Anthrax Vaccine Immunization Program (AVIP)
Questions and Answers

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Anthrax Vaccination Program
Questions and Answers

Adapted from the Immunization Action Coalition (with permission) and the Centers for Disease Control and Prevention (CDC).

Current Policy

Current Policy

1) What is the current DoD policy for anthrax vaccinations?
• Vaccinations are mandatory for DoD Service members, emergency essential designated civilians, and contractor personnel performing mission-essential services assigned to:

o Central Command area of responsibility for 15 or more consecutive days.
o Korean Peninsula for 15 or more consecutive days
o Special units with bio-warfare or bio-terrorism related missions
o Specialty units with approved exception to policy

• Vaccinations shall begin, to the extent feasible, up to 120 days prior to deployment or arrival in higher threat areas.

• Vaccinations are voluntary for DoD Service members and U.S. Government civilian employees of DoD who are not in the mandatory groups and have received at least one dose of anthrax vaccine adsorbed during or after 1998.

• Vaccinations are voluntary for DoD civilians and adult family members; contractors and their accompanying U.S. citizen family members: Residing in Central Command area of responsibility for 15 or more consecutive days or Residing on Korean Peninsula for 15 or more consecutive days.

• Vaccine manufacturing and research personnel and others, as designated by the ASD (HA)

2) Is anthrax vaccination now mandatory for all Service members?
No. Anthrax vaccination is mandatory for DoD Service members, emergency essential designated civilians, and contractor personnel performing mission-essential services assigned to:

• Central Command area of responsibility for 15 or more consecutive days.

• Korean Peninsula for 15 or more consecutive days.

• Special units with bio-warfare or bio-terrorism related missions.

• Specialty units with approved exception to policy.

3) Is it mandatory to complete the series once I am no longer in a higher threat area?
No. Vaccinations are voluntary for DoD Service members who are not in the mandatory groups and have received at least one dose of anthrax vaccine adsorbed during or after 1998.

4) What are the recent changes for the route of administration and dosing schedule for the administration of anthrax vaccine?
On December 11, 2008, the Food and Drug Administration (FDA) approved a change in route of administration for the anthrax vaccine adsorbed (AVA) from a subcutaneous (SC) injection to intramuscular (IM). The FDA also approved a change in the vaccination series by removing the 2 week dose and asserting the safety and effectiveness of the new 5 dose regimen. This is a change from the originally licensed 6 dose regimen.

5) Does the change in route of administration and dosing schedule effect the policy?
The policy remains unchanged. Anthrax vaccination is mandatory for uniformed personnel and all emergency essential and equivalent civilian personnel assigned to the CENTCOM area of responsibility (AOR) or to the Korean Peninsula for 15 or more consecutive days. The vaccine will be offered on a voluntary basis to family members 18-65 years of age accompanying Department of Defense (DoD) military and civilian personnel for 15 or more consecutive days to the CENTCOM area of responsibility (AOR) or Korean Peninsula.

6) Given the new anthrax dosing schedule, will the recommendation for receiving at least three doses before deploying change to two?
Yes. Eliminating the 2-week dose does not change the immune status. Receiving a minimum of two doses of vaccine, at day 0 and 4 weeks, prior to arrival in theater is the new recommendation.

7) While in a voluntary status, will military members be informed about their right to refuse vaccination?
Yes, Service members will be informed about DoD policy that allows for individual consent to vaccination while in voluntary status. They will also be told that the military and civilian leadership of DoD strongly recommends that they be vaccinated. Anthrax is a deadly infection and anthrax vaccine is an important force protection measure. In the fall of 2001, 22 cases of anthrax resulted from attacks with anthrax spores. Five people died in these attacks. Anthrax vaccine is not experimental, not investigational, and does not require special authorization or informed consent. Anthrax vaccine was licensed for general use on November 4, 1970. It is a routine, common vaccination for people whose occupation places them at-risk for exposure to anthrax. No one will be required to sign consent forms. Members will be informed in writing about the vaccine and told that they have the option to refuse with no punishment of any kind and no adverse personnel action while in voluntary status.

8) How long will this current policy be in effect?
This current policy will be in effect until the senior civilian leadership directs the Services otherwise.

9) Will those people who received anthrax vaccinations in the past be allowed to continue the six-dose series?
Yes. Vaccinations are voluntary for DoD Service members who are not in the mandatory groups and have received at least one dose of anthrax vaccine adsorbed during or after 1998.

10) What happens to those of us who have received several doses of anthrax vaccine previously but choose not to continue under voluntary status?
There is no reason for concern that stopping the anthrax series will cause any harm. However, when anthrax vaccine is reintroduced to your body (you get your next dose); published evidence shows that your body has a good immune memory and will have a good antibody response. Each dose of anthrax vaccine is like walking up a set a stairs. You may remain on one step longer than originally planned, but the next dose of vaccine will resume development of protective immunity (climbing further up the stair case).

11) What are the recent events regarding the anthrax vaccine, the injunction, the EUA, the FDA Final Order, and the resumption of the program?
• Following a suit filed by several unnamed Service members, the U.S. District Court of Washington, D.C. placed an injunction against the DoD's mandatory anthrax vaccination program on 27 October 2004.

• DoD immediately issued orders to comply with the court decision, stopping anthrax vaccinations for all personnel on 27 October 2004, pending resolution of all legal issues.

• Following the procedure established by law, the Deputy Secretary of Defense (under authority assigned by the Secretary) determined that a significant potential for a military emergency exists that involves a heightened risk of U.S. military forces of attack with anthrax spores. To avoid the harm to the Armed Forces associated with stopping the vaccination program for high-risk personnel, DoD sought an Emergency Use Authorization.

• The Assistant Secretary of Defense for Health Affairs (ASD (HA)) submitted to the FDA a detailed summary of the evidence for safety and effectiveness that form the scientific foundation for the current FDA license for anthrax vaccine. • The ASD (HA) asked the Commissioner of FDA to approve the EUA.

• The Commissioner of FDA considered the evidence regarding the safety and effectiveness of anthrax vaccine for protection against anthrax disease via inhalation exposure, consulted with the Centers of Disease Control and Prevention and National Institutes of Health, and then issued the Emergency Use Authorization on 27 January 2005.

• On April 6, 2005, the District Court modified it's injunction to allow program resumption under EUA.

• On December 15, 2005, the FDA issued a Final Rule and Final Order on the license status of anthrax vaccine adsorbed (AVA). After reviewing extensive scientific evidence and carefully considering comments from the public, the FDA again determined that AVA is licensed for the prevention of anthrax infection regardless of route of exposure.

• On 12 October 2006 Deputy Secretary of Defense approved resumption of a mandatory AVIP program for military and civilian personnel in higher risk areas or with special mission roles. The policy allows voluntary vaccinations for other groups.

• The Under Secretary of Defense for Personnel and Readiness released DoD implementation guidance for the AVIP on 6 December 2006

• Service implementation plans were approved by the Assistant Secretary of Defense for Health Affairs on 08 February 2007

• On December 11, 2008, the Food and Drug Administration (FDA) approved a change in route of administration and the dosing schedule for the anthrax vaccine.

Countering the Threat

Anthrax Weapons -- The Threat

1) Why is anthrax vaccination needed?
Anthrax is highly lethal and relatively easy to produce in large quantities for use as a weapon. Anthrax spores are easily spread in the air over a large area and can be stored and remain viable 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. On February 24,

2004, CIA Director George Tenet told the Senate Select Intelligence Committee: “Although gaps in our understanding remain, we see al-Qaeda’s program to produce anthrax as one of the most immediate terrorist CBRN [chemical, biological, radiological, nuclear] threats we are likely to face.”

2) Has any country ever used anthrax as a weapon?
There is some evidence that the Japanese used anthrax as a biological weapon (BW) 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 spores 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 when the 1972 Biological and Toxin Weapons Convention (BTWC) took effect. The BTWC 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 the former Soviet Union city of Sverdlovsk in 1979 resulted in at least 79 cases of anthrax infection and 68 human deaths and demonstrated the lethal potential of anthrax aerosols. Members of Aum Shinrikyo, the group responsible for the 1995 Tokyo sarin attack, reportedly experimented with biological agents in Japan before resorting to chemical agents. A lengthy article in the May 26, 1998, edition of the New York Times reported that members of Aum Shinrikyo released anthrax spores and botulinum toxin in Tokyo, Yokohama, and Yokosuka in 1990, targeting Japanese government and U.S. Navy facilities. Fortunately, no one was injured in these events.

Anthrax spores have also been used as a weapon inside the United States by unknown terrorists in the Fall of 2001. The attack killed 5 people and infected at least 17 others.

3) Has anthrax vaccine ever been used in the past? How often?
Yes, since licensure in November 1970, anthrax vaccine has been administered to people at risk (both civilian and military) -- veterinarians, laboratory workers, and some people working with livestock for several decades. The manufacturer and FDA report that about 68,000 doses of anthrax vaccine were distributed between 1974 and 1989. The Army has purchased anthrax vaccine since its approval by the FDA in 1970, for use by about 1,500 at-risk laboratory workers. Anthrax vaccine was administered during the Gulf War to about 150,000 Service members, to protect U.S. forces against the threat of Iraq’s biological weapons. The DoD vaccinated over 1.5 million DoD personnel with over 5.9 million doses since the beginning of the AVIP in March 1998.

4) How are biological agents deployed?
Biological agents can be dispersed in many ways, ranging from mailed envelopes, intentional human vectors, spray devices, bombs, to ballistic missiles. Biological agents are often hard to detect. Symptoms are delayed. Without preventive medical efforts, such as vaccination, the results can be devastating and widespread. A 1993 report by the U.S. Congressional Office of Technology Assessment estimated that between 130,000 and 3 million deaths could follow the aerosolized release of 100 kg of anthrax spores upwind of the Washington, DC area -- truly a weapon of mass destruction. An anthrax aerosol would be odorless, invisible, and capable of traveling many miles.

5) Has the threat of biological warfare changed?
The threat of biological warfare has been a risk to U.S. forces for many years. 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. DoD analysts maintain an updated evaluation of the level of

threat, adjusting the information as necessary to reflect the risk to U.S. operations. Assessment of the potential offensive biological threat facing American Service members indicates it is necessary to have a robust biological defense program today. The threat is real and the consequences are grave. On 16 October, 2006, Assistant Secretary of Defense for Health Affairs William Winkenwerder said, "… anthrax remains a deadly infection that's been used as a bioterrorism weapon against our own population. The threat environment and unpredictable nature of terrorism makes it necessary to include biological warfare defense as part of our force protection measures."

6) Who is at greater risk from a biological attack? Soldiers? Sailors? Airmen? Marines? Front line? Rear area? Logistical units?
Anthrax weapons have the potential to contaminate wide areas of the battlefield. It is difficult to determine who would be at a greater risk from a biological threat. All Service members meeting the criteria to receive the vaccine need to be protected, regardless of Service, specialty, or location within higher threat areas.

7) What preparations have been made to respond to an anthrax release in a high-threat area?
We are taking necessary steps to develop optimal protection against the threat of anthrax and other potential bio-weapon agents, including improved intelligence, detection, surveillance capabilities, protective clothing and equipment, new generation vaccines, and other medical countermeasures. In addition, we have stockpiled antibiotics in pre-positioned locations and medical personnel are better educated in the treatment of anthrax.

8) If we vaccinate against anthrax, couldn't our adversaries just switch to a different biological weapon?
If the DoD anthrax vaccination program causes adversaries to switch to a different weapon, it can be considered a success. Other biological weapons are less stable, less predictable, or less effective than anthrax weapons.

9) Are vaccines being developed for other biological agents?
Yes. As potential biological warfare threats are identified, DoD works with other government agencies and industry partners to develop medical countermeasures. Vaccines are being developed, whenever appropriate, for all validated biological threat agents. More information is provided in the specific Q & A section entitled -- Biological Warfare - Overview.

Anthrax -- The Disease

1) What is anthrax?
Anthrax is a rapidly progressing acute infection caused by spore-forming bacteria called Bacillus anthracis. Anthrax most commonly occurs in warm-blooded animals, especially goats, cattle, and sheep, but it can also infect humans. Anthrax spores can be easily produced in a dry form for biological weapons. Spores can survive many years in adverse conditions and still remain capable of causing disease. When inhaled by humans, these spores cause respiratory failure that can lead to death within a week.

Anthrax can make an excellent weapon of mass destruction. The spores may be used as a weapon in a variety of delivery systems. They can be produced in large quantities without sophisticated equipment. All it takes is a single breath of aerosolized anthrax to inhale enough spores to cause the disease. Then, if serious symptoms occur, it kills 99% of unprotected people. Even if a person with symptoms receives antibiotics, the death rate is still about 50%. Anthrax spores are odorless, colorless, and tasteless.

2) Who gets infected with anthrax?
Animals and people can get anthrax disease. Anthrax is most commonly found in agricultural regions where goats, sheep, cattle or other plant-eating animals have not been vaccinated. When anthrax infects humans, it is usually due to an occupational exposure to infected animals or their products, especially hides, hair, wool, bones or bone products. Less commonly, ingesting undercooked, contaminated meat can infect humans.

3) What are the symptoms of anthrax?
- Fever (over 100 degrees F). The fever may be accompanied by chills or night sweats.
- Flu-like symptoms.
- Cough, usually a non-productive cough, chest discomfort, shortness of breath, fatigue, muscle aches, sore throat followed by difficulty swallowing, enlarged lymph nodes, headache, nausea, loss of appetite, abdominal distress, vomiting or diarrhea.
- A sore, especially on the face, arms or hands, that starts as a raised bump and develops into a painless ulcer with a black area in the center.

4) How can I know my cold or flu is not anthrax?
Many human illnesses begin with what are commonly referred to as “flu-like” symptoms, such as fever and muscle aches. However, in most cases anthrax can be distinguished from the flu because the flu has additional symptoms. In previous reports of anthrax cases, early symptoms usually did not include a runny nose, which is typical of the flu and common cold.

5) Where is anthrax usually found?
Anthrax is found around the globe. It is more often a risk in countries that do not vaccinate their livestock, or that have substandard or ineffective public-health programs.

6) What are the types of anthrax infection? How is anthrax transmitted?
There are three forms of anthrax disease, varying by the route of infection. People can get anthrax in the following three ways:

1. Through a break in the skin (cutaneous anthrax). Most (about 95%) anthrax infections occur when the bacterium enters a cut or abrasion on the skin, such as when handling contaminated wool, hides, leather, or hair products (especially goat hair) of infected animals. About 20% of untreated cases of cutaneous anthrax will result in death and less than 1% resulting in death with antibiotic treatment
2. By eating inadequately cooked contaminated meat (gastrointestinal anthrax). Initial signs of nausea, loss of appetite, vomiting, fever are followed by abdominal pain, vomiting of blood, and severe diarrhea. Intestinal anthrax results in death in about 25% to 60% of cases.
3. By breathing in bacteria or spores (inhalational anthrax). Inhalational anthrax does not typically spread from person to person. Inhalational anthrax is usually fatal. Although case-fatality estimates for inhalational anthrax are based on incomplete information, the rate is extremely high even with all possible supportive care including appropriate antibiotics.

Because anthrax spores can live in the soil for many years, animals can get anthrax by grazing or drinking water in contaminated areas. Weaponized anthrax could be used against people in almost any location, and in many different ways. The greatest threat with the most deadly consequences comes from inhaled anthrax.

7) Can people spread anthrax to each other?
Direct person-to-person spread of inhalational anthrax is "very rare," according to the American Public Health Association’s Control of Communicable Diseases Manual. Presumably, person-toperson spread

would require contact with contaminated skin lesions.

8) Can anthrax be transmitted by insects?
One report suggested that black flies may have transmitted anthrax from animals to humans, where there was a large outbreak in the animal population. Insects are not a major factor in the spread of anthrax.

9) Can I get screened or tested to find out whether I have been exposed to anthrax?
There is no screening test for anthrax; there is no test that a doctor can do for you that says you have been exposed to or carry it. The only way exposure can be determined is through a public health investigation.

10) What is a nasal swab test?
A nasal swab involves placing a swab inside the nostrils and taking a culture. The CDC and the U.S. Department of Health and Human Services do not recommend the use of nasal swab testing by clinicians to determine whether a person has been exposed to Bacillus anthracis, the bacteria responsible for anthrax, or as a means of diagnosing anthrax. At best, a positive result may be interpreted only to indicate exposure; a negative result does not exclude the possibility of exposure. Also, the presence of spores in the nose does not mean that the person has inhalational anthrax. The nose naturally filters out many things that a person breathes, including bacterial spores. To have inhalational anthrax, a person must have the bacteria deep in the lungs, and also have symptoms of the disease.

Another reason not to use nasal swabs is that most hospital laboratories cannot fully identify anthrax spores from nasal swabs. They are only able to tell that bacteria that resemble anthrax bacteria are present.

11) How is anthrax diagnosed?
Anthrax is diagnosed by isolating the bacteria, Bacillus anthracis, from the blood, skin, or cerebral spinal fluid, or by measuring specific antibodies in the blood of suspected cases. Generally, diagnosis by antibodies is done weeks or months after the infection occurs, too late to aid in treatment. The best protection is vaccination before exposure, combined with the appropriate Mission-Oriented Protective Posture (MOPP), including protective clothing and detection equipment.

12) For More Information:
Advisory Committee on Immunization Practices. Use of anthrax vaccine in the United States. MMWR-Morbidity & Mortality Weekly Report 2000;49(RR-15, Dec 15):1-20.
http://www.cdc.gov/mmwr/PDF/rr/rr4915.pdf

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Turnbull PCB. Guidelines for the Surveillance and Control of Anthrax in Humans and Animals, 3rd ed., WHO Report WHO/EMC/ZDI/98.6. http://www.co-infectiousdiseases.com/pt/re/coinfdis/abstract.00001432-200004000-00004.htm;jsessionid=FRZCbn15JMK9npLt12pBYDyZHTbdLSmz7Msn3Kvn1s1x75nCS8YR!736553971!-949856145!8091!-1

13) If patients are suspected of being exposed to anthrax, should they be quarantined or should other family members be tested?

Anthrax is not known to spread from one person to another person. Therefore, there is no need to quarantine individuals suspected of being exposed to anthrax or to immunize or treat contacts of persons ill with anthrax, such as household contacts, friends, or coworkers, unless they also were also exposed to the same source of infection. For more information on laboratory testing, go to http://www.bt.cdc.gov/agent/anthrax/faq/labtesting.asp.

14) Why vaccinate at all? Why not treat with antibiotics after exposure?

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.

The Anthrax Vaccine

Independent Scientific Reviews of the Anthrax Vaccine

1) Have any independent scientific panels outside the Department of Defense rendered opinions about anthrax vaccine?
Yes, since 1978, seven independent civilian panels affirmed the safety and efficacy of anthrax vaccine. These include (each discussed in detail below):

Panel on Review of Bacterial Vaccines & Toxoids
Armed Forces Epidemiology Board (AFEB); Now named the Defense Health Board (DHB)
Advisory Committee on Immunization Practices (ACIP)
Cochrane Collaboration
Working Group on Civilian Bio-defense
Anthrax Vaccine Expert Committee (AVEC)
National Academy of Sciences – Institute of Medicine

2) Why has anthrax vaccine been subjected to so many independent reviews? Is this the normal process for a licensed vaccine?
All vaccines used in the United States are subjected to independent scientific review before and after licensing. The same is true for anthrax vaccine. Because the Anthrax Vaccine Immunization Program (AVIP) is actively opposed by small vocal groups of people, additional scientific panels have evaluated anthrax vaccine. Although anthrax vaccine critics are committed and dedicated; they base their opposition largely on emotion and assumption. To determine the truth based in science about anthrax vaccine, the Department of Health & Human Services (DHHS) and the Department of Defense (DoD) turn to America's senior vaccine experts for objective findings and advice. The DoD uses facts determined by these scientific bodies for the messages and education material DoD distributes to Service members, their families, and the public.

3) What is the National Academy of Sciences Institute of Medicine (IOM) Committee on the Safety and Efficacy of Anthrax Vaccine, and what did they do?
The IOM committee reached two major conclusions: that anthrax vaccine works and that anthrax vaccine is as safe as other vaccines. Regarding effectiveness:

"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 all known or plausible engineered strains of B. anthracis." [Pages 7 and 58].

The whole report is available at the website of the National Academy Press: Joellenbeck LM, Zwanziger L, Durch JS, Strom BL, editors. The Anthrax Vaccine: Is it Safe? Does it Work? Washington, DC: National Academy Press, March 2002, 235 pages. http://www.nap.edu/catalog/10310.html

4) What was the Panel on Review of Bacterial Vaccines & Toxoids, and what did they find?
When responsibility for vaccine regulation shifted from the National Institutes of Health (NIH) to the Food & Drug Administration (FDA) in 1972, FDA convened a series of civilian advisory panels.

The FDA commissioned these panels to determine whether sufficient evidence of safety and

effectiveness existed for vaccine licenses to be continued. These panels considered every vaccine used in America at that time, including such "old" vaccines as polio vaccine, tetanus toxoid, measles vaccine, and many others. The Panel on Review of Bacterial Vaccines & Toxoids met first in 1978 and published their report in 1985 in the Federal Register (1985; 50:51002-117).

The panel consisted of prominent infectious disease experts and other physicians and scientists with expertise in pharmaceutical manufacturing quality. The panel recommended that the federal licenses for each bacterial vaccine be continued, but the panel recommended that several other product licenses be terminated. In the case of anthrax vaccine, this civilian panel concluded: "The Panel recommends that this product be placed in Category I and that the appropriate license(s) be continued because there is substantial evidence of safety and effectiveness for this product." The FDA accepted this recommendation completely. FDA revoked the licenses for the other products, following the recommendations of the civilian panel.

5) What is the Defense Health Board (DHB), and what did they find?
The Defense Health Board (DHB), formerly known as Armed Forces Epidemiological Board (AFEB), has a proud 60-year heritage of protecting the health of America's Armed Forces. The DHB consists of civilian physicians and scientists selected to advise the Surgeons General of the Armed Services (http://www.ha.osd.mil/DHB/default.cfm).

From its first reviews of anthrax vaccine under DoD Directive 6205.3, the DHB has affirmed the value of this vaccine. In August 1994, the DHB concluded: "The licensed anthrax vaccine is suitable for use in personnel assigned, pre-designated or scheduled for deployment to areas with a validated higher threat under its approved indications." In November 1996, the Defense Health Board reported that it "endorses the proposed DoD anthrax vaccine implementation plan under the current vaccine protocol [i.e., dosing schedule]."

The DHB reaffirmed its recommendations to use anthrax vaccine for bio-defense of military personnel in 1999 and 2000. A March 25, 1999, report states "The DHB continues to strongly endorse the current DoD Anthrax Vaccine Immunization Program."

On March 29, 2000, the DHB reported: "…we are (DHB) concerned and somewhat surprised at the criticism surrounding the program given the high level of professionalism that had characterized this effort. … Anthrax vaccine is a fully licensed FDA vaccine.

The vaccine does cause local side effects, but has an excellent safety profile. The Anthrax Vaccine Immunization Program has carefully tabulated person-specific immunization data and has assiduously investigated reported complications associated with receipt of anthrax vaccine. These data have been regularly reviewed by the board and attest to the safety of the vaccine."
http://www.anthrax.mil/resource/library/afeb.asp

The DHB continues to receive regular updates regarding implementation of the Anthrax Vaccine Immunization Program and the variety of safety surveillance methods used by the Department of Defense to monitor the vaccine's use.

6) What is the Advisory Committee on Immunization Practices (ACIP), and what did they find?
The Advisory Committee on Immunization Practices (ACIP) consists of America's preeminent vaccine scientists, civilian physicians who advise the Centers for Disease Control & Prevention (CDC) (http://www.cdc.gov/nip/publications/ACIP-list.htm). The ACIP sets national standards for vaccine delivery. ACIP guidelines for the nation are published in the CDC's weekly journal, the Morbidity & Mortality Weekly Report (MMWR).

Between fall 1999 and June 2000, an ACIP working group reviewed published and unpublished information about anthrax vaccine adsorbed (AVA). In June 2000, the ACIP unanimously adopted a report finding anthrax vaccine effective and safe for the prevention of anthrax. The report notes that: "The efficacy of AVA is based on several studies in animals, one controlled vaccine trial in humans, and immunogenic data for both humans and lower mammalian species. … Routine vaccination with AVA is indicated for persons engaged in work involving production quantities or concentrations of B. anthracis cultures and in activities with a high potential for aerosol production."

The ACIP recognizes that it is the role of the Defense Health Board (DHB) to advise the military Surgeons General on vaccination policies for military personnel. Nonetheless, the ACIP noted that "For the military and other select populations or for groups for which a calculable risk can be assessed, pre-exposure vaccination may be indicated." Advisory Committee on Immunization Practices. Use of anthrax vaccine in the United States MMWR-Morbidity & Mortality Weekly Report 2000; 49(RR-15):1-20. http://www.cdc.gov/mmwr/PDF/rr/rr4915.pdf

7) What is the Cochrane Collaboration, and what did they find?
The Cochrane Collaboration is an internationally respected group of scientists who apply principles called evidence-based medicine to discern the most objective use of medications. The Cochrane Collaboration is based in Oxford, England (http://www.cochrane.org).

In 1998, the Cochrane Infectious Diseases Group reviewed the evidence for effectiveness and safety of two anthrax vaccines, manufactured in the United States and the former Soviet Union. "Trial quality assessment and data extraction was conducted independently by the six authors."

This international group of scientists found that "Killed anthrax vaccines appear to be effective in reducing the risk of contracting anthrax with a relatively low rate of adverse effects. Further research should be restricted to testing new vaccines only." (http://www.cochrane.org/cochrane/revabstr/ab000975.htm) This review was later published in the peer-reviewed medical journal Vaccine: Demicheli V, Rivetti D, Deeks JJ, Jefferson T, Pratt M. The effectiveness and safety of vaccines against human anthrax: A systematic review. Vaccine 1998;16:880-4. http://www.vaccines.mil/documents/library/Demicheli%201998%20Vaccine%20p.%20880.pdf

8) What is the Working Group on Civilian Biodefense, and what did they find?
The Working Group on Civilian Bio-defense included 23 representatives from staff of major academic medical centers and research, government, military, public health, and emergency management institutions and agencies. The original consensus statement of 1999 resulted from a synthesis of published information and the revision of three drafts. Members of the working group reviewed anthrax literature again in January 2002, with special attention to articles following the anthrax attacks of 2001. Members commented on a revised document with proposed revisions being incorporated in the final product put out by The Center for Civilian Bio-defense Strategies (http://www.hopkins-biodefense.org/). The working group concurred with the findings of the March 2002 IOM report on the safety and efficacy of AVA, that AVA is effective against inhalational anthrax and concluded that if given with appropriate antibiotic therapy, it may help prevent the development of disease after exposure. The working group also found that: “Pre-exposure vaccination of some persons deemed to be in high-risk groups should be considered when substantial supplies of vaccine become available.”

The working group also addressed the use of anthrax vaccine in children: "The U.S. anthrax vaccine is licensed for use only in persons aged 18 to 65 years because studies to date have been conducted exclusively in this group. No data exist for children, but based on experience with other inactivated vaccines, it is likely that the vaccine would be safe and effective." Inglesby TV, O'Toole T, Henderson

DA, Bartlett JG, Ascher MS, Eitzen E, Friedlander AM, Gerberding J, Hauer J, Hughes J, McDade J, Osterholm MT, , Parker G, Perl TM, Russell PK, Tonat K, Working Group on Civilian Bio-defense. Anthrax as a biological weapon, 2002: Updated recommendations for management. Journal of the American Medical Association 2002; 287:2236- 52. http://jama.ama-assn.org/cgi/content/short/287/17/2236

9) What is the Anthrax Vaccine Expert Committee (AVEC), and what did they find?
In October 1998, DoD requested that the U.S. Department of Health and Human Services (DHHS) establish an Anthrax Vaccine Expert Committee (AVEC) to review reports to the Vaccine Adverse Events Reporting System (VAERS) involving anthrax vaccine. A distinguished university professor chaired this review committee of civilian physicians with expertise in immunology, internal medicine, neurology, rheumatology, and microbiology. The AVEC independently reviewed all anthrax vaccine-related reports. The Committee met every 3 to 6 weeks, along with nonvoting representatives of DoD, CDC, FDA, and DHHS. The AVEC reviewed the quality of the submitted information, evaluated the reported event in the context of expected and unexpected adverse events to vaccines, and assessed the cause-and-effect relationship of the event with anthrax vaccine. The Committee also looked for any significant patterns in the aggregate data. The review performed by the AVEC is unprecedented for a licensed vaccine. To date, the AVEC reports it found no unexpected patterns in the side-effect profile of anthrax vaccine.

10) Besides the six scientific panels described in detail above, have any other independent scientific individuals or groups rendered opinions about anthrax vaccine?
Gerald R. Burrow, MD, reviewed the health and medical aspects of the Anthrax Vaccine Immunization Program (AVIP) in 1998 before the program began. This is also discussed below. The Society of Medical Consultants to the Armed Forces (SMCAF) endorsed the anthrax vaccination program in September 1999.

11) Who is Gerald Burrow, MD, and what did he find?
On December 15, 1997, Secretary of Defense William Cohen approved the plan to immunize the Total Force against anthrax, contingent on four conditions: (1) supplemental testing for potency, purity, sterility, and general safety; (2) plans for execution and communication; (3) a system for fully tracking anthrax vaccinations; and (4) review of the health and medical aspects of the program by an independent expert. To achieve condition (4), Secretary Cohen asked Gerald R. Burrow, MD, to make the review. Dr. Burrow served as dean of medicine at the University of California at San Diego and dean of medicine and special assistant to the president of Yale University. Dr. Burrow was one of a few physicians elected as a member of the prestigious National Academy of Sciences, one of the nation's most prestigious scientific honors.

On February 19, 1998, Dr. Burrow reported: "I have made several visits to the Pentagon, have had a number of telephone conferences and have consulted extensively with experts in allergy, immunology and infectious disease." Based on his review, Dr. Burrow concluded: "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 vaccine stockpile." (http://www.defenselink.mil/other_info/burrows.html)

12) What is the Society of Medical Consultants to the Armed Forces (SMCAF), and what did they say?
The Society of Medical Consultants to the Armed Forces was formed in 1946 to disseminate the knowledge of military medicine gained in both armed conflict and peacetime practice and research, and to respond promptly to the call of the Surgeons General for advice on issues of professional importance in the Armed Forces (http://www.smcaf.org).

In September 1999, the Society expressed its support of the Anthrax Vaccine Immunization Program of the Department of Defense. In letters to the Secretary of Defense and the Surgeons General, President Nicholas Rock, MD, furnished documentary evidence of the need for and the safety of the Immunization Program, and declared that "The Society of Medical Consultants to the Armed Forces endorses the decision of the Surgeons General to proceed with priority attention, to provide protection against anthrax for our military forces."

13) Where can I find supporting scientific information about the safety and effectiveness of anthrax vaccination? What about more information regarding the military vaccination program?
Additional information concerning the scientific data that supports the safety and efficacy of the anthrax vaccine can be found at the following locations:

• The National Academy of Sciences report on the safety and effectiveness of anthrax vaccine: www.nap.edu/catalog/10310.html

• Summary for General Public: http://www.iom.edu/Object.File/Master/4/149/0.pdf

• Summary for Policy Makers: http://www.iom.edu/Object.File/Master/4/149/0.pdf

• Detailed safety information: http://www.vaccines.mil/documents/854AVASafetyRvw.pdf

• Additional programmatic information: www.anthrax.mil

Overview

1) What is anthrax vaccine?
Anthrax vaccine is known officially to the FDA as "Anthrax Vaccine Adsorbed." It is abbreviated AVA. It is also referred to by its trade name “BioThrax.” This vaccine is a sterile product, made from filtrates of microaerophilic cultures of an avirulent nonencapsulated strain of Bacillus anthracis. This means that the vaccine is the solution that results after filtration of a culture of anthrax bacteria. If you’ve ever seen percolated coffee, you know that liquid coffee is the filtrate and the coffee grounds are what are left in the filter. These bacteria are grown with very little oxygen (microaerophilic conditions). The bacteria cannot cause disease themselves (they are avirulent). They are from a strain of anthrax that does not have a capsule around the bacterial cells (they are nonencapsulated). The master seed used for vaccine manufacturing was transferred from Fort Detrick to Lansing in 1970 and is identified as Bacillus anthracis strain V-770-NPI-R1. Adsorbed refers to the fact that the vaccine is deposited on the surface of ("adsorbed to") a chemical called aluminum hydroxide. Aluminum hydroxide is added to the vaccine to increase the amount of antibodies that the body makes in response to vaccination. Aluminum hydroxide is called a vaccine adjuvant. Adjuvant comes from the Latin word meaning "to help." Anthrax vaccine is a cell-free filtrate vaccine, which means that it contains no whole bacteria, neither live nor dead. The vaccine is manufactured and distributed by BioPort Corporation (formerly the Michigan Biologic Products Institute), in Lansing, Michigan.

2) Isn’t anthrax vaccine based on old (archaic) technology?
Anthrax vaccine was invented using mid-century technology that also led to highly successful vaccines against tetanus, diphtheria, and other infectious diseases. Today’s manufacturing of anthrax vaccine by BioPort meets all current Food and Drug Administration standards of production.

3) Who licensed the availability of anthrax vaccine in the United States?

The vaccine was developed in the United States during the 1950s and 1960s for humans. The vaccine was licensed by the National Institutes of Health's Division of Biologics Standards for general use on November 4, 1970. In 1972, responsibility for vaccine regulation was transferred from NIH to the Food & Drug Administration (FDA). It is customary to refer to anthrax vaccine as "FDA-licensed." Since 1970, at-risk veterinarians, laboratory workers, and livestock handlers in the United States have used anthrax vaccine. FDA officials report that about 68,000 doses of anthrax vaccine were distributed in the United States between 1974 and 1989.

4) What do I do if I am late for my next scheduled dose?
The vaccine schedule should be followed as closely as possible. However, if a person is late for a dose, the next dose should simply be given as soon as possible. Then subsequent doses should be given according to the standard dosing intervals from the most recent dose. This applies to anthrax vaccine, as well as other vaccines, according to the Centers for Disease Control & Prevention. http://www.cdc.gov/mmwr/PDF/rr/rr4915.pdf

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 five doses is complete, the primary series is never repeated.

5) What is the new standard dosing schedule for the anthrax vaccine?
The current FDA-licensed schedule calls for doses to be administered intramuscularly in the deltoid according to the following schedule (the first dose is considered "week 0"): 0, 4 weeks; 6 months, 12 months, and 18 months.

Recipients receive the first shot, then the second shot four weeks later, and then the third shot five months after the second shot. Six months after the third shot, recipients receive the fourth shot. Six months after that, they receive the fifth shot. The entire primary series takes 18 months to complete. Annual booster doses of the vaccine are required for ongoing protection.

6) When did the route of administration of anthrax vaccine change from subcutaneous to intramuscular and the number of doses in the initial series change from six to five doses?
On 11 Dec 08, the Food and Drug Administration (FDA) approved two updates to the package insert for the anthrax vaccine. The route of administration was changed from a subcutaneous injection over the deltoid to an intramuscular injection in the deltoid. The FDA also approved a change in the vaccination series by removing the 2-week dose. The new schedule is now 0, 4 weeks, and 6 months, 12 months, 18 months, and annual boosters.

7) Why was the dosing schedule and route of administration for the anthrax vaccine changed?
The Centers for Disease Control and Prevention (CDC) conducted a randomized double-blind clinical trial investigating the safety and efficacy of a dose reduction and route change for the anthrax vaccine. The FDA has confirmed and approved the results of the clinical trial that Anthrax Vaccine Adsorbed (AVA) is safe and effective as a five-dose regimen for the primary series and administration of the vaccine is safe via the intramuscular route.

8) Will I receive the same level of protection from the five-shot anthrax vaccine series?
Yes. Researchers at the Centers for Disease Control and Prevention (CDC) conducted a randomized double-blinded study and found that dose reduction from 6 doses to 5 doses, over an 18 month period to include annual boosters, receive the same benefit of protection from anthrax vaccine.

9) If I have started my vaccination series while on the six-dose series, do I need to start my

series over?
No. You will not start your primary anthrax series over. You will continue with your next scheduled dose in the series.

10) Can I get vaccinated ahead of schedule?
No. If you get vaccinated "too soon," the body's immune system might not have had enough time to prepare for the next dose, and you may not develop as good an antibody response as if you had complied with the standard schedule. Stay on schedule.

11) What does the anthrax vaccine do to make a person immune?
The anthrax vaccine, like other vaccines, stimulates your body to produce protective antibodies. These antibodies help your immune system to prevent the anthrax bacteria from producing toxins that could otherwise kill you, if you became infected with anthrax. Nearly everyone who receives two doses of anthrax vaccine has some antibody response. The full series plus annual booster doses provides maximum and on-going protection.

12) Do pilots who have received the anthrax vaccine have any troubles with FAA flight certification?
No, taking the anthrax vaccine has no effect on civilian or military aviation status. An excellent independent source for definitive information regarding aviation-related matters and the anthrax vaccine can be found at http://www.faa.gov/about/office_org/headquarters_offices/avs/offices/aam/. The Federal Aviation Administration reports that people vaccinated against anthrax are not disqualified from performing civilian airman duties.

13) Can people who have received the anthrax vaccine donate blood?
Yes, the American Association of Blood Banks (AABB) and the Food & Drug Administration allow blood donations following anthrax vaccination without any vaccine-related restrictions. For more information, see the Internet resources of the Armed Services Blood Program Office (http://www.militaryblood.dod.mil/). Sometimes people will not be allowed to donate blood for other reasons. For example, the Armed Services Blood Program has ordered Department of Defense blood banks to defer blood donations from all military personnel who were stationed in Saudi Arabia, Kuwait, Iraq, Bahrain, Qatar, the United Arab Emirates, Oman and Yemen at any time since August 1, 1990. This action was taken in response to a small number of diagnosed cases of leishmania infection -- a tropical disease -- among military personnel returning from that area. For more information regarding the temporary donor deferral related to Leishmaniasis http://www.fda.gov/bbs/topics/ANSWERS/ANS00360.html Data Source: The American Association of Blood Banks (http://www.AABB.org), 1801 Glenbrook Road, Bethesda, MD 20814-2749, 301-907-6977, Standards for Blood Bank and Transfusion Services, 19th ed., Standard B2.600.

14) After anthrax vaccination, is one able to donate a kidney or bone marrow?
Yes. Anthrax vaccine contains no live bacteria and poses no safety risk. There is no bar (contraindication) regarding donating organs or marrow after being vaccinated. In fact, your bone marrow might confer temporary immunity to the diseases to which you are immune to the marrow recipient. The immune response to anthrax vaccine would have no adverse effect on the internal organs of the kidney or marrow recipient. Anthrax vaccine is a sterile product made from filtrates of inactivated bacterial cultures. Sterile filtration during manufacturing yields a vaccine containing no whole organisms, thereby presenting no possibility of infection to the recipient, whether immunodeficient or not.

15) Has the anthrax vaccine ever been reviewed by any civilian medical review board?
Yes, seven times. See the separate Q&A page on Independent Scientific Reviews of Anthrax Vaccine" for details.

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 (http://www.cdc.gov/mmwr/PDF/rr/rr4915.pdf) and the Johns Hopkins Center for Civilian Bio-defense Studies (http://jama.ama-assn.org/cgi/content/short/287/17/2236) recognize the anthrax vaccine as part of the national preparedness against biological terrorism.

16) In some DoD documents it states that veterinarians have been "routinely administered" anthrax vaccinations. Why do some people dispute this statement?
Anthrax is not a widespread disease in the United States. Therefore, primarily at-risk veterinarians within the U.S. are vaccinated. "Routinely" was not intended to imply that veterinarians are universally vaccinated (i.e., that they are all vaccinated), but rather that if the person is potentially exposed to anthrax, vaccination is routine, a customary practice.

Also, other at-risk workers such as laboratory personnel and livestock handlers are routinely vaccinated. Other non-military personnel have been vaccinated, including workers at an Alabama sweater factory from 1977-1996. The manufacturer and FDA report that about 68,000 doses of anthrax vaccine were distributed between 1974 and 1989.

Anthrax vaccine is not experimental, not investigational, and does not require special authorization, nor informed consent. Anthrax vaccine was licensed for general use on November 4, 1970. It is a routine, common vaccination for people whose occupation places them at-risk for exposure to anthrax.

17) Which antibiotics does CDC recommend for prevention of inhalational anthrax?
In selecting an antibiotic, we will be guided by the organism's culture and sensitivity results, history of allergic reactions, age and health status factors and antibiotic availability. When no information is available about the antimicrobial susceptibility of the implicated strain of B. anthracis, initial therapy with ciprofloxacin or doxycycline is recommended for adults and children, or levofloxacin for adults.

18) If an anthrax event occurs, should people buy and store antibiotics?
There is no need to buy or store antibiotics, and indeed, it can be detrimental to both the individual and to the community. First, only people who are exposed to anthrax should take antibiotics, and health authorities must make that determination. Second, individuals may not stockpile or store the correct antibiotics. Third, under emergency plans, the federal government can ship appropriate antibiotics from its stockpile to wherever they are needed.

19) What drugs are FDA-approved for treatment of anthrax?
Ciprofloxacin, doxycycline and penicillin are FDA-approved for the treatment of anthrax in adults and children.

20) What happens to those individuals who were court-martialed or given non-judicial punishment for refusing to take anthrax vaccine?
This is a matter for long-established appeals processes and the Board for the Correction of Military Records.

21) How many DoD personnel have been vaccinated?
We have vaccinated over 1.5 million DoD personnel with over 5.9 million doses since the beginning of the AVIP in March 1998.

22) For More Information:
Advisory Committee on Immunization Practices. General recommendations on immunization. MMWR-Morbidity & Mortality Weekly Report 2002;51(RR-2):1-35

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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.vaccines.mil/documents/338field_eval.pdf

Advisory Committee on Immunization Practices. Use of anthrax vaccine in the United States. MMWR-Morbidity & Mortality Weekly Report 2000; 49(RR-15):1-20. http://www.cdc.gov/mmwr/PDF/rr/rr4915.pdf

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Turnbull PCB. Guidelines for the Surveillance and Control of Anthrax in Humans and Animals, 3rd ed., WHO Report WHO/EMC/ZDI/98.6.

Anthrax Vaccine-Civilian Inquiries

1) Can civilians get the anthrax vaccine?
The vaccine's manufacturer, Emergent BioSolutions of Lansing, MI, offers anthrax vaccine for sale to licensed physicians in the United States. Emergent BioSolutions sells the vaccine, under the trade name BioThrax.

2) How would one respond to a bioterrorist attack involving anthrax?
The course of action for preventing anthrax after exposure in the civilian population would be with antibiotics, or a combination of anthrax vaccine and antibiotics.

3) How can bioterrorist attacks be detected?
The investigative skills, diagnostic techniques, and physical resources required to detect and diagnose a disease outbreak are the same ones required to identify and respond to a silent bioterrorist attack. A key component to success will continue to be the sharing of information among all components of the public health system so that early diagnosis and response can happen as quickly as possible.

4) How will I know what to do, if there is a bioweapon attack near me?
If there was an incident, people would be notified by the emergency public announcement system by federal, state, or local authorities about what to do or where to go to obtain treatment. The closest source of emergency assistance will come from your city, county, or state. Contact your state or local Health Department to find out procedures for handling possible bioterrorist incidents in your area.

5) What other reliable information is available from health authorities?
Advisory Committee on Immunization Practices. Use of anthrax vaccine in the United States. MMWR-Morbidity & Mortality Weekly Report 2000;49(RR-15, Dec 15):1-20. http://www.cdc.gov/mmwr/PDF/rr/rr4915.pdf l CDC BioTerrorism Preparedness and Response: www.bt.cdc.gov l CDC Public Inquiry line: 1-800-311-3435 l CDC National Immunization HOTLINE 1-800-232-2522 Civilian Panel on Review of Bacterial Vaccines & Toxoids, advising the FDA from 1978 to 1985. Federal Register 1985;50:51002-117. http://www.anthrax.mil/documents/205Fed_Reg.pdf Armed Forces Epidemiological Board (AFEB), civilian scientists advising the Surgeons General, from 1994 to present. Cochrane Collaboration, the international evidence-based medicine group from Oxford. Demicheli V, Rivetti D, Deeks JJ, Jefferson T, Pratt M. The effectiveness and safety of vaccines against human anthrax: A systematic review. Vaccine 1998;16:880-4. http://www.vaccines.mil/documents/library/Demicheli%201998%20Vaccine%20p.%20880.pdf Anthrax Vaccine Expert Committee (AVEC), civilian physicians selected by the Department of Health & Human Services, who independently evaluate VAERS reports, 1998 to present: http://www.vaccines.mil/documents/library/AVEC_ms.pdf http://www.vaccines.mil/documents/library/SeverArticle.pdf

Anthrax Vaccine-Eligibility Criteria

1) Who should not take the anthrax vaccine?
Those with a true hypersensitivity reaction (serious allergic reaction) to a previous dose of the anthrax vaccine, people infected with HIV, people who have other kinds of immune suppression, pregnant women, and people under 18 and over 65 years of age. Other temporary reasons for deferring anthrax vaccination include an acute respiratory disease or active infection, and a temporary course of immune-suppressing drugs such as steroids (e.g., prednisone). Vaccinations should be resumed when these issues are resolved. If a person has an active infection or is taking a prescription medication that suppresses the immune system, a decision to give the anthrax vaccine will be made on a case-by-case basis.

2) Should people with lupus (SLE) get vaccinated?
People who have been diagnosed with lupus should talk with their physician about whether or not they should be vaccinated, considering the state of their disease, the medications they take, and their personal risk for specific infections. Several medical studies have shown that people with lupus can be safely and effectively vaccinated against influenza, hepatitis B, pneumococcal disease and other diseases that would pose a significant risk if they were infected. For military personnel with lupus, providers are authorized to grant medical exemptions according to the patient's specific situation. Medical specialists can advise how to get the best benefit from vaccination in such circumstances.

3) Why doesn't DoD policy include giving anthrax vaccine to people younger than 18 years or older than 65 years?
The FDA has only licensed the anthrax vaccine for use in people between ages 18 and 65. FDA does not perform its own clinical research; it reviews the quality of research performed by others. FDA can only determine the effectiveness of a vaccine in the same kind of population as the vaccine was tested in. No formal studies of children, adolescents, or the elderly have been performed to date. Once such studies are performed, FDA can determine if sufficient evidence is available. Individual physicians can treat individual people in ways that are outside the limitations of a package insert (these are called "off-label" uses of drugs). Indeed, DoD knows of no example of a vaccine that is effective among adults that is not also effective in the elderly or in adolescents. DoD policy is to abide by the age ranges in the FDA-approved labeling for its Anthrax Vaccine Immunization Program.

4) Why aren't HIV-positive or immunodeficient people included in DoD's Anthrax Vaccine Immunization Program?
Anthrax vaccine's package insert says "anyone that is immunodeficient should not receive the vaccination." This precaution refers to the fact that the recipient, being immunodeficient, would be less likely to mount a full immune response to the vaccine, thus reducing the vaccine's intended benefit. Inactivated vaccines are not considered to be harmful to immunodeficient people. HIV-positive and other immunodeficient people should receive the anthrax vaccine if exposure occurs or is imminent. These personnel should be counseled that the vaccine is not expected to harm them, but they may not mount as complete an immune response to protect against anthrax as other people do. Under these conditions, the adage "some protection is better than none" would apply.

5) For More Information:
Advisory Committee on Immunization Practices. General recommendations on immunization. MMWR-Morbidity & Mortality Weekly Report 2002;51(RR-2):1-35. http://www.cdc.gov/mmwr/pdf/rr/rr5102.pdf

Anthrax Vaccine-Effectiveness

1) Why do we think the anthrax vaccine will protect people if anthrax inhalation occurs? What scientific evidence do we have?
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." 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 inhalational forms of anthrax infection that occurred. No inhalational anthrax occurred among the vaccinated workers, while five cases of inhalational anthrax occurred among workers who had not been vaccinated. The total number of inhalation cases was judged too few to show statistically conclusive proof of protection by itself. However, results from several animal studies provide additional evidence that the vaccine protects against anthrax challenge with hundreds of times the lethal dose of anthrax by inhalation. This information coupled with the encouraging results of the effectiveness and immune response in humans assures us that the vaccine will greatly increase the chances of soldiers surviving exposure to inhalational 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.

2) I heard that the vaccine used in the 1962 Brachman study isn't the same as the vaccine used today. Is that true?
Yes, it is true that the current vaccine has more protective antigen (PA) in it than Brachman's vaccine

formula, and also that the current vaccine is more highly purified than the vaccine used in the Brachman study. Between the time of the Brachman study and the licensing of the vaccine produced in Lansing, the conditions under which the anthrax bacteria were cultured were changed. These changes resulted in a purer, more potent vaccine. Government authorities were aware of and approved the changes at that time the license application was considered in 1970. The independent, civilian review panel advising the FDA was aware of the changes, and described them in its 1985 report. Both vaccine formulas are based on protective antigen (PA), the key protein common to all strains of anthrax.

3) What will happen if personnel are exposed to anthrax before they gain immunity through vaccination?
Personnel will be treated with antibiotics if there is a known exposure to anthrax before gaining immunity through vaccination. Antibiotics are effective in treating animals, including primates, exposed to inhalational anthrax, but only if started before symptoms develop. This would usually mean starting antibiotics in the first 24 hours after exposure. Unfortunately, servicemembers may not know they have been exposed until symptoms develop; by then, the infection is nearly always fatal within a few days, whether antibiotics are given or not. The best protection to counter inhalational anthrax is the use of the anthrax vaccine combined with the appropriate Mission Oriented Protective Posture (MOPP), including protective clothing and detection equipment.

4) If you receive all the shots, are you 100% protected?
No medication, no vaccine is 100% effecticve. The antibodies that result from any vaccine theoretically could be overwhelmed if one is exposed to extremely large doses of any pathogen. Even if vaccinated, one may not be completely safe if one is close to the point of release of the biologic agent. Antibiotics for such people will offer additional protection. That's why vaccination is only one part of force health protection efforts, which also includes protective gear and detection equipment. For continued protection, annual booster doses are required.

5) Does anthrax vaccine protect against disease if someone inhales anthrax spores?
The original studies of anthrax vaccine showed 93% fewer anthrax infections (combining both cutaneous and inhalational cases of anthrax) among vaccinated people, compared to unvaccinated people. In those original studies, no cases of inhaled (inhalation) anthrax occurred among vaccine recipients, while five cases of anthrax occurred among unvaccinated or incompletely vaccinated people. This difference involved too few people to be statistically conclusive, although the trend is obvious. It is unethical to intentionally expose human beings to inhaled anthrax to test the vaccine. Instead, anthrax vaccine was tested on rhesus monkeys. After 65 animals received one or two doses of vaccine, 95% survived aerosol challenge in full health. One animal died from anthrax exposure two years after the second dose of vaccine. This illustrates the importance of annual booster doses of anthrax vaccine. These data lead us to expect that anthrax vaccine would be quite effective in preventing inhaled anthrax.

6) How long does it take after the first shot before protection begins?
Antibodies begin to develop within a week or two after the first dose of vaccine. Protection levels increase as shots in the series are given, like walking up a set of stairs. The entire sixshot series is needed for full protection as licensed by the Food & Drug Administration.

7) Will this anthrax vaccine protect soldiers from all forms of anthrax, including the ones reportedly developed in Russia?
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." 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 (including 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.

8) Is the anthrax vaccine licensed for use against biological agents?
The anthrax vaccine is licensed for people at risk for exposure to anthrax spores. Biological weapons are designed to deliver aerosolized anthrax spores that will result in inhalational anthrax. The FDA concurs that the use of the anthrax vaccine to protect against inhalational anthrax is consistent with indications for use of the vaccine.

9) What is FDA's position about the effectiveness of anthrax vaccine?
For years, FDA has held that anthrax vaccine prevents anthrax infection regardless of the route of exposure. On December 15, 2005, the Food and Drug Administration released a Final Rule and Final Order for anthrax vaccine. After reviewing extensive scientific evidence and carefully considering comments from the public, the FDA determined that anthrax vaccine is safe and effective in preventing anthrax disease regardless of route of exposure, including inhalation anthrax.

10) For More Information:
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Anthrax Vaccine-Ingredients

1) What are the ingredients of the anthrax vaccine?
Anthrax vaccine is a sterile product made from filtrates of microaerophilic cultures of an avirulent nonencapsulated strain of Bacillus anthracis. These bacteria are grown with very little oxygen (microaerophilic conditions). The bacteria cannot cause disease themselves (they are avirulent). They are from a strain of anthrax that does not have a capsule around the bacterial cells (they are nonencapsulated). This means that the vaccine is the solution that results after filtration of a culture of anthrax bacteria. If you've ever seen percolated coffee, you know that liquid coffee is the filtrate and the coffee grounds are what are left in the filter. In this example, the vaccine is like the cup of coffee. Anthrax vaccine is known officially to the Food & Drug Administration (FDA) as "Anthrax Vaccine Adsorbed," generating its abbreviation "AVA." Adsorbed refers to the fact that the vaccine is deposited on the surface of ("adsorbed to") a chemical called aluminum hydroxide. Aluminum hydroxide is added as an adjuvant to the vaccine to increase the amount of antibodies that the body makes in response to vaccination. Anthrax vaccine is a cell-free filtrate vaccine, which means that it contains no whole bacteria, neither live nor dead. The bacteria used to make the vaccine cannot cause disease themselves. For these two reasons, it is impossible to contract the anthrax disease from the anthrax vaccine. The final product is formulated to contain 600 micrograms aluminum per 0.5ml, added as aluminum hydroxide in 0.85% sodium chloride. The product is formulated to contain 25 mg/mL benzethonium chloride and 100 mg/mL formaldehyde, added as preservatives.

2) Why is aluminum in anthrax and other vaccines?
Aluminum is an adjuvant. The word adjuvant comes from the Latin, meaning "to help." Adjuvants are added to vaccines to increase antibody responses to vaccination. Aluminum salts are the only kind of adjuvant so far licensed by the FDA and the only kind of adjuvant used in anthrax vaccines for humans in the United States. Anthrax vaccine contains aluminum hydroxide, as do FDA-licensed diphtheria, Haemophilus influenzae type b, hepatitis A, hepatitis B, Lyme disease, pertussis, and tetanus vaccines.

3) What is benzethonium chloride?
Benzethonium chloride is used as a preservative in the anthrax vaccine. It is also a common component

in other injectable and nasal medications (such as thrombin, ketamine, orphenadrine [Norflex], and butorphanol [Stadol]). Benzethonium chloride is sometimes also called Phemerol, a trade name.

4) Does anthrax vaccine contain mercury?
No. The preservative of anthrax vaccine is benzethonium chloride.

5) Formaldehyde is not approved for human consumption. Why is it used in the anthrax and other vaccines?
Material Safety Data Sheets correctly warn people not to swallow formaldehyde. Small amounts of formaldehyde are approved by the FDA for use in manufacturing several vaccines, including vaccines against anthrax, diphtheria, hepatitis A, influenza, Japanese encephalitis, and tetanus. A small amount of formaldehyde, less than 2 parts per 10,000 (0.02%), is permitted by FDA to remain in the anthrax vaccine. Formaldehyde has been used in vaccine manufacturing since the 1960s, if not earlier. Literally billions of people around the world have been given tetanus toxoid processed with formaldehyde (as anthrax vaccine is), which is recognized as safe. FDA closely monitors all the ingredients and processing steps of all vaccines and other medications before they can be distributed for widespread use. Material Safety Data Sheets (MSDS) are a method to explain chemical hazards, according to OSHA standards (see http://www.osha-slc.gov/SLTC/smallbusiness/sec16.html). For any given chemical, health hazards vary by amount of chemical (concentration), duration of exposure (time), and route of exposure (skin, stomach, lungs, etc.). FDA's decision to permit formaldehyde to be present as residues in vaccines is based, in part, on the low concentrations and infrequent exposures involved. While it might not be prudent to have formaldehyde contact the skin every day at work, or to inhale formaldehyde fumes repeatedly, a few minute doses of formaldehyde in vaccines are recognized as safe.

6) Does the anthrax vaccine contain pork or egg products?
Anthrax vaccine adsorbed is a sterile, cell-free (filtered) bacterial vaccine that contains no live or dead organisms. It is not made from or with pork or egg products.

7) Does the anthrax vaccine contain any fetal tissue?
No human tissues of any kind are used in the process of making the anthrax vaccine.

8) Does the anthrax vaccine contain squalene?
In September 2000, DoD became aware of FDA test results finding trace amounts of squalene in three out of three US vaccines tested: anthrax, diphtheria, and tetanus. The level of squalene identified by the FDA test is so minute that it is likely the result of squalene in the oil of a fingerprint not cleaned from lab glassware. The trace level of squalene found by the FDA in anthrax vaccine is less than the concentration normally present in human blood (250 parts per billion).

9) Is the Food & Drug Administration concerned about the quantity of squalene found in these vaccines?
No. In Congressional testimony on 3 October 2000, FDA's Mark Elengold said that the trace quantities of squalene detected were "within the realm of both naturally occurring and safe."

10) Does the anthrax vaccine use squalene as an adjuvant?
No, the adjuvant in the anthrax vaccine is aluminum hydroxide.

11) For More Information:
Food & Drug Administration. Biological products; Bacterial vaccines and toxoids; Implementation of efficacy review. Federal Register 1985;50:51002-117.
http://www.anthrax.mil/documents/205Fed_Reg.pdf

Food & Drug Administration. Biological products; Bacterial vaccines and toxoids; Implementation of efficacy review. Federal Register 2004;29:78281-93.
http://www.anthrax.mil/documents/library/bvactox.pdf

Safety

1) Is the anthrax vaccine safe?

Yes, this vaccine has been safely administered in the U.S. to at-risk veterinary and laboratory workers, livestock handlers, and servicemembers since licensure by the Food & Drug Administration (FDA) in 1970. The FDA certifies the safety and efficacy of all pharmaceuticals (medications) used in the U.S. One of FDA's primary missions is to ensure that pharmaceuticals released for use by the American public are tested for both safety and efficacy. Like all vaccines, anthrax vaccine may cause soreness, redness, itching, swelling, and lumps at the injection site. About 30% of men and 60% of women report these local reactions, but they usually last only a short while. Lumps can persist a few weeks, but eventually disappear. Injection-site problems occur about twice as often among women. For both genders, between 1% and 5% report reactions of 1 to 5 inches in diameter. Larger reactions occur in about one in a hundred vaccine recipients. Beyond the injection site, from 5% up to 35% will notice muscle aches, joint aches, headaches, rash, chills, fever, nausea, loss of appetite, malaise, or related symptoms. Again, these symptoms usually go away after a few days. Over-the-counter medications before or after the anthrax vaccine may help reduce bothersome symptoms. Like all vaccines, most adverse events are minor and temporary. Serious events, such as those requiring hospitalization, are rare. They happen about once per 200,000 doses. Severe allergic reactions can occur after any vaccination, less than once per 100,000 doses. Anthrax vaccine is as safe as other vaccines. Like other vaccines, deaths have been reported rarely after anthrax vaccination. Each of these cases is carefully reviewed by CDC, FDA, and DoD, to make vaccinations as safe as possible. For independent information about vaccines and vaccine safety see: Centers for Disease Control & Prevention's National Immunization Program: http://www.cdc.gov/nip

2) What about long-term side effects?

There are no known long-term side effects to anthrax vaccine. At Fort Detrick, more than 1,500 laboratory workers followed for up to 10 to 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 such injections during their tenure at Fort Detrick. The first report of this group of vaccine recipients was published in the Bulletin of the Johns Hopkins Hospital in 1958. Two follow-up reports were printed in the Annals of Internal Medicine in 1965 and 1974. An updated manuscript is currently being finalized. These employees have been followed annually. None developed unexplained symptoms due to repeated doses of this or other vaccines they received. From this and other monitoring, no patterns of delayed side effects to anthrax vaccine have been found. Monitoring continues. An extension of this long-term study is underway to determine, in even greater detail, whether people who received multiple vaccines, including anthrax vaccine, during their past employment at Fort Detrick demonstrated any adverse health effects over the long term. A total of 570 study and control volunteers have been enrolled in this case-control study begun in 1996. All volunteers signed an informed-consent document. The study methods include a 9-page health history questionnaire, extensive blood tests and urinalysis. The questionnaire queries mental and physical conditions of progeny as well as the health of volunteers. Study end points include symptoms, symptom complexes (including the complex of symptoms reported by veterans of the Persian Gulf War), diseases, and abnormal laboratory and urine tests. Study subjects will be compared to two to three race-, gender-, and age-matched control subjects to determine if any long-term medical effects exist among this unique group of study subjects. Analysis of the data from the extensive health history questionnaire and numerous laboratory tests is currently in progress. An October 2004 review of over 716,000 active-duty service members discharge rates shows

anthrax vaccination does not increase risk of disability. Overall, the disability evaluation rate in the Army was very low for the 4.25 years covered by this study, and there appeared to be no effect of exposure to anthrax vaccine on the risk of disability evaluation.

3) Is there a requirement for long-term follow-up after the anthrax vaccine is administered?
No. Like other FDA-licensed products, the anthrax vaccine does not require follow-up monitoring of healthy vaccine recipients. Nonetheless, the DoD has already conducted such studies and is conducting more. No data collected to date shows any patterns of adverse events developing years after people have been vaccinated with anthrax vaccine or any other vaccine.

4) Is this an experimental vaccine?
No, the anthrax vaccine has been FDA licensed since 1970. License No. 99 was issued on November 4, 1970. It is neither "experimental" nor "investigational." Since 1970, this vaccine has been administered to people at risk for anthrax exposures including certain veterinary and laboratory workers and civilians who work with animal products. FDA officials reported that about 68,000 doses of anthrax vaccine were distributed in the United States between 1974 and 1989. Since licensure in 1970, the U.S. Army purchased this vaccine for use by at-risk laboratory workers, and it was used during the Gulf War (approximately 150,000 recipients) to vaccinate U.S. forces against Iraq's production of biological weapons. The military currently vaccinates people working in at-risk jobs and some 3,000 personnel assigned to special operations units, the Army Technical Escort Unit and the Marine Corps Chemical-Biological Incident Response Force (C-BIRF). The Centers for Disease Control and Prevention's 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 is consistent with the Food and Drug Administration-licensed use of the vaccine. When Emergent BioSolutions bought the facilities of the Michigan Biologic Products Institute, License No. 1260 was substituted for License No. 99.

5) What about sterility or impairment of fertility?
In nearly 30 years of licensed use, there is no evidence of any sterility or fertility impairment from anthrax vaccine. Regarding reproductive health, the Center for Disease Control and Prevention's Advisory Committee on Immunization Practices states, "there is no convincing risk from vaccinating pregnant women with inactivated virus or bacterial toxoids."

In the March 27, 2002, issue of the Journal of American Medical Association, two Army physicians published their peer-reviewed findings that women get pregnant at the same rate, whether anthrax-vaccinated or unvaccinated. These physicians from Fort Stewart, Georgia, also showed that women deliver offspring at the same rate, whether anthrax-vaccinated or unvaccinated. The Fort Stewart study found no difference in birth defect rates, but the study may have been too small to detect small differences. [Wiesen AR, Littell CT. Relationship between pre-pregnancy anthrax vaccination and pregnancy and birth outcomes among U.S. Army women. Journal of the American Medical Association (JAMA) 2002; 287:1556-60. http://jama.ama-assn.org/content/vol287/issue12/index.dtl.

Preliminary data from the Naval Health Research Center raised a tentative signal that there may be an association with an increased rate of birth defects if vaccinated in the first trimester of pregnancy. This signal is being investigated thoroughly, to determine which of several explanations for the signal is most likely.

Long-standing Defense policy is to defer routine vaccinations in women until after pregnancy. This policy has always applied to anthrax vaccine. Women are asked if they are pregnant before

vaccination. Women who are not sure are offered pregnancy tests.

Data about anthrax vaccination was obtained from men at time of oocyte and sperm retrieval. Researchers assessed characteristics of male gametes, including 254 vaccinated men and 791 unvaccinated men. The two groups were comparable for semen concentration (million sperm per milliliter), sperm motility (movement), sperm morphology (shape), need for intracytoplasmic sperm injection, and rate of fertilization of mature oocytes, embryo transfer, and clinical pregnancy. A diagnosis of male-factor infertility was less common in anthrax-vaccinated men than in unvaccinated men. The researchers concluded that anthrax vaccination of men did not impair semen parameters, fertilization rate, embryo quality, or clinical pregnancy rates.

6) Are there any other groups or agencies besides DoD that advocate the use of the anthrax vaccine?
In addition to the Department of Defense, other agencies and groups advocate or support the use of the anthrax vaccine. The Food & Drug Administration licensed the anthrax vaccine in 1970. The Centers for Disease Control & Prevention, the World Health Organization, the Defense Health Board, and many other respected public health organizations support use for people at risk or exposed to Bacillus anthracis. Information about the AVIP is available on the Internet (a variety of DoD web sites as well as the Centers for Disease Control & Prevention (www.cdc.gov) and the Food & Drug Administration web sites), which includes facts about the anthrax vaccine, history, side effects, purpose for immunizations and more. [See the Q&A page on independent scientific reviews.] 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, 17th ed. James Chin, ed. "An official report of the American Public Health Association," Washington, DC, 2000.

Guide for Adult Immunization, 3rd ed, Philadelphia: American College of Physicians, 1994.

Immunization Against Infectious Disease. Her Majesty's Stationery Office, London: British Joint Committee on Vaccination and Immunization, 1996. Report of the Committee on Infectious Diseases, 26th edition, Elk Grove Village, IL: American Academy of Pediatrics, 2003.

ImmunoFacts: Vaccines & Immunologic Drugs. Saint Louis: Facts and Comparisons, Inc., 2006.

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.

Similarly, anthrax vaccination is specifically endorsed in the Working Group on Civilian Bio-defense position paper on preparedness against anthrax (Inglesby, et al. Anthrax as a Biological Weapon, 2002.

Journal of the American Medical Association (JAMA) 2002;287:2236- 52).

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.

7) Is the Department of Defense continuing to research safety aspects of the anthrax vaccine?
Thirty (30) years of experience with anthrax vaccine in the United States suggests it has a similar side effect profile compared to other commonly used vaccines. Nonetheless, the Department of Defense

continues to monitor the safety of the anthrax vaccine during program execution. As the National Academy of Sciences pointed out, the most scientifically powerful way of assessing vaccine safety is by comparing and contrasting people vaccinated and unvaccinated against anthrax. In addition, DoD scientists are currently conducting more long-term research and designing yet more studies. In designing these studies, we will draw from the accumulated experience of some of the nation's best vaccine researchers at CDC and FDA. One of the methods used is a surveillance technique used by CDC in post-marketing studies: large, linked databases. DoD uses the large, linked database approach in its long-term research efforts through access to its immunization tracking programs database and though the medical databases maintained by the Defense Medical Surveillance System (DMSS).

8) Is there any risk of cancer or mutagenesis (genetic mutations)?
In nearly 30 years of use, there is no evidence that the anthrax vaccine causes cancer or mutagenesis. As with most other vaccines or other pharmaceuticals, studies regarding carcinogenesis or mutagenesis has not been performed with anthrax vaccine. Such studies have not been performed, in large part, because in over 200 years of administering vaccines to humans, no vaccine has ever been shown to cause cancer or genetic mutations.

9) I don't have a spleen. Can I still get vaccinated?
Yes, you may receive the anthrax vaccine if your spleen was removed in surgery or if your spleen no longer works properly. Several vaccines are specifically recommended for people without a spleen (asplenic people), to improve the body's defense against infections. In general, inactivated or killed vaccines (including anthrax vaccine) are recommended for people without spleens. In many cases, such vaccines may be life-saving by preventing overwhelming infection. The American College of Physicians (ACP) specifically names anthrax vaccine in its 1994 guidelines for people at risk of exposure to this bacterium. People without a spleen should get some live vaccines and avoid others. Spleens help people fight infections. People who do not have a spleen have a hard time protecting themselves against bacteria. Without a spleen, people are at risk of severe bacteremia (infection in the blood) from many types of bacteria. Some people lose their spleens during surgery to repair abdominal injuries suffered during accidents or their spleen is removed to help them respond to certain kinds of cancer. Certain diseases, especially sickle cell disease, destroy the spleen, while other people may be born without a spleen. According to the American College of Physicians (ACP), people without spleens or people whose spleens don't work properly should be vaccinated against the following diseases, if they are susceptible to them: Tetanus, diphtheria, pneumococcal, Haemophilus influenzae type b (Hib), meningococcal, and influenza. These people should be vaccinated against anthrax, cholera, hepatitis B, measles, mumps, plague, poliovirus (injectable vaccine), rabies, rubella, and typhoid fever (injectable vaccine), if these vaccines are needed. The ACP concludes by saying "In addition, the importance of anti-malarial prophylaxis must be emphasized for those planning foreign travel to areas where malaria occurs." (Guide for Adult Immunization, 3rd ed. Philadelphia: 1994) The American Academy of Pediatrics and the CDC's Advisory Committee on Immunization Practices provide similar recommendations on vaccines for persons with surgical or functional asplenia.

10) Should people with lupus (SLE) get vaccinated?
People who have been diagnosed with lupus should talk with their physician about whether or not they should be vaccinated, considering the state of their disease, the medications they take, and their personal risk for specific infections. Several medical studies have shown that people with lupus can be safely and effectively vaccinated against influenza, hepatitis B, pneumococcal disease and other diseases that would pose a significant risk if they were infected. For military personnel with lupus, providers are authorized to grant medical exemptions according to the patient's specific situation. Medical specialists can advise how to get the best benefit from vaccination in such circumstances.

11) What information about potential risks of vaccination will DoD provide people who will be

vaccinated against anthrax?
DoD will ensure potential vaccine recipients receive the most current educational trifold brochure available . An Individual's Briefing will be available at all immunization sites. Potential vaccine recipients will be educated about the threat of anthrax and the benefits and risks of vaccination.

12) How will the side effects of anthrax vaccinations be monitored?
DoD will continue its enhanced safety surveillance program, which features:

• Encouraging healthcare workers and vaccine recipients to report adverse events to the Vaccine Adverse Events Reporting System (VAERS, www.vaers.hhs.gov)

• Systematic monitoring of the health of recipients of anthrax vaccine adsorbed (e.g., cohort studies using the Defense Medical Surveillance System databases).

13) How will DoD track who receives anthrax vaccinations?
DoD will track anthrax vaccinations through Service-specific automated immunization tracking systems and the DEERS central repository. Where electronic immunization tracking is unavailable all vaccinations will be recorded in the individual health record and "yellow shot card" (PHS-731) (if provided).

14) What compensation is available for individuals who claim injury from anthrax vaccine?
Established military and civilian worker's programs provide compensation for injuries or illnesses resulting from military service or civilian job requirements.

15) For More Information:
Advisory Committee on Immunization Practices. General recommendations on immunization. MMWR-Morbidity & Mortality Weekly Report 2002;51(RR-2):1-35.
ftp://ftp.cdc.gov/pub/Publications/mmwr/rr/rr5102.pdf

American College of Obstetricians & Gynecologists, Committee Opinion, Immunization During Pregnancy, 2003;282:1-6. http://www.acog.org/from_home/publications/misc/bco282.pdf

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http://www.anthrax.mil/documents/338field_eval.pdf

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http://www.vaccines.mil/documents/library/Fertility&Sterility.pdf

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Singleton JA, Lloyd JC, Mootrey GT, Salive ME, Chen RT, VAERS Working Group. An overview of the vaccine adverse event reported system (VAERS) as a surveillance system. Vaccine 1999;17:2908-17. Turnbull PCB. Guidelines for the Surveillance and Control of Anthrax in Humans and Animals, 3rd ed., WHO Report WHO/EMC/ZDI/98.6. http://www.who.int/emcdocuments/zoonoses/whoemczdi986c.html

White CS III, Adler WH, McGann VG. Repeated immunization: Possible adverse effects: Reevaluation of human subjects at 25 years. Annals of Internal Medicine 1974;81:594 600. http://www.vaccines.mil/documents/library/Repeated.pdf

Long Term Safety

1) What do we know about the long-term safety of anthrax vaccine?
Based on multiple objective sources of data, there are no known long-term side effects to anthrax vaccine.

2) When people talk about "long term," what do they mean?
There is no universal definition for "long term." When applied to vaccines, scientists may consider "long term" to be 6 months to 1 year or longer.

3) I have heard people say that "no data has been collected more than 48 hours after anthrax vaccination." Is that statement true?
No. Twenty safety studies of various types have been performed to assess anthrax vaccine. Several of these studies actively collected data for weeks or months after each vaccination:

Brachman study: 24 and 48 hours after each dose

Fort Bragg study: 1, 2, 3, 7, and 30 days after each dose

Fort Detrick route-change study: 1, 2, 3, 7, and 30 days after each dose

Tripler Army Medical Center study: 7 days or more after each dose

Korea study: 2 weeks to 5 months after each dose

4) I have heard people say "there are no long-term safety studies of anthrax vaccine." Is that statement true?

No. Unlike the safety studies of single-dose vaccines, the 6-dose vaccination schedule for anthrax vaccine requires that individual vaccine recipients be observed for multiple months or years. Numerous studies have assessed the health of anthrax vaccine recipients over extended periods of time. The following list shows how much time elapsed after individual anthrax vaccine recipients received their first dose of anthrax vaccine:

Vaccine Adverse Event Reporting System (VAERS) minutes to years

Army Disability Discharge Study: 4.5 years

Fort Detrick route-change study: 6 months

Korea study: 6 months

USAF vision study: at least 6 months

Langley AFB study: at least 6 months

Tripler Army Medical Center study: at least 1 year

Brachman study: at least 1.5 years

Inpatient/outpatient cohort study: at least 6 to 18 months

Fort Detrick and US Army Medical Research Institute of Infectious Diseases (USAMRIID) 10 years or more

5) Laboratory workers at Fort Detrick, Maryland, have been vaccinated against anthrax since the 1940s. What do we know about the long-term health of those workers?
At Fort Detrick, Maryland, 99 laboratory workers were evaluated 10 to 20 years after receiving anthrax vaccine. Most of these workers received 150 to 200 doses of various vaccines (including anthrax vaccine); some received more than 300 such injections during their tenure at Fort Detrick. This study "failed to produce evidence that development of neoplasms, amyloidosis, or autoimmune diseases was associated with the vaccine dosages and frequencies used at Fort Detrick. The authors concluded "These data and the accompanying evaluation of an intensively immunized population provide evidence that no obvious adverse effects result from repeated immunization." The first report of this group of vaccine recipients was published in the Bulletin of the Johns Hopkins Hospital in 1958. Two follow-up reports were published in the Annals of Internal Medicine in 1965 and 1974.

An extension of this long-term study is underway at the U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID) to determine, in even greater detail, whether people who received multiple vaccines, including anthrax vaccine, during their past employment at Fort Detrick demonstrated any adverse health effects over the long term. More than 1,500 employees have been followed annually there. In a case-control study begun in 1996, vaccinated and unvaccinated volunteers have been enrolled. All volunteers signed an informed-consent document. The study methods include a 9-page health history questionnaire, extensive blood tests and urinalysis. The questionnaire queries mental and physical conditions of the volunteers, as well as the health of their offspring. Study end points include symptoms, symptom complexes (including symptoms reported by veterans of the Persian Gulf War), diseases, and abnormal laboratory and urine tests. Study subjects will be compared to two to three race-, gender-, and age-matched control subjects to determine if any long-term medical effects exist among this unique group of study subjects. Analysis of the data from the extensive health history

questionnaire and numerous laboratory tests are currently in progress. No unexplained symptoms due to repeated doses of anthrax or other vaccines have been found. From this and other monitoring, no patterns of delayed side effects to anthrax vaccine have been found. Monitoring continues.

White CS III, Adler WH, McGann VG. Repeated immunization: Possible adverse effects: Reevaluation of human subjects at 25 years. Annals of Internal Medicine 1974; 81:594-600.

Mail Handling Safety

1) How can mail get cross-contaminated with anthrax?
CDC does not have specific studies to address this, however, cross-contamination of the mail could occur during the processing, sorting, and delivery of mail when an envelope comes in contact with an envelope, piece of equipment (e.g., an electronic sorting machine), or other surface that is contaminated with Bacillus anthracis spores. In addition, airborne spores in contaminated postal facilities before they were cleaned might play a role.

2) When there is a known incident, how can I prevent anthrax exposure from cross-contaminated mail?
There are no scientifically proven recommendations for preventing exposure. However, there are some common-sense steps people can take:

- Do not open suspicious mail
- Keep mail away from your face when you open it
- Do not blow or sniff mail or mail contents
- Avoid vigorous handling of mail, such as tearing or shredding
- Wash your hands after handling the mail
- Discard envelopes after opening mail.

3) What should people do when they get a letter or package with powder?
Handling of Suspicious Packages or Envelopes:

- Do not shake or empty the contents of any suspicious package or envelope.
- Do not carry the package or envelope, show it to others or allow others to examine it.
- Put the package or envelope down on a stable surface; do not sniff, touch, taste, or look closely at it or at any contents which may have spilled.
- Alert others in the area about the suspicious package or envelope. Leave the area, close any doors, and take actions to prevent others from entering the area. If possible, shut off the ventilation system.
- WASH hands with soap and water to prevent spreading potentially infectious material to face or skin. Seek additional instructions for exposed or potentially exposed persons.
- If at work, notify a supervisor, a security officer, or a law enforcement official. If at home, contact the local law enforcement agency.
- If possible, create a list of persons who were in the room or area when this suspicious letter or package was recognized and a list of persons who also may have handled this package or letter. Give this list to both the local public health authorities and law enforcement officials.

These recommendations were published on October 26, 2001, in “Update: Investigation of bioterrorism-related anthrax and interim guidelines for exposure management and antimicrobial therapy” MMWR 2001; 50(42):909-919.

4) What is the risk for getting anthrax from handling my own mail?
If there is a risk for inhalational anthrax associated with exposure to cross-contaminated mail, it is very low. For example, about 85 million pieces of mail were processed on the few days in 2001 after envelopes containing Bacillus anthracis (addressed to two U.S. senators) passed through the New Jersey and District of Columbia sorting facilities until they were closed. Despite the fact that both of these facilities had evidence of widespread environmental contamination with B. anthracis spores and the fact that public health officials had been aggressively looking for anthrax cases, no new cases of anthrax were identified during that time.

5) When the possibility of cross-contamination of the mail exists, should I take antibiotics?
Preventive antibiotics are not recommended for persons who routinely open or handle mail, either at home or at the workplace. Antimicrobial prophylaxis is recommended only in certain specific situations such as for persons exposed to an air space known to be contaminated with aerosolized Bacillus anthracis or for persons in a postal sorting facility in which an envelope containing B. anthracis spores was processed. CDC's complete recommendations on antimicrobial prophylaxis are contained in the November 9, 2001 MMWR. Additional recommendations for use of vaccine as part of post-exposure prophylaxis are contained in the November 15, 2002 MMWR 51(45):1024-1026.

6) What kinds of anthrax worker safety guidelines have been issued?
The recommendations are divided into four categories. They are engineering controls, administrative controls, housekeeping controls, and personal protective equipment for workers. The guidelines describe measures that should be implemented in mail-handling/processing sites to prevent potential exposures to B. anthracis spores.

Vaccination and Reproductive Health

1) Can the anthrax vaccine be taken by military members who are pregnant?
It is DoD policy not to give anthrax vaccine to women who are pregnant or who think they may be pregnant. This is consistent with the general practice of withholding most medications from women who are pregnant. Most vaccinations are routinely deferred until after pregnancy, unless immunity is needed during pregnancy. Tetanus, meningococcal, hepatitis B, and influenza vaccines, for example, are specifically recommended for susceptible women during their pregnancy. As with other vaccines in the U.S., studies on possible reproductive side effects by intentionally giving anthrax vaccine to pregnant women have not been performed. However, there has been no confirmed evidence of infertility, miscarriages, or other reproductive problems with the use of inactivated vaccines. Because the anthrax vaccine is a sterile, cell-free (filtered) bacterial vaccine, it is non-infectious and is not expected to cause any harm to the fetus. If a pregnant woman is known to have been exposed to anthrax, she could be offered the vaccine as a potential life-saving measure. Women who believe that they may be pregnant should inform their health-care provider before vaccination. Once pregnancy is confirmed, anthrax vaccinations will be deferred until the woman is no longer pregnant. Once a woman is no longer pregnant, deferred anthrax vaccination will resume. A woman can safely become pregnant any time after vaccination that she wishes. Preliminary data from the Naval Health Research Center raised a tentative signal that there may be an association with an increased rate of birth defects. This signal is being investigated thoroughly, to determine which of several explanations for the signal is most likely.

2) Have any studies revealed birth defects among babies born to women who received anthrax vaccine during their pregnancy?
A recent study by the Department of Defense (DoD) Center for Deployment Health Research with the Naval Health Research Center and the National Center for Birth Defects and developmental Disabilities indicated that women who received anthrax vaccinations during their first trimester of pregnancy could

have a slightly higher risk of birth defects than women receiving anthrax vaccine at other times before or after the first trimester. The study is still under review. Results are pending.

3) Are the chances for birth defects increased if both parents have received anthrax vaccination?
There is no evidence in the above mentioned study to indicate that anthrax vaccination in both parents increases the risk for birth defects in babies born to those parents.

4) What happens to vaccinated women who later get pregnant?
In the March 27, 2002, issue of the Journal of American Medical Associations, two Army physicians published findings that women get pregnant at the same rate, whether anthrax-vaccinated or unvaccinated. These physicians from Fort Stewart, Georgia, also showed that women deliver offspring at the same rate, whether anthrax-vaccinated or unvaccinated. The Fort Stewart study found no difference in birth defect rates, either, but the study may have been too small to detect small differences. Long-standing Department of Defense policy is to defer routine vaccinations in women until after pregnancy. This policy has always applied to anthrax vaccine. Women are asked if they are pregnant before vaccination. Women who are not sure are offered pregnancy tests.

5) What about men who get vaccinated? Should they delay fathering a child?
No. For all the same reasons mentioned above, there is no reason for a man to delay fathering a child after vaccination. A man can safely father a child any time after vaccination that he wishes. Data about anthrax vaccination was obtained from men at time of oocyte and sperm retrieval. Researchers assessed characteristics of male gametes, including 254 vaccinated men and 791 unvaccinated men. The two groups were comparable for semen concentration (million sperm per milliliter), sperm motility (movement), sperm morphology (shape), need for intracytoplasmic sperm injection, and rate of fertilization of mature oocytes, embryo transfer, and clinical pregnancy. A diagnosis of male-factor infertility was less common in anthrax-vaccinated men than in unvaccinated men. The researchers concluded that anthrax vaccination of men did not impair semen parameters, fertilization rate, embryo quality, or clinical pregnancy rates.

6) What about a woman who is taking fertility-enhancing drugs in an effort to become pregnant?
No drug interactions are known between fertility medications (such as clomiphene, Clomid) and any vaccination. Women on fertility-enhancing drugs receive all DoD vaccinations on schedule until they have a positive pregnancy test. At this point, further vaccinations are deferred as described above.

7) I don't have any children now, but hope to one day and I'm currently taking the anthrax vaccination. Will this vaccination cause birth defects in my future children?
There is no increased risk of birth defects when receiving anthrax vaccination before becoming pregnant. If you are trying to become pregnant or think you may be pregnant, be sure to request a pregnancy test. Inactivated vaccines are generally considered safe in pregnancy.

8) I'm scheduled to start/restart my anthrax vaccination series, but I want to start trying to get pregnant. Should I delay getting pregnant?
There is no increased risk of birth defects when receiving anthrax vaccination before becoming pregnant. If you are trying to become pregnant or think you may be pregnant, be sure to request a pregnancy test. DoD policy is to temporarily exempt women who are pregnant.

9) Why is anthrax vaccine not contraindicated with breast-feeding?
Women who are breast-feeding may safely receive any vaccine. As an inactivated vaccine, anthrax vaccine contains no living or dead organisms and is non-infectious. No ill effects to the infant are anticipated through breast-feeding. As recommended by the Advisory Committee on Immunization

Practices of the Centers for Disease Control and Prevention (CDC), there is no need to interrupt breast-feeding (lactation) for inactivated vaccines.

10) For More Information:
Advisory Committee on Immunization Practices. General recommendations on immunization. Morbidity & Mortality Weekly Report (MMWR) 2002; volume 51 (No. RR-2): pages 1-36; http://www.cdc.gov/mmwr/pdf/rr/rr5102.pdf)

American College of Obstetricians & Gynecologists, Committee Opinion, Immunization During Pregnancy, 2003; 282:1-6. http://www.acog.org/from_home/publications/misc/bco282.pdf

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United States Army Regulation 40-562; Navy Bureau of Medicine & Surgery Instruction 6230.15; Air Force Joint Instruction 48-110; Coast Guard Commandant Instruction M6230.4E. Immunizations & Chemoprophylaxis. Washington, DC, 1 November 1995.

Wiesen AR, Littell CT. Relationship between pre-pregnancy anthrax vaccination and pregnancy and birth outcomes among U.S. Army women. Journal of the American Medical Association (JAMA) 2002; 287:1556-60. http://jama.ama-assn.org/content/vol287/issue12/index.dtl

Anthrax and the Persian Gulf War

1) Is the anthrax vaccination program a result of lessons we learned from the 1990-1991 Persian Gulf War?
Yes. Building upon the lessons of past wars and leveraging superior technologies available today and in the future, the AVIP is one of the cornerstones of Force Health Protection. Additionally, the current world threat environment and the unpredictable nature of terrorism make it prudent to include biological warfare defense in all our force protection planning. We also learned that we need to put more effort into documentation of vaccinations in Service Members' medical records. This is the reason for the new immunization tracking systems operated by each of the military services.

2) Anthrax vaccine was administered to personnel deployed in the Persian Gulf War. How many Service Members received vaccines against biological weapons during the Gulf War?
During the Persian Gulf War approximately 150,000 Service Members (about 1 in 5 of the people who served in the operation) received at least one dose of anthrax vaccine to vaccinate U.S. forces against Iraq's weaponization of Bacillus anthracis. Approximately 8,000 doses of botulism vaccine were also administered during the Gulf War.

3) Was the anthrax vaccine FDA-licensed at the time it was given to Gulf War veterans?
Yes. The FDA licensed the anthrax vaccine in 1970. All of the anthrax vaccine administered during the Persian Gulf War was produced at the Lansing facility and release according to the lot-release test criteria for potency, purity, safety, and sterility.

4) Has the anthrax vaccine been linked to illnesses among Persian Gulf War veterans?
No. Several independent nationally renowned scientific groups have addressed this issue and have found no evidence to link anthrax vaccine with illnesses among Gulf War veterans. Symptoms have been reported both by Gulf War veterans who were vaccinated and those who were not. The Institute of Medicine, the Presidential Advisory Committee on Gulf War Veterans' Illnesses, National Institute of Health, and the Defense Science Board have reviewed the correlation and concluded that the anthrax vaccine does not explain the reported chronic effects associated with illnesses among Gulf War veterans. There have been several unsubstantiated allegations in the media and elsewhere about experimental vaccines that may have contained non-FDA-licensed substances. Only the FDAlicensed anthrax vaccine was used then or now.

5) What did the Centers for Disease Control and Prevention find in their study?
One study of the health of Gulf War veterans was coordinated by scientists at the CDC. The clinical evaluation portion of their study assess 158 Gulf War veterans from one Air Force unit, regardless of health status. Portions of their research report is reprinted verbatim here: METHODS: "...To screen for exposure (either by vaccination or in combat) to 2 widely discussed putative biologic warfare agents, we tested serum samples for antibodies to toxin produced by Clostridium botulinum and Bacillus anthracis. Serum samples were screened at the Division of Bacterial and Mycotic Diseases, CDC, for antibodies to type A botulinum toxin. Serum samples were assayed at the US Army Medical Research Institute of Infectious Diseass, Washington, DC [sic], for antibodies against anthrax protective antigen and lethal factor...." RESULTS: "...There was no association between seropositivity to various infectious agents and chronic multisymptom cases. ... Ten subjects reacted to botulina [sic] toxin and 14 to anthrax protective antigen, but there were no differences between cases and noncases...." COMMENT: "We tested participants for exposure to several infectious agents that are important health problems in the Gulf region, that may have been used in vaccines, and that might be associated with a chronic illness. ... Similarly, we found no association between illness and antibody against the other viruses, rickettsiae, parasites or bacteria for which we assayed...." CITATION: Fukuda K, Nisenbaum R, Stewart G. Thompson WW, Robin L, Washko RM, Noah DL, Barrett DH, Randall B, Herwaldt BL, Mawle AC, Reeves WC. Chronic multisystem illness affecting Air Force veterans of the Gulf War. Journal of the American Medical Association (JAMA) 1998;280:981-8.

6) Where can I get more information about reputable studies of Gulf War illnesses?
The Special Assistant for Gulf War Illnesses, Dr. Bernard Rosker, published an info paper entitled "Vaccine Use During the Gulf War" (http://www.gulflink.osd.mil/va/). 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 related 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 vaccine and any illness common to Gulf War veterans. These reports include:

Presidential Advisory Committee on Gulf War Veterans' Illnesses: Final Report, December 1996. Pages of Interest: second page, Executive Summary, plus pages 112-114 of the original document (Chapter 4 in the web version).

Institute of Medicine, Health Consequences of Service During the Persian Gulf War:

Recommendations for Research & Information Systems, 1996. (http://books.nap.edu/books/0309055369/html/1.html)Pages of Interest: 49-52, 55, 100.

National Institutes of Health, Technology Assessment Workshop: The Persian Gulf Experience and Health, 29 April 1994.

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.

Three specific studies looking into the health of Gulf War veterans and their families were published in the New England Journal of Medicine. The postwar hospitalization experience of U.S. veterans of the Persian Gulf war. New England Journal of Medicine 1996; 335:1505-13. 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; 336:1650-6. The authors concluded that "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. 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."

A DoD-funded British team at King's College, London, reported in the 20 May 00 issue of British Medical Journal that multiple vaccinations given in a theater of war, but not before deployment, were associated with multi-symptom illness, fatigue, psychological distress, health perception, and physical functioning. The analysis was limited to veterans who kept vaccination records.

Exposures other than vaccination were not controlled for, except pesticide use. Anthrax vaccine was not analyzed independently. The lead author was Matthew Hotopf; the research team included Catherine Unwin. The authors recommend that Armed Forces be vaccinated before deployment: "It would be folly to allow Service personnel to be committed to a modern battlefield without all necessary means of protection against endemic infection and biological weapons." The accompanying editorial calls Hotopf's evidence "inconclusive," citing design limitations and contradictory findings.

Next Generation Anthrax Vaccine (NGAV)

1) Is the Department of Defense (DoD) pursuing an improved anthrax vaccine?
Yes. DoD is actively pursuing a next-generation anthrax vaccine (NGAV) in cooperation with the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH).

2) Why is DoD pursuing another anthrax vaccine? Doesn't the one you have now work?
The National Academy of Sciences and its Institute of Medicine (IOM) stated in no uncertain terms that "AVA [the current FDA-licensed anthrax vaccine], as licensed, is an effective vaccine to protect humans against anthrax, including inhalational anthrax." This was in its March 2002 report, which can be found at: http://www.nap.edu/catalog/10310.html.

3) Then why are you pursuing a next-generation anthrax vaccine?
We want to explore whether a newer anthrax vaccine would be easier to produce and require fewer doses to achieve immunity. The IOM study also recognized the advantages of developing a next-generation anthrax vaccine when it said, "the production, testing, and licensure of a new vaccine requiring fewer doses and producing fewer local reactions are needed." Aviators consistently seek better airplanes. Similarly, we seek better vaccines.

4) What efforts does DoD have underway? Who are DoD's partners?
DoD and the National Institutes of Health (NIH) have been working on a next-generation anthrax vaccine (NGAV). Specifically, the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and the Joint Vaccine Acquisition Program (JVAP) collaborated to develop an NGAV that uses state-of-the-art recombinant technology. The NIAID collaborates with this effort by preparing the NGAV product and sponsoring human clinical phase-1 trials. The NIAID is independently pursuing multiple "recombinant protective antigen" (rPA) candidate vaccines, to identify and develop the most promising next-generation vaccine as quickly as possible. This is a parallel effort from the DoD/NIAID cooperative effort on the DoD NGAV candidate.

5) What advantages could an NGAV offer?
NGAV is a much more highly defined product (a single highly purified protein). As a result, there should be more consistency from production lot to production lot, making release testing more predictable. Additionally, it might be possible to achieve immunity with fewer doses, because higher and more consistent doses of the protective-antigen protein may be administered. It might also be possible to use an intramuscular injection route, which may cause fewer adverse events after vaccination (i.e., be less reactogenic). However, this possibility won't be known until human clinical trials of the vaccine are completed. Finally, the rPA is produced in non-sporeforming bacteria that permit the vaccine to be made in the same production facility as other vaccines, unlike anthrax vaccine adsorbed (AVA).

6) How will this new anthrax vaccine be produced?
The next-generation anthrax vaccine (NGAV) is based on a protein called "recombinant protective antigen" (rPA). rPA is a single purified protein that protects animals against aerosol exposure to deadly Bacillus anthracis spores. rPA can be produced in several genetically-engineered bacteria

7) Will a next-generation anthrax vaccine protect as well as the current anthrax vaccine?
That is our goal, yes. Until completion of human clinical trials, we do not know how much protective antibody human volunteers will produce. Preliminary data from non-human primates (rhesus monkeys) seems to indicate similar protection profiles compared to anthrax vaccine adsorbed (AVA).

8) What has to be done before we can use an NGAV?
NIH is in the beginning stages of clinical testing of an NGAV. Phase I tests in a few dozen people will study this new vaccine's safety. Next, a preliminary Phase II test in a few hundred people will test antibody responses to the new vaccine. Expanded Phase III testing among thousands of volunteers will produce pivotal information about both safety and immune responsiveness required for product licensing. Advanced studies (post-clinical trials) will be conducted in animals to define the protective immune response induced by the NGAV candidate. Additionally, studies will be performed to optimize the vaccine's formula and immunization schedule. In addition, results from the study of the current FDA-

licensed anthrax vaccine, being conducted by the Centers for Disease Control & Prevention (CDC), will provide critical information on immune responses that will be required to license an NGAV. Finally, the FDA will study all of the data and eventually determine if the NGAV will become a licensed product.

9) When will human clinical trials of next-generation anthrax vaccines (NGAV) begin?
These clinical trials began in fall 2002.

People Issues

Educational Materials

1) Will anthrax vaccine recipients receive any educational information about the anthrax vaccine? How will this information be presented?
Commanders and health care professionals will provide anthrax vaccine recipients information about the vaccine. Information has been provided to military personnel and DoD civilians through command channels and internal and external public affairs programs to include web sites, commanders' calls, military newspapers, television, radio and messages.

2) Anthrax vaccine information is also available through:
DoD and Service Web Sites
- www.anthrax.mil
- www.vaccines.mil/anthrax

AVIP Information
- Anthrax Vaccine Trifold Brochure
- Information Paper
- Individual Briefing
- Leader's Briefing
- Health-Care Providers briefing
- Toll-free information line (877-GET-VACC)
- Email question-and-answer service (vaccines@amedd.army.mil)

Other agencies, including:
- Centers for Disease Control & Prevention (http://www.bt.cdc.gov/)
- Food & Drug Administration (http://www.fda.gov/)
- World Health Organization (http://www.who.int/)

Plasma Donation

1) Why is the Department of Health and Human Services (DHHS) collecting plasma from anthrax-vaccinated people?
Despite treatment with highly active antibiotics there is still a significant mortality from inhalational anthrax. Because of this, the DHHS Biomedical Advanced Research and Development Authority (BARDA) Office, funded under Project Bioshield, is working to make a new kind of anthrax medication by collecting blood plasma from people who have been vaccinated against anthrax. Antibodies found in this plasma fight anthrax infections and will be used to create a medication which will be known as anthrax immune globulin or AIG.

Over 1.8 million people have received anthrax vaccine since 1998; most of which were U.S. service members. DHHS asked the U.S. Department of Defense (DoD) to assist with the AIG plasma program to improve the Nation's medical defenses against anthrax attack. The DoD agreed to distribute information about this voluntary DHHS BARDA office program to service members.

2) Who is in charge of this project?
The Department of Health and Human Services (DHHS) BARDA office is in charge of this project. Through Project Bioshield, the DHHS contracted with Cangene Corporation (www.cangene.com) to collect the plasma from anthrax vaccinated people and make AIG. Cangene Corporation has contracted with plasma-donation centers in cities near selected military bases to collect plasma for this program. Visit www.cangene.com/AIGPDP.locations.a.htm for a complete list of donation centers.

3) Why is AIG needed?
AIG is needed because severe cases of anthrax infection are often fatal, despite current therapies. DHHS and DoD became more interested in AIG after the anthrax bioterrorism attacks of fall 2001. Among the 11 cases of inhalational anthrax, 5 (45%) died despite intensive care and antibiotic therapy. The goal of AIG is to reduce the risk of death among people with severe anthrax in case of another anthrax attack. The need for medications such as AIG to use with antibiotics would be even greater for anthrax infections resistant to antibiotics.

4) How would this AIG be used, once it is manufactured?
After it is made, the AIG will be stored for emergency use to treat patients with severe anthrax infection. This emergency supply called the Strategic National Stockpile (SNS), has large quantities of medicine and medical supplies to help citizens across the country, including troops and their families. The Strategic National Stockpile (SNS) managed by the CDC is overseen by the Department of Health and Human Services as provided in Project Bioshield legislation.

5) Who is eligible to donate plasma for this project?
Per the brochure, eligible plasma donors who have received at least 4 or more doses of the anthrax vaccine, with the most recent dose within the past 21 days, are eligible for immediate donation without further vaccination.

In addition at some locations, individuals can also participate if they have ever received:

- 4 or more doses of anthrax vaccine*, or
- 1 or more doses of anthrax vaccine*, or
- Zero doses of anthrax vaccine

*Last dose of anthrax vaccine not within the last 21 days.

These additional AIG programs vary by location, so please contact your nearby plasma center for more details. A list of plasma centers can be found at www.cangeneplasma.com.

6) Do donors have to be in the Service to donate? What if you're a civilian employee or contractor who got vaccinated against anthrax?
No, donors don't have to be in the Service to donate. Anyone is welcome to donate plasma for this DHHS BARDA office project, as long as they meet the requirements for donation.

7) Will plasma donors be compensated for their time and travel?
Yes! Standard practice at U.S. plasma centers is to compensate plasma donors for their time and effort. Plasma donors are paid for each plasma donation; bonuses may also be paid to those who donate for multiple consecutive weeks.

8) How often can a plasma donor donate?
FDA standards allow plasma donation as often as twice a week.

However, USAMRIID and DoD laboratory workers are allowed to donate only once per week, if they are involved in duties that involve the risk of potential occupational exposure.

9) Where are donations going to occur?
Donations will occur at specific plasma-donation centers contracted by Cangene Corporation for this project. These centers are licensed by the Food and Drug Administration (FDA) and are known technically as plasmapheresis centers. The specific centers for this project are near military bases which have large numbers of anthrax-vaccinated service members. Visit http://www.cangeneplasma.com for a complete list of donation centers.

10) Can someone go to any plasma center other than the designated centers involved with this project?
No, not for this project. Only the designated plasma centers that are part of this DHHS BARDA office program are collecting plasma to produce AIG at this time. Plasma donated at other centers will not go toward this project.

11) How soon after donating whole blood can someone donate plasma? What about vice versa?
After donating a unit of whole blood, the usual recommendation is to wait 8 weeks before donating plasma. After donating plasma, the usual recommendation is to wait 2 to 3 days before donating whole blood, assuming the blood donor is in good health.

12) What is involved in donating plasma?
Donating plasma is similar to donating blood. A sterile needle is put in your vein and attached to sterile IV tubing. Blood goes out into the tubing, then into a spinning centrifuge, to separate plasma from the blood cells. Plasma is the straw-colored portion of the blood and is made up of 90% water. Plasma contains various proteins, including albumin, fibrinogen (to help clotting) and globulins (including antibodies). The blood cells are then returned to you through the same tubing and needle. A sterile saline ("salt water") solution may be given to you by IV after the donation, to help your body replace fluid removed during donation. If the saline solution is not given, the body will replace the fluid naturally within 48 hours. This process of removing whole blood and separating it into its two main parts: blood cells and plasma is called plasmapheresis.

13) Will my immunity against anthrax decrease after giving plasma?
Not in any substantial way. Plasma donation does remove anthrax-fighting antibodies from the bloodstream. The reduction is small, compared to total blood volume and the cells that make antibodies are not removed by plasma donation. Therefore the donor does not lose its ability to make more anthrax-fighting antibodies. Here is an analogy. You own an orchard with apple trees. You give away some of the apples, but keep the rest of the apples and the trees for yourself. Then you grow more apples. Similarly, the plasma donor gives away some antibodies, but keeps the rest of the antibodies and the cells that make more antibodies. Then the donor makes more antibodies to replace the donated antibodies.

14) Will plasma donors sign an informed-consent document?
Yes. Plasma donors will sign a consent form to record that they voluntarily donate the plasma. This will be done at the plasma center. Plasma donors will not be the subject of any research project.

15) What side effects can happen during or after plasma donation?

Side effects are similar to those related to donating blood. Some donors may feel faint or lightheaded during or right after donating plasma. This usually occurs when the donor did not eat or drink enough just before donating. Inserting the needle may cause a bruise. Some donors may have discomfort in the arm during donation from the needle. This can usually be solved by adjusting the needle's position. Some donors may have a metallic taste or tingling in their tongue or feet. This is caused by a blood thinner used to keep the blood from clotting. If this happens, slowing or stopping the plasma donation will stop the feeling. Allergic reactions could occur, but are rare. People with allergic reactions might have a rash, hives, itching, shortness of breath, or wheezing. If you have any of these feelings during or just after donating, tell the plasma center staff right away. Before donating you will be told about the risks of donating plasma, possible side effects, and be given an opportunity to have your questions answered.

16) What happens to the plasma after donation?
After donation, the plasma is promptly frozen, then shipped to Cangene Corporation for processing. Antibodies, including anthrax antibodies, are separated from other parts of the plasma. Then the antibodies are processed to kill any germs that might be present, and packaged into vials.

17) Can somebody get AIDS or some other infection from donating plasma?
No. It is not possible to acquire any disease through donating plasma, because new, disposable, sterilized equipment is used for each donation. Plasma is collected in a highly controlled, sterile environment by professionally trained staff. Any equipment that touches the donor's blood or plasma is used only once, eliminating the possibility of transmitting any infection to the donor by the donation process. All items used — the finger lancet, the needle, cotton balls, swabs and solutions — are thrown away after a single use. Each plasma center is also periodically inspected by FDA representatives.

18) Will plasma donation increase the odds of adverse reactions to the next anthrax vaccination?
No. Plasma donation has never been found to cause adverse events after subsequent vaccinations.

19) Will plasma donors be able to get their next anthrax vaccinations on time?
Yes. Plasma donation does not affect vaccination schedules.

20) Is a product like Anthrax Immune Globulin (AIG) likely to work or be guaranteed to be used?
AIG is not yet licensed by the FDA; it is considered an investigational new drug, also called an IND. Products like AIG were commonly used before antibiotics became available in the 1930s and 1940s. Additional research is being done to understand the value of AIG better but animal studies suggest AIG will be useful.

AIG may also go unused if there is no emergency or if some other event arises that prevents its use.

21) How can one get more information about this plasma-donation project?
Contact the designated plasma center participating in the DHHS BARDA office program. For more information about eligibility or how to contact the center, contact the Military Vaccine (MILVAX) Agency by visiting their website www.anthrax.mil/AIG or calling 877-GET-VACC (877-438-8222). Also visit www.cangeneplasma.com for additional information.

Production Issues

Production Issues

1) The production facility for the anthrax vaccine, located in Lansing, Michigan, changed ownership in 1998. Who are the current owners?
The State of Michigan opened its first laboratory to manufacture vaccines and antibodies in Lansing in 1925, over 75 years ago, receiving license #99 to manufacture biological medications. On 7 July 1998, the State of Michigan approved the sale of the United States' only licensed manufacturer of anthrax vaccine to a for-profit company. The state-owned entity known as the Michigan Biologic Products Institute (MBPI) was sold effective 5 September 1998 to become BioPort Corporation. The facility's license is now listed as license #1260, with the sale of MBPI to Emergent BioSolutions Incorporated http://www.emergentbiosolutions.com.

Multiple shareholders own Emergent BioSolutions, whose headquarters remain in Lansing, Michigan. The two main companies that make up Emergent BioSolutions are Intervac, headed by William Crowe and Fuad El-Hibri, and Michigan Biologic Products Inc., which is made up of seven managers from the era when the State of Michigan owned the plant, headed by Robert Myers. The former state employees were specifically permitted by the Michigan State Legislature to bid on the sale. The legislators hoped that retaining local management as investors would help keep the plant and its 200 jobs in Michigan. Admiral William Crowe, Jr., is a former Chairman of the Joint Chiefs of Staff and the U.S. ambassador to Britain until 1997. Fuad El-Hibri, a U.S. citizen of Lebanese descent, transformed a British government plant for vaccine production into a successful private venture.

As Admiral Crowe testified to the U.S. Congress in October 1999, that the government's decision to vaccinate the Armed Forces was made after several years of internal analysis that culminated in a December 1997 decision. These events occurred well before the State of Michigan chose to sell its vaccine-production facilities to Emergent BioSolutions Incorporated.

2) Did the Food and Drug Administration revoke Emergent BioSolutions' license to manufacture anthrax vaccine?
No. Emergent BioSolutions' predecessor, the Michigan Biological Products Institute (MBPI), owned by 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 licenses issued to MBPI. MBPI 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. Emergent BioSolutions submitted a highly detailed set of quality control documents to FDA in fall 2001. FDA approved Emergent BioSolutions' facilities and processes, as they relate to the manufacture of anthrax vaccine, on January 31, 2002.

3) The manufacturing facility owned by Emergent BioSolutions was renovated. Was this due to any findings made by the inspections by the Food & Drug Administration?
The planning for renovations to the physical plant began in 1996. Construction began in early 1998 and was completed in May 1999. The Food and Drug Administration approved the renovations to Emergent BioSolutions' anthrax vaccine manufacturing facilities and processes January 31, 2002.

The FDA has steadily approved release of anthrax vaccine lots manufactured by Emergent BioSolutions ever since. Over the years, the State of Michigan appropriated money to upgrade and expand its existing facility in a staged fashion, as improvements in current Good Manufacturing Practices (cGMPs) were adopted by the U.S. pharmaceutical industry. In January 1993, FDA as part of a routine program inspected the anthrax vaccine manufacturing facility at Emergent BioSolutions. To improve its operations, a renovation to the Lansing facility was approved by the State of Michigan in July 1993 with funding coming in later years. The manufacturer closed the anthrax vaccine production line in January 1998 for planned renovation. 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 production requirements. This renovation project cost $3.7 million and 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.

In 1994, after Michigan authorities had approved the renovation schedule, the FDA conducted a rigorous inspection of Michigan's plasma-derivatives operation. Then, in 1995, the FDA issued a warning letter to Michigan concerning plasma operations and rabies vaccine manufacturing. After a November 1996 inspection, findings showed that corrections to the previous areas had not been completed. The FDA issued a "Notice of Intent to Revoke" (NOIR) letter in March 1997, threatening to begin a multi-step process to revoke Michigan's license to manufacture vaccines.

Michigan responded quickly to the NOIR letter, developing a strategic plan for compliance within 30 days. FDA later testified to Congress that Michigan "had made progress in achieving its compliance goals."

The FDA conducted a pre-approval inspection of the newly renovated production facility at Emergent BioSolutions in November 1999. The FDA inspection reported 30 observations to Emergent BioSolutions management that needed to be corrected as well as identified process validation steps that needed to be addressed for FDA to approve the new facility. FDA completed its approval of Emergent BioSolutions' physical renovations, as well as its extensive process-validation documentation in December 2001.

4) There have been questions raised about the anthrax vaccine due to the results of the FDA inspections over the past few years. Are there reasons to be concerned about the inspection results?
No. All lots of anthrax vaccine that have ever been released, including those used in the DoD's immunization program, met all FDA release criteria: general safety, purity, sterility, and potency. All stockpiled lots that have been used in the DoD immunization program have met DoD-mandated supplemental testing criteria and oversight of that testing has been provided by an independent DoD-contractor, Mitretek Systems, Inc.

Over the years the FDA acknowledged that the manufacturer was making progress in achieving compliance with FDA standards and regulations. FDA found no deficiencies serious enough to warrant recall of the anthrax vaccine, which is within FDA's authority. Link to FDA Enforcement Reports http://www.fda.gov/opacom/enforce.html.

Results of more recent FDA inspections of Emergent BioSolutions, both in Nov 1999 and Oct 2000, have indicated BioSolutions progress toward licensure in an environment of increasingly stringent FDA standards for process validation and for demonstrating consistency of manufacturing. FDA's actions in December 2001 and January 2002, approving all aspects of anthrax vaccine manufacture, reflect the FDA's satisfaction with Emergent BioSolutions' renovations and quality controls. FDA officials have visited Emergent BioSolutions several times since. FDA officials visit all vaccine manufacturers periodically.

5) Is there a connection between deficiencies found in the 20 February 1998 FDA Inspection Report and the fact that MBPI suspended anthrax vaccine production?
There is no connection between the deficiencies found on the 20 February 1998 FDA inspection report and the fact that MBPI ceased production of anthrax vaccine in its original production suite. FDA did not order MBPI to suspend production. DoD in coordination with MBPI determined several years ago that the current production line would require scheduled renovation. The start of the renovation was contingent upon MBPI completing the production requirements needed to meet the terms of the

production contract (DAMD 17-97-D1139). MBPI fulfilled the contract in December 1997, and the planned renovations began shortly thereafter.

6) Given the nature of the problems identified by the FDA in their inspection of the Michigan Biological Products Institute (now BioPort) in 1996, what safeguards did DoD take to assure that the anthrax vaccine is safe and effective?
DoD directed that supplemental testing be done on all lots in the stockpile at MBPI produced under contract DAMD 17-97-D0003. Of these lots, only lots of vaccine that passed supplemental testing were approved for shipment and use by DoD and Coast Guard personnel.

7) Emergent BioSolutions recently received a full go-ahead from FDA. What did it take to earn this FDA approval?
Emergent BioSolutions ceased manufacturing to renovate its vaccine production facility in February 1998. When the manufacturing process or equipment in a renovated facility or establishment differs materially from that in the former facility or establishment (CFR 21.314.70), a Biologics License Application (BLA) Supplement must be submitted for Agency approval before production can be resumed. Emergent BioSolutions' BLA Supplement consisted of many parts. Included in the BLA supplement were data validating an updated potency test, process validation test results, and information concerning the qualification and testing of three fermentation systems, raw material quality and acceptance criteria and updated procedures for operating the new facility. In addition, Emergent BioSolutions submitted test data to demonstrate that the potency, safety, sterility and composition of the vaccine were maintained when Hollister-Stier LLC, Emergent BioSolutions' contract filling facility in Spokane, WA, filled AVA into vials for distribution. Emergent BioSolutions produced three separate lots of vaccine in the renovated facility. These were analyzed to assure consistency of production. The results were submitted to the FDA for approval. After the FDA received Emergent BioSolutions' BLA supplement, a review committee was established consisting of personnel from the following Offices: Vaccines Research & Review (OVRR), Biostatistics & Epidemiology, and Compliance & Biologics Quality. This committee completed an in-depth review of the submission. An integral part of the review included an on-site inspection by the FDA of production activities at both Emergent BioSolutions and Hollister-Stier. The inspectors reviewed hundreds of documents and physically inspected areas and processes associated with the manufacture and vialing of anthrax vaccine. Following these inspections, Emergent BioSolutions was granted approval for the renovations to the AVA manufacturing suite on December 21, 2001. Hollister-Stier was approved as a contract manufacturer for the vialing of AVA on January 31, 2002.

8) Since 1970, how many times has FDA inspected the anthrax vaccine production facility in Lansing?
The FDA or the National Institute of Health (NIH) has inspected MBPI's (Emergent BioSolutions') Lansing facilities more than 50 times since 1969. Each inspection focused on one or more of three manufacturing activities: bacterial vaccines and toxoids, viral vaccines, or plasma derivatives. Examined during each of these inspections were elements common to the manufacturing of all products at the Lansing site, including the manufacture of anthrax vaccine. The anthrax vaccine manufacturing facilities specifically have been inspected 12 times in the years following licensure. Further, the FDA did not force Emergent BioSolutions to close its facility and rebuild. The decision to renovate the anthrax vaccine manufacturing facilities was made in an effort to meet the demand for vaccine from the Department of Defense.

9) Since 1970, has anthrax vaccine been subject to additional FDA evaluation or testing?
Some lots of the anthrax vaccine have been tested and evaluated in accordance with procedures approved by the Food & Drug Administration (FDA) for extending the shelf life of vaccines. The approved procedure used to extend the usable life of the anthrax vaccine is the same procedure

applied to any other vaccine. This was funded under a DoD stability-testing contract.

10) What is required before releasing the anthrax vaccine into interstate commerce?
Each lot of vaccine is approved and released by the Food & Drug Administration, after specific tests for potency, purity, safety, and sterility. General Safety: General safety is determined in the following manner: two animals each of two species (mouse and guinea pig) are given doses of the vaccine and observed for 7 days for adverse effects. Each animal must survive the test period, gain weight, and show no adverse reaction. Three vials per lot will be tested for safety. General safety tests are required for lot release. Other safety studies have been performed that establish that anthrax vaccine adsorbed has a side-effect profile similar to that of other vaccines. Potency: Potency is determined in the following manner: guinea pigs are vaccinated with one of several serial dilutions of vaccine or no vaccine (control group). All guinea pigs are injected with known amounts of virulent anthrax 14 days after vaccination, and average time to death is calculated for each group. The test vaccine must be no less potent than the FDA's reference vaccine. Sterility: Sterility testing is performed on sub-lots and on final product to detect the presence of bacterial contamination. Twenty vials per lot will be tested for sterility. Purity: Requirements exist calibration and controls. Purity testing consists of four individual tests for aluminum, benzethonium chloride, sodium chloride, and formaldehyde. One vial per lot will be tested for purity.

11) Is it unusual for a vaccine to be manufactured by only one company in the United States?
No. About half of FDA-licensed vaccines are produced by only one manufacturer. These include: Japanese encephalitis vaccine, measles vaccine, meningococcal vaccine, mumps vaccine, pneumococcal 7-valent vaccine, pneumococcal 23-valent vaccine, injectable poliovirus vaccine, rubella vaccine, live typhoid vaccine, injectable typhoid vaccine, varicella vaccine, and yellow fever vaccine. Vaccines available from multiple manufacturers include: diphtheria toxoid, tetanus toxoid, pertussis vaccine, Haemophilus influenzae type b (Hib) vaccine, hepatitis A vaccine, hepatitis B vaccine, influenza vaccine, and rabies vaccine.

12) Why was supplemental testing ordered for some lots of the anthrax vaccine by the Department of Defense? What tests are involved?
The Secretary of Defense ordered supplemental testing of all lots of anthrax vaccine in the Lansing stockpile when he authorized the Anthrax Vaccine Immunization Program in December 1997. DoD requested the supplemental testing because of FDA concerns, raised during routine inspections, about the facility's quality control procedures. Supplemental testing repeats the original FDA required tests for sterility, purity, potency, and general safety. Supplemental tests were performed by the manufacturer and overseen by an independent contractor (Mitretek, McLean, Virginia). Supplemental tests are not performed on lots 040 or higher, because these lots underwent the same tests for sterility, purity, potency, and general safety more recently and the data were independently reviewed by the FDA to determine whether the lots meet approval criteria for FDA release. Lot-release tests performed by the manufacturer include: general safety, purity, potency and sterility (see question 8 for a description of each). Supplemental testing reports may be accessed at the AVIP web site.

FDA Inspections

1) FDA Inspections of the Anthrax Vaccine Manufacturing Facility

1. September 9, 1969
2. August 3-4, 1970
3. April 11-12, 1972
4. September 18-19, 1972
33. September 26-27, 1988
34. May 30- June 1, 1989
35. July 10-12, 1989
36. September 12-13, 1990

5. July 24-25, 1973
6. July 26, 1973
7. October 15-16, 1974
8. April 16, 1975
9. October 21, 1975
10. April 5, 1976
11. October 28-29, 1976
12. March 14, 1977
13. April 13-14, 1978
14. May, 3,5,8,10,12,15,1978
15. June 6-8, 1979
16. October 18, 19, 25, 26, Nov 6, 1979
17. April 20, May 1, 1980
18. May 21, 1980
19. March 25, 1981
20. June 28-29, 1982
21. July 11, August 11, 1982
22. October 26-28, 1982
23. May 2-4, 1983
24. September 21-22, 1983
25. June 25-27, 1984
26. August 15-16, 1984
27. July 8-9, 1985
28. November 18-20, 1985
29. August 6-8, 1986
30. June 4-5, 1987
31. August 26-28, 1987
32. April 26-27, 1988
37. September 9-10, 1991
38. June 30- July 1, 1992
39. July 29-31, 1992
40. August 31- September 2, 1992
41. January 14-15, 1993
42. May 4-7, 1993
43. May 31- June 3, 1994
44. July 25-26, 1994
45. April 24- May 5, 1995
46. November 18-27, 1996
47. February 4-20, 1998
48. October 19-23, 1998
49. November 15-23, 1999
50. October 10 - 26, 2000
51. December 11-14, 2001
52. September 4-13, 2002
53. May 11-20, 2004
54. May 9-18, 2006

2) What were the recent FDA actions related to the anthrax vaccine (BioThrax)?
On December 15, 2005, the Food and Drug Administration released a Final Rule and Final Order for anthrax vaccine. After reviewing extensive scientific evidence and carefully considering comments from the public, the FDA determined that anthrax vaccine is safe and effective in preventing anthrax disease regardless of route of exposure, including inhalation anthrax.

The Facts on Squalene

1) Executive Summary
A few people claim the Department of Defense (DoD) added squalene to anthrax vaccine to stretch the vaccine supply. Four civilian panels have looked into these allegations since 1999 and repeatedly found them groundless. Neither DoD nor anybody else added squalene to anthrax vaccine for our troops. DoD does not conduct illegal experiments. Details and links to independent sources of data appear below.

2) What is squalene?
Squalene is a naturally occurring substance found in plants, animals, and humans. Squalene is

manufactured in the liver of every human body and circulates in our bloodstreams. Squalene is present in the oil left by human fingerprints (Asano et al, 2002). Humans cannot live without squalene, because we use squalene as an essential building block to make hormones and other substances in our bodies. Squalene is also found in a variety of foods (for example: eggs, olive oil (0.7%), cookies, yeast, meat), cosmetics (for example: eye makeup, lipstick, baby powder), over-the-counter medications, and health supplements. Squalene in olive oil may contribute to the low cholesterol levels of people who consume Mediterranean-style diets (Smith, 2000). People can purchase squalene at health food stores. It is more commonly known as “shark liver oil.”

3) Does the anthrax vaccine use squalene as an adjuvant?
No, the adjuvant in the anthrax vaccine is aluminum hydroxide. An adjuvant is a substance to improve the body’s immune response to a vaccine (Vogel et al, 1998; Burdin et al, 2004).

4) Does the anthrax vaccine contain squalene?
Maybe. Some lab tests come up positive for squalene. Because of the difficulty of removing squalene-containing fingerprint oils from laboratory glassware, it is hard to know whether the squalene is truly present in some lots of the vaccine or is introduced by the testing process itself. DoD, the Food & Drug Administration (FDA), and several civilian advisory committees agree that squalene at such low levels has no adverse health consequences. In September 2000, DoD became aware of FDA test results finding trace amounts of squalene in three out of three US vaccines tested: tetanus, diphtheria, and anthrax. The level of squalene identified by the FDA test is so minute that it is likely the result of squalene in the oil of a fingerprint not completely cleaned from lab glassware. It is hard to completely remove fingerprint oils from glassware. Before they go looking for squalene, lab workers have to use a chemical solvent such as hexane to completely remove their own fingerprint oils from lab glassware. When lab workers intentionally tested an extract of fingerprint oil, the squalene reading went off the chart. Before the FDA test results became known, Stanford Research International (SRI), under DoD contract, looked for squalene in anthrax vaccine. At the limit of detection of its test, 140 parts per billion, SRI found no squalene in several lots of anthrax vaccine. The FDA’s test, which was developed later, is more sensitive. It is able to detect as little as 10 parts per billion. The FDA found squalene at 10 to 83 parts per billion in diphtheria toxoid, tetanus toxoid, and anthrax vaccine. The trace level of squalene found by the FDA in anthrax vaccine is less than the concentration naturally present in human blood (250 parts per billion) (Miettinen, 1982; Nikkila et al, 1992). After the FDA reported its results, DoD asked SRI to refine its assay. Using an improved method that could detect as little as 1 part per billion, SRI found no squalene in 32 out of 33 lots of anthrax vaccine tested (including lots in which FDA found low levels of squalene). In one lot, they found up to 9 parts per billion. The details appear below.

5) Should we be concerned about the presence of trace quantities of squalene in tetanus, diphtheria, and anthrax vaccines?
No. The trace level of squalene found by the FDA and SRI in diphtheria, tetanus, and anthrax vaccines is well below the concentration naturally present in human blood (250 parts per billion). Injecting trace amounts of squalene are unlikely to have any biological effect, given that it is already present in the body. In fact, without squalene in the body to manufacture hormones and other substances in our bodies, we would die. In Congressional testimony on 3 October 2000, FDA official Mark Elengold said that the trace quantities of squalene detected were “both naturally occurring and safe."

6) Can squalene cause harm?
Some animal research to study arthritis used injections of tuberculosis-like bacteria (mycobacteria) dissolved in squalene (e.g., arthritis-prone rats, mice). Other studies assessed 100% squalene injected into rat tails or injected directly into joints. (Yoshino & Yoshino, 1994; Lorentzen, 1999; Kuroda et al, 2004) The relevance of findings in susceptible animal species to humans is unclear (IOM/Sox, 1999; Kuroda et al, 2004). Based on other research, it is clear that whether squalene causes harm or not is

related to selected conditions of concentration, dose, route of application, and other factors (Benisek et al, 2004).

7) If you wanted to use squalene as an adjuvant, what form would it take?
If you wanted to use squalene as an adjuvant (to boost immune responses) you would have to multiply the amount of squalene found by the FDA about 1 million times, as well as change it from a simple liquid (its natural state) to an emulsion. An emulsion is a stable suspension of tiny droplets, like an oil-and-vinegar mixture that doesn't separate. This double difference is like the difference between a teaspoon of oil and 2,000 pounds of mayonnaise. [If you emulsify oil with eggs, you get mayonnaise.] Squalene in the form of an emulsion (emulsified squalene, such as an adjuvant called MF59) has been added as an adjuvant to some investigational vaccines in the U.S. (Burdin et al., 2004) There is no squalene adjuvant in any US-licensed vaccine. Whatever the arguments for or against squalene as a vaccine adjuvant, the fact is that none of the anthrax vaccine administered to U.S. troops contained squalene as an adjuvant. Based on manufacturing records, FDA can verify that no squalene was added to any vaccine formulation used during the Gulf War. This includes the anthrax vaccine. To date, the FDA has licensed, and US manufacturers have used, only aluminum salts (for example, aluminum hydroxide, aluminum phosphate, aluminum potassium sulfate) as adjuvants.

8) What do we know about the European influenza vaccine that uses MF59 (an adjuvant containing squalene).
In 1997, European health agencies approved emulsified squalene (with influenza virus in the center of each droplet) for use as an adjuvant in an influenza vaccine (Fluad, Chiron Corporation, Marburg, Germany, and Siena, Italy, http://www.forumimpfen.de/impfnavigator/packungsbeilage/5205fluad.pdf; Sesardic & Dobbelaer, 2004). Some clinicians consider influenza vaccine with MF59 adjuvant to be better able to induce immunity in elderly people (Banzhoff et al, 2003). To make this influenza vaccine work, researchers needed a squalene concentration of 1.95% (about 2 parts per hundred or 20 million parts per billion) to boost the immune response. This squalene had to be in the form of an emulsion (a mixture of tiny droplets) to be recognized by the immune system. Squalene in its oily state is naturally present inside the human body. Tens of millions of doses of this European influenza vaccine have been administered safely since 1997.

9) What testing has been done?
Three sets of US tests have been performed: Initial tests by SRI, tests by FDA, and improved tests by SRI. Each is described below.

10) What did SRI find the first time?
To determine whether squalene was present in anthrax vaccine, the DoD contracted with an independent civilian laboratory, Stanford Research Institute (SRI) International of Menlo Park, California www.sri.com, to test for the presence of squalene in anthrax vaccine. SRI developed a laboratory method to detect squalene as dilute as 140 parts per billion (ppb). At this level of detection, extraordinary measures must be taken to avoid contaminating samples, glassware, and equipment with squalene from the skin, because squalene is a natural component of the oils in our skin. The SRI test used a technique called high-pressure liquid chromatography (HPLC) with ultraviolet detection at a wavelength of 203 nanometers. SRI tested 17 lots of anthrax vaccine: FAV008, FAV017, FAV019, FAV020, FAV024, FAV030, FAV031, FAV033, FAV034, FAV036, FAV037, FAV038, FAV041, FAV043, FAV044, FAV047, and FAV048B. SRI reported "based on triplicate analysis, no squalene was detected in the sample. The limit of detection is 70 nanograms per 0.5 milliliter dose (140 ppb)." (Spanggord et al., 2002)

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12) What did the FDA find?
Using a more sensitive test, developed after the initial SRI test, the Food & Drug Administration (FDA) found trace amounts of squalene in three out of three US vaccines tested in Jun 1999: diphtheria toxoid, tetanus toxoid, and anthrax vaccine (http://www.vaccines.mil/documents/library/Squalene1.pdf). The FDA test used a technique called gas chromatography with flame-ionization detection. The FDA method could detect squalene as dilute as 10 parts per billion (ppb). Testing five lots of anthrax vaccine and two lots each of diphtheria and tetanus vaccines, FDA concluded, "there were only trace amounts of squalene in the lots tested." Based on manufacturing records, FDA verified that no squalene was added to any vaccine formulation used during the Gulf War. The amounts of squalene identified in the specific lots were:
Anthrax lot FAV020 11.3 ppb
Anthrax lot FAV030 10.1 ppb
Anthrax lot FAV038 27.1 ppb
Anthrax lot FAV043 40.0 ppb
Anthrax lot FAV047 82.9 ppb
Diphtheria lot 3710 22.5 ppb
Tetanus lot 7271 28.7 ppb
Squalene is constantly present in the human blood stream at 250 ppb (250 nanograms per milliliter), a concentration 3 to 25 times higher than the level detected in the FDA test. The amount of squalene added as an adjuvant to a European-approved influenza vaccine is 4 grams per 100 ml (4 parts per hundred), which is about 1,000,000 times more than the concentration of squalene detected in the FDA test. This European influenza vaccine has been administered safely to hundreds of thousands of people.

13) What did SRI find after it revised its test procedures?
After the FDA released its findings in September 2000, SRI revised its squalene test, lowering its limit of detection of 1 ppb or 0.5 nanograms per 0.5 ml. With this more sensitive test, SRI found no squalene in 32 out of 33 lots tested. SRI found squalene in each of three vials of lot FAV008, at 1, 7, and 9 ppb. SRI found no squalene in lots 12, 13, 18, FAV001, FAV002, FAV003, FAV004, FAV005, FAV006, FAV007, FAV009, FAV012, FAV016, FAV017, FAV018, FAV019, FAV020, FAV022, FAV024, FAV030, FAV031, FAV032, FAV033, FAV034, FAV036, FAV037, FAV038, FAV041, FAV043, FAV044, FAV047, and FAV048B. SRI also tested some non-vaccine injectable pharmaceuticals. SRI found no squalene in human insulin regular U-100, human insulin isophane (NPH) U-100, lidocaine 2% solution, sodium chloride 0.9% solution, or potassium chloride 2 mEq/ml solution.

14) Did DoD mislead or lie to anybody about the squalene tests conducted by SRI?
No. DoD truthfully and fully reported its findings at each step since May 1999, when SRI first developed its squalene test. DoD did not know of FDA's findings until they were publicly released. At the initial limit

of detection of its test, 140 parts per billion, SRI found no squalene in anthrax vaccine (Spanggord et al., 2002). It was scientifically proper to say ‘no squalene was found to the limit of detection of the assay,’ which DoD officials sometimes oversimplified to say ‘there is no squalene present.’

15) Has anyone, anywhere found squalene added as an adjuvant to any US-licensed vaccine?
No

16) Where did the squalene FDA found in its anthrax vaccine tests come from?
The most likely source of the trace squalene in the FDA tests is the result of squalene in the oil of a fingerprint not cleaned from lab glassware. Squalene is not added to anthrax vaccine or any US-licensed vaccine. It is hard to completely remove fingerprint oils from glassware. Lab workers have to use a chemical solvent such as hexane to completely remove fingerprint oils from lab glassware.

17) What did 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) http://veterans.senate.gov/Reports/chapt3.pdf (chapter 3, page 23 of 55) 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 certain 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.

18) Did the British government test its anthrax vaccine for squalene?
Yes, The United Kingdom’s Ministry of Defence arranged for an independent laboratory to test 11 lots of the British anthrax vaccine manufactured at Porton Down, as well as other vaccines. No squalene was detected in those lots of vaccine, with a limit of detection of 0.1 microgram/ml (100 parts per billion).

19) What are the claims about anti-squalene antibodies?
In an effort to explain the health problems of some Gulf War veterans, a few people have theorized that a vaccine adjuvant may have caused an autoimmune disease in veterans. A Vanity Fair article by Gary Matsumoto, "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, its magazine Insight on the News, and the (Wilmington) Delaware News Journal, have made similar allegations regarding “secret medical experiments” and the like. Investigators cited in these articles (Pamela Asa, Ph.D., Memphis, TN, and Robert Garry, Ph.D., Tulane University School of Medicine, New Orleans, LA) report they developed in 1997 and patented a test for anti-squalene antibodies (ASA). Autoimmune Technologies, LLC, of New Orleans, has an exclusive license on the use of this test. The investigators report that they detected anti-squalene antibodies in the blood of ill Gulf War veterans. Their methods were published in the February 2000 and August 2002 issues of the journal Experimental and Molecular Pathology. In the February 2000 article, the authors themselves conclude: "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." Asa and colleagues published a second article in the August 2002 issue of Experimental and Molecular Pathology, but it also provides no validation of the original assay. As a result, the findings of the second article are also in question. The authors' comment that the Matyas article of Nov 2000 supports their findings is mistaken.

20) Have any independent panels evaluated the claims of researchers to find anti-squalene

antibodies in the blood of ill Gulf War veterans?
Yes, four independent civilian panels considered the February 2000 article by Asa and colleagues and other allegations related to squalene and anti-squalene antibodies. When the Institute of Medicine (part of the National Academy of Sciences) Committee on Gulf War and Health (the "Sox committee") evaluated the 2000 Asa claims of anti-squalene antibodies in the blood of ill Gulf War veterans, it concluded that the paper contains shortcomings, some serious, that combine to invalidate the authors' conclusions. The report says: "The committee does not regard this study as providing evidence that the investigators have successfully measured antibodies to squalene." See http://www.nap.edu/books/030907178X/html, pages 311-312. The civilian experts on the Armed Forces Epidemiological Board (AFEB) said in July 2000, "the research reported in this paper does not support this claim; … it remains unclear if the assay actually measures antibodies to squalene, as the authors assert…" http://www.ha.osd.mil/afeb/reports/squalene.pdf Regarding assertations that Service Members who received anthrax vaccination from the five lots cited in the FDA squalene tests experienced more or more severe adverse events after vaccination, the civilian physicians on the Anthrax Vaccine Expert Committee (AVEC) evaluated adverse events by lot and geographic location. They found no meaningful differences based on lot or on geographic location. (Sever et al. 2002 http://www.vaccines.mil/documents/library/AVEC_ms.pdf, especially pages 198-200, and Sever et al, 2004 http://www.vaccines.mil/documents/library/SeverArticle.pdf, especially pages 13-15) Of note, the five lots cited in the FDA squalene tests were shipped to multiple DoD installations. In addition, Dover AFB received lots other than the five lots mentioned above. After the comprehensive review of anthrax vaccine safety by the National Academy of Sciences (the "Strom committee," March 2002, www.nap.edu/catalog/10310.html), which included hearing from personnel from Dover AFB and elsewhere concerned that they suffered adverse events after anthrax vaccination, the civilian physicians and scientists concluded that "The [SRI] study report, dated August 14, 2001, found that 1 lot of over 30 lots tested contained measurable levels of squalene. Three samples from that lot [FAV008] contained squalene at 7, 9, and approximately 1 parts per billion, respectively. Use of vaccine from that lot has not been associated with elevated rates of adverse events. … Because the available data ... demonstrate that the presence of trace amounts of squalene is not associated with an increase in the rates of adverse events following vaccination with AVA, the committee concludes that further investigation of possible AVA contamination is not warranted at this time."

21) Are these panels really independent?
The IOM committee members were selected by the National Academy of Sciences to be fully independent of both the Department of Defense and the Department of Veterans Affairs. The AVEC committee members were selected by the Department of Health & Human Services to be fully independent of the Department of Defense. The DHB is appointed by the Secretary of the Army to advise the Surgeons General of the military Services. These civilians constitute a highly accomplished and widely respected scientific advisory board. These civilians are free to render whatever opinions they wish, and their candidness is important to ensuring that DoD is using the best possible medical information.

22) What did the GAO say about squalene testing and what are DoD researchers doing?
In March 1999, the U.S. General Accounting Office (GAO, now the Government Accountability Office) 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." The proper first step is to show that the test for squalene antibodies measures what it 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. To investigate the anti-squalene antibody theory, 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 competitively 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.

23) What did the competitively funded research project find regarding squalene antibodies?
In April 2000, the research project published its first peer-reviewed report, describing an enzyme-linked immunosorbent assay (ELISA) that could detect antibodies to squalene induced in mice. Use of squalene alone did not produce a significant amount of anti-squalene antibodies. A special chemical was needed to induce the antibodies against squalene in mice. After injecting mice with liposomes (fat globules) containing 71% squalene (710 million parts per billion), plus a second chemical called lipid A, antibodies to squalene were readily induced in mice. The validity of the method was established using positive and negative controls to preclude false positive and false-negative test results. The investigators concluded that squalene is a weak antigen (a weak inducer of antibodies). (Matyas et al., 2000).

By September 2001, researchers reported improving the assay and ensuring these tests were reproducible and sensitive enough to detect 80 ng/ml of anti-squalene antibody. The test was also reproducible from experiment to experiment (Matyas et al., 2001). The third study from this research effort, published in 2004, adapts the test described above so that it could detect anti-squalene antibodies if present in human serum. Serum from three groups of people were tested: retired employees of the U.S. Army Medical Research Institute of Infectious Diseases (average 68 years of age, 88% of whom received anthrax vaccine, mean = 26 doses per person) , civilian volunteers of similar age from Frederick, Maryland (none of whom received anthrax vaccine), and random blood donors from Fort Knox, Kentucky (vaccination status unknown), This next study indicates that anti-squalene antibodies are found in 7.5% of the vaccinated USAMRIID alumni, 15% of the unvaccinated Frederick civilians, and in 0% of the Fort Knox blood donors. The antibodies described in the previous sentence were a type of antibody called IgG. Researchers found another type of anti-squalene antibody called IgM in all three groups (37%, 32%, and 19%). The researchers found that anti-squalene antibodies are more common with increasing age (a characteristic also found in mice). The presence of anti-squalene antibodies was unrelated to anthrax vaccination status. They concluded that anti-squalene antibodies occur naturally in humans (Matyas et al., 2004).

24) Has DoD ever tested squalene-adjuvanted vaccines in humans against any disease?
Yes. The DoD conducted several human clinical trials exploring the value of investigational vaccines containing squalene-based adjuvants to prevent malaria and HIV infection. The squalene-containing adjuvants principally involved products known as MF59 (licensed from Chiron Corporation) and AS02A (licensed from GlaxoSmithKline). Each of these studies involved an FDAapproved scientific plan in human volunteers told the contents of the vaccine. Malaria: Hoffman et al, 1994; Epstein et al, 2004; Wang et al, 2004. HIV: Nitayaphan et al, 2000; Pitisuttithum et al, 2003. The Department of Defense (DoD) has never exposed any military member or civilian to any squalene-adjuvanted investigational

product without the person's informed consent, abiding by FDA regulations. Civilian researchers, including some funded by the National Institutes of Health, have conducted clinical trials of these and other squalene-adjuvanted vaccines on human volunteers, ranging from infants to the elderly.

25) Could squalene concerns have anything to do with various reported clusters of illnesses among people given anthrax vaccine?
A panel of civilian physicians selected by the Department of Health & Human Services reviewed all reports of adverse events after anthrax vaccination from 1998 to 2001 (Sever et al, 2002; Sever et al, 2004). This panel was known as the Anthrax Vaccine Expert Committee (AVEC).

To evaluate assertations that Service Members who received anthrax vaccination from the five lots cited in the FDA squalene tests experienced more or more severe adverse events after vaccination, these civilian physicians evaluated adverse events by lot and geographic location. They found no meaningful differences based on lot or on geographic location. Of note, the five lots cited in the FDA squalene tests were shipped to multiple DoD installations. In addition, Dover AFB received lots seven lots other than the five test-positive lots mentioned above.

26) Bottom line, is there any reason for alarm here?
No. Squalene is not added to any US-licensed vaccine, including anthrax vaccine. The background level of squalene found by the FDA is less than the concentration normally present in human blood. The FDA confirms that these trace levels are "naturally occurring and safe." Improved tests found no squalene in the lots where FDA found it. Nonetheless, DoD continues to compile additional knowledge about squalene and anti-squalene antibodies.

Biological Warfare Issues

Joint Program Office for Biological Defense

1) What mechanism exists to ensure supply of the anthrax vaccine for a complete series of shots for all personnel?
The Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) - http://www.jpeocbd.osd.mil is responsible to the Secretary of Defense for maintaining an adequate stockpile of biological warfare defensive vaccines and defined production capabilities, as determined by the Joint Staff and Services' demands. The JPEO-CBD has developed an anthrax vaccine production model to use as a tool to balance the total annual requirement for production with vaccination and inventory requirements to support total force vaccination.

Emergent BioSolutions recently received full FDA approval for the newly renovated manufacturing suite and its contract filler, Hollister-Stier LLC this will ensure production of the anthrax vaccine. To be used by DoD, each vial of anthrax vaccine must meet all FDA requirements. Additionally, a stockpile exists that could be used in an emergency situation.

2) Is biological agent detection a part of the JPEO-CBD mission?
Yes. Please see the JPEO-CBD website for more information (http://www.jpeocbd.osd.mil/).

3) Is the AVAPP part of the Joint Vaccine Acquisition Program (JVAP)?
Yes, the AVAPP is part of the JVAP, a component of the Chemical and Biological Medical Systems management office, Frederick, Maryland. The JVAP manages the production of licensed vaccines and the advanced development, testing and licensing of vaccines and therapeutic blood products against other biological warfare agents. There are several bio-defense products in development by the JVAP.

For more information on the JVAP go to http://www.jpeocbd.osd.mil/

4) What is the mission of the Anthrax Vaccine Adsorbed Production Program, Joint Program Executive Office for Chemical-Biological Defense (JPEO-CBD)?
The mission of the Anthrax Vaccine Adsorbed Production Program (AVAPP) is to provide an assured supply of Food and Drug Administration (FDA) licensed Anthrax Vaccine Adsorbed (AVA), BioThrax™, to meet the requirements of the Department of Defense's Anthrax Vaccine Immunization Program (AVIP). The AVAPP provides technical, managerial, financial, scientific, regulatory, program management and quality oversight of the production of AVA and serves as a liaison between the AVIP and the manufacturer, Emergent BioSolutions. This mission is accomplished by both an on-site presence at the manufacturing site and a program management office.

Myths and Facts

Myths and Facts About Anthrax Vaccine

1) What are some of the common myths and facts about the anthrax vaccine?
MYTH: Anthrax vaccine is dangerous and can cause death.
FACT: Anthrax vaccine is as safe as any other vaccine. Like any vaccine, death can occur after vaccination, but so few deaths can plausibly be associated to a specific vaccine or event that it is hard to evaluate the risk. For any vaccine, any death reported to the Vaccine Adverse Event Reporting System (VAERS) is thoroughly examined to ensure that it is not a new vaccine related problem. The Department of Defense, Food and Drug Administration, Centers for Disease Control and Prevention, and an independent panel of civilian physicians review reports of death or serious illness 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. "

MYTH: Anthrax vaccine causes terrible side effects.
FACT: Based on over 30 years of anthrax vaccine use, we know that severe, but temporary, injection site reactions can occur. It is known that from 30 to 60 percent of people who receive anthrax vaccine will develop an injection site reaction (less than one inch). About 1 in 100 develops a reaction five inches in diameter or larger. The rate of side effects away from the injection site is about the same as other vaccines: from 5 to 35 percent, with these events going away within a few days. The National Academy of Sciences' Institute of Medicine reported in March 2002, "Local events, especially redness, swelling, or nodules at the injection site, are associated with receipt of AVA [U.S. anthrax vaccine], are similar to the events observed following receipt of other vaccines currently in use by adults, and are fairly common" and "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."

MYTH: Women have long-term side effects from anthrax vaccine more than men.
FACT: Women experience more small injection site 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.

MYTH: Antibiotics are more effective than anthrax vaccine.
FACT: There is no better around-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 dire. This is not a risk DoD can afford to take. DoD will therefore vaccinate ahead of time for the best protection.

MYTH: Anthrax vaccine only protects against cutaneous anthrax.
FACT: While no vaccine is 100% effective, this vaccine will greatly reduce 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." FDA Agrees.

MYTH: Anthrax vaccine won't protect against all strains of anthrax.
FACT: Every disease-causing strain of Bacillus anthracis produces the same protein that is required to cause disease. The vaccine induces the production of antibodies that neutralizes 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."

MYTH: Some lots of anthrax vaccine cause more problems than other lots.
FACT: 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 (FDA). The Department of Defense uses only vaccine lots that the FDA released as meeting all applicable standards.

MYTH: The anthrax vaccine is based on old technology.
FACT: Anthrax vaccine was invented using mid-century technology that also led to highly successful vaccines against tetanus, diphtheria, and other infectious diseases. Today's manufacturing process for anthrax vaccine by Emergent BioSolutions meets all current Food and Drug Administration (FDA) production standards.

MYTH: The Department of Defense added squalene, oil naturally produced in the human body, to the vaccine in 1990-91 to stretch the supply.
FACT: No one added squalene to anthrax vaccine. 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 processing during FDA tests (squalene is present in the oil in fingerprints). The FDA called the squalene in vaccines "naturally occurring and safe."

MYTH: The Food and Drug Administration revoked the license of Emergent BioSolutions, the Department of Defense's vaccine supplier, because of manufacturing problems.
FACT: Emergent BioSolutions' predecessor, the Michigan Biological Products Institute (MBPI), owned by 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 licenses issued to MBPI. MBPI 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. Emergent BioSolutions submitted a highly detailed set of quality control documents to FDA in fall 2001. FDA approved

Emergent BioSolutions' facilities and processes, as they relate to the manufacture of anthrax vaccine, on January 31, 2002.

MYTH: The Centers for Disease Control and Prevention use of anthrax vaccine for Congressional staff and U.S. Postal Service workers was "experimental" and "investigational," requiring informed consent, so the Department of Defense's use of anthrax vaccine requires consent from Service members as well.
FACT: The Department of Defense's use of anthrax vaccine in the Anthrax Vaccine Immunization Program for pre-exposure prevention using six doses over eighteen 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 prophylaxis" in three doses. This is not a Food and Drug Administration-licensed use of the vaccine, therefore, in that case (post-exposure), the vaccine was administered under an "investigational new drug" protocol, with informed consent.

MYTH: The anthrax vaccine can cause miscarriages.
FACT: There is no study to support this claim. Consistent with the national standard and the Centers for Disease Control and Prevention recommendation, the Department of Defense policy does not vaccinate pregnant woman. Women who receive the vaccine get pregnant and deliver children at the same rates as unvaccinated women.