizations. We are supporters of the Last Patrol, and Rolling Thunder.

PROPOSALS & INFORMATION REQUESTED ON THE 26th of MAY 1998, IN WASH.,D.C.

1. Continue existing protocols, and standard tests such as MRI (Magnetic Resonance Imaging). for those presenting with Neurological symptoms. However, when continued neurological difficulties are exhibited, and the initial or follow up MRI reports render findings such as; "Within normal limits", "Essentially within normal limits", "Foggy", or other elusiveness',

   We proposed Neuro Imaging such as SPECT (Single Photon Emission Computer Tomography), or PET scans, to be added to the protocol of tests within both the DoD & VA Medical Centers. (SPECT scans, on the average, are approximately 1.5 times the cost of one MRI. However, when it is indicated that two or more MRI s may be required, the monetary savings of the SPECT scan justifies itself.) Moreover, SPECT / PET scans highlight areas of the brain abnormalities resulting from; 1) Head Trauma, 2) Stroke, or 3) Organic brain abnormalities / damage resulting from toxins. This test has been instrumental in providing expeditious answers to both veterans and physicians, resulting in lessor time, appointments, travel, and needless testing. Thusly, more immediate "provisional" diagnosis', result in more immediate recommendations for appropriate medical treatment regimens, medications, and recognition of the physiological origin of neurologically stemmed medical disorders. Regardless of whether the initial causation is known or [recognized], critical time factors (continued degradation of health, useless testing, appointments, needless travel, and monetary expenditures) are greatly reduced. Whether loss of life will be reduced or eliminated, is undetermined, however the probability for salvaging the quality of life, is undisputed by those who have been fortunate to have had the testing done. Determining and "pinpointing" physical neurological disability, eliminates the continued pre-assumption or misdiagnosis' of somatic, or psychosomatic disorders within an otherwise healthy and mentally reliable veteran population. Further reducing stresses incurred upon veterans, & families, physicians, clinicians, or administrators. (DoD and VA created & proliferated PTSD)

2. I (we) proposed and requested mandatory testing of all PGW veterans, whether presenting with symptoms or not, for Mycoplasmas. In specific, Mycoplasma Fermentans, *incognitus strain.* (Further referred to as, MFI) We urged strongest consideration by the Department of Defense, and the Veterans Administration, to add this to the existing protocol, to assist in establishing a baseline reference for veterans and or family members [and possibly health care providers]. The proposal was met with some resistance by Dr. Kilpatrick, but not totally rebuffed, once he was reminded we were aware of ongoing research and testing regarding the matter. We further recommended that the test procedure be administered, or overseen by, Dr. Garth L. Nicolson, Chief Scientific Officer & Research Professor of Internal Medicine, The Institute For Molecular Medicine. Dr. Nicolson utilizes very exacting, and controlled PCR - DNA test procedures. Again, we cited that regardless of the causation of infection / introduction, the fact that over 50 percent of PGW veterans tested are double positive for MFI, and it is in our blood, is most significant. Additionally, veterans are most concerned and disturbed, when our spouses / intimate relationships, test positive as well in many instances. And, in some cases the children / extended family members.

Though Dr. Nicolson's research, testing, and results have been challenged or attacked by some members of DoD and VA, to include Dr. Kilpatrick, his work is strongly supported by many within the scientific & medical community. It was noted to Dr. Kilpatrick that we were aware that earlier this year, DoD had sent a team to, The Institute For Molecular Medicine, to interface with, and observe Dr. Nicolson's research methods at a cost exceeding $45,000.00.

3. We proposed and requested mandatory DU (Depleted Uranium) testing be added to existing protocols. Again, establishing baseline data. And more importantly, recognition and treatment of medical problems with physiological evidence to the same. Dr. Kilpatrick immediately retorted with words to the effect of,

"You do know that after a few weeks, DU will not show up in Urinalysis tests.... "

Not being researchers, medical doctors, or specialists in Internal Nuclear Medicine, we replied with the best information we had at the time. And proposed hair sample testing. (A method that many veterans have taken in seeking answers and treatment.) Dr. Kilpatrick stated, "Oh, yes. That's right." (We have since learned that we were incorrect, and that hair samplings years after exposure are no more reliable than Urinalysis. Due to varying contaminating factors throughout the course of an individual's lifetime.) And accurate results are found by bone marrow testing. This may include individuals with embedded fragments as well.

(Others throughout the course the Board proceedings, will address Depleted Uranium contamination, and appropriate test procedures, and terminology with greater clarity than I have capabilities to do.)

4. We proposed and requested that DoD begin centralized testing, with subsequent releases of findings. Possibly we were misinterpreted. We were seeking answers, not the ongoing retaining of information that has existed for almost 8 years now. We did however, provide the opportunity for DoD and VA to recover credibility so sorely needed regarding veteran's issues. As you will find in the supporting documents their response was to keep all research and testing with; Walter Reed, VA, the Uniformed Services University of Health Sciences, the National Institute of Health, the Armed Forces Institute of Pathology, and the National Naval Medical Center.

(The same locations that have produced very little to the veterans, public and Congress. Other than biased and politically correct information, which has served to produce minimum progressive activity.)

The previous proposals and requests were the only medically specific areas we took to the table. We stressed that we did not believe, imply, or suggest the issues spoken of were all inclusive, of what our troops were exposed to or given, whether in or out of theatre.

The door was opened by us to hopefully cease continued "warring" between veterans, Department of Defense, and the Veterans Administration.

At that time, there were approximately 1,500 PGW Veterans who had been rated by the VA with "Undiagnosed" illnesses. Therefore we proposed to Dr. Kilpatrick, and Mr. Joe Gordon, that in an effort to alleviate possible "political" sensitivities, opposition, and be as cost effective as possible, that those persons be tested first, in each of the proposed areas; 1- The use of SPECT / PET scans. 2 - Testing for Mycoplasma Fermentans, *Incognitus strain*. And, 3 - Depleted Uranium.

Those 1,500 had already crossed the "politically sensitive" line. And, some had already received the mentioned tests, whereby reducing costs again.

If those tested indicated a significantly high percentage, and the results were made known, then we felt it would certainly justify our requests for mandatory additions to the existing DoD and VA protocols.

To the faces of all present that day, Dr. Kilpatrick agreed that was a sensible outlook, and approach. That was the 26th of May 1998. The number of "Undiagnosed Illnesses" is now approx. 2,000.

OTHER NON-MEDICAL REQUESTS OR PROPOSALS MADE ON 26 MAY 1998

1. We asked why Col. Gerald Schumaker was never authorized to deploy the only real-time Biological Detector capability, the PACER / PBS unit. This unit sat in a warehouse throughout the entire DSS Operation. We stated there is a real credibility problem with that information on behalf of the Department of Defense. (And specifically, the "Leave No Stone Unturned" administration, and DoD team.)

Dr. Kilpatrick replied that, " Yes, that is a credibility problem. One that we are having to address." He further stated that that was why he and his Navy unit were deployed. When asked where he was deployed to, he stated, "Cairo, but we had field teams in Saudi, checking different unit locations, reporting dysentery, and things like that."

We were told that they would be getting back with us on that subject.

(For the record, I am providing a taped video of Col. Gerald Schumaker's statements and a transcription of the same to the members of this Board. The transcription was provided to Mr. Rostker and team at the Camp LeJeune Town Hall Meeting)

Dr. Kilpatrick asked us to demonstrate cooperation, and provide assistance to his office in finding U.S. personnel who had been in close contact with, S.A.N.G. units, or individual S.A.N.G. personnel.

We found the request needless, since DoD has greater data resources, however, we thought it was their way to determine our willingness to reciprocate. So, we did. You will find attached documentation to verify our efforts, with Dr. Kilpatrick's response, and approval.

In addition to the attached documents, I state today that at the NGWRC Conference, held in Washington D.C., I was approached by Mr. Joe Gordon, and Mr. Prather. At that time I was told, "You know, Joe, we simply haven't been able to find out a thing about anything called a PACER. Or, what was it you called it? Was that an acronym or something like that? Let us know if you can find out more about it, and we will do everything we can. But, we are just at wits end."

This was witnessed by two other persons, when the statements and questions were posed to me.

Approximately one month later, at the Camp LeJeune, Town Hall Meeting, I cited the PACER / PBS units again. At that time, I suggested to Mr. Rostker, Cpt. Kilpatrick, and Mr. Prather, the following;

"Since no one in your office can find out anything about the PACER / PBS Biological Detector units, Maybe you can find Col. Gerald Schumaker, you seem to be able to find anyone else that you want to."

Maybe the members of this Oversight Board will be able to get some answers, for the sake of our nation.
/----------END OF WRITTEN PUBLIC STATEMENT----------/

Joe P. Poe, Jr.

Subj: **PRIVATE - NEED IN PUT - PART 1**
Date: 7/20/98 7:05:26 AM Eastern Daylight Time
From: [redacted]
To: [redacted]
To: [redacted]
To: [redacted]
To: [redacted]
CC: [redacted]

First, Apologies to all for the length of this message.... However, I feel it is required to give the full picture at this point.... in regard to asking your advice. [redacted] have not made comms with you, due to the understandable request of family and friends to allow you ample recovery time, so if it is still too early, sincerest apologies... and a simple reply..... to let you be, would be in order, and no offense would be taken. [redacted] you are amoung the numbers who were present in D.C, when we met with Rostker's boy's, and are key players in this matter. To [redacted] without the knowledge you passed on to Marilyn and me, I would not have known of specific test (SPECT) scan to demand while in Birmingham VA, and would still be that much more in the dark. To [redacted] you have much experience in Veteran matters, are a key player, aware of my case, and know that my abilities to produce results are steadily declining. To [redacted] your knowledge, dedication, and confidentiality can be trusted. [redacted] To ALL, we are approaching to 60 day mark, since I (we) gave DOD the proposal to incorporate 1) SPECT / PET Brain scans, 2) DU tests - via hair - follicle samples, 3) DNA - PCR Blood tests for Mycoplasma Fermentans Incognitus.... into the standard protocal for PGW veterans. Additionally, we requested an official answer from DOD in reference to the somehow forgotten subject of why our PACER Biological Detection units were not authorized deployment into theatre, and sat in Dover the whole time, and also we inquired into the status of forensic studies that have been done on deceased PGW vets...to wit the reply was *none have been done*. .... Joe Gordon and Mike Klipatrick, in turn asked us to assist DOD in finding personnel who had contact with S.A.N.G. personnel while in theatre, we have done so, and have gotten responses. We did not ask for the whole mountain, just a part of it that could make an immediate difference for thousands of personnel. With this said, I submit to you all contact to date, in sequence, please note the order of things..... and help me with some perspective....at present time, I do not find DOD's requested interview to be beneficial to the cause of our veterans....and feel that they are attempting somehow to destroy what we set out to do.....

<< Subj: **US - SANG contact**
Date: 5/29/98 12:38:24 PM EST
From: UVAC2
To: VetCenter

Your assistance is requested in locating / contacting, Persian Gulf War veterans who had contact with the **SANG - Saudi National Guard.** This is being done in an effort to aid various medical researchers who are continuing to pursue answers and treatment for the many different medical maladies experienced by our Gulf War veterans and or families. This is important, as you may know, coalition forces have been, and are experiencing many of the same signs and symptoms as our's have. Any help in this matter will be greatly appreciated. The categories include but are not limited to the following. Individuals who : 1) Had close personal contact with SANG Forces. 2) Performed joint missions / projects with SANG. 3) Trained SANG personnel / units. 4) Were in close proximity to SANG units. Respondents should be prepared to give their names, unit they served with, duty capacity, dates in country, and if they have in the past, or are currently experiencing medical difficulties due to service in the Gulf (**particularly " unexplained " or " undiagnosed "**), and if they are on the DOD or VA registry. When possible, they should describe; locations, dates, and mission / project designators, in regard to items 1-4. Also, the individuals should note if they have reported information of this nature before, either while in country, or through the established DOD Hotline for incident reporting . ***Once again this is specifically related to SANG contact.*** *Please post to your* various web-sites, message boards, etc. Individuals should E-mail to, **uvaxo@intrstar.net** or **UVAC2@aol.com**. Please enter **SANG** in subject box. " Vires Per Unum " Joe P.Poe, Jr., UNIFIED VETERANS OF AMERICA .

>>.....

Subj: **Re: US - SANG contact**
Date: 5/29/98 2:34:20 PM Eastern Daylight Time
From: mkilpatr@gwillness.osd.mil
To: UVAC2@aol.com

The message looks clear and comprehensive. Looking forward to talking with you on Monday - I've had some very positive interactions with all organizations, including the VA.

<< Subj: **Vets meet with members of DoD's Office for GW Illness**
Date: 6/3/98 5:26:36 PM EST
From: (b)(6)
To: VetCenter@aol.com (VetCenter)

Press Release:

Vets Meet with Members of DoD's Office for Gulf War Illnesses

On Monday, 26 May 98, at 1000 hours individual members of the Last Patrol, Unified Veterans of America, Inc. and Rolling Thunder met with members of Bernard Roskers, PhD. staff. The members of Rosker's staff were CAPT Michael Kilpatrick, MD, USN, Director, Medical and Health Benefits Collaboration and Col Joe Gordon, USMC Ret. Director of Public Affairs. The meeting directly involved Mike Woods of the Last Patrol, Joe Poe of Unified Veterans of America (UVA) and Mike Ange of UVA, however, about 15 vets and family members were in attendance and several of them provided invaluable input to the meeting. Our purpose for establishing the meeting was to determine if an effective cooperation could be developed with a goal of locating REAL treatment options for Veterans suffering from the so called "Gulf War Syndrome".

As most of you know, past contacts between Rosker's staff and Gulf War (GW) Veterans have been very confrontational. While confrontation is understandable, we did not feel it was producing productive responses. Due to the adversarial nature of past meetings with this office and the political nature of some questions we face, some agreements were made up front. Among those agreements was an understanding that we are not focusing our efforts on the causative factors of GWI. It was decided that the more important issue was "immediate, accurate and effective treatment" for GW vets. If corrective treatment was not possible, then adequate compensation to insure a reasonable standard of living for affected vets was our second primary goal.

Mike Woods introduced a proposal to unify the research process. Specifically, he proposed that DoD start completing all of the viable testing available in one centralized location for as many veterans as possible. We proposed the continued use of traditional test with the addition of the following test as a minimum starting point. A battery of neurological imaging tests including new tests such as SPECT (Single Photon Emission Computed Tomography)

Scans and PET Scans that should address areas not covered by more traditional testing methods, this should eliminate some of the misdiagnosis experienced by GW vets previously. Additionally, we have requested that testing for mycoplasma fermentans incognitus, depleted uranium and any possible chemical or biological warfare agent exposures be included.

In order to remove as much political opposition as possible from the research process, we proposed using the 1500 plus vets already accepted by the VA as having undiagnosed illnesses from the Gulf War as the FIRST people tested. Data from these individuals could then be compared to baseline data from a healthy control group of similar demographics (age, ect.). According to our proposal this study would then be used to establish a protocol for the most efficient and effective testing of other veterans having gulf related problems. The research would also lead to the establishment of a uniform treatment protocol based upon the GW vet's specific problems. We also discussed why forensic pathological studies (autopsies) of deceased veterans had not been conducted to date.

As most GW vets are aware, The Department of Defense has had demonstrable difficulty with the accuracy of released information regarding Gulf War Troop Exposures generally and the factors impacting Gulf War Syndrome specifically. (Specific instances include an on the record admission by General Swartzkoff that he provided false testimony to The U.S. Congress regarding chemical exposures of troops under his command in the Gulf War, as well as other documented instances.) In order to provide an impetus for spontaneous integrity, we proposed the formation of a panel of observers to closely watch this research process. This panel will be composed entirely of individuals selected by the veteran's groups, including vets and professionals that meet certain criteria for professional background and training. Acceptance of this proposal by the DoD is necessary to obtain our cooperation in what has become another research process.

The initial meeting concluded with the selection of Mike Ange as the primary point of contact for the veteran's organizations present. It was also agreed that DoD would have 1 week to research the validity and feasibility of the proposals made and that specific information about the meeting would not be released prior to that deadline. The deadline for contact was set for close of business on 1 Jun 98.

On Monday, 1 Jun 98, Mike Ange, Joe Poe and Eric Truesdale participated in a conference call with Col Gordon and CAPT Kilpatrick. Basically, the call confirmed the general acceptance by The DoD of the proposals made by the veterans. There were some modifications. Due to the infeasiblity of testing all veterans at Walter Reed, additional facilities were included in the list of research facilities to be used. The list of agencies now includes:

The Veteran's Administration, The Uniformed Services University of Health Sciences, Walter Reed, The National Institute of Health, The Armed Forces Institute of Pathology, and The National Naval Medical Center.

A draft of the proposed research protocol is currently being developed. This protocol will have impact on the qualifications required in the panel to be selected by the veteran's organizations. It is expected that the required qualifications will be available to the veterans groups within two weeks. CAPT Kilpatrick anticipates that this study should be operational within 3 to 4 months. Simultaneously, DoD is developing a proposed protocol for pathological studies to be conducted on deceased veterans with Gulf War illnesses. This procedure is expected to require permission of the immediate family members and forms for that purpose are also being developed.

As veterans, we need to keep this door open and try to impact the future of our own medical care as much as we can. While we are accepting the efforts of DoD as one step in the right direction, we are doing so with extremely guarded optimism. This one step cannot erase a well-established legacy. However, shouting at each other over a podium will not secure the end results our veterans need. Hopefully, we are finally on a road that has the potential to lead to results.

Veterans or family members desiring more information on Gulf War Illnesses should contact Unified Veterans of America at email address unifiedvet@aol.com or The Last Patrol at lpatrol@aol.com. There are numerous groups supporting GW vets and these two resources can answer questions or forward you to an active group in your area. For details specific to this article contact (b)(6)

>>.....

..... Then, on 6/9/98, I get called at home from " Ivory" in Bernie's office, wanting to do a telephone interview.... interesting, why me, I am not their friend. Told her I don't do phone interviews with anyone.... to easy to have words turned about. resulting in..

..... Subj: **Veterans Spotlight article**

Date: 6/9/98 12:22:22 PM Eastern Daylight Time

From: (b)(6)

To: (b)(6)

Good morning Mr Poe

Thank you for speaking with me earlier this morning. My name is Ivory and I am a Public Affairs writer with Joe Gordon's team.

As I mentioned in our phone conversation we are interested in writing an article on you for our Veterans Spotlight section in our newsletter, GulfNEWS. The spotlight article highlights a vet who provides a motivational example for others. You can see past spotlight articles that

have been written on GulfLINK. Just click on News. I thought it would be more convenient for you if we corresponded via e-mail instead of a telephone interview. If you and your wife don?t mind us doing an article on you I have written several questions I would like to start out with.

1. Where were you stationed during your time in the gulf and how long were you there? What unit were you with?

2. How long after your return did you begin to experience symptoms?

3. Did you register with the Comprehensive Clinical Evaluation Program (CCEP) or VA Registry to receive your medical evaluation? If so, where and when?

4. How have the medical symptoms you have experienced affected your life and your family?s life?

5. Please explain a little about the medical protocol that you have proposed for the care of Gulf War veterans.

6. Please explain a little about the work the United Veterans of America hopes to accomplish

I am trying to conduct the interview and get the article written within the next few days. If you have any questions you can e-mail me at (b)(6) or you can call (b)(6)

Even though their office knows the answers to each of the questions, I responded

Subj: Re: Gulfnews Spotlight
Date: 6/9/98
To: (b)(6)

Dear Miss Graham,

Your initial line of questioning looks reasonable. My statement regarding my wife to you, was done in a light-hearted manner. I'm sure you know that. The reason I will not do a phone interview is that inevitably there will be questions requiring locations, dates, etc., or other specifics. Any and all answers rendered by me, will be accurate and complete, and that usually requires referring back to paperwork for accuracy. My question to you at this point is if you still want to interview me..... Will my answers be printed in their entirety? I do not use obscenities, or go into wild accusations. I do speak with confirmed facts, regardless of the subject matter. Bear in mind, I am not pleased with all that has transpired in regard to the Persian Gulf War, and it's after effects. The war's attrition rate has been at home. I still believe in strong National security, and the establishment of a REAL working relationship between DOD, VA, and our Veteran community, however " Blind Faith" trust to anyone or any department is not my forte. You have a job to do, and so do I, we are not adversaries, only patriots, from probably very different perspectives.I am far different than MSG Pedro Coll. Are you sure you still want to do this? Regardless of your decision, thank you for the interest.

Sincerely, Joe.

Apologies if I got your title wrong (Miss or Ms), These are the '90's, and Clinton is president.

THEN

Subj: Re: Gulfnews Spotlight
Date: 6/9/98 3:29:02 PM Eastern Daylight Time
From: (b)(6)
To:

Thanks for your response. I appreciate your effort to provide accurate and complete information. We will print your full responses as much as possible. We are limited by space constraints but we will not print any of your statements in a manner in which they may be taken out of context. We are still interested in hearing what you have to say and writing your story.

Oh and no offense taken. Miss or Ms is fine or just Ivory.

Subj: **Re: Gulfnews Spotlight**
Date: **6/9/98**
To: (b)(6)
CC:

"Ivory", I am slow, and my speech is not so good anymore. Joe Gordon and Mike Kilpatrick can vouch that I am not the best orator nowadays. So, thank you for agreeing to do this by E-mail. Plus, it is a courtesy to you. to not have to sort though somewhat unintelligible words or phrases. I will maintain as much brevity as possible in answering your questions. Joe.–

The same evening, I was taken to the E.R., and admitted to the VA for a few days. When I returned home, I was in the middle of putting together a reply, when we received word of a death in the immediate family, which took me out of state for a few days. When we returned home, this was on my E-mail ———

Subj: **Update**
Date: 6/22/98 5:02:47 PM Eastern Daylight Time
From: (b)(6)
To:
CC (b)(6)

The planned trip to Ft Bragg for the week of July 14 has to be rescheduled. The Special Oversight Board appointed by the President to monitor what the Special Assistant for Gulf War Illnesses does has requested to be briefed by the office on July 16 and 17. This conflict has caused us to have to reschedule Ft Bragg. Joe Gordon will let you know when that rescheduled time will be.

I spent June 16-19 at the meetings for Federally funded researchers on Gulf War Illnessess while the OSAGWI team went to Ft Campbell. Needless to say, little got done at the office with everybody out. I have identified Dr Jim Smimiotopoulos at the Uniformed Services University of Health Sciences as the neuroimaging specialist to develop the protocol to compare the diagnostic capabilities of the SPECT scan to other types, including the PET scan and the f-MRI, among others. I will need to work with him to develop the details of patient selection, etc. I can't tell you a time line yet on the protocol, but will pass something more after I talk with him tomorrow.

I read that the PAC recommended a "civilian advisory committee" for all epidemiological studies. I think that concept is consistent with what we discussed to have veterans in on the ground floor when research concepts are put together to do a reality check. Think if there is a better or more comfortable title. I'm not sure about the word "civilian".

Look forward to your reply, and will update you as I have more.

Subj: **Neuroimaging study**

Date: 6/24/98 9:05:08 AM Eastern Daylight Time

From: (b)(6)

To:

CC: (b)(6)

I spoke with Dr Jim today - he is leaving for a 2 week meeting/holiday in Greece. To get a research protocol intitiated that makes scientific sense, it is necessary to have some background information on the patients who will participate (this is general information and not individual specific). I know we talked about the 1500 patients who have been categorized as undiagnosed illness by the VA. I'm not familiar with the medical workup that would lead to this category or if it was the same for each patient. To get lift off on this part, I either need to talk with a knowledgeable physician at a VA that has made this diagnosis on patients, or I need the names of patients willing to have me request the VA to review their records to give me that information. I don't have access to the VA medical records due to privacy restrictions. One way to perhaps enlist people to participate is to state that those who come forward will be the first ones to be evaluated with the battery of neuroimaging studies. It is not necessary to do a random selection of the 1500 patients since we are looking for a test which identifies a "marker" for diagnosis of Gulf War illnesses.

The protocol for this study needs to state a purpose, so we need to understand the general conditions of the Gulf War veterans in the undiagnosed illness category. We need to know if some/any/or all have had MRI's, for example. We need to know what the major problems are they are experiencing, for example headache, short term memory loss, physical neuromuscular problems, muscle and joint pain, etc. We will look at reports of SPECT scans to see what type of scans are being done and what is being "read" as the results. Putting the protocol together by mid-July should be a timetable goal for us. I will be sure LtCol Engle includes his programatic portion, and I will also coordinate with him about Mycoplasma fermentans incognitus testing since he is coordinating the DoD effort on testing with Dr Garth Nicolson (who I met for the first time last week). Once drafted, the protocol will have to be presented to the Research Working Group and be reviewed by the external scientific review board. Then funds are allocated if the scientific review scores are high. I believe there is enough interest in the right places to expedite this process and to assure there is enough "seed" money to at least get this off the ground.

One of the critical parts is to have a panel of experts, recognized by the neuroimaging community as experts, to simultaneously read all the scans so that there is a consensus opinion. The " veterans' advocates" (I just made that up) advisory committee would get activated once the drafting of the proposal is initiated. This could be a small number of people here in the DC area who could meet with Dr Jim as he thinks the protocol through.

June 24 - just found this in my draft box, thought I had sent it yesterday. Sorry about the delay. If you need any more details, just ask. I have a very unscheduled day today, so I'll be able to respond in a timely manner.

Now, while discussing with some of the others, exactly what to make of what had transpired up to this point, and how to respond in the most appropriate manner, I received the following

Subj: **PRIVATE - INPUT REQUESTED - PART 2**
Date: 7/20/98 7:05:30 AM Eastern Daylight Time
From: UVAC2

[redacted]

In a message dated 7/1/98 10:21:59 AM EST, (b)(6) writes:

<< Subj: **Fw: Squalene as an Adjuvant**
Date: 7/1/98 10:21:59 AM EST
From: (b)(6)
To (b)(6)

—Original Message—
From: (b)(6)
To (b)(6)
Date: Wednesday, July 01, 1998 6:35 AM
Subject: Squalene as an Adjuvant

>
>
>
>
>Dear Mr. President,
>
>In keeping with your policy to get to the bottom of why Gulf War Veterans'
>
>are ill, I believe that before the DOD can rule out the use of a synthetic
>
>adjuvant called squalene and currently used by WRAIR in Malaria and HIV
>
>vaccines; veterans' testing positive through Tulane University and John
>
>Hopkins University should also be tested by the Department of Defense as
>
>well. Many of us have had numerous tested performed outside of the
>
>established agencies, DOD, and DVA. in order to prove that our illnesses
>
>are based upon sound medical evidence and not psychosomatic stress related
>
>diagnosis. My medical results include hair analysis by Doctor's Data,
>
>Chicago, IL, showing abnormalities resulting from malabsorption, brain
>
>SPECT exam abnormalities, and positive test results for an uncommon
>
>mycoplasma found particularly in only the Gulf War Veterans' population.
>
>As you can see, all these tests have supported my claim that my immune
>
>system is shot. I am one of the fortunate ones who is ill enough to

>
>receive health care benefits from Social Security Disability and the
>
>Department of Veterans' Affairs. However, I am also one of these veterans'
>
>still waiting on the DVA to adjudicate my Persian Gulf Claims, as well as ,
>
>service connection for secondary illnesses due to diabetes mellitus. I
>
>intend to have even more tests run to prove this is not psychosomatic but
>
>underlying medical causes are to blame. At this very time, 8 out of 11
>
>Gulf War Veteran Brain SPECT Exams at the OKC, VAMC, have significant brain
>
>abnormalities, and a request for funding based upon these findings is
>
>forthcoming to the DOD for consideration for clinicl trials.
>
>I would appreciate it if the Department of Veterans' Affairs test for
>
>synthetic squalene as well, and I believe and expect an answer to my
>
>request within a reasonable period of time leaving, "NO STONE UNTURNED!"
>
>Sincerely,
>
>Dannie Wolf
>
>http://www.lawtonok.net/wa/pgvf.htm
>
>PGVF Webmaster
>
> Initial email message
>
>Response:
>Dear Mr. Wolf
>
> Thank you for your recent e-mail to President Clinton regarding
>squalene as a possible cause of Gulf War illnesses. This is Robin,
>and I am responding on behalf of Dr. Bernard Rostker, the Special
>Assistant for Gulf War Illnesses.
>
> Allow us to reiterate a few statements we have told you before
>that
>address the major points of your e-mail to the President:
>
> -- Squalene was NOT used as an adjuvant in any vaccines given to U.S.
>troops in the Persian Gulf conflict.
> -- Squalene is an experimental adjuvant under development for HIV and
>malaria vaccines. Neither were administered to U.S. troops who
>participated
>in the Gulf War.
> -- All tests to determine the presence of squalene or squalene
>antibodies
>are experimental and currently unproven. We will contact Tulane and
>Hopkins to learn more about what tests they are conducting.

> --All tests for mycoplasma fermentans (incognitus) are experimental
>and,
>as of yet, unproven. The Department of Defense is currently working with
>Dr. Nicolson to validate the reproducibility of his testing methods.
> --Civilians with chronic fatigue syndrome who were never in the Gulf
>are
>reported to have a 50 percent positive rate for mycoplasma fermentans
>incognitus.
> --Spect scans are indicative of blood flow changes, but do not confirm
>an
>anatomical lesion responsible for symptoms.
> --As you know, this office is encouraging investigators with expertise
>in
>neuroimaging to develop a protocol to evaluate and compare new
>technologies.
>
> We also invite your attention to the most recent Annual Report
>to
>Congress from the Department of Veterans Affairs Persian Gulf Veterans
>Coordinating Board Research Working Group concerning the Federally
>Sponsored Research on Gulf War Veterans' Illnesses for 1997 released
>in March 1998. You can download this very large document from the
>Internet at (http://www.va.gov/resdev/pgrpt97.htm).
>
> Thank you for your continued interest in the progress of our
>investigation into what happened in the Gulf that has made some of our
>veterans ill. We know our investigation is important to you.
>950701

After looking at the course of events..... reading some of what had been sent out from ...Robin of Rostker's dream team..... and taking all into what I hope is still perspective, I believe that they are attempting to jerk me around to become a seal on their ball..... I am tired, and trying to keep peices together in many other directions simultaneously..... Will all of you please give my tired butt some thought on this situation. I do not want to harm any efforts that have already taken place by so many dedicated persons. Please send your replies to each I have listed, so we are all on same sheet of music..... But please to no others....Screwed but not through, Joe.....MY PHONE IS[redacted]

"Pacer" Units Reportedly Never Deployed During Gulf War

"U.S. forces or U.S. Intelligence or someone,
did not want a real-time detection system
[for biological agents]
on the battlefield."...LTC Schumaker

A Special Gulf War Illness Report by
The Northwest Veterans Newsletter
with information provided by 'The Unified Veterans of America'

September 1998

We now know that the Pentagon has admitted to the possibility of low-level chemical exposures during the Gulf War, or possibly from Allied demolitions of Iraqi bunkers. However all evidence of such exposures is generally referred to as "anecdotal" and chemical alarms from all equipment, no matter the sophistication, cannot be "substantiated" with a paper-trail. How convenient...

We also know that opinions of possible biological exposure, such as former CIA analyst Patrick Eddington and several doctors - notably Prof. Garth Nicolson - are purely "opinions" since I have found that the Allies had no means of detecting biological agents in the Persian Gulf.

But what I now find of great interest is a television report by the 'American Investigator,' hereafter referred to as "AI." I have obtained a video-taped copy from a Mr. Joe Poe, Jr. (See Footnote)

Mobile Biological Sprayers:

In the video tape, it is brought to the viewers attention that prior to the Gulf War, the Pentagon was most aware we did not have equipment that could produce real-time detection of biological agents. I was led to believe when questioning the detection of biological agents that such equipment did not exist. The AI report goes on to explain about mobile sprayers. These sprayers could be deployed in the rear of a pickup truck and dispense approximately 20 gallons of biological agent. AI reported that prior to the Gulf War the CIA had learned that Iraq had purchased 52 of these mobile sprayers from an unnamed "allied" government. In turn, according to the AI investigation and from information provided by a then active-duty Lieutenant

Colonel, the CIA purchased two of these mobile sprayers for testing of their effectiveness prior to the Gulf War. CIA findings, according to AI, discovered that just TWO of these mobile sprayers deployed at the leading-edge of and offensive could result in the deaths of 100,000 Coalition Forces.

Pacers and PBS:

The AI report centers on the reports of LTC Gerald Schumaker, Army, 91st Division and Vietnam veteran. It is a fascinating story to say the least. LTC Schumaker was part of a project to urgently update a biological detection system dating back to the mid-70's, known as "Pacers." This antiquated Pacer system took a minimum of 18 hours to develop results. Obviously this would be of no value during a war, and thus a crash program was initiated to develop 'real-time' testing that could provide such results.

According to LTC Schumaker, they accomplished that goal. But the PBS unit was never deployed to the Gulf despite repeated efforts by LTC Schumaker. Below is a transcript of what follows in the video. The transcript begins with LTC Schumaker's comments to AI regarding a scheduled meeting with a Lt. Gen Harrison. The purpose of this meeting was to persuade an apparently reluctant Lt. Gen. Harrison (the Commanding Officer) to deploy Schumaker's PBS unit to the Gulf prior to the shooting war.

LTC. Schumaker:

> "...On the third day I walked into General Harrison's office, to brief him, at a scheduled appointment.
>
> "Lt. Gen. Harrison waived his hand at me and said; 'Colonel I don't even want to hear about it. This project is dead and you are not going anywhere.' "

Comments: At this time in the video tape, AI points out that perhaps the PBS detection equipment was not needed in the Gulf "...because the troops had been vaccinated for anthrax." AI at this point stated that LTC Schumaker disagreed, and that the Colonel had reported that only 10% of the ground forces had received the anthrax vaccine. In fact it was made obvious that LTC Schumaker considered the widely publicized report of the anthrax vaccination as intended 'misinformation' to Iraq. A 'report' to make the Iraqis believe

that the use of biological weapons would be of no value whatsoever .

The tape now goes back to LTC Schumaker...

LTC. Schumaker:

> "Three times in that conversation, General Harrison reached for the phone. One time he picked it up and actually started to dial it. Then he set it back down and said; 'No Colonel, you and your team are not going.' "

AI:

> "Has there been a system in place that could determine whether biological weapons were ever used in the Gulf?"

LTC. Schumaker:

> "The only capability the U.S. military had to even come close to real-time detection of biological agents on the battlefield never made it out of the warehouse.
>
> "When I read Department of Defense reports that repeatedly state; '...there is no evidence of biologicals used...' in my gut...what goes through my mind...is that we never deployed the only capability we could have had to determine whether that fact existed or didn't exist."

AI:

> "Has there ever been a mention of the mobile biological sprayers in the public record, previous to this interview?"

LTC. Schumaker:

> "Not anywhere I've ever read, in any document, in any place..."

Comments: AI reported that four separate approaches to get intervi ews
with the Pentagon had failed concerning the mobile sprayers. This included attempts to get an interview with Colin Powell and AI sta ted,

"Why the reluctance to talk about this?"

LTC. Schumaker:

"I'm not suggesting that there is some massive conspiracy here of people who joined together to not talk about the sprayers. I mean, there is a handful of people who, for some reason...who haven't talked about the sprayers.

"U.S. forces or U.S. Intelligence or someone, did not want a real-time detection system [for biological agents] on the battlefield.

"The very far extreme...was someone worried that detectors would go off, a lot?"

AI:

"Are you worried about personal repercussions?"

LTC. Schumaker:

"Yes I am. I intentionally did this interview before I retired from active duty because I resent the fact that so many officers and government officials such as McNamara and others, after they had nothing to lose, tell the world the way it really was.

"I feel they could not have been a man of ethics and values if they wait until there are no risks to themselves."

AI:

"Why are you coming forward with this story?"

LTC. Schumaker:

"We aren't trained to defend against this! And I can no longer sit idly by, wait another five years, another 10,000 soldiers going to the Gulf now, to say...'Well, gee, if they really turn them on [the sprayers] I guess we'll have to deal with it.'

"We need to deal with it NOW before they turn

them on. I think before we put our soldiers in harm's way, again, we need to fix the problem. We need to develop the protection. We need to be able to defend ourselves. And most of all, we need to be able to treat those soldiers and their families that are now suffering."

[End of video as I received it from Joe Poe, Jr.]

~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

Food for thought...

AP 9/1/98, regarding the report released by the Committee on Veter ans'
Affairs Special Ivestigation Unit on Gulf War Illnesses:

"The report backs up Pentagon officials who deny any cover-up of chemical weapons exposure to troops, a suspicion that emerged after the disappearance of one-fifth of the logs that would record such activity. The report blamed 'negligence rather than conspiracy...' "

~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

Roger Young -- The Northwest Veterans Newsletter
E-mail: (b)(6)

For additional information, contact Joe Poe, Jr.,
E-mail: (b)(6)

Footnote: Joe Poe, Jr. first entered the Army in 1972 and served with honor his entire career which culminated following the Gulf War. Joe today, just a few short years following the Gulf War, is one Desert Storm veteran with a 100% disability, but not in spirit or intelligence!

Mr. Poe now heads 'The Unified Veterans of America, Inc.' based in North Carolina which supports ALL veterans -- Roger Young

End Notes

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pacers.txt

Released to Joe Poe, Jr. 20 October 1998 at his request

(100)

OFFICE OF THE SECRETARY OF DEFENSE
1000 DEFENSE PENTAGON
WASHINGTON, DC 20301-1000

SPECIAL ASSISTANT
FOR
GULF WAR ILLNESSES

APR 21 2000

MEMORANDUM FOR ASSISTANT SECRETARY OF DEFENSE
(ATTN: HEALTH AFFAIRS, LTCOL NORRIS)
OFFICE OF THE SURGEON GENERAL
(ATTN: AVIP, LTC GRABENSTEIN)
UNITED STATES ARMY MEDICAL RESEARCH
INSTITUTE OF INFECTIOUS DISEASES
(ATTN: COL MCKEY)

SUBJECT: Recoordination of Information Paper – Vaccine Administration During the Gulf War

Please review the revised draft information paper, Vaccine Administration During the Gulf War (attached). This recoordination addresses the issues raised in the initial review of the information paper. Concurrence/ nonconcurrence and comments are requested by Friday, May 12, 2000. Direct your responses to our point of contact, (b)(6) fax (b)(6). Requests to view documents referenced in the narrative should also be directed to Mr. (b)(6)

The Vaccine Administration During the Gulf War information paper is a draft document. The release of the document for external coordination does not constitute authority for public release. The document is expected to be released promptly at the conclusion of the coordination process.

Michael H. Abram COL US Army
Dale A. Vesser
Deputy Special Assistant

Attachment

Information Paper

Vaccine Use During the Gulf War

Information papers are reports of what we know today about military equipment and/or procedures used in the 1990-1991 Gulf War. This particular information paper on vaccine use during the Gulf War is not an investigative report, but is meant to provide the reader with a basic understanding of the vaccine policies and practices during the war. This paper provides background information on vaccines and vaccine-related issues, shows how the military develops and implements its vaccination policies, and reviews what we now know about vaccine use in the Gulf War. This is an interim paper, not a final paper. We hope that you will read this and contact us with any information that would help us better understand and report on vaccine use during the Gulf War. Please contact my office to report any new information by calling:

1-800-497-6261

Bernard Rostker
Special Assistant for Gulf War Illnesses
Department of Defense

1999012-0000011
Ver 1.0

Last Update: December 7, 2000

Many veterans of the Gulf War have expressed concern that their unexplained illnesses may have resulted from their experiences in that war. In response to veterans' concerns, the Department of Defense established a task force in June 1995 to investigate incidents and circumstances relating to possible causes. The Office of the Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses assumed responsibility for these investigations on November 12, 1996, and continues to gather information on vaccine use during the Gulf War. The office's interim report is contained here.

To inform the public about the progress of this office, the Department of Defense is publishing on the Internet and elsewhere accounts that may contribute to the discussion of possible causes of illnesses among Gulf War veterans, along with documentary evidence or personal testimony used in compiling the accounts. This information paper will aid in understanding how US forces used vaccines during the Gulf War.

TABLE OF CONTENTS

I. SUMMARY

Since the return of American military personnel deployed to Southwest Asia during Operations Desert Shield and Desert Storm, illnesses have been reported that may relate to service in the Gulf War. A number of veterans and others have expressed concern that the use of vaccines may have contributed to these illnesses. This paper provides information for veterans and other concerned individuals about vaccines, their use by the military, and particularly about issues arising from the administration of biological warfare vaccines in the Gulf War. It includes discussion of several related and contemporary issues, and concludes with some observations that reflect both accomplishments and continuing challenges. This paper also complements a recent report from the Institute of Medicine that evaluates the published scientific research on the health effects of specific vaccines used during the Gulf War.

Vaccines are commonly used health interventions that broadly benefit populations as well as individuals. Because of its unique and diverse mission, the military employs vaccines as critical countermeasures against infectious diseases and biological warfare agents. Differences in vaccination policies among the military services reflect variations in their respective training cycles, missions, and expected levels of exposure. Military vaccine programs are also constantly being updated to incorporate advances in preventive medicine, as well as in response to changing health threats.

During the Gulf War, anthrax and botulinum toxoid vaccines were used to protect US forces against the threat of Iraq's biological weapons. Administration of these vaccines during Operations Desert Shield and Desert Storm was characterized by several difficult issues, including obtaining sufficient quantities of the vaccines to protect all forces at risk; prioritizing military units for vaccination because of limited availability of both vaccines; using the investigational botulinum toxoid vaccine; providing servicemembers with information about the vaccines and obtaining their informed consent; employing voluntary and mandatory vaccinations; dealing with operational security considerations; and documenting vaccines in health records.

Military personnel today are increasingly facing routine deployments overseas, exposures to environmentally hazardous battlefields, and risks associated with biological warfare agents. The Gulf War experience has brought to light some shortfalls in vaccine administration and generated improvements in force health protection. Ensuring adequate production sources and maintaining sufficient stockpiles of safe and effective military-unique vaccines—especially vaccines in investigational status—remain daunting challenges, as does the communication of associated health risks to servicemembers. Importantly, progress has been demonstrated in vaccine tracking and documentation for deployments, and robust research on military vaccine development is ongoing. The Department of Defense should continue to build upon lessons learned from the Gulf War to ensure that advances in vaccine development and administration keep pace with changing health threats to military personnel.

II. INTRODUCTION

A. Origin of the Issue

Nearly 700,000 American military men and women deployed to Southwest Asia at the time of the Gulf War. Since their return, some veterans have experienced persistent and unexplained illnesses possibly related to their service in the Gulf. Some veterans also have been concerned that the vaccines they received before and during this deployment may have caused or contributed to these illnesses. Other veterans have questions about which vaccines were used and why they were chosen. These concerns have focused attention on vaccine use during the Gulf War.

B. Purpose of the Paper

To better understand how vaccines were used during the Gulf War deployment, the Office of the Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses has prepared this information paper. It discusses why the military considered the need for vaccines and how they chose to use them in the Gulf War. It provides information about vaccines administered to maintain general readiness as well as information about vaccines chosen for specific use during the Gulf War deployment, including vaccines directed against biological warfare agents. The paper also discusses related issues of concern to veterans, such as adverse reactions associated with these vaccines, information about the vaccines available to servicemembers, and the use of investigational vaccines. It ends with some general observations on vaccine administration.

For veterans, this paper should provide some context in which vaccines were used and some reasonable explanations for difficulties surrounding their use. No individual health records were reviewed and this paper cannot provide detailed information on the specific vaccines that an individual servicemember may have received. In-depth discussion of such issues as investigational products, record keeping, and risk communication is also beyond the scope of this paper, but general references for these issues are provided. A listing of definitions for acronyms, abbreviations, and medical terminology used in the paper can be found in Tab A.

C. Vaccines and Vaccination[1]

Vaccines are powerful health interventions that benefit both individuals and populations. They work by stimulating the body to produce a state of immunity, or protection from disease when the individual is later exposed to an infectious agent. Some vaccines may require only one or two doses (injections or tablets) to produce this immunity; others may require several doses. Some vaccines also require extra (or booster) doses after that in order to maintain this protection.

In many cases, antibodies (protective substances) produced in vaccinated individuals can be measured as a guide to the strength of the protection. Of course, the best evidence that a vaccine

[1] The terms *vaccination* and *immunization* are used interchangeably in this paper. See the glossary in Tab A for more exact definitions of these terms and the differences between them.

has created adequate protection is for the vaccinated individual to be exposed to the infectious agent and not develop the disease, but this is not always possible. For example, some biological warfare agents occur too infrequently as natural infections, so the protection of vaccinated individuals cannot be adequately tested this way. In such cases, the effectiveness of the vaccine may be demonstrated in animals, but there are always concerns as to whether this information would apply to humans. In the United States, the Food and Drug Administration (FDA) carefully reviews research on the effectiveness of a particular vaccine (as well as its safety) before the vaccine is licensed for general use. Before this testing is complete, the vaccine is considered *investigational*, meaning that it is approved for more limited use in humans pending full study and approval for general use. Both licensed and investigational vaccines were used in the Gulf War.

Vaccines vary in their ability to protect and are not always successful in stimulating immunity in the individuals who receive them. As examples, tetanus toxoid will work to prevent lockjaw (tetanus) most of the time, whereas cholera vaccine may work to prevent the diarrheal disease (cholera) only half the time. Even when vaccines do not provide full protection against the disease, they may still reduce the severity of the illness. Some vaccines are more likely to cause adverse reactions (undesired side effects) than others, and nearly all vaccines can cause serious ill effects, although these are rare. Civilian and military health authorities carefully weigh advantages and disadvantages of vaccines to ensure that the benefit in protection from disease far exceeds the risk of taking a vaccine.

There are other specific countermeasures for some diseases, like antibiotics for anthrax, meningococcal disease, and typhoid fever, and injections of pre-formed antibodies, like immune globulin for hepatitis A or antitoxin for botulism. Yet whenever safe and effective vaccines are available, they offer protection that is long lasting, easily administered, and available well in advance of the expected exposures. These advantages make a strong case for vaccines in both civilian public health and military force health protection.

III. VACCINE USE BY THE MILITARY

Vaccines are one of the principal countermeasures the Department of Defense (DoD) uses against infectious diseases and other biological hazards, so military personnel routinely receive many immunizations. These immunizations help protect servicemembers from the infectious diseases they may encounter in ordinary times between deployments, as well as the infectious diseases and biological warfare agents they may encounter during deployments. Differences in vaccination policies and practices among the military services are based upon their different training cycles, different missions, and different levels of exposure to biological threats.[2] Because of the missions they are prepared to undertake, military personnel are more broadly immunized than civilians against a variety of infectious diseases and biological warfare agents.[3]

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[2] Institute of Medicine, Strategies to Protect the Health of Deployed U.S. Forces: Medical Surveillance, Record Keeping, and Risk Reduction, Joellenbeck, Lois M., Philip K. Russell, and Samuel B. Guze, eds., Washington, DC: National Academy Press, 1999, p. 103.

[3] Institute of Medicine and National Research Council, Chemical and Biological Terrorism: Research and

Vaccine policy for the US Armed Forces is based on the recommendations of both military and civilian medical experts. For vaccines of special importance to the military, two organizations play central roles. The Armed Forces Epidemiological Board is composed of civilian experts in the fields of public health, preventive medicine, and environmental health, and advises the DoD on various disease prevention issues, particularly in the area of vaccines and immunization policy.[4] The Armed Forces Medical Intelligence Center, an activity of the Defense Intelligence Agency, provides the DoD with medical intelligence, including information on worldwide infectious disease and environmental health risks.[5]

For vaccines not unique to the military, the Centers for Disease Control and Prevention (CDC), an agency of the Department of Health and Human Services whose activities include vaccine, infectious disease, and travelers' health programs, provides much of the necessary information.[6] The CDC's Advisory Committee on Immunization Practices provides guidance and recommendations on general immunization issues and the use of specific vaccines.[7] These organizations also consider the reports of worldwide disease surveillance, regulatory documents, and travel-related health reports published by the World Health Organization.[8]

Military immunization policies, procedures, and responsibilities during the Gulf War were contained in DoD and joint service publications. DoD Instruction 6205.2 provides broad policy guidance regarding military immunizations. Among the directive's key points are that DoD is to follow the recommendations of the US Public Health Service, as developed by the CDC's Advisory Committee on Immunization Practices and published in CDC's *Morbidity and Mortality Weekly Report*. The directive also points out that military immunization procedures are to be developed in consultation with the Armed Forces Epidemiological Board and the Armed Forces Medical Intelligence Center. Particular emphasis is to be given to conditions that affect operational readiness, pose a risk in the community or occupational environment, or are unique to a particular geographic or cultural setting. DoD organizations are also directed to comply with communicable disease and adverse reaction reporting requirements established by civilian (e.g., public health) authorities.[9]

The 1988 joint regulation on immunizations implemented the DoD instruction and applied during the Gulf War to active and reserve components of the Army, Navy, Air Force, Marine Corps, and Coast Guard. It incorporated more detailed guidance for the military medical services regarding their respective immunization programs. This guidance indicated that all immunizing agents for use by the Armed Forces were to meet the minimum requirements of the Department of Health and Human Services, as well as standards acceptable to the Food and Drug

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Development to Improve Civilian Medical Response, Washington, DC: National Academy Press, 1999, p. 111.

[4] Department of Defense Memorandum, from the Deputy Secretary of Defense, Subject: "Executive Agent for the Armed Forces Epidemiological Board," May 21, 1998.

[5] Armed Forces Medical Intelligence Center web site, www.armymedicine.army.mil/ (as of June 29, 2000).

[6] Centers for Disease Control and Prevention web site, www.cdc.gov (as of June 29, 2000).

[7] Advisory Committee on Immunization Practices web site, www.cdc.gov/od/ads/acip (as of June 29,2000).

[8] World Health Organization, "Communicable Disease Surveillance and Response (CSR)," web site, www.who.int/emc/ (as of June 29, 2000).

[9] Department of Defense Instruction 6205.2, "Immunization Requirements," October 9, 1986, par. 3.

Administration; that medical personnel were to keep current on the Advisory Committee on Immunization Practices recommendations for immunizing agents and requirements for international travel; and that adverse reactions to immunizing agents were to be appropriately recorded and reported. (See also *Adverse Reactions to Vaccines*, section V.) It also allowed for commanders of unified commands to establish specific immunization requirements for deploying personnel based on special threat assessments.[10]

The current version of this joint publication includes updated recommendations by the US Public Health Service, expanded guidance on reporting adverse events, and specific guidance on immunizations for biological warfare defense.[11] This 1995 publication is now undergoing review and revision.[12]

The DoD published a new directive in 1993 outlining the policies, responsibilities, and procedures for the development, acquisition, and stockpiling of biological defense vaccines. Broadly stated, it is DoD policy that military personnel should be immunized against validated biological warfare threat agents, for which suitable vaccines are available, in sufficient time to develop immunity before deployment to high-threat areas.[13]

Because of the military's unique mission, the DoD requires several vaccines (e.g., anthrax, plague, and certain adenovirus vaccines) that have limited or no commercial market. Consequently, it has been difficult for the DoD to maintain a reliable manufacturing base to supply these vaccines. Procurement of vaccines against Iraq's biological warfare threat was a challenging problem during the Gulf War, and recent experiences with DoD's anthrax vaccination program demonstrate that optimal solutions have yet to be found.[14]

Vaccines are an integral part of DoD's new strategy of force health protection, which was developed in part from lessons learned from the Gulf War.[15] Force health protection uses preventive health techniques and emerging technologies in environmental surveillance and combat medicine to protect servicemembers before, during, and after deployment. It is designed to improve individual health, proactively address medical threats, and provide care for any illness or injury that does occur.[16] Vaccines can help ensure that military forces are healthy and fit to

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[10] Army Regulation 40-562, Navy Medical Command Instruction 6230.3, Air Force Regulation 161-13, and Coast Guard Commandant Instruction M6230.4D, "Immunizations and Chemoprophylaxis," October 7, 1988, p. 1 and par. 2-1a, 3-1b, 3-11a, 4-4.

[11] Air Force Joint Instruction 48-110, Army Regulation 40-562, Navy Bureau of Medicine Instruction 6230.15, and Coast Guard Commandant Instruction M6230.4E, "Immunizations and Chemoprophylaxis," November 1, 1995, par. 12, 47-49.

[12] Department of Defense (Health Affairs) E-mail, from a staff member, Subject: "Status of Joint Service Immunization Policy," June 1, 2000.

[13] Department of Defense Directive 6205.3, "DoD Immunization Program for Biological Warfare Defense," November 26, 1993, par. 4.1.

[14] Institute of Medicine, Strategies to Protect the Health of Deployed U.S. Forces: Medical Surveillance, Record Keeping, and Risk Reduction, Joellenbeck, Lois M., Philip K. Russell, and Samuel B. Guze, eds., Washington, DC: National Academy Press, 1999, p. 105-106.

[15] Joint Staff Force Health Protection Brief, J4 web site, www.dtic.mil/jcs/j4 (as of June 27, 2000).

[16] Department of Defense Force Health Protection web site, www.forcehealth.com (as of June 8, 2000).

fight, as well as prevent casualties from biological warfare and endemic diseases.[17]

IV. VACCINES USED DURING THE GULF WAR

A. Vaccines for Routine Preparedness

At the time of the Gulf War most servicemembers would already have been vaccinated against several common infectious diseases, either during recruit training or at later times, as required by the joint guidance on immunizations. Table 1, which is taken from this guidance, shows detailed information on these vaccine requirements.[18]

Table 1. Vaccinations for military personnel (at the time of the Gulf War)

IMMUNIZING AGENT	ARMY	NAVY	AIR FORCE	MARINE CORPS	COAST GUARD
Adenovirus (types 4 and 7)	B	B	B	B	H
Cholera	F	F	F	F	F
Hepatitis B	E,G,H	E,G,H	E,G,H	E,G,H	G,H
Influenza	A,B,X	A,B,R	A,B,R	A,B,R	B,C,H
Measles	B,G	B,G	B,G	B,G	B,G
Meningococcal (A,C,Y,W135)	B,H	B,H	B,H	B,H	B,H
Mumps	G,H	G,H	G,H	G,H	G
Plague	C,D,E,G	D,G	E	A,G	E
Polio	A,R	A,R	A,R	A,R	A
Rabies	D,G,H	D,G,H	D,G,H	D,G,H	H
Rubella	B,G	B,G	B,G	B,G	B
Smallpox	B,H	B,H	B,H	B,H	B,H
Tetanus-diphtheria	A,B,R	A,B,R	A,B,R	A,B,R	A,B
Typhoid	C,E,H	H	C,E,H	H	E
Yellow fever	C,D,E	A,R	C,E	A,R	B,E

Legend:
A: All active duty personnel
B: Recruits
C: Alert forces
D: Special Operating Forces components
E: When deploying or traveling to high risk areas
F: Only when required by host country for entry
G: High risk occupational groups
H: As directed by applicable Surgeon General
R: Reserve components
X: Reserve component personnel on active duty for 30 days or more during influenza season.

[17] Joint Staff Force Health Protection Vision Document, J4 web site, www.dtic.mil/jcs/j4 (as of June 27, 2000); American Forces Information Service News Article, Gillert, Douglas J., "Force Protection Covers All Aspects of Troop Health," June 1998.

[18] Army Regulation 40-562, Naval Medical Command Instruction 6230.3, Air Force Regulation 161-13, and Coast Guard Commandant Instruction M6230.4D, "Immunizations and Chemoprophylaxis," October 7, 1988.

Many of the vaccines required by the military as part of routine preparedness (like those against polio, measles, mumps, rubella, influenza, tetanus, and diphtheria) were in widespread use in both civilian and military communities. These vaccines are not discussed in detail in this paper. Other vaccines were used more broadly or solely by the Armed Forces, because military personnel are more likely to acquire these diseases under certain conditions (as during initial training periods), or might be quickly deployed to areas where these diseases are more common (as for the alert and special operating forces), or work in occupations that are generally at higher risk of infection (like laboratory and medical workers). The following paragraphs provide abbreviated information on the vaccines for which the military had special requirements and on the diseases these vaccines were designed to prevent.[19]

Adenovirus Vaccines (types 4 and 7). These vaccines were given as tablets to Army, Navy, and Marine Corps recruits on a one-time basis early in their initial (basic) training. The Air Force did not use these vaccines unless an actual outbreak of disease occurred. Adenoviruses can cause acute respiratory diseases that are common under basic training conditions. While the vaccines reduced respiratory diseases in recruits, the military no longer uses them because the sole manufacturer stopped production for commercial reasons in the late 1990s.[20]

Meningococcal Vaccine. This vaccine was given to all recruits on a one-time basis early in their initial training in order to prevent meningococcal diseases, which are more common under basic training conditions. The US Central Command (CENTCOM) also recommended this vaccine for personnel deploying to Southwest Asia, and it is more fully discussed in the following subsection. (See *Vaccines for the Gulf War Deployment,* section IV.) The military continues to use this vaccine for recruits.

Plague Vaccine. At the time of the Gulf War, only Marine Corps recruits and selected special operating forces received the plague vaccine. Plague is a bacterial infection, acquired by flea bite, which causes fever and lymph node swelling. Without appropriate treatment, this disease can spread widely throughout the body and be life threatening. The available vaccine was at least partially protective against plague, reducing the severity while not always preventing the disease. Plague may also result from inhaling the bacteria, but the vaccine had not been proven useful against this form of the disease. It is the ability to aerosolize the bacteria that makes plague a potential biological warfare disease. (See *Vaccine Use by Coalition Forces,* section V.) After the Gulf War, routine immunization of Marine Corps recruits was discontinued. The vaccine is currently out of production due to low commercial demand.[21]

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[19] Unless otherwise noted, the information about specific diseases and vaccines is taken from the following: Chin, James, ed., Control of Communicable Diseases Manual, American Public Health Association, 17th ed., Washington, DC: 2000; and Grabenstein, John D., ImmunoFacts: Vaccines and Immunologic Drugs, St. Louis, MO: Facts and Comparisons, 2000. Detailed information on vaccines can also be found at the CDC Advisory Committee on Immunization Practices web site, www.cdc.gov/nip.

[20] Institute of Medicine, Strategies to Protect the Health of U.S. Forces: Medical Surveillance, Record Keeping, and Risk Reduction, Joellenbeck, Lois M., Philip K. Russell, and Samuel B. Guze, eds., Washington, DC: National Academy Press, 1999, p.105.

[21] Inglesby, Thomas V. et al., "Plague as a Biological Weapon: Medical and Public Health Management," *Journal of the American Medical Association (JAMA),* May 3, 2000, vol. 283, no. 17, p. 2285.

Rabies Vaccine. This vaccine provides good protection against rabies. It is also used to prevent rabies after exposure. The rabies virus is usually acquired from the bite of an infected animal and can cause a disease of the brain (encephalitis) that is nearly always fatal. Selected military personnel with greater risk of exposure to this virus (like veterinarians) as well as special operating forces routinely received this vaccine. The military continues to use the vaccine for these purposes.

Smallpox Vaccine. Because smallpox had been eradicated worldwide, the military phased out use of the smallpox vaccine during the late 1980s.[22] Yet many servicemembers who deployed to the Gulf War would have received the smallpox vaccine when they first entered military service. A report of an adverse reaction to this vaccine during the Gulf War deployment suggests that it may also have been given to some individuals at that time. (See *Adverse Reactions to Vaccines,* section V.) The smallpox virus is highly communicable and infection generally causes fever and skin rash; in some cases, it can be fatal. (Smallpox virus also has been considered a potential biological warfare agent.) The vaccine is no longer commercially available, although some vaccine is maintained by the Centers for Disease Control and Prevention.

Typhoid Vaccine. Vaccine against typhoid fever, a bacterial infection, was used regularly for alert forces, and for military personnel deployed to areas where the disease is common. CENTCOM also recommended this vaccine for personnel deploying to Southwest Asia, and it is more fully discussed in the following subsection. (See *Vaccines for the Gulf War Deployment,* section IV.) Since the Gulf War, the manufacturer has discontinued production of the vaccine generally used by the military, although other typhoid vaccines are commercially available.

Yellow Fever Vaccine. The Navy and Marine Corps routinely used this vaccine against the yellow fever virus for all active duty and reserve forces. The Army and Air Force used it only for personnel deployed to areas of high risk. CENTCOM also recommended this vaccine for personnel deploying to Southwest Asia, and it is more fully discussed in the following subsection. (See *Vaccines for the Gulf War Deployment,* section IV.) Following the Gulf War, the Navy and Marine Corps continued the routine uses of this vaccine noted above.

Vaccines for routine preparedness were usually given to servicemembers who required them at the time of recruitment, at times of periodic health assessment or record review, or when preparing for deployment to areas of high risk.

In the years following the Gulf War, the military revised its requirements for vaccines in keeping with progress in preventive medicine. New vaccines were added, uses for some vaccines were modified, and a few vaccines were discontinued. The revised joint guidance on immunizations includes these changes. Table 2, which is taken from that publication, shows detailed vaccine requirements following the Gulf War.[23]

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[22] United States Army Medical Research Institute of Infectious Diseases, Public Health Training Network, Centers for Disease Control and Prevention, and Food and Drug Administration, "Biological Warfare and Terrorism: The Military and Public Health Response," Satellite Broadcast, September 21-23, 1999, p. 41.

[23] Air Force Joint Instruction 48-110, Army Regulation 40-562, Navy Bureau of Medicine and Surgery Instruction 6230.15, and Coast Guard Commandant Instruction M6230.4E, "Immunizations and Chemoprophylaxis," November

Table 2. Vaccinations for military personnel (after the Gulf War)

IMMUNIZING AGENT	ARMY	NAVY	AIR FORCE	MARINE CORPS	COAST GUARD
Adenovirus (types 4 and 7)	B	B	G	B	G
Cholera	E	E	E	E	E
Hepatitis A	G	G	C,D	G	G
Hepatitis B	F,G	F,G	F,G	F,G	F,G
Influenza	A,B,X	A,B,R	A,B,R	A,B,R	B,C,G
Japanese Encephalitis	D	D	D	D	G
Measles	B,F	B,F	B,F	B,F	B,G
Meningococcal (A,C,Y,W135)	B,D	B,D	B,D	B,D	B,G
Mumps	F,G,	B,F,G	F,G	B,F,G	G
OPV (Oral Polio)	B,D,R	B,R	B,R	B,R	A
Plague	D,F	F	F	F	F
Rabies	F	F	F	F	G
Rubella	B,F	B,F	B,F	B,F	B
Tetanus-diphtheria	A,B,R	A,B,R	A,B,R	A,B,R	A,B
Typhoid	C,D	C,D	C,D	C,D	D
Varicella (Chickenpox)	F,G	F,G	F,G	G	F,G
Yellow Fever	C,D	A,R	C,D	A,R	B,C,E

Legend:
A: All active duty personnel
B: Recruits
C: Alert forces
D: When deploying or traveling to high risk areas
E: Only when required by host country for entry
F: High risk occupational groups
G: As directed by applicable Surgeon General
R: Reserve components
X: Reserve component personnel on active duty for 30 days or more during influenza season.

B. Vaccines for the Gulf War Deployment

In addition to updating routine vaccinations in need of a booster—as with tetanus-diphtheria and oral poliovirus vaccines—the guidance from CENTCOM in August 1990 recommended additional countermeasures for personnel deploying to Southwest Asia that included meningococcal, typhoid, and yellow fever vaccines, and immune globulin to protect against hepatitis A. Smallpox, plague, cholera, and rabies vaccines were not recommended in this guidance.[24] The services sometimes modified these recommendations as indicated in the discussion of specific vaccines below. The biological warfare vaccines, anthrax and botulinum toxoid, are discussed in a following subsection.

Meningococcal Vaccine (groups A, C, Y, and W-135). This vaccine was routinely given to military recruits for protection against meningococcal disease during initial training. (See

1, 1995.

[24] CENTCOM Message, from USCINCCENT/CCCS, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 101700Z Aug 90.

previous subsection.) Meningococcal infections usually begin with growth of the bacteria in the respiratory tract. Serious meningococcal diseases can spread to the lining of the brain and spinal cord (meningitis) or to the bloodstream (meningococcemia), and without rapid treatment are often fatal. The vaccine is considered 85 to 95 percent effective in preventing meningococcal disease associated with four of the five common strains of these bacteria (namely, groups A, C, Y, and W-135; there is no licensed vaccine for group B strains).[25] Meningococcal disease had been reported in Saudi Arabia, especially at the times of annual religious pilgrimages.[26]

During Operation Desert Shield, CENTCOM recommended meningococcal vaccine for personnel deploying to the Gulf who had not had it within five years and who would be expected to have prolonged close contact with local nationals, especially children, but not for those who would have only occasional casual contact.[27] The Army recommended it for all personnel, especially for those with the contacts mentioned above (civil affairs and medical personnel were given as examples), but indicated that solders could deploy without it.[28] The Navy, Air Force, and Marine Corps essentially reiterated the original CENTCOM guidance for this vaccine.[29] Later guidance reinforced the need for this vaccine, restated the position that it was not necessary for all personnel, and suggested that there might have been shortages, requiring some servicemembers to receive the vaccine after arriving in the Gulf.[30] There were reports of meningococcal disease in two American servicemembers during the Gulf War, one of whom died of meningococcal meningitis.[31] Given the scope of this paper, we do not know whether these individuals had received the vaccine.

Typhoid Vaccine. Typhoid fever is a bacterial infection characterized by prolonged fever, which is usually acquired from contaminated food or water. It is debilitating and can be life threatening. Of the typhoid vaccines available at the time of the Gulf War, the military generally

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[25] Grabenstein, John D., "Meningococcal Polysaccharide Vaccine: Groups A, C, Y, and W-135," (section written February 1999), ImmunoFacts: Vaccines and Immunologic Drugs, St. Louis, MO: Facts and Comparisons, 2000, p. 92g-94a.

[26] Centers for Disease Control and Prevention, "Meningococcal Disease Among Travelers Returning from Saudi Arabia," *Morbidity and Mortality Weekly Report (MMWR)*, August 28, 1987, vol. 36, no. 33, p. 559; Gasser, Robert A. et al., "The Threat of Infectious Disease in Americans Returning from Operation Desert Storm," *The New England Journal of Medicine*, March 21, 1991, vol. 324, no. 12, p. 862.

[27] CENTCOM Message, from USCINCCENT/CCCS, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 101700Z Aug 90.

[28] Army Message, from CDRFORSCOM/FCMD-PM, Subject: "Consolidated Immunization and Preventive Medicine Requirements and Information," 141815Z Aug 90.

[29] Navy Message, from CNO/932, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 131510Z Aug 90; Air Force Message, from NGB/SGA, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 131500Z Aug 90; Marine Corps Operations Plan, "USMARCENT OPLAN Desert Storm," January 1, 1991, p. D-3-C-2.

[30] Air Force Message, from NGB/SGP, Subject: "Malaria Chemoprophylaxis and Meningococcal Vaccination for Operation Desert Shield," 101528Z Oct 90; Desert Shield Preventive Medicine Situation Summary Report, 29 September to 12 October 1990; Army Message, from CINCFOR/FCJ3-CAT, Subject: "Medical/Dental Screening During Desert Shield - At Home Station and During POM," 061600Z Oct 90.

[31] Presidential Advisory Committee on Gulf War Veterans' Illnesses, Final Report, December 1996, p. 117; Information Paper, Subject: "Post Operations Desert Shield/Desert Storm (ODS/DS) Medical Issues," September 15, 1993.

used the more effective acetone-inactivated vaccine. This vaccine's effectiveness ranged between 75 percent to 94 percent; other typhoid vaccines were somewhat less effective.[32] CENTCOM recommended typhoid vaccine for all deploying personnel who had not had it within three years.[33] The Army required this vaccine; the Navy, Air Force, and Marine Corps essentially reiterated the original CENTCOM guidance.[34] No confirmed cases of typhoid fever were reported among US personnel deployed to the Gulf.[35]

Yellow Fever Vaccine. The Navy and Marine Corps used this vaccine for all active duty and reserve forces; the Army and Air Force used it only for personnel deployed to areas with high risk of contracting this disease. Yellow fever, usually acquired from a mosquito bite, is a potentially serious viral disease that can affect the liver and kidneys, and that can be life threatening. An available vaccine is highly effective in preventing this disease. While the initial CENTCOM guidance recommended yellow fever vaccine for deployment to Southwest Asia, the Army specifically noted it was not required.[36] The Navy, Air Force, and Marine Corps reiterated the CENTCOM guidance.[37] Yellow fever is not generally present in Southwest Asia, and we are not aware of any reports of servicemembers who acquired this disease during the Gulf War.[38]

Immune Globulin. Immune globulin is not a vaccine, but it protected servicemembers against hepatitis A in a similar way.[39] Hepatitis A is a disease of the liver that can be debilitating, although full recovery is the rule. It is spread by direct contact with infected individuals, or by food or water contaminated with the virus, and is common in Southwest Asia.[40] Immune

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[32] Grabenstein, John D., "Typhoid Vaccines (Parenteral)," (section written May 1995), ImmunoFacts: Vaccines and Immunologic Drugs. St. Louis, MO: Facts and Comparisons, 2000, p. 110.

[33] CENTCOM Message, from USCINCCENT/CCCS, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 101700Z Aug 90.

[34] Army Message, from CDRFORSCOM/FCMD-PM, Subject: "Consolidated Immunization and Preventive Medicine Requirements and Information," 141815Z Aug 90; Navy Message, from CNO/932, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 131510Z Aug 90; Air Force Message, from NGB/SGA, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 131500Z Aug 90; Marine Corps Operations Plan, "USMARCENT OPLAN Desert Storm," January 1, 1991, p. D-3-C-2.

[35] Hyams, Kenneth C. et al., "The Impact of Infectious Diseases on the Health of U.S. Troops Deployed to the Persian Gulf During Operations Desert Shield and Desert Storm," *Clinical Infectious Diseases*, June 1995, vol. 20, p. 1499.

[36] CENTCOM Message, from USCINCCENT/CCCS, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 101700Z Aug 90; Army Message, from CDRFORSCOM/FCMD-PM, Subject: "Consolidated Immunization and Preventive Medicine Requirements and Information," 141815Z Aug 90.

[37] Navy Message, from CNO/932, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 131510Z Aug 90; Air Force Message, from NGB/SGA, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 131500Z Aug 90; Marine Corps Operations Plan, "USMARCENT OPLAN Desert Storm," January 1, 1991, p. D-3-C-2.

[38] Centers for Disease Control and Prevention, National Center for Infectious Diseases, "Comprehensive Yellow Fever Vaccination Requirements," web site, www.cdc.gov/travel/diseases/yelfever (as of June 30, 2000).

[39] Immune globulin already contains antibodies against hepatitis A; a vaccine stimulates the body to produce them. Either way, the individual is protected, but the duration of protection from immune globulin is brief (months), while that produced by a vaccine would be long-lasting (years).

[40] Centers for Disease Control and Prevention, National Center for Infectious Diseases, "Hepatitis, Viral, Type A," web site, www.cdc.gov/travel/diseases/hav (as of May 2, 2000); Gasser Robert A. et al., "The Threat of Infectious

globulin—also known as immune serum globulin, gamma globulin, and immune globulin intramuscular—is 80 to 95 percent effective in preventing hepatitis A disease. During Operation Desert Shield, CENTCOM recommended the use of immune globulin as an injection of either 2.0 cc if servicemembers were only to be in the areas of exposure for three months or less, or a larger amount of 5.0 cc if they were to stay longer.[41] The Army required the larger amount for all individuals.[42] The Navy, Air Force, and Marine Corps reiterated the original CENTCOM guidance.[43] Shortages of this product caused the military to seek additional sources. Immune globulin from a second source was approved by the FDA, but was not administered to US servicemembers.[44] The shortages of immune globulin may have limited the size of the initial dose in some cases and this, along with extensions of the deployment, required that some servicemembers be given additional doses in theater. Only a few cases of hepatitis A were reported among deployed US personnel, reflecting the effectiveness of immune globulin along with other preventive medicine measures.[45] A vaccine against Hepatitis A is now available and is used by the military to prevent this disease.[46]

These deployment vaccinations (along with updating of the more routine vaccinations) were generally carried out at the home stations or at the mobilization stations. Some were also given in theater due to initial shortages, as was the case with meningococcal vaccine and immune globulin, or because the requirement for a particular vaccine was seasonal, as with influenza vaccine.[47]

Disease in Americans Returning form Operation Desert Storm," *The New England Journal of Medicine*, March 21, 1991, vol. 324, no. 12, p. 862.

[41] CENTCOM Message, from USCINCCENT/CCCS, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 101700Z Aug 90.

[42] Army Message, from CDRFORSCOM/FCMD-PM, Subject: "Consolidated Immunization and Preventive Medicine Requirements and Information," 141815Z Aug 90; Army Message, from CDRFORSCOM/FCMD, Subject: "Updated Immunization and Preventive Medicine Guidance," 201145Z Nov 90.

[43] Navy Message, from CNO/932, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 131510Z Aug 90; Air Force Message, from NGB/SGA, Subject: "Preventive Medicine Guidance for Operation Desert Shield," 131500Z Aug 90; Marine Corps Operations Plan, "USMARCENT OPLAN Desert Storm," January 1, 1991, p. D-3-C-2.

[44] Army Memorandum, from the Chief of the Preventive and Military Medicine Consultants Division, Subject: "Purchase of Immune Serum Globulin (ISG) from Foreign Manufacturer," November 29, 1990; Office of the Special Assistant for Gulf War Illnesses E-mail, from a staff member, Subject: "Contaminated Immune Globulin (Gamma Globulin) and the Gulf War," April 15, 1997; Office of the Special Assistant for Gulf War Illnesses Letter, from the Special Assistant, January 30, 1998.

[45] Hyams, Kenneth C. et al., "The Impact of Infectious Diseases on the Health of U.S. Troops Deployed to the Persian Gulf During Operations Desert Shield and Desert Storm," *Clinical Infectious Diseases*, June 1995, vol. 20, p. 1501.

[46] Department of Defense (Health Affairs) Memorandum, from the Assistant Secretary of Defense for Health Affairs, Subject: "Recommendation Regarding the Use of the Newly Licensed Hepatitis A Vaccine in Military Personnel," April 19, 1995.

[47] Ledford, Frank F., "From the Surgeon General of the Army: Medical Support for Operation Desert Storm," *The Journal of the US Army Medical Department*, January/February 1992, p.5; Hyams, Kenneth C. et al., "The Impact of Infectious Diseases on the Health of U.S. Troops Deployed to the Persian Gulf During Operations Desert Shield and Desert Storm," *Clinical Infectious Diseases*, June 1995, vol. 20, p. 1498; Air Force Message, from NGB/SGP, Subject: "Malaria Chemoprophylaxis and Meningococcal Vaccination Guidelines for Operation Desert Shield," 101528Z Oct 90; Desert Shield Preventive Medicine Situation Summary Report, 29 September to 12 October 1990.

Casualties from infectious diseases during Operations Desert Shield and Desert Storm were extremely low, reflecting at least in part an extensive preventive medicine program.[48] From available records, it appears that few servicemembers required medical evacuation for diseases that were potentially vaccine-preventable.[49] The death from meningococcal meningitis was the only reported death from an infectious disease.[50]

C. Biological Warfare Vaccines

From the onset of Operation Desert Shield, the military was concerned that Iraq might use biological weapons. In August 1990, the Central Intelligence Agency believed Iraq possessed two biological warfare agents, botulinum toxin and *Bacillus anthracis* (the bacterium that causes anthrax).[51] The Armed Forces Epidemiological Board reviewed intelligence data to determine the need for biological agent vaccines against anthrax and botulism, and in August 1990 recommended that immunization of forces at risk begin as soon as possible.[52]

Anthrax Vaccine. Anthrax is a bacterial disease that ordinarily occurs through contact with infected animals or contaminated animal products, or by ingestion or inhalation of infected dust from hides, wool, or similar substances. Naturally occurring anthrax affects small numbers of people who often work in environments with occupational exposure to the anthrax spores (one form of the bacterium). The spores are quite hardy, can be produced in large quantities, and can be spread by aerosols, making anthrax useful as a biological warfare agent. Anthrax infection acquired through inhalation generally starts within a few days with symptoms of fatigue, fever, and cough, and progresses to severe breathing difficulty and shock. At this point the mortality is very high.[53] Even less seriously ill servicemembers would substantially weaken the military force. While protective masks provide a barrier against this infection, and antibiotics given early in the infection can be useful, adequate warning of an attack would be unlikely, so a vaccine would clearly offer the best pre-combat protection for military personnel.

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[48] Defense Science Board, "Task Force on Persian Gulf War Health Effects," June 1994, p. 47; Hyams, Kenneth C. et al., "The Impact of Infectious Diseases on the Health of U.S. Troops Deployed to the Persian Gulf During Operations Desert Shield and Desert Storm," *Clinical Infectious Diseases*, June 1995, Vol. 20, p. 1497.

[49] Global Patient Movement Requirements Center, "Desert Shield/Desert Storm Moves, August 1990-August 1992," February 9, 1998.

[50] Writer, James V., Robert F. DeFraites, and John F. Brundage, "Comparative Mortality Among US Military Personnel in the Persian Gulf Region and Worldwide During Operations Dessert Shield and Desert Storm," *Journal of the American Medical Association (JAMA)*, January 10, 1996, vol. 275, no. 2, p. 119, Table 1.

[51] Central Intelligence Agency Assessment, "Iraq's Biological Warfare Program: Saddam's Ace in the Hole," August 8, 1990.

[52] Armed Forces Epidemiological Board Memorandum, from the Board President and the Executive Secretary, Subject: "Recommendations Concerning Immunization Policies," August 30, 1990.

[53] Friedlander, Arthur M., "Anthrax," *Medical Aspects of Chemical and Biological Warfare*, Sidell, Frederick R. et al., eds., Textbook of Military Medicine, Zajtchuk, Russ, et al., eds., Washington, DC: Office of the Surgeon General, 1997, p. 471-472.

After the testing and review process, the Food and Drug Administration licensed an anthrax vaccine in 1970.[54] In field trials with textile workers prior to licensure, vaccinated workers did not develop inhalational anthrax, while some unvaccinated workers did; however, the total number of individuals studied was small.[55] At the time of the Gulf War, the anthrax vaccine, which was slightly different from the earlier tested version, contained aluminum hydroxide as an adjuvant. (See also *Vaccine Adjuvants*, section V.) The recommended schedule was a series of six injections over 18 months, followed by yearly booster injections to maintain protection.[56] The vaccine was produced by the Michigan Department of Public Health (MDPH). In the 20 years preceding the Gulf War, the MDPH had distributed more than 70,000 doses of the vaccine, which had been given to more than 10,000 veterinarians, laboratory workers, workers in the hide and wool industries, and others who were most likely to come in contact with anthrax spores.[57] Adverse reactions were generally tolerable and limited. (See also *Adverse Reactions*, section V.) During the early period of the Gulf War deployment, additional animal studies were done to further support the vaccine's effectiveness against inhalational anthrax.[58]

Botulinum Toxoid Vaccine. Botulism is a disease caused by toxins produced by the bacterium, *Clostridium botulinum*. The bacteria are commonly found in soil, and natural disease can occur from ingestion of toxin-containing food or direct contamination of a wound. Though contamination of food sources was possible, the military was most concerned that botulinum toxin could be aerosolized as a biological warfare agent and inhaled by military personnel. Within a day or so of exposure, sometimes longer, the toxins cause progressive muscle weakness with difficulty swallowing, speaking, and breathing, and finally respiratory paralysis. While prompt administration of prepared anti-toxins can neutralize botulinum toxins, and intensive respiratory support can be life saving, the effects on the military force could be incapacitating. The military viewed vaccination as the best available pre-combat protection for the forces.

A botulinum toxoid vaccine was available as an investigational product at the time of the Gulf War. (See also *Investigational Vaccines*, section V.) According to data collected by the CDC, the vaccine had been used since 1970 to protect high-risk laboratory workers against botulism. The vaccine contained aluminum phosphate as an adjuvant.[59] (See also *Vaccine Adjuvants*, section V.) Vaccine recipients developed levels of antibody considered protective when compared to studies in animals, but protection in humans was more difficult to demonstrate since botulism from any cause is a rare disease. The vaccine required a series of three injections over

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[54] Grabenstein, John D., "Anthrax Vaccine" (section written May 2000), ImmunoFacts: Vaccines and Immunologic Drugs, St. Louis, MO: Facts and Comparisons, 2000, p. 35a.

[55] Friedlander, Arthur M., Phillip R. Pittman, and Gerald W. Parker, "Anthrax Vaccine: Evidence for Safety and Efficacy Against Inhalational Anthrax," Journal *of the American Medical Association (JAMA)*, December 8, 1999, vol. 282, no. 22, p. 2104-2106.

[56] Michigan Department of Public Health, Anthrax Vaccine Package Insert (Information Sheet), October 1987.

[57] Johnson-Winegar, Anna, Information Paper, Subject: "Anthrax Vaccine and Botulinum Vaccines," September 27, 1990.

[58] Department of Defense Ad Hoc Working Group for Medical Defense Against Biological Warfare, After Action Reports of Meetings on August 20, 1990, October 19, 1990, and November 2, 1990.

[59] Centers for Disease Control and Prevention, "Pentavalent Botulinum Phosphate Adsorbed," Progress Report #31 BB-IND 161, March 2, 1996 to March 1, 1997.

12 weeks, with subsequent booster injections to maintain antibody levels. Between 1970 and the Gulf War, over 10,000 injections of the vaccine had been given, mostly to volunteers and laboratory workers. Adverse reactions were generally tolerable and limited. (See also *Adverse Reactions*, section V.)

Availability of Biological Warfare Vaccines. The peacetime demand for anthrax and botulinum toxoid vaccines was not large. The Michigan Department of Public Health was the sole producer of both vaccines. In October 1990, in an effort to expand the industrial base for biological vaccine production, the Secretary of Defense directed the Assistant Secretary of Defense for Health Affairs to acquire a second source for these biological vaccines.[60] In response, the Assistant Secretary established a tri-service vaccine task force, subsequently named "Project Badger." Project Badger reviewed the MDPH capabilities and the probable vaccine delivery timelines based upon the projected needs for the Gulf War. The task force also conducted a survey to find out if other manufacturers (including manufacturers of veterinary vaccines) could produce anthrax and botulinum toxoid vaccines. The feasibility of purchasing vaccines from a foreign source and producing the vaccines at Fort Detrick, Maryland and other Army facilities was also explored.[61]

The search for alternative sources was not successful. The MDPH had suspended further production of botulinum toxoid vaccine in order to produce the anthrax vaccine.[62] Veterinary vaccine manufacturers used processes different from those used to produce human vaccines.[63] One potential manufacturer would not have been able to deliver any vaccine until April 1991.[64] Only one foreign manufacturer was identified.[65] Production of botulinum toxoid vaccine at Fort Detrick was feasible, but would require substantial renovation and equipment purchases.[66] Production at Army facilities other than Fort Detrick was not feasible.[67] In the end, only anthrax and botulinum toxoid vaccines produced by the MDPH were used by US forces during the Gulf

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[60] Department of Defense Memorandum, from the Secretary of Defense, Subject: "Expansion of Industrial Base for Biological Vaccine Production," October 3, 1990.

[61] Department of Defense (Health Affairs) Memorandum, from the Assistant Secretary of Defense for Health Affairs, Subject: "Expansion of Industrial Base for Biological Vaccine Production," October 5, 1990; Army Memorandum for Record, from the Commander, US Army Medical Research and Development Command, Subject: "Second Tri-Service Task Force Meeting to Evaluate the Industrial Capability to Produce Anthrax and Botulinum Toxin Vaccines," October 12, 1990.

[62] Joint Chiefs of Staff, Logistics Directorate (J4), "Biological Defense Chronology," MPOD #3821, February 12, 1992, p. 10.

[63] Army Memorandum for Record, from the Task Force Chairman, Subject: "Third Tri-Service Task Force (Project Badger) Meeting," October 18, 1990; Chronology for Project Badger (Long Term), October 24, 1990.

[64] Army Memorandum for Record, from the Task Force Chairman, Subject: "Sixth Tri-Service Task Force (Project Badger) Meeting," November 9, 1990.

[65] Army Memorandum for Record, from the Task Force Chairman, Subject: "Third Tri-Service Task Force (Project Badger) Meeting," October 18, 1990.

[66] Army Memorandum for Record, from the Deputy Director of Professional Services, Office of the Surgeon General, Subject: "BW Vaccine Surge Meeting," December 6, 1990.

[67] Army Memorandum for Record, from the Task Force Chairman, Subject: "Fourth Tri-Service Task Force (Project Badger) Meeting," October 26, 1990.

War deployment.[68]

Since supplies of the two biological warfare vaccines were limited, the DoD allocated the vaccines only to personnel they believed to be at greatest risk of exposure to these biological warfare agents.[69] Vaccine shortages were likely responsible for reducing the anthrax vaccine doses required to two, with the knowledge that two doses would provide at least partial protection to most individuals, and for reducing the botulinum toxoid vaccine to three doses, as recommended by an earlier working group. Shortages may also have led to holding some anthrax vaccine in reserve to use along with antibiotics for unprotected servicemembers who may be exposed, and to acquiring botulinum anti-toxin for use under similar conditions.[70] Most servicemembers who received the biological warfare vaccines received them in the Gulf during early 1991, but at least some special forces personnel received them stateside during the latter part of 1990.[71] The initial shipment of the anthrax and botulinum toxoid vaccines was flown from the US to the Gulf accompanied by members of a tri-service vaccination team. This team helped ensure safe transport of the vaccines and assisted with finalization of the plan to distribute the vaccines in theater.[72]

Biological Warfare Vaccine Use in the Gulf. In late December 1990, following discussions with the Joint Staff, the US Central Command (CENTCOM) established immunization priorities for the use of biological warfare vaccines.[73] CENTCOM messages in January 1991 initiated the anthrax and botulinum toxoid vaccination programs.[74]

The anthrax vaccination guidelines directed that only personnel assigned to fixed units within the areas designated by CENTCOM were to be vaccinated at that time. No transient or shipboard personnel were to be vaccinated. Exceptions were pathologists and medical laboratory personnel. The guidelines indicated that sufficient quantities of anthrax vaccine would be available by May 1991 to vaccinate all personnel in the area of responsibility. It was anticipated that the relatively long period between exposure and onset of illness (when compared to botulism) would make anthrax an agent more likely to be used against fixed and rearward units.

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[68] Army Memorandum, from the Commander, US Army Research Institute of Infectious Diseases, Subject: "Response to LEAD [Lead Sheet] Report," June 29, 1999.

[69] Army Memorandum, from the Director of Health Care Operations, Subject: "Request for Anthrax and Botulinum Vaccine and Botulinum Antitoxin Requirements," April 12, 1991; Caudle, Lester C. III, "The Biological Warfare Threat," *Medical Aspects of Chemical and Biological Warfare*, Sidell, Frederick R. et al., eds., Textbook of Military Medicine, Zajtchuk, Russ, et al., eds., Washington, DC: Office of the Surgeon General, 1997, p. 462.

[70] CENTCOM Message, from USCINCCENT/CCSG, Subject: "Biological Warfare Defense Medical Guidelines," 051444Z Jan 91; Department of Defense Ad Hoc Desert Shield Biological Warfare Working Group, Minutes of Meeting on January 18, 1991.

[71] Office of the Special Assistant for Gulf War Illnesses E-mail, from a staff member, Subject: "Phone Conversation," May 2, 2000; Navy roster of SEAL personnel, June 24, 1998.

[72] Army Memorandum, from the Army Operations Deputy, Subject: "Alert Message to Prepare for Initiation of the BW Vaccination Program," December 14, 1990.

[73] CENTCOM After Action Report, "Medical Defense against Biological Warfare Summary," March 12, 1991, p. 6.

[74] CENTCOM Message, from USCINCCENT/CCSG, Subject: "Biological Warfare Vaccination Guidelines," 071203Z Jan 91; CENTCOM Message, from USCINCCENT/CCSG, Subject: "Biological Warfare Vaccination Guidelines," 171632Z Jan 91.

The guidance called for two doses of vaccine approximately 14 days apart.[75] CENTCOM directed that personnel in the following areas and units would be vaccinated: Riyadh, Dhahran-Damman, King Khalid Military City (KKMC), Logistics Bases A/B/C/D/E, Headquarters VII Corps and XVIII Airborne Corps, 1st Cavalry Division, and Bahrain.[76] Available records indicate that anthrax vaccine from (at least) lot numbers 19, FAV002, FAV003, FAV004, FAV005, and FAV006 was distributed in theater.[77]

The botulinum toxoid vaccination guidelines specified that only personnel in units prioritized by CENTCOM, namely the Army VII Corps and the 1st Marine Expeditionary Force, were to be vaccinated at that time, and that limited additional quantities of botulinum toxoid vaccine would be available in February and March 1991 to vaccinate additional designated personnel in the area of responsibility. It was anticipated that the relatively brief period between exposure and onset of illness (when compared to anthrax) would make botulinum toxin an agent likely to be used against forward units. The guidance called for two doses of vaccine approximately two weeks apart, followed by a third dose 10 weeks after the second dose.[78] Available records indicate that botulinum toxoid vaccine from (at least) lot number PBP001 was distributed in theater.[79]

Although informed consent was not required for either the anthrax or the botulinum toxoid vaccines, in practice both were administered as voluntary to some extent. A post-conflict status report indicates that anthrax vaccinations were not portrayed as mandatory, but as highly recommended.[80] This is substantiated by an affidavit documenting the voluntary refusal of a servicemember to take the anthrax shot.[81] Subsequent testimony by the CENTCOM Surgeon indicated that the botulinum toxoid vaccine was also voluntary: "And, again I mention, there wasn't enough vaccine for everybody. And it seemed reasonable enough to give them the choice, based upon the fact that you gave them the information upon which to base a choice."[82] Reports indicate that the botulinum toxoid vaccine was likely declined by several thousand servicemembers.[83]

A CENTCOM message in March 1991 terminated the biological warfare vaccine programs and instructed any personnel who began the series that they need not complete the immunization

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[75] CENTCOM Message, from USCINCCENT/CCSG, Subject: "Biological Warfare Vaccination Guidelines," 071203Z Jan 91.

[76] Army Message, from COMUSARCENT/CG, Subject: "Biological Warfare Vaccination Guidelines," 080700Z Jan 91.

[77] Army Forms 3161, "Request for Issue or Turn-in," January 10 through February 18, 1991.

[78] CENTCOM Message, from USCINCCENT/CCSG, Subject: "Biological Warfare Vaccination Guidelines," 171632Z Jan 91.

[79] Army Forms 3161, "Request for Issue or Turn-in," February 7 and 18, 1991.

[80] CENTCOM Message, from USCINCCENT/CCSG, Subject: "Investigational Drug Status," 081808Z Mar 91.

[81] Affidavit (voluntary refusal to take the anthrax shot), signed February 23, 1991.

[82] Belihar, Robert, Testimony before the Presidential Advisory Committee on Gulf War Veterans' Illnesses, January 12, 1996, web site, www.gwvi.ncr.gov (as of July 28, 2000).

[83] CENTCOM After Action Report, "Medical Defense Against Biological Warfare," March 12, 1991; Belihar, Robert, Testimony before the Presidential Advisory Committee on Gulf War Veterans' Illnesses, January 12, 1996, web site, www.gwvi.ncr.gov (as of July 28, 2000).

programs.[84] At the end of hostilities, personnel from the US Army Medical Research Institute of Infectious Diseases traveled to Saudi Arabia to recover remaining stocks of anthrax and botulinum toxoid vaccines, which were stored at the 47th Medical Supply, Optical, and Maintenance facility in Dhahran.[85] The team reported that there were two refrigeration malfunctions in April and May 1991 that may have affected the quality of the vaccines. The team recommended disposal of the anthrax vaccine and re-testing of the botulinum toxoid vaccine.[86]

There is no accurate count of how many servicemembers received these vaccines. The DoD estimated that 150,000 servicemembers received at least one immunization against anthrax and that 8,000 servicemembers received at least one immunization of botulinum toxoid.[87] A recent survey of Gulf War veterans suggests the numbers of servicemembers who received these vaccines may be higher.[88]

The Office of the Special Assistant now holds a collection of rosters showing biological warfare vaccines administered to individual servicemembers, but this collection is incomplete. The information included in many of these rosters is insufficient and difficult to interpret. Some of the rosters appear original, others apparently were created in response to a post-war call for this information. (See also *Vaccine Record Keeping*, section V.)

After the war, Iraq acknowledged that it had conducted research into the offensive use of biological warfare agents, including anthrax and botulinum toxin. During the Gulf War, Iraq had filled some weapons with these two biological warfare agents (and also with aflatoxin, a toxin for which there is no vaccine), but did not use them.[89] A report by the Central Intelligence Agency also concluded that Iraq did not use biological warfare agents during the Gulf War.[90] The best evidence available to the Presidential Advisory Committee on Gulf War Veterans' Illnesses indicated that US personnel were not exposed to biological warfare agents during the Gulf War.[91]

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[84] CENTCOM Message, from USCINCCENT/CCSG, Subject: "Termination of Anthrax and Botulism Vaccination Programs," 041803Z Mar 91.

[85] Army Information Paper, from an Army staff officer, Subject: "Medical Products Recovery Team," May 13, 1991.

[86] Army Information Paper, from an Army staff officer, Subject: "Potential Loss of Anthrax and Botulism Vaccines and Botulinum Antitoxin in Saudi Arabia (SA)," May 24, 1991.

[87] Army Memorandum for Record, from an Army NBC staff officer, Subject: "Drug and Vaccine Usage During Operation Desert Shield/Storm," December 9, 1991; Army Information Paper, from an Army staff officer, Subject: "Numbers of Service Members Vaccinated During Operation Desert Storm," October 9, 1991; Presidential Advisory Committee on Gulf War Veterans' Illnesses, Final Report, December 1996, p. 98.

[88] Kang, Han K., et al., "Illnesses Among United States Veterans of the Gulf War: A Population-based Survey of 30,000 Veterans." *Journal of Occupational and Environmental Medicine*, May 2000, vol. 42, no. 5, p. 496-7, 499.

[89] US Government White Paper, "Iraq Weapons of Mass Destruction Programs," released February 13, 1998, p. 2-3 and 7; Caudle, Lester C. III, "The Biological Warfare Threat," *Medical Aspects of Chemical and Biological Warfare*, Sidell, Frederick R. et al., eds., Textbook of Military Medicine, Zajtchuk, Russ, et al., eds., Washington, DC: Office of the Surgeon General, 1997, p. 462.

[90] Central Intelligence Agency, "Intelligence Related to Possible Sources of Biological Agent Exposure During the Persian Gulf War," August 2000, p. 2.

[91] Presidential Advisory Committee on Gulf War Veterans' Illnesses, Final Report, December 31, 1996, p. 38.

Because anthrax remains a biological warfare threat, the Department of Defense has decided to vaccinate the total military force against this disease.[92] The DoD's Anthrax Vaccine Immunization Program office manages this effort and regularly provides updated information on its web site.[93] The military also continues an active research program to develop new and better vaccines against a variety of biological warfare agents.

V. RELATED ISSUES

A. Adverse Reactions to Vaccines

By far the most common reactions to vaccines are local reactions at the site of injection, usually soreness and swelling. Fever is also associated with some vaccines. These reactions generally last only a few hours or days, although the soreness and swelling occasionally may be more severe and prolonged. Some vaccines are more likely than others to produce these reactions. For example, influenza vaccines may cause mild soreness and fever in 20 to 30 percent of individuals;[94] the typhoid vaccine generally used by the military may have caused local soreness in 50 to 80 percent of recipients, and headache, muscle aches, and fever in up to 30 percent.[95] Serious reactions to vaccines are much less common. Most vaccines can cause allergic reactions that can be life-threatening (anaphylaxis), but this is rare.[96]

At the time of the Gulf War, joint guidance required that adverse reactions to vaccines be described in the individual's medical record. Reactions requiring hospitalization or resulting in significant time lost from duty were also to be reported on a CDC form. The more common and limited reactions need not be reported unless contaminated lots of vaccines were suspected.[97]

While there are no detailed listings for all adverse reactions to vaccines experienced by servicemembers during the Gulf War deployment, a database maintained by the Army's Center for Health Promotion and Preventive Medicine lists 58 vaccine reaction incidents for which servicemembers were hospitalized. Typhoid vaccine was the most frequent cause of reactions attributed to a single vaccine (rather than to combinations of vaccines or to various unidentified vaccines). Two incidents listed in this database might have been life threatening: a severe allergic reaction to typhoid vaccine (anaphylaxis) and a widespread skin rash from smallpox

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[92] Department of Defense Memorandum, from the Secretary of Defense, Subject: "Implementation of the Anthrax Immunization Program for the Total Force," May 18, 1998.

[93] Anthrax Vaccine Immunization Program web site, www.anthrax.osd.mil.

[94] Grabenstein, John D., "Influenza Virus Vaccines, Trivalent, Types A and B," (section written August 2000), ImmunoFacts: Vaccines and Immunologic Drugs, St. Louis, MO: Facts and Comparisons, 2000, p. 132.

[95] Grabenstein, John D., "Typhoid Vaccines (Parenteral)," (section written May 1995), ImmunoFacts: Vaccines and Immunologic Drugs, St. Louis, MO: Facts and Comparisons, 2000, p. 111.

[96] Grabenstein, John D., ImmunoFacts: Vaccines and Immunologic Drugs, St. Louis, MO: Facts and Comparisons, 2000, p. 67, 99, 123, 132, 186, 201.

[97] US Army Regulation 40-562, US Naval Medical Command Instruction 6230.3, US Air Force Regulation 161-13, and Coast Guard Commandant Instruction M6230.4D, "Immunizations and Chemoprophylaxis," October 7, 1988, par. 3-11a.

vaccine (generalized vaccinia).[98]

Information was also limited on adverse reactions to the biological warfare vaccines, anthrax and botulinum toxoid. A communication from mid-January 1991 indicated that there was no formal feedback program for gathering information on adverse reactions from anthrax vaccinations, but noted that about half of personnel vaccinated in the first week of the program developed local irritation that went away in three to four days, and that no serious reactions were observed.[99] A survey of 169 aircrew members found that 92 percent reported some reaction from the anthrax vaccine, primarily local tenderness and redness, while 30 percent reported fever, headache, and muscle aches; only 3 percent felt their reactions were serious enough to affect flying duties.[100] Adverse reactions from anthrax vaccine used before the Gulf War included local reactions in 30 percent with a tendency toward increased reactions with later doses in the series. This and other information about adverse reactions expected to occur with this vaccine was noted in the package insert that accompanied the vaccine.[101] We are aware of one hospitalization during the Gulf War possibly related to anthrax vaccine.[102]

We are not aware of any reports of severe reactions to the botulinum toxoid vaccine. A 1995 Institute of Medicine report notes that the 1st Marine Expeditionary Force conducted a postcard survey in August 1991 of 123 Marines who received one or more doses of the vaccine in the Gulf. Of the 121 who responded, 12 percent reported mild local reactions; 14 percent reported pain that limited use of the arm temporarily; and 2.5 percent reported systemic symptoms that did not limit activity.[103] By comparison, the CDC had noted reaction rates in earlier vaccine recipients of 5.8 percent for moderate and severe local reactions and 3 percent for systemic reactions.[104]

A system for reporting complaints about medical materiel to the Defense Personnel Support Center (DPSC) was also in place during the Gulf War (although this system was not designed primarily for vaccine reactions). Complaints about medical materiel included any of the following: Type I, complaints about materiel determined by use or tests to be harmful or defective enough to cause death, injury, or illness; Type II, complaints about materiel other than equipment suspected of being harmful, defective, deteriorated, or otherwise unsuitable for use; and Type III, complaints about equipment determined to be unsatisfactory because of

[98] Center for Health Promotion and Preventive Medicine, Medical Surveillance Activity Report, "Adverse Reactions to Vaccines Among Soldiers Deployed to Persian Gulf War," November 21, 1996.

[99] Letter from an Army staff officer (concerning Gulf War biological warfare vaccination and medical defense program), January 15, 1991.

[100] Air Force Aerospace Medicine Consolidated After Action Report, "Desert Shield/Desert Storm," January 1992, p. 13.

[101] Michigan Department of Public Health, Anthrax Vaccine Package Insert (Information Sheet), October 1987.

[102] Although the initial hospital diagnosis sheet stated "Seizure activity (possible reaction to anthrax)," both the condition and the cause were less clear at the time of subsequent evaluation, i.e., "Pseudoseizures vs. seizure activity."

[103] Institute of Medicine, Health Consequences of Service During the Persian Gulf War: Initial Findings and Recommendations for Immediate Action. Washington, DC: National Academy Press, 1995, p. 55.

[104] Army Medical Research Institute of Infectious Diseases, "Administration of Pentavalent Botulinum Toxoid to At-Risk Individuals During Operation Desert Shield," September 14, 1990.

malfunction, design, and defects.[105] The DPSC was to immediately notify the Defense Medical Standardization Board (DMSB) and the Food and Drug Administration of all Type I complaints. According to DMSB staff, the Board received no Type I complaints for any vaccines used during the Gulf War. Documentation was not available at the DMSB regarding Type II or Type III complaints involving vaccines for the same period.[106]

Following the Gulf War, revised joint guidance on immunizations continued to require the recording and reporting of adverse reactions as before, but reactions previously reported to CDC were now to be reported to the FDA through the newer Vaccine Adverse Events Reporting System (VAERS).[107] VAERS is a combined FDA and CDC program that requires reporting of certain events (and encourages reporting of any other events considered important) that occur after the administration of vaccines. This system uses the term "adverse event" rather than "adverse reaction" to indicate that it is not always possible to make a causative connection between events experienced and vaccines administered. Medical personnel, vaccine manufacturers, and vaccine recipients submit reports through VAERS.[108]

Reactions to the anthrax vaccine used in the current DoD immunization program have been documented through surveys of military personnel. Because the program began in early 1998, the majority of the servicemembers had received fewer than the full series of doses at the time of these surveys. Most of the reported reactions have been localized, minor, and limited, but these reactions were more frequent in women.[109] The DoD's Anthrax Vaccine Immunization Program office maintains a web site with updated information on this issue.[110]

The CDC and the FDA continue to monitor licensed and investigational vaccines closely, and to suspend use of vaccines whenever there is substantial evidence that they may cause serious side effects.

Currently there are no established connections between vaccines and the persistent and unexplained illnesses reported by some veterans, although research continues on this issue. A recent report from the Institute of Medicine (IOM) reviewed the published scientific research in order to assess the potential adverse health effects of the biological warfare vaccines. The report concluded that anthrax and botulinum toxoid vaccinations are associated with transient acute local and systemic effects (e.g., redness, swelling, fever) typically associated with other

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[105] Defense Logistics Agency Regulation 4155.28, "Reporting and Processing Medical Materiel Complaints," June 16, 1986.

[106] Lead Sheet #26394, Interview of a staff assistant for the Pharmaceutical Division, Defense Standardization Board, October 16, 1998.

[107] Air Force Joint Instruction 48-110, Army Regulation 40-562, Navy Bureau of Medicine and Surgery Instruction 6230.15, and Coast Guard Commandant Instruction M6230.4E, "Immunizations and Chemoprophylaxis," November 1, 1995, par. 12.

[108] Vaccine Adverse Event Reporting System (VAERS) web site, www.fda.gov/cber/vaers (as of July 5, 2000).

[109] Centers for Disease Control and Prevention, "Surveillance for Adverse Events Associated with Anthrax vaccination: US Department of Defense, 1998-2000," Morbidity *and Mortality Weekly Report (MMWR)*, April 28, 2000, vol. 49, no. 16, p. 341-345.

[110] Anthrax Vaccine Immunization Program web site, www.anthrax.osd.mil.

vaccinations, but that there is inadequate/insufficient scientific evidence to determine whether these vaccinations are associated with long-term adverse health effects. It noted that the small number of published studies on this issue is not unusual, as few vaccines have been monitored for adverse effects over long periods of time. The report recommended long-term studies of recipients of these vaccines. The IOM also assessed the possible health effects of multiple vaccinations, and again concluded that there is inadequate/insufficient scientific evidence to determine whether multiple vaccinations are associated with long-term adverse health effects, with further research needed.[111]

B. Vaccine Adjuvants

Adjuvants are substances included in some vaccines in order to improve the immune response to these vaccines. Not all vaccines contain adjuvants; some don't need them to produce protection in recipients. The addition of an adjuvant to a vaccine preparation can sometimes increase local reactions to the vaccine, but there is substantial benefit in producing an earlier, stronger, or more persistent protection from the vaccine. Aluminum compounds are common adjuvants in licensed vaccines and have been used safely for many years. Some of the vaccines given to servicemembers during the Gulf War deployment, including the anthrax, botulinum toxoid, hepatitis B, and tetanus-diphtheria vaccines, contained aluminum compounds as adjuvants.[112]

To improve the effectiveness of vaccines, research has continued on a large number of newer adjuvant formulations that appear stronger than the aluminum compounds. Some of these newer adjuvant formulations contain squalene as an oil component in the formulation. Squalene itself is commonly found in certain cosmetics and foods, and in the body as a part of normal human metabolism. Both the Department of Defense and the National Institute of Allergy and Infectious Diseases (a division of the National Institutes of Health) have sponsored research clinical trials of vaccines that include squalene-containing adjuvants. Some of these trials were done at the time of the Gulf War. Because these vaccines were investigational products, FDA guidelines required informed consent from the volunteers. (See also *Investigational Vaccines*, Section V.) The DoD has also conducted research with squalene-containing adjuvants in animals, including research on newer anthrax vaccines. The General Accounting Office noted that the DoD considered but did not use vaccines containing adjuvants other than aluminum during the Gulf War. According to DoD officials, the use of new adjuvant formulations for the anthrax vaccine was rejected because any alteration in the licensed vaccine would require re-licensure, and DoD would not receive FDA approval in time.[113]

Since the Gulf War, one group of researchers has reported finding antibodies to squalene in Gulf War veterans with unexplained illnesses and has suggested that squalene, or antibodies to

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[111] Institute of Medicine, Gulf War and Health: Volume 1. Depleted Uranium, Sarin, Pyridostigmine Bromide, Vaccines, Fulco, Carolyn E., Catharyn T. Liverman, Harold C. Sox, eds., Washington, DC: National Academy Press, 2000, p. 1-5, 14-18.

[112] Grabenstein, John D., ImmunoFacts: Vaccines and Immunologic Drugs, St. Louis, MO: Facts and Comparisons, 2000, p. 35, 69, 127, 513.

[113] General Accounting Office, "Gulf War Illnesses: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved," March 29, 1999, p. 3, 5, 6.

squalene, may have contributed to these illnesses.[114] This research is preliminary and will require confirmation.[115]

C. Information Available to Servicemembers

Communication of information to servicemembers about the health hazards of war and about the benefits and risks of medical countermeasures like vaccines is essential, but problematic. The information must be made understandable to all vaccine recipients, yet it may be impossible to completely avoid technical concepts. The communication of complex risks might be particularly difficult when the information is presented during the hurried and stressful times of deployment.

Risk communication might be considered successful when "it raises the level of understanding of relevant issues for those involved and satisfies them that they are adequately informed within the limits of available knowledge." It most often involves a two-way exchange of information in order to maximize this level of understanding, but this dialogue may not be feasible or appropriate for all military situations. Sometimes a simple one-way briefing may suffice; at other times feedback and discussion may be necessary.[116] Successful risk communication, as applied to the use of vaccines, would make it clear that the scientific information is rarely complete, that the risks of the diseases and the vaccines are neither overstated nor understated, and that the decisions made are in the best health interests of the servicemembers. Such communications should lead to improvements in mutual respect and trust.

During the Gulf War, the policy for informing servicemembers about the biological warfare vaccines was contained in the CENTCOM guidelines and was classified in order to preserve operational security. Prepared statements were to be read to servicemembers at the time of vaccination, but were not to be distributed, and vaccine recipients were cautioned not to discuss the vaccinations with anyone.[117]

For the anthrax vaccine, the information in the statement included the reasons for the vaccine, the schedule of injections, and the expected reactions to the vaccine. It indicated that the vaccine was supplementary to the primary protection provided by masks and to treatment with available antibiotics.[118] For the botulinum toxoid vaccine, the information also included a brief description of botulism, indications that the vaccine was investigational, and details about the

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[114] Asa, Pamela B., Yan Cao, and Robert F. Garry, "Antibodies to Squalene in Gulf War Syndrome," *Experimental and Molecular Pathology*, February 2000, vol. 68, p. 55-64.

[115] Armed Forces Epidemiological Board Memorandum, from the Board President and the Executive Secretary, Subject: "Armed Forces Epidemiological Board (AFEB) Recommendations Regarding Review of the Paper, 'Antibodies to Squalene in Gulf War Syndrome' by P.B. Asa, Y. Cao and R.F. Garry," July 11, 2000.

[116] Institute of Medicine, Strategies to Protect the Health of Deployed U.S. Forces: Medical Surveillance, Record Keeping, and Risk Reduction, Joellenbeck, Lois M., Philip K. Russell, and Samuel B. Guze, eds., Washington, DC: National Academy Press, 1999, p. 93.

[117] Army Message, from COMUSARCENT/CG, Subject: "Biological Warfare Vaccination Guidelines," 080700Z Jan 91; CENTCOM Message, from USCINCCENT/CCSG, Subject: "Biological Warfare Vaccination Guidelines," 171632Z Jan 91.

[118] Army Message, from COMUSARCENT/CG, Subject: "Biological Warfare Vaccination Guidelines," 080700Z Jan 91.

reactions that had occurred with previous uses of the vaccine.[119] An additional statement was added to the information sheet for botulinum toxoid vaccine for signature by the vaccine recipient. The statement indicated that the recipient had read and understood the information, and had voluntarily submitted to the vaccine series.[120]

These policies for vaccine information appear to have been implemented with varying consistency and success. A preventive medicine officer reported that "...despite the hush-hush nature of the [anthrax] vaccine's employment..., there developed some groundswell of unease and anxiety among units who were not on the distribution list.... I had to do some scrambling just to find out what the principles of prioritization were."[121] A medical detachment commander expressed similar concerns: "The reasons why some units were chosen to receive the [anthrax] vaccine and not other units was not made clear to all units. There was poor communication about the vaccine itself leading to many fears among those potentially receiving the vaccine. Many commanders made the immunization mandatory.... Other commanders made it optional.... There was a great deal of misinformation about the anthrax vaccine among the soldiers. Very many thought that the vaccine was not FDA approved and was an experimental drug. Many feared drastic systemic side effects."[122] Some servicemembers reported that they were provided no information on why the anthrax and botulinum toxoid vaccines were being given.[123]

Following the Gulf War, the Department of Defense developed policy that reflects a heightened awareness of the importance of informing personnel of health threats and risks associated with deployment.[124] The DoD now provides several web sites with information about vaccines and links to other governmental and non-governmental sources of information.[125] Each of these sites is an attempt by DoD to establish improved lines of communication with servicemembers about the role of vaccines in force health protection.

D. Investigational Vaccines

The administration of botulinum toxoid vaccine to US forces during the Gulf War highlighted

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[119] CENTCOM Message, from USCINCCENT/CCSG, Subject: "Biological Warfare Vaccination Guidelines," 171632Z Jan 91.

[120] Botulinum toxoid vaccine information sheet [undated].

[121] Army Memorandum, from an Army Preventive Medicine Officer, Subject: "Operation Desert Storm Update," February 12, [1991].

[122] Army Memorandum, from a Medical Detachment Commander, Subject: "Desert Shield After Action Report," March 10, 1991; Army Memorandum, from a Medical Detachment Commander, Subject: "Anthrax Vaccination Program in LBC [Log Base Charlie]," March 4, 1991.

[123] Lead Sheet #14758, Interview of a physician, May 4, 1998; Lead Sheet #14216, Interview of a nurse, May 11, 1998; Lead Sheet #14536, Interview of a physician, July 16, 1998.

[124] Department of Defense Directive 6490.2, "Joint Medical Surveillance," August 30, 1997, par. 4; Department of Defense Instruction 6490.3, "Implementation and Application of Joint Medical Surveillance for Deployments," August 7, 1997, par. 6.

[125] Department of Defense (Health Affairs) web site, www.tricare.osd.mil/immunization (as of May 30, 2000); Center for Health Promotion and Preventive Medicine web site, chppm-www.apgea-army.mil/depm (as of July 10, 2000); Anthrax Vaccine Immunization Program web site, www.anthrax.osd.mil.

the concerns and challenges surrounding the military use of investigational drugs and vaccines.[126] Generally speaking, the term "investigational" applies to drugs and vaccines that have not been fully approved and licensed by the Food and Drug Administration. Such is the case with the botulinum toxoid vaccine. Conversely, the anthrax vaccine used during the Gulf War had been licensed by the FDA for many years, and thus was not an investigational product.[127]

The FDA grants licensure for drugs and vaccines that have been shown to be both safe and effective (generally for a specific use). Products developed to protect against biological warfare agents can be shown to be safe in humans using fairly well established procedures. However, the human trials usually required by the FDA to prove vaccine effectiveness are not possible when the disease does not occur naturally with sufficient frequency, or when studies in humans are too dangerous (i.e., exposure to harmful doses). Consequently, a number of much-needed products under development in military research programs cannot satisfy the current requirements for licensure by the FDA and remain in an investigational status.[128]

Investigational drugs and vaccines are tested in volunteer subjects under FDA-approved guidelines. Use and study of these investigational products require review by an institutional review board, informed consent from the recipients of the products, and the maintenance of detailed records of the products' administration and test results.[129]

In assessing countermeasures to Iraq's biological threats during the Gulf War, the DoD determined that it needed to be prepared to use investigational products such as the botulinum toxoid vaccine. At the same time, the DoD was concerned that the rules for administering investigational products could not be followed under battlefield conditions. Therefore, in late October 1990, the DoD recommended that the FDA provide a mechanism for waiving informed consent requirements for investigational products that might be considered the best preventive or therapeutic treatments available for US military personnel serving in the Gulf. In its recommendation, the DoD noted that "...In all peacetime applications, we believe strongly in informed consent and its ethical foundations.... But military combat is different. If a soldier's life will be endangered by nerve gas, for example, it is not acceptable from a military standpoint to defer to whatever might be the soldier's personal preference concerning a preventive or therapeutic treatment that might save his life, avoid endangerment of other personnel in his unit, and accomplish the combat mission."[130]

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[126] Investigational products include both drugs and "biologics;" vaccines are considered among the biologics. The official term "investigational new drug" or "IND" is taken to mean both drugs and biologics.

[127] Presidential Advisory Committee on Gulf War Veterans' Illnesses, Interim Report, February 1996, p. 20.

[128] Institute of Medicine, Strategies to Protect the Health of Deployed U.S. Forces: Medical Surveillance, Record Keeping, and Risk Reduction, Joellenbeck, Lois M., Philip K. Russell, and Samuel B. Guze, eds., Washington, DC: National Academy Press, p. 111.

[129] Institute of Medicine, Strategies to Protect the Health of Deployed U.S. Forces: Medical Surveillance, Record Keeping, and Risk Reduction, Joellenbeck, Lois M., Philip K. Russell, and Samuel B. Guze, eds., Washington, DC: National Academy Press, p. 112.

[130] Department of Defense (Health Affairs) Letter, from the Assistant Secretary of Defense for Health Affairs, October 30, 1990 (as published in the Federal Register, December 21, 1990, p. 52814-52815).

The FDA responded to the DoD recommendation by publishing an interim rule in the *Federal Register* in December 1990. This rule permitted the FDA to determine that obtaining informed consent from military personnel for the use of an investigational drug or biologic is not feasible in certain battlefield or combat-related situations, and that withholding treatment would be contrary to the best interests of military personnel. The published rule stated that "...FDA will consider investigational products proposed for military use on a case-by-case basis, and the agency is prepared to waive the requirement of informed consent where it can be documented that use of these agents in combat-related situations serves the best interests of individual soldiers and the military combat units in which they serve."[131]

As required by this interim rule, the DoD then submitted a written request to the FDA, asking for a determination that obtaining informed consent would not be feasible for the botulinum toxoid vaccine because of the military combat exigencies associated with Operation Desert Shield.[132] The FDA Commissioner concurred and provided a written determination to the Assistant Secretary of Defense for Health Affairs in late December 1990, noting that "...I find that there is no available satisfactory alternative therapy for the prevention of botulism, and I concur with your assessment that informed consent is not feasible and that withholding treatment would be contrary to the best interests of military personnel."[133] (A detailed discussion of the issues surrounding this interim rule may be found in a 1999 RAND report.[134] Information on vaccine record keeping is included in the following subsection of this paper.)

Media reports about "experimental" vaccines, combined with limited vaccine supplies, were apparently key factors in a decision by CENTCOM to modify the agreed-upon protocol and allow servicemembers the choice of declining the botulinum toxoid vaccine. In post-Gulf War testimony before the Presidential Advisory Committee on Gulf War Veterans' Illnesses (PAC), the CENTCOM Surgeon expressed concern about the impact of media-fueled rumors on the morale of military personnel. He further stated that since there was not enough botulinum toxoid vaccine for all servicemembers, it seemed reasonable to give them the information and let them make the choice.[135] In subsequent correspondence with the FDA, the DoD commented that while this decision had been made without notice to the Pentagon until after the fighting stopped, "...in retrospect, it was quite proper to give the responsible military command the option to decide whether actual military circumstances unfolding in the theater of operations truly required the standardized use of the vaccine."[136]

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[131] Department of Health and Human Services, Food and Drug Administration, Interim Rule, "Informed Consent for Human Drugs and Biologics; Determination That Informed Consent Is Not Feasible," Federal Register, December 21, 1990, p. 52814-52817.

[132] Department of Defense (Health Affairs) Letter, from the Assistant Secretary of Defense for Health Affairs, December 28, 1990.

[133] Department of Health and Human Services, Food and Drug Administration Letter, from the Commissioner of Food and Drugs, December 31, 1990.

[134] RAND, Military Use of Drugs Not Yet Approved by the FDA for CW/BW Defense: Lessons From the Gulf War, National Defense Research Institute, 1999.

[135] Belihar, Robert, Testimony before the Presidential Advisory Committee on Gulf War Veterans' Illnesses, January 12, 1996, web site, www.gwvi.ncr.gov (as of July 28, 2000).

[136] Department of Defense (Health Affairs) Letter, from the Assistant Secretary of Defense for Health Affairs, September 13, 1996.

Other investigational vaccines were also considered for use during the Gulf War. In December 1990, the DoD briefly considered establishing a "Manhattan-like project" to accelerate the testing and development of several new vaccines in an operational setting.[137] The proposed project was evaluated by a tri-service medical working group, which felt that the timing was not right at that point in the conflict, although such a proposal might be possible if the Gulf War became prolonged.[138] The project was referred for further consideration, but was not supported and a draft memorandum establishing a project task force was never signed by the Army Surgeon General.[139]

Following the Gulf War, progress in resolving the issues surrounding the military's use of investigational drugs under deployment conditions has been slow. The PAC noted that the DoD and the FDA had "deliberated carefully" before allowing the use of investigational products without informed consent during the Gulf War. However, the DoD was unable to produce records of who received these products and had not been responsive to the recommendation that it routinely inform servicemembers about the possible use of investigational products for chemical and biological warfare defense; the FDA had failed to devise better long-term methods governing military use of these products and had taken too much time before soliciting public comment on alternatives to the interim rule.[140] In a summary report, the PAC again noted the FDA's slowness in making progress on these issues, as well as DoD's acknowledgement of its failures to comply with federal regulations pertaining to these investigational products in both the Gulf War and in the subsequent deployment to Bosnia.[141]

In 1998, Congress passed legislation stipulating that only the President, at the request of the Secretary of Defense, can waive the requirement for informed consent involving investigational products. The law states that for informed consent to be waived, it must be found to be not feasible, contrary to the best interest of the servicemember, or not in the best interests of national security.[142] In 1999, a presidential order expanded on the requirements of the 1998 law, and called for the DoD to provide ongoing training and health risk communication to servicemembers on investigational drugs in support of military operations.[143] The FDA then revoked its 1990 (Gulf War) interim ruling and published a new interim rule that establishes criteria for the President to apply in making a determination that informed consent is not feasible or is contrary

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[137] Army Memorandum, from the Army Infectious Diseases Consultant, Subject: "Tri-Service Vaccine Task Force (Appendix A)," December 7, 1990.

[138] Army Memorandum, from the Working Group Chairperson, Subject: "Minutes of the Desert Shield Medical Issues Working Group," December 27, 1990.

[139] Army Memorandum, from the Director of the Military Infectious Disease Research Program, Subject: "Infectious Disease (ID) Products Used in Operation Desert Shield," September 5, 1997; Army Memorandum, from the Army Surgeon General, Subject: "Tri-Service Task Force" [undated].

[140] Presidential Advisory Committee on Gulf War Veterans' Illnesses, Interim Report, February 1996, p. 22-23; Presidential Advisory Committee on Gulf War Veterans' Illnesses, Final Report, December 1996, p. 27.

[141] Presidential Advisory Committee on Gulf War Veterans' Illnesses, Special Report, October 1997, p. 8-10.

[142] Public Law 105-261, "Strom Thurmond National Defense Authorization Act for Fiscal Year 1999," October 17, 1998, Sec. 731.

[143] Executive Order 13139, "Improving Health Protection of Military Personnel Participating in Particular Military Operations," September 30, 1999.

to the best interests of the individual servicemember.[144]

The military will likely have need for investigational vaccines in future deployments, but use of these vaccines will be difficult. As noted, some investigational vaccines cannot be adequately tested in humans in order to satisfy current requirements for licensure, and all investigational vaccines have proven difficult to administer under deployment conditions.

E. Vaccine Record Keeping

Documentation of health care (including immunizations) during the Gulf War is addressed in detail in an earlier information paper released by the Office of the Special Assistant.[145] Guidance on documentation of immunizations during the Gulf War was complicated by the need for operational security in the use of the biological warfare anthrax and botulinum toxoid vaccines, and by special record keeping requirements for the investigational botulinum toxoid vaccine.

In January 1991, CENTCOM and Army messages—originally classified SECRET and since declassified—provided guidelines for the theater-wide anthrax and botulinum toxoid vaccination programs. These messages stated that the vaccinations may be recorded on the yellow shot record (PHS 731), or on the *Immunization Record* (SF 601), as Vacc A and Vacc A-2 for the anthrax series, and Vacc B, Vacc B-2, and Vacc B-3 for the botulinum toxoid series.[146] A later memorandum indicated these vaccines may also have been recorded as "Anthrax," "A Vaccination," "A-Vax," "Botulinum," "Bot-Tox," "B Vaccination," "B-Vax," or something similar.[147] For the anthrax vaccine, it appears that a roster of personnel receiving the vaccine was required. For the botulinum toxoid vaccine, personnel were required to sign an information sheet about the vaccine, indicating that they had read and understood the information and had voluntarily submitted to this immunization.[148]

Whatever the initial guidance, there appeared to be substantial confusion about where, even whether, these vaccinations were to be recorded. Additional guidance, issued after the cease-fire and termination of the vaccination program, specifically required that the vaccinations be entered in the individual health records, and that rosters of immunized personnel be forwarded

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[144] Department of Health and Human Services, Food and Drug Administration, "Human Drugs and Biologics: Determination that Informed Consent is Not Feasible or is Contrary to the Best Interests of Recipients; Revocation of 1990 Interim Final Rule; Establishment of New Interim Final Rule," Federal Register, October 5, 1999, p. 54180-54189.

[145] Office of the Special Assistant for Gulf War Illnesses (Information Paper), "Military Medical Recordkeeping During and After the Gulf War," August 11, 1999, web site, www.gulflink.osd.mil.

[146] CENTCOM Message, from USCINCCENT/CCSG, Subject: "Biological Warfare Vaccination Guidelines," 171632Z Jan 91; Army Message, COMUSARCENT/CG, Subject: "Biological Warfare Vaccination Guidelines," 080700Z Jan 91.

[147] Army Memorandum, from the Army Deputy Surgeon General, Subject: "Medical Records and Rosters Related to Vaccination Against Biological Warfare Agents," May 21, 1991.

[148] CENTCOM Message, from USCINCCENT/CCSG, Subject: "Biological Warfare Vaccination Guidelines," 171632Z Jan 91; Army Message, COMUSARCENT/CG, Subject: "Biological Warfare Vaccination Guidelines," 080700Z Jan 91.

through the chain of command.[149] Post-conflict discussions with Gulf War veterans further indicated that documentation of anthrax and botulinum toxoid immunizations was irregular, perhaps owing to the need for operational security in the administration of both vaccines, and to the uncertain guidance regarding the documentation of the investigational (botulinum toxoid) vaccine.[150]

The most current (1995, but being revised) joint guidance covering the Armed Forces immunization program, along with service-specific medical record keeping directives, reflect the post-Gulf War policies for documenting immunizations. According to these directives, immunizations for Army, Navy, and Marine Corps personnel continue to be recorded on both the *Immunization Record* (SF 601) in the individual health record and the *International Certificates of Vaccination* (PHS 731). Air Force immunizations are recorded on the *Adult Preventive and Chronic Care Flowsheet* (AF 1480A) in the member's health record as well as on the PHS 731.[151] These policies, in turn, have been affected by the 1998 issuance of an *Adult Preventive and Chronic Care Flowsheet* (DD 2766). The Navy[152] and the Army[153] now direct that immunizations be documented in the individual health record using the DD 2766 instead of the SF 601, and the Air Force has designated the DD 2766 as a replacement for the AF 1480A,[154] as well as a record for documenting medical care during deployments.[155]

The documentation of investigational drugs and vaccines remains a difficult issue. In its 1997 request for comments on the rule that waived the requirements for informed consent for investigational products taken during the Gulf War, the FDA recognized that the rule did not work

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[149] Marine Corps Message, from FIRST MARDIV/CG, Subject: "Biological Warfare Vaccination Program," 200932Z Mar 91; Army Letter, from the Commander, Medical Group (Provisional), Subject: "Documentation Guidelines for Anthrax Immunization," July 9, 1991; Army Memorandum, from a 98th Division staff member, Subject: "Medical Records and Rosters Related to Vaccination Against Biological Warfare (BW) Agents," June 25, 1991; National Guard Bureau Memorandum, from the Chief of the Office of the Army Surgeon, Subject: "Medical Records and Rosters Related to Vaccination Against Biological Warfare Agents," June 24, 1991; Army Message, from CDRFORSCOM/FCJ1, Subject: "Medical Records and Rosters Related to Vaccination Against Biological Warfare (BW) Agents," 191755Z Jun 91; Army Memorandum, from the Army Deputy Surgeon General, Subject: "Medical Records and Rosters Related to Vaccination Against Biological Warfare Agents," May 21, 1991.

[150] Lead Sheet #10934, Interview of a hospital technician, May 22, 1997; Lead Sheet #5553, Interview of a hospital corpsman, July 22, 1997; Lead Sheet #14606, Interview of a clearing company physician, March 27, 1998; and Lead Sheet #9882, Interview of an air search and rescue member, February 11, 1997.

[151] Air Force Joint Instruction 48-110, Army Regulation 40-562, Bureau of Medicine Instruction 6230.15, and Coast Guard Commandant Instruction M6230.4E, "Immunizations and Chemoprophylaxis," November 1, 1995, par. 50-53; Army Regulation 40-66, "Medical Record Administration," July 20, 1992, p. 26, par. 5-17; Navy Manual P-117, "Manual of the Medical Department," December 23, 1994, p. 16-71, art. 16-59; Air Force Instruction 41-210, "Patient Administration Functions," July 26, 1994, p. 34, par. A5.4.2.2.

[152] Navy Memorandum, from the Chief of the Bureau of Medicine and Surgery, Subject: "Adult Preventive and Chronic Care Flowsheet for Implementation of Put Prevention Into Practice (PPIP)," July 7, 1998; Department of Defense (Health Affairs) Memorandum, from the Acting Assistant Secretary of Defense for Health Affairs, Subject: "Put Prevention Into Practice (PPIP) – Policy," March 31, 1998.

[153] Army Letter, from DASG-HS, Subject: "The Use of DD Form 2766 and DD Form 2766C," March 26, 1999.

[154] Air Force Memorandum, from the Commander, Air Force Medical Operations Agency, Subject: "Deployment Medical Surveillance," August 17, 1998.

[155] Air Force Pamphlet 44-155, Implementing Put Prevention Into Practice, February 1, 1999, par. 4.1.5.

as anticipated. The FDA specifically mentioned problems with record keeping, and requested comments on whether and how record keeping should be addressed in the rule.[156] In its reply, the DoD indicated that it believed existing FDA regulations on record keeping were adequate, and noted ongoing initiatives to develop automated record keeping and immunization tracking systems.[157]

Recognizing that increasing the number of vaccines and the complexity of immunization schedules require more efficient methods of recording and tracking immunizations, the DoD has established an interim tracking system for its anthrax vaccination program. Currently, the Army uses the Medical Occupational Data System (MODS), the Air Force uses its Military Immunization Tracking System (MITS), and the Navy and the Marine Corps use the Shipboard Automated Medical System (SAMS). Each system transmits a core set of information to the DoD's Defense Eligibility Enrollment System (DEERS), allowing decentralized confirmation of an individual's vaccination status and updating the servicemember's immunization record.[158]

Responding to the Secretary of Defense's direction to establish an anthrax vaccination program,[159] each of the services has developed plans to emphasize the importance of command-level support.[160] These plans, along with a subsequent Army regulation,[161] provide guidance on the medical record keeping and documentation of anthrax immunization program information.

F. Vaccine Use by Coalition Forces

While all coalition partners had vaccination programs, only some of them used vaccines directed against biological warfare agents. As part of the coalition response to Iraq's invasion of Kuwait, the United Kingdom (UK) also conducted an immunization program against biological warfare agents. Details of the UK program are contained in two reports published by the Ministry of Defence in October 1997 and January 2000.[162]

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[156] Department of Health and Human Services, Food and Drug Administration, "Accessibility to New Drugs for Use in Military and Civilian Exigencies When Traditional Human Efficacy Studies Are Not Feasible: Determination Under the Interim Rule That Informed Consent is Not Feasible for Military Exigencies; Request for Comments," Federal Register, July 31, 1997, vol. 62, p. 40996-41001.

[157] Department of Defense (Health Affairs) Letter, from the Acting Assistant Secretary of Defense for Health Affairs to the Lead Deputy Commissioner, Food and Drug Administration [undated].

[158] Department of Defense Report to Congress, "Medical Tracking System for Members Deployed Overseas," May 1998, p. 8-9.

[159] American Forces Information Service News Article, Gilliert, Douglas J., "Pentagon Plans Mass Anthrax Vaccinations," December 16, 1997.

[160] Army Memorandum, from the Army Vice Chief of Staff, Subject: "Army Anthrax Vaccine Immunization Program Plan," April 28, 1998; Secretary of the Navy Instruction 6230.4, "Department of the Navy (DON) Anthrax Vaccination Implementation Program (AVIP)," April 29, 1998; Air Force Memorandum, from the Air Force Chief of Staff, Subject: "Air Force Anthrax Immunization Plan," March 9, 1998.

[161] Army Medical Command Regulation 40-39, "Anthrax Vaccine Adsorbed (AVA) Immunization Documentation," June 28, 1999.

[162] United Kingdom Ministry of Defence, "Background to the Use of Medical Countermeasures to Protect British Forces During the Gulf War (Operation Granby)," October 1997; United Kingdom Ministry of Defence, "Implementation of the Immunisation Programme Against Biological Warfare Agents for UK Forces During the Gulf Conflict 1990/1991," January 2000; United Kingdom Ministry of Defence web site, www.gulfwar.mod.uk (as of

The British program, like the US program, was classified SECRET at the time of the Gulf War. It consisted of an anthrax vaccine and a plague vaccine for use against the UK-assessed threat of Iraq's biological warfare agents, and a pertussis vaccine for use as an adjuvant to accelerate the immunization effect of the anthrax vaccine.[163] The anthrax vaccine was produced from a strain of the bacteria different from that used for the US vaccine and was to be delivered in a series of four injections rather than six. This schedule was reduced to three doses and combined with pertussis vaccine in order to complete the vaccination series in the limited time available.[164] Instead of a botulinum toxoid vaccine, the UK procured botulinum antitoxin for use as a post-attack therapy.[165] The vaccines were intended to be voluntary and their usage was to be recorded. British troops were also to be briefed on the reasons for the vaccine program as well as characteristics of the vaccines.

The British estimate that over 75 percent of all personnel deployed to the Gulf region, and close to 100 percent in many units, received the first anthrax-pertussis injection. Fewer personnel received the second dose of anthrax-pertussis vaccine, which was often accompanied by the first plague vaccine injection. Additional doses of these vaccines were rare. Similar to the US vaccination program, implementation varied: vaccine information was not always made available to UK service personnel, medical officers, or commanders; the voluntary nature of the program was not universally understood or fully implemented; and documentation of immunizations was inconsistent.[166]

Recently, researchers have reported an association in UK veterans between multiple vaccinations given after arriving in the Gulf and later ill health. This work is subject to limitations noted by the authors and others, and will require additional research.[167]

Canada was another coalition partner that had a vaccination program against biological warfare agents during the Gulf War. Like the British forces, Canadian forces used a plague vaccine as well as an anthrax vaccine with pertussis vaccine as an adjuvant.[168]

September 8, 2000).

[163] United Kingdom Ministry of Defence, "Implementation of the Immunisation Programme Against Biological Warfare Agents for UK Forces During the Gulf Conflict 1990/1991," January 2000 (statement by the Ministry of Defence to accompany publication of the report).

[164] United Kingdom Ministry of Defence, "Background to the Use of Medical Countermeasures to Protect British Forces During the Gulf War (Operation Granby)," October 1997, par. 42-44.

[165] United Kingdom Ministry of Defence, "Implementation of the Immunisation Programme Against Biological Warfare Agents for UK Forces During the Gulf Conflict 1990/1991," January 2000, par. 67.

[166] United Kingdom Ministry of Defence, "Implementation of the Immunisation Programme Against Biological Warfare Agents for UK Forces During the Gulf Conflict 1990/1991," January 2000 (Summary).

[167] Hotopf, Matthew et al., "Role of Vaccinations as Risk Factors for Ill Health of Veterans of the Gulf War: Cross Sectional Study," *British Medical Journal*, May 20, 2000, vol. 320, p. 1363; Shaheen, Seif, "Shots in the Desert and the Gulf War Syndrome," *British Medical Journal*, May 20, 2000, vol. 320, p. 1351; Institute of Medicine, Gulf War and Health: Volume 1, Depleted Uranium, Sarin, Pyridostigmine Bromide, Vaccines, Fulco, Carolyn E., Catharyn T. Liverman, Harold C. Sox, eds., Washington, DC: National Academy Press, 2000, p. 17-18.

[168] Canadian Department of National Defence, "Health Study of Canadian Forces Personnel Involved in the 1991 Conflict in the Persian Gulf," vol. II, app. E (Canada in the Gulf War), Canadian Department of National Defence web site, www.dnd.ca (as of August 30, 2000).

VI. OBSERVATIONS

The following are some general observations on vaccine use during the Gulf War deployment. They are intended primarily for veterans who continue to have concerns about the way in which the vaccine programs were planned and implemented. They include areas of success and areas of continuing challenge in the ongoing effort to provide safe and effective vaccines for the protection of military personnel. These observations have been forwarded to the Lessons Learned Implementation Directorate of the Office of the Special Assistant for coordination with applicable offices within the military departments to help ensure that identified issues are appropriately addressed.

- The decisions to select and use specific vaccines for the Gulf War deployment were based on accurate assessments of the infectious diseases and biological warfare agents that servicemembers were likely to encounter. The low number of reported casualties from infectious diseases is due in part to the vaccines given to servicemembers before and during the deployment.

- Shortages of the biological warfare vaccines and delays in implementing this program meant that substantial numbers of servicemembers either did not receive the protection affordable by these vaccines, or received fewer than the desirable number of doses to gain the maximum benefit from these vaccines.

- Information available to servicemembers about vaccinations, especially the biological warfare and investigational vaccines, was inconsistent. Operational security required for the biological warfare vaccines, the necessary prioritization of vaccine recipients, confusion about whether the vaccines were mandatory or voluntary, and the uncertain guidance as to how and where vaccinations would be recorded, all likely contributed to the concern among servicemembers about taking these vaccines. Military personnel at all levels need to appreciate the health risks inherent in military operations, including the relative risks of infectious diseases and biological warfare agents on the one hand, and of the vaccines available as countermeasures on the other.

- Inadequate medical record keeping, especially for the biological warfare vaccines, has made it difficult to know which vaccines were given to individual servicemembers, and has complicated research on possible connections between vaccines and the persistent and unexplained illnesses in some Gulf War veterans. Newer and largely electronic vaccine record keeping systems now in place for at least some vaccines will also need to capture immunizations given during the accelerated tempo of a major deployment.

- For some vaccines of special use to the military, production during the Gulf War was insufficient to meet the needs of the forces. It will still be necessary to find ways to regularly supply vaccines in amounts sufficient for routine use and to increase production at times of major deployments.

- Research by the military has played a substantial role in vaccine development and testing,

including some vaccines used during the Gulf War. As vaccines are potentially the easiest and best countermeasures, the military should continue its active research program to improve existing vaccines and to develop new vaccines for the infectious diseases and biological warfare agents servicemembers may encounter in future deployments.

- Difficult issues remain concerning the demonstration of effectiveness of vaccines that cannot be adequately tested in humans. Similarly, there is a need for better resolution of problems that accompany the use of investigational vaccines during deployments, especially the needs for adequate record keeping and informed consent, which are difficult to achieve under these conditions. The Department of Defense and the Food and Drug Administration should continue to work toward resolution of these issues.

This information topic remains open. Should additional information become available, it will be incorporated. If you have records, photographs, recollections, or find errors in the details reported, please call 1-800-497-6261.

TAB A – Acronyms, Abbreviations, and Glossary

Acronyms and Abbreviations

ACIP ..... Advisory Committee on Immunization Practices
AFEB ..... Armed Forces Epidemiological Board
AFMIC ..... Armed Forces Medical Intelligence Center
AOR ..... area of responsibility
ARCENT ..... Army Central Command
ASD(HA) ..... Assistant Secretary of Defense (Health Affairs)
AVIP ..... Anthrax Vaccine Immunization Program
BW ..... biological warfare
CDC ..... Centers for Disease Control and Prevention
CDRFORSCOM ..... Commander, Forces Command
CENTCOM ..... Central Command
CINC ..... Commander in Chief
CINCCENT ..... Commander in Chief, Central Command
CINCFOR ..... Commander in Chief, Forces Command
CW ..... chemical warfare
DD ..... Department of Defense (form)
DEERS ..... Defense Eligibility and Enrollment Reporting System
DNBI ..... disease and non-battle injury
DoD ..... Department of Defense
FDA ..... Food and Drug Administration
FORSCOM ..... Forces Command (Army)
GAO ..... General Accounting Office
HHS ..... Department of Health and Human Services
HSC ..... Health Services Command (Army)
ICD ..... International Classification of Diseases
IND ..... investigational new drug
IOM ..... Institute of Medicine
J4 ..... Joint Staff, Logistics Directorate
MARDIV ..... Marine division
MEDCOM ..... Medical Command (Army)
MEDPROS ..... Medical Protection System (Army)
MEDSOM ..... Medical Supply, Optical, and Maintenance
MDPH ..... Michigan Department of Public Health
MITS ..... Military Immunization Tracking System (Air Force)
MMWR ..... Morbidity and Mortality Weekly Report
MOD ..... Ministry of Defence (United Kingdom)
MPOD ..... Medical Plans and Operations Division (J4)
NBC ..... nuclear, biological, and chemical
NCID ..... National Center for Infectious Diseases
NGB ..... National Guard Bureau
PAC ..... Presidential Advisory Committee on Gulf War Veterans' Illnesses

PHS ..... Public Health Service
PIC ..... personal information carrier
SAMS ..... Shipboard Automated Medical System (Navy)
SF ..... standard form
UK ..... United Kingdom (of Great Britain and Northern Ireland)
USACHPPM ..... US Army Center for Health Promotion and Preventive Medicine
USAMRIID ..... US Army Medical Research Institute of Infectious Diseases
USAMRMC ..... US Army Medical Research and Materiel Command
VA ..... Department of Veterans Affairs
VAERS ..... Vaccine Adverse Events Reporting System
WHO ..... World Health Organization

Glossary

Active immunity — Immunity produced by the person's own immune system. This type of immunity can be brought about by a natural infection or by a vaccine. It is usually long lasting. (Compare with *passive immunity*.)

Adjuvant — A substance added to a vaccine preparation to increase the body's immune response to the vaccine.

Adverse event — Any undesirable event that occurs following vaccination. An adverse event could be a true vaccine reaction, or just a coincidental event, with further research needed to distinguish between them.

Adverse reaction — An unintended side effect of a vaccine. (The intended effect of a vaccine is to produce immunity.) Adverse reactions may be local, systemic, or allergic.

Allergy — A condition in which the body has an exaggerated (immune) response to a substance, like a vaccine. Also known as *hypersensitivity*.

Antibiotics — Drugs (medicines) used to treat or prevent infectious diseases.

Antigen — A foreign substance (like a bacterium or virus, or parts of them) which triggers an immune response. Vaccines also contain antigens in order to trigger an immune response that is protective against subsequent disease.

Attenuated vaccine	A vaccine prepared from live bacteria or viruses, which have been weakened so they produce immunity but do not cause disease. Also called *live attenuated vaccines.* (Compare with *inactivated vaccine.*)
Bacteria	Tiny one-celled organisms present throughout the environment. Some bacteria cause disease (like diphtheria, tetanus, and typhoid fever).
Biological warfare agent	A tiny organism (or toxin produced by it) used as a weapon to cause disease.
Biologics	A classification of products derived from living sources, such as humans, animals, bacteria and viruses. Vaccines, immune globulin, and anti-toxins are biologics.
Booster	An additional dose of a vaccine needed periodically to "boost" the immune system (e.g. tetanus-diphtheria vaccine every 10 years).
Chemoprophylaxis	The use of a drugs to prevent infectious diseases (e.g., the use of anti-malarial pills).
Effectiveness (or Efficacy)	The ability of a vaccine to produce the desired beneficial effect, i.e., to protect against a disease.
Endemic (disease)	(A disease) occurring continually in a population or geographic area.
Epidemic (disease)	(A disease) occurring in a population or geographic area in excess of what would be normally be expected.
Epidemiology	The study of the frequency and distribution of disease in human populations.
Exposure	Contact with infectious agents (bacteria or viruses) in a manner that promotes transmission and increases the likelihood of disease.
Immune system	A complex system in the body which fights disease by recognizing bacteria and viruses as foreign and developing a defense against them (the *immune response*). Vaccines protect against disease by stimulating the immune system to produce this immune response.
Immunity	Protection against or resistance to disease. Immunity may be long lasting or temporary. It generally follows natural infections and is the goal of vaccinations. (See also *active* and *passive* immunity.)
Immunization	The process of inducing protection against a disease, usually by

	administering an antigen (as in a vaccine) or antibodies (as in immune globulin). (See also *vaccination*, but these terms are often used interchangeably.)
Inactivated vaccine	A vaccine prepared from killed whole bacteria or viruses, from parts of them, or from products (like toxins) produced by them.
Investigational vaccine	A vaccine that has been approved by the Food and Drug Administration (FDA) for use in clinical trials on humans. However, investigational vaccines are still in the testing and evaluation phase and are not licensed for use in the general public. For more detailed information, see the FDA web site at www.fda.gov/cder.
Natural infection (or disease)	An infection (or disease) from bacteria or viruses found in the environment, such as measles, chicken pox, etc.
Passive immunity	Immunity produced in an animal or person and transferred to another person, usually by injection. It is effective but usually disappears in a few weeks to months. (Immune globulin and botulinum antitoxin provide passive immunity.)
Side effect	An undesirable effect of a vaccine. (See also *adverse reaction.*)
Systemic	Affecting the whole body.
Toxin	A poisonous substance produced by a living organism (e.g., a bacterium, a plant, or an animal). Some toxins can cause diseases, such as botulism and tetanus.
Toxoid	A vaccine prepared from an inactivated bacterial toxin. (Botulinum toxoid vaccine and tetanus-diphtheria toxoid vaccines are examples.)
Vaccination	The introduction into the body of bacteria or viruses (or parts or products of them) that have previously been treated to make them harmless for the purposes of inducing the development of immunity. (See also *immunization.*)
Vaccine	A preparation of weakened or killed microorganisms (or parts or products of them) used to produce immunity to a particular disease.
Virus	A tiny organism that multiplies within cells and can cause disease. Measles, mumps, chickenpox, and hepatitis are diseases caused by viruses.

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