ANTHRAX VACCINATION IMMUNIZATION PROGRAM

Proven Protection Against a Documented Threat

STATEMENT BY

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INTRODUCTION

Chairman Warner and Distinguished Committee Members, I am honored to appear before your Committee today to address your questions on the Department of Defense (DOD) Anthrax Vaccine Immunization Program (AVIP). I am Rudy deLeon, Deputy Secretary of Defense. I am accompanied by the Honorable David Oliver, Principal Deputy Under Secretary of Defense, Acquisition and Technology, Lieutenant General Ronald R. Blanck, Surgeon General of the Army, and Major General Randy L. West, Special Advisor for Biological Defense, Office of the Secretary of Defense. At your request, our testimony will specifically address the anthrax threat, the safety and efficacy of the anthrax vaccine, an update on the immunization program and program reports on the procurement of new vaccine.

THE THREAT

General - Currently, about a dozen nation states are known to possess, or have in development, a biological warfare capability. The is also evidence that a small number of terrorist groups appear to be interested in biological agents. The production of biological warfare agents does not require specialized equipment or advanced technology. When comparing equal amounts of biological and chemical warfare agents, the biological agent is far more potent. Small quantities of biological agents can produce large numbers of casualties. Biological agents can be delivered through a number of means including aerial bombs, artillery shells, long-range missiles, agricultural sprayers, and spray tanks carried by aircraft, ships, boats or even automobile. Many of the materials and equipment that are used to produce biological warfare agents are available from legitimate sources and intended for other uses such as pharmaceuticals or biopesticides. This makes it difficult to limit the spread of biological warfare technologies and capabilities.

Anthrax Itself - Anthrax is an infectious disease caused by the bacterium *Bacillus anthracis* and is spread by contact with infected animals, handling infected products, eating infected meat, or inhaling weapon-dispersed anthrax spores. Of all known biological warfare agents, anthrax spores are the top choice in biological weapons for "germ warfare." Several of the countries that have or are developing offensive biological warfare capabilities are most likely working with anthrax. Iraq has admitted to producing and weaponizing anthrax. The anthrax accident at Sverdlovsk in 1979 illustrated Russia's military research with the organism.

Anthrax Facts - Compared to many other pathogens with BW potential, anthrax cultures are relatively easy to obtain. Large quantities of the bacterium can be produced in readily obtainable fermentation vessels. The organism can convert to a spore form that can be stored as bulk agent or in filled munitions. When disseminated in air, the spores remain viable much longer than other types of infectious agents. The size of the spores (approximately 1-micrometer) is such that when inhaled, they tend to be retained in the lung. The effects are usually lethal unless rapid diagnosis is made and a combination of appropriate medical measures is administered immediately. One deep breath can inhale enough spores to result in fatality. Initial symptoms can begin as early as 1 to 3 days after exposure and mimic a common cold or the flu. For the vast majority of inhalation anthrax victims, it is too late for help, once symptoms occur. Post-exposure vaccination or antibiotic treatment for these victims will not likely be effective. The vaccination must be administered prior to symptom onset, in order to be effective.

Anthrax is a deadly and stealth disease that is colorless, odorless, and tasteless, making it very difficult to detect. And, if detection does not occur, there may not be enough time to warn, prepare or diagnose so that effective medical treatment can be administered. If untreated, death is almost certain and, depending on the exposure, can occur within 1 to 5 days after symptoms first

begin. Lethality approaches 100% for unvaccinated persons who are contaminated and do not receive antibiotics, before symptoms appear.

Anthrax is considered an effective biological weapon because:

- Spores can be produced in large quantities using basic knowledge of biology.
- Spores can be stored for years without losing viability.
- Spores can be easily spread in the air by missiles, rockets, artillery, aerial bombs & sprayers.

SAFETY AND EFFICACY

The Department is using a vaccine that is proven both safe and effective for individuals at risk of exposure to anthrax spores. The anthrax vaccine has been licensed since 1970 and utilized for decades. It has proven to be a safe vaccine. The vaccine was also re-assessed in the 1980s when responsibility for biological medicine transferred from the National Institutes of Health's Division of Biological Standards to the FDA. Other independent civilian review panels have also recognized the value of anthrax vaccine, including the Armed Forces Epidemiological Board. Twenty-nine plus years of usage and a decade of increased scrutiny confirms the vaccine's safety and has increased our confidence in its efficacy.

Coordinated Surveillance for Anthrax Vaccine Safety - The Department of Defense conducts an aggressive, multi-faceted surveillance program to assess vaccine safety. In fact, the safeguards for vaccine administered to DOD personnel meet or exceed every standard for vaccine administration to the civilian population. Our program includes a wide variety of activities that can be grouped into three main scientific method categories: clinical studies of vaccine recipients; database analysis of vaccine recipient automated medical records; and spontaneous reports.

DOD distinguishes between adverse events adverse reactions. Adverse events are adverse outcomes, for which a cause-and-effect relationship with an exposure (to a medication or vaccine) has not yet objectively been determined. An ***adverse event*** becomes an ***adverse reaction*** once objective evidence is available to establish a cause-and-effect link between an exposure and an adverse outcome. Table A lists some of the criteria proposed many years ago by famed epidemiologist Sir Austin Bradford Hill that help us make the determination of causal association.

Table A: Causal Association Criteria

1. How strong is the association between the exposure and the outcome?
2. What is the quality of the evidence for an association?
3. Is there a dose-response relationship?
4. Is there consistency among several studies?
5. Is there a specific cause for the effect observed?
6. Did the cause exist before the effect occurred?
7. Is the outcome plausible, given what we know about biology?

Adapted from: Rothman KJ, Greenland S. Modern Epidemiology, 2nd ed. Philadelphia: Lippincott-Raven, 1998:24-28.

The CDC publication, *Epidemiology and Prevention of Vaccine-Preventable Disease*, 6th ed., January, 2000, discusses the most reliable and conclusive ways to establish causal relationships for vaccine adverse events — and they are relatively few. Causal links between a vaccine and an adverse event may be established if they produce a unique laboratory result, a unique clinical syndrome, or if an epidemiological study shows vaccinated persons are more likely than unvaccinated persons to experience the adverse event. Numerous clinical studies have been conducted on the safety of the anthrax vaccine. Among them are twelve clinical studies using more than 16,000 vaccine recipients. The known adverse events from anthrax vaccine as demonstrated by these and other studies include local injection site reactions, headache, slight fever, joint pain, and fatigue.

Additional Long -Term Study – While the DOD leadership, its physicians and its research experts are confident of the safety and efficacy of the anthrax vaccine, they are aware of and respect the concerns expressed by a small number of service members about possible long-term health effects. The Department wants to address these concerns using the best, most appropriate scientific knowledge and practices. We will continue demonstrating an ongoing commitment to ensuring the health of our men and women as we implement the AVIP.

To that end, the Anthrax Vaccine Immunization Program Agency convened a team of civilian and military medical experts to design a set of studies to assess the long-term safety of the anthrax vaccine, in response to requests from Service Members, their families and recommendations of the General Accounting Office. In designing these studies, we have drawn from the accumulated experience of some of the nation's best vaccine researchers at CDC and FDA.

A new long term study is also underway to determine whether individuals who received multiple vaccines, including the anthrax vaccine, during their past employment at Ft. Detrick, MD demonstrated any adverse health effects over the long term. A total of 570 study and control volunteers have been enrolled in this case-controlled study that began in 1996. All volunteers signed an approved informed consent document. The study media included 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 Gulf War Illness complex of symptoms), diseases, abnormal laboratory and urine tests. Study subjects will be compared to 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.

We have also initiated a $20 million multi-year research study, under the auspices of the CDC, with the collaboration from the Department of Defense, the Food and Drug Administration, and the National Institutes of Health. This four-objective comprehensive effort will examine risk factors for adverse events, including gender reaction differences, alternate routes of administration, reduced dosage schedule, and immunogenicity build-up and retention. In addition, we are looking at instituting a network for improving the quality of vaccine heath care delivery in the DoD.

Member Concerns- The Department strongly encourages all members who have received the vaccine and feel they have had a negative reaction to report it through the Vaccine Adverse Event Reporting System (VAERS). Not only are members encouraged to submit a report but families or anyone personally aware of a situation can as well. We listen. We are concerned. This has included listening to many members on a one-to-one basis. Members of my staff have personally met with dozens of service members who have voiced concern for the reactions the members believe they have experienced, and talked to or corresponded with many, many more.

Education & Communication – When we spoke to the members on a one-on-one basis we realized that improvements in the program were needed and we have begun them. We want this program to be the best it can be. To do this we have initiated the research I mentioned earlier and have published polices for both administrative and medical exemption. Now, personnel with 180 days or less left before separating from the service, may elect to not receive the vaccine. In addition, there is a written medical waiver policy for personnel who have experienced what could be adverse reactions. While waivers have always been available, they have been reiterated in the waiver policy. The Department is also

committed to fully educating our Service Member population and their families on the purpose and value of anthrax vaccination in an unprecedented manner. We use each of the following communications media to accomplish this goal:

◆ A sophisticated anthrax specific website www.anthrax.osd.mil with multiple layers of information and methods for communicating with our Service Member population, their families, and other DOD beneficiaries and concerned members of the American public.

◆ Three Service - specific anthrax websites hyper-linked to all known military and civilian websites discussing anthrax, biological weapons, health care, domestic preparedness, terrorism, VAERS reporting, preventive medicine, infectious disease, etc.

◆ Quad-fold information sheets individually tailored for Service Members, Family Members and Civilians. DOD has provided each Service Member receiving the vaccine with printed silent training aides since administering the first doses in March 1998. The current quad-fold brochure explains the threat of biological weapons, the benefits of anthrax vaccination and the known risks from the vaccine. The Quad-fold also includes information aimed specifically at Reserve Component personnel accessing care.

◆ DOD Leaders Briefing required to be given to all Service Members prior to receiving the anthrax immunization. Distributed by each Service and prominently posted on the www.anthrax.osd.mil website.

◆ DOD Health Care Providers Briefing given to all DOD health care providers administering the anthrax vaccine — who then serve as teachers, coaches, mentors for supervisors, commanders, Service Members and their families. Distributed by each Service and prominently posted on the www.anthrax.osd.mil website.

◆ Open House/Speakers Bureau briefings and open educational forums for all Service Members and their families.

◆ A 1.877.GETVACC telephone hotline.

◆ A variety of anthrax vaccine ‘silent training aids’. These highly visible training aids emphasize the key themes of the anthrax threat, safety and efficacy of the vaccine, adverse event reporting, etc.

◆ Armed Forces Information Service news media, local installation print, radio and television news service initiatives.

◆ A state-of-the-art Anthrax Education CD-ROM is in development and it will provide Service Members, their families, supervisors, commanders and health care providers with tailored, multimedia information on the anthrax threat, safety and efficacy of the vaccine, signs, symptoms and prevention of the anthrax disease.

◆ An Anthrax Vaccine Immunization Program Videotape explaining the threat, safety, efficacy of the vaccine. The video features prominent civilian and Government scientists and vaccine experts explaining and endorsing the vaccine.

◆ DOD is currently collaborating with CDC to array this information in the format of a Vaccine Information Statements (VISs) the standard vaccine information format that civilian health care providers around the country give America’s children, adolescents, and adults during routine vaccinations (e.g. measles, polio, tetanus).

◆ Clinical Practice Guidelines for Management of Adverse Events After Any Vaccination that are based on a consensus panel of civilian and military physicians experienced both in immunology and the general provision of health care.

Our anthrax vaccine program is one of the most studied, reviewed and examined programs in the Defense Department. The most current are reviews by the General Accounting Office and the Inspector General. We are aware of the issues raised in these studies and are taking steps to address them. There is concern for the stockpile and we, as a Department, are addressing the issue objectively with interim requirement dosage supply contingency plans being developed. We are also aware of the financial condition of the anthrax vaccine manufacturer BioPort Corporation. The company, and its management, have improved over the past quarter and seem determined to continue in that direction.

Another issue is FDA licensing. The need for FDA approval of BioPort's Supplemental Biologics Application License (BLA) is also an area of media and opponent attention. We expect BioPort to achieve FDA approval of the BLA Supplement for assured production of the vaccine this calendar year. Continuing the program uninterrupted until FDA approves the BLA supplement requires FDA release approval of additional lots previously manufactured by Michigan Biologic Products Institute (MBPI). BioPort has submitted information on several lots and we are optimistic sufficient amounts will be released to continue Phase I uninterrupted.

PROCUREMENT AND PROGRAM

Anthrax Vaccine Adsorbed is produced by the BioPort Corporation of Lansing, Michigan, which is the only FDA licensed establishment for the Anthrax Vaccine Adsorbed. BioPort's facility has been licensed to manufacture the anthrax vaccine since 1970.

In the fall of 1998, BioPort became the sole licensed producer of the anthrax vaccine via a privatization process initiated by the State of Michigan. In September 1998, BioPort was awarded a contract for production of the anthrax vaccine. In August 1999, DOD renegotiated the contract and provided extraordinary contractual relief under authority of PL 85-804.

This action was necessary to preserve the company's financial viability and ensure uninterrupted production of the anthrax vaccine. The necessity to renegotiate BioPort's contract resulted from poor accounting of production costs prior to privatization and a lack of adequate resources. Even though, during state ownership the Michigan taxpayers subsidized the Defense Department's procurement of Anthrax vaccine, BioPort discovered that more work was required to bring the facility up to the state of the art, and that, the vaccine cost more to produce than anticipated. The Defense Contract Audit Agency verified the need for the extraordinary contractual relief and a recent DOD IG report validated that it had been done in accordance with Federal Acquisition Regulations. The Department of Defense continues to work with BioPort, the only FDA licensed manufacturer of the anthrax vaccine, to ensure the viability of the facility with the production capability to provide a sufficient supply of the vaccine to meet Department of Defense requirements. If BioPort enters into bankruptcy, the immunization program to protect the U.S. service members is at risk and our warfighters will be vulnerable to the extremely lethal and present danger of anthrax exposure resulting from biowarfare or bioterrorism.

SUMMARY

Our Service men and women in at least two major theaters go to work everyday in areas where bioweapons could be delivered at any time. There is a limited availability of Bio-detectors and sensitivity is a concern. Protective clothing and equipment are available, but they cannot be comfortably used for long periods of time. Antibiotics are available, but must be used in the first few hours of exposure, before initial symptoms appear. Those same service personnel would also be incapacitated with severe diarrhea for a period of time. The superior form of protection is vaccination.

Our personnel deserve our best and fullest protection. The FDA licenses the current vaccine for that full protection with the complete six-shot regimen. We cannot wait until the balloon goes up to begin the vaccination. Being vaccinated may very well save the life of thousands of America's men and women in uniform, should some state or terrorist organization elect to employ what we know they are already capable of using. It would be a dereliction of duty to have the anthrax vaccine capability we presently have and not make it part of the arsenal of protection that we provide to our servicemen and women. We hope anthrax is never used as a weapon, but if it is, we must be ready!