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THE DEPARTMENT OF DEFENSE ANTHRAX VACCINE IMMUNIZATION PROGRAM: UNPROVEN FORCE PROTECTION

FOURTH REPORT

BY THE

COMMITTEE ON GOVERNMENT REFORM

together with

DISSENTING AND SUPPLEMENTAL VIEWS

Available via the World Wide Web: http://www.house.gov/reform
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APRIL 3, 2000.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

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LETTER OF TRANSMITTAL

HOUSE OF REPRESENTATIVES,
Washington, DC, April 3, 2000.

Hon. J. DENNIS HASTERT,
Speaker of the House of Representatives,
Washington, DC.

DEAR MR. SPEAKER: By direction of the Committee on Government Reform, I submit herewith the committee's fourth report to the 106th Congress. The committee's report is based on a study conducted by its Subcommittee on National Security, Veterans Affairs, and International Relations.

DAN BURTON,
Chairman.

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Union Calendar No. 304

106TH CONGRESS, *2d Session* } HOUSE OF REPRESENTATIVES { REPORT 106–556

THE DEPARTMENT OF DEFENSE ANTHRAX VACCINE IMMUNIZATION PROGRAM: UNPROVEN FORCE PROTECTION

APRIL 3, 2000.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

Mr. BURTON, from the Committee on Government Reform submitted the following

FOURTH REPORT

On March 9, 2000, the Committee on Government Reform approved and adopted a report entitled, "The Department of Defense Anthrax Vaccine Immunization Program: Unproven Force Protection." The chairman was directed to transmit a copy to the Speaker of the House.

I. SUMMARY

Responding to service members' complaints of program insensitivity to adverse health effects, inadequate medical record-keeping, and heavy-handed program operation, the Subcommittee on National Security, Veterans Affairs, and International Relations initiated an oversight investigation into the design and implementation of the Department of Defense [DOD] force-wide, mandatory Anthrax Vaccine Immunization Program [AVIP]. Because the anthrax vaccine is still being studied as a potential causative or contributing factor in Gulf war veterans' illnesses,[1] the subcommittee measured the program against this standard: Any expanded use of the same vaccine should be undertaken only with the greatest care and only to the extent necessary.

As currently designed and implemented, the anthrax vaccine program fails on both counts. The AVIP lacks a consistent standard of care and is designed to reach far beyond those at risk.

[1] Public Law 105–277, title XVI, sec. 1603(d).

Based on the testimonial and documentary record,[2] the subcommittee finds the AVIP a well-intentioned but overwrought response to the threat of anthrax as a biological weapon. Against the so-called "asymmetric" threats to U.S. conventional military superiority posed by a growing range of chemical and biological weapons, the anthrax vaccine program represents a medical maginot line, a fixed fortification protecting against attack from only one direction.

UNREALISTIC PROGRAM

As a mandatory, force-wide countermeasure to the real threat of weaponized anthrax on the battlefield, the vaccine effort is unrealistic. It expands and distorts the use of invasive, dated medical technology to address perceived weaknesses in detection technology and external physical protection against biological attack. Born of a post-Gulf war panic over apparent weaknesses in chemical and biological [CB] warfare defenses, the AVIP is an unmanageably broad military undertaking built on a dangerously narrow scientific and medical foundation.

At best, the vaccine provides some measure of protection to most who receive it. Just how much protection is acquired, by whom, for how long, and against what level of challenge are questions DOD answers with an excess of faith but a paucity of science.

Many members of the armed forces do not share that faith. They do not believe merely suggestive evidence of vaccine efficacy outweighs their concerns over the lack of evidence of long term vaccine safety. Nor do they trust DOD has learned the lessons of past military medical mistakes: atomic testing, Agent Orange, Persian Gulf war drugs, and vaccines. Heavy handed, one-sided informational materials only fuel suspicions the program understates adverse reaction risks in order to magnify the relative, admittedly marginal, benefits of the vaccine.

As a military operation, the AVIP rests on weak conceptual and logistical footing. It suffers from poor planning, inflexible execution, and over-extended supply lines. As a health care effort, the AVIP compromises the practice of medicine to achieve military objectives.

The decision to use the 1950's era vaccine, which requires an elaborate inoculation regime of six shots over 18 months, presents daunting, perhaps insurmountable, logistical challenges to reach a force of 2.4 million active duty and reserve component members. Research to support a shorter, more manageable inoculation regimen was not completed before the AVIP was launched. Development of a purer, potentially less reactogenic anthrax vaccine using recombinant technologies was not pursued aggressively.

UNSTABLE SUPPLY

The sole-source procurement strategy leaves the program vulnerable to supply shortages and price increases. Because Food and Drug Administration [FDA] regulations require a dedicated production facility for spore-based biologics, other pharmaceutical firms

[2] In response to the subcommittee's investigative requests, DOD provided more than 100,000 pages of documentary and electronic records on the anthrax vaccine program from 1991 to the present. Five subcommittee hearings were held in 1999, encompassing 20 hours of testimony from 46 witnesses. The full Committee on Government Reform also heard testimony on the subject of vaccines for military defense on Oct. 12, 1999.

will not commit the time and capital needed to manufacture an old vaccine for a very limited market. As a result, DOD and the sole vaccine maker are locked in a mutually dependent relationship.

The manufacturer, struggling to reopen a plant with a checkered regulatory history, clings to a captive customer. Threats to stop production render DOD unable to resist demands for extraordinary financial relief and pressure to permit the use of publicly funded improvements to monopolize the private domestic and foreign markets as well.

UNCERTAIN SAFETY

Incurious reliance on FDA approval of the vaccine as "safe" for occupational exposure blinds the program to potential adverse reaction trends in a vastly expanded, demographically diverse population of vaccine recipients. Adverse events following vaccination are reported by women at twice the rate among men. The vaccine may be as safe as many other approved products, but valid data to support, or refute, that proposition will not come from the AVIP. Preposterously low adverse report rates generated by DOD point to a program far more concerned with public relations than effective force protection or the practice of medicine.

The AVIP raises an ominous question: Who protects the force from ill-conceived force protection? The anthrax vaccine effort is designated a "commander's program," not a medical program, so DOD doctors appear unable to act as advocates for individual patients in the face of command pressure to meet force-wide inoculation levels. FDA regulations reach only the vaccine producer, the BioPort Corp., not the activities of the vaccine purveyor, the Pentagon, although for purposes of the AVIP the distinction is meaningless.

UNTESTED EFFICACY

Administration of the anthrax vaccine for mass prophylaxis against biological warfare should be considered an off-label use of the product to treat an indication for which it is not explicitly licensed. DOD's operational use of a standard of "functional protection" after three inoculations constitutes a *de facto* alteration of the approved six shot regimen. Both the new indication and the new schedule should be undertaken only pursuant to FDA regulations governing clinical trials of investigational new drugs [IND].

Under supervision of the FDA and an Institutional Review Board [IRB], DOD would be required to inform vaccine recipients adequately, obtain informed consent, and gather data on vaccine safety consistently. If necessary, DOD could request the President waive the informed consent requirement for certain deployed personnel under the statute, regulation, and Executive order that provide far greater protections to service members than the process used for similar waivers during the Gulf war.[3]

[3] 10 U.S.C. 1107(f); 21 CFR Part 50; Executive Order No. 13139 of Sept. 30, 1999.

Findings in Brief

1. The AVIP is a well-intentioned but over-broad response to the anthrax threat. It represents a doctrinal departure overemphasizing the role of medical intervention in force protection.

2. The AVIP is vulnerable to supply shortages and price increases. The sole-source procurement of a vaccine that requires a dedicated production facility leaves DOD captive to old technology and a single, untested company. Research and development on a second-generation, recombinant vaccine would allow others to compete.

3. The AVIP is logistically too complex to succeed. Adherence to the rigid schedule of six inoculations over 18 months for 2.4 million members of a mobile force is unlikely, particularly in reserve components. Using an artificial standard that counts only shots more than 30 days overdue, DOD tolerates serious deviations from the Food and Drug Administration [FDA] approved schedule.

4. Safety of the vaccine is not being monitored adequately. The program is predisposed to ignore or understate potential safety problems due to reliance on a passive adverse event surveillance system and DOD institutional resistance to associating health effects with the vaccine.

5. Efficacy of the vaccine against biological warfare is uncertain. The vaccine was approved for protection against cutaneous (under the skin) infection in an occupational setting, not for use as mass protection against weaponized, aerosolized anthrax.

Recommendations in Brief

1. The force-wide, mandatory AVIP should be suspended until DOD obtains approval for use of an improved vaccine. To accomplish this:

2. DOD should accelerate research and testing on a second-generation, recombinant anthrax vaccine; and,

3. DOD should pursue testing of the safety and efficacy of a shorter anthrax inoculation regimen; and,

4. DOD should enroll all anthrax vaccine recipients in a comprehensive clinical evaluation and treatment program for long term study.

5. While an improved vaccine is being developed, use of the current anthrax vaccine for force protection against biological warfare should be considered experimental and undertaken only pursuant to FDA regulations governing investigational testing for a new indication.

II. BACKGROUND

THE PROGRAM

On December 15, 1997, after what DOD described as "a detailed, deliberative process" spanning almost 4 years,[4] Secretary of Defense William S. Cohen announced a program to immunize all active duty personnel against anthrax, a bacterial disease that in

[4] *Anthrax Immunization Program,* 106th Cong., 1st sess., p. 8 (1999) (Subcommittee on National Security, Veterans Affairs, and International Relations hearing of Mar. 24, 1999, No. 106–17) [hereinafter "NSVAIR anthrax hearing (I)"] (prepared statement of Dr. Sue Bailey).

spore form can be used as a biological weapon. The effort is called the Anthrax Vaccine Immunization Program [AVIP].[5]

The program was designed to be implemented in three phases:[6]

Phase I (3/98–1/00) forces assigned or rotating to high threat areas 400,000

Phase II (1/00–1/04) early deploying forces into high threat areas 1,000,000

Phase III (10/02–9/06) remainder of the total force, boosters, et cetera 1,000,000

The AVIP is a medical force protection effort undertaken by DOD pursuant to a 1993 policy calling for immunizations "against validated biological warfare threat agents, for which suitable vaccines are available, in sufficient time to develop immunity before deployment to high-threat areas . . ."[7]

According to the DOD news release announcing the vaccine program, "After a three year study, Secretary of Defense William S. Cohen concluded that the vaccination is the safest way to protect highly mobile U.S. military forces against a potential threat that is 99 percent lethal to unprotected individuals."[8] Cohen added, "To be effective, medical force protection must be comprehensive, well documented, and consistent. I have instructed the military to put such a program in place."[9]

Accordingly, Secretary Cohen set four conditions on the start of vaccinations:

1) supplemental testing to assure sterility, safety, potency, and purity of the vaccine stockpile;

2) implementation of a system for fully tracking anthrax immunizations;

3) approval of operational plans to administer the vaccine and communications plans to inform military personnel; and

4) review of medical aspects of the program by an independent expert.[10]

In 1998, supplemental testing of the anthrax vaccine stockpile began.[11] An elaborate interim recordkeeping and tracking system was designed to combine vaccination data from the three military services into an existing central data base, the Defense Enrollment Eligibility Reporting System [DEERS].[12] A more efficient, centralized immunization records system is under development.[13] Communication plans were approved centered around a "tri-fold" brochure

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[5] DOD media release, "Defense Department to Start Immunizing Troops Against Anthrax," No. 679–97, Dec. 15, 1997.

[6] AVIP briefing slides (in subcommittee files).

[7] DOD Directive 6205.3, "DOD Immunization Program for Biological Warfare Defense." Nov. 26, 1993. Other elements of force protection include intelligence about threats, detection capability, physical protection (suits, masks, et cetera), post-exposure treatment with antisera and antibiotics, and strategic deterrence. In the Gulf war, up to 150,000 U.S. service personnel received one or two doses of the anthrax vaccine along with other immunizations and medications. Due to poor or non-existent recordkeeping, however, DOD is unable to conduct a systematic follow-up on the health effects, if any, of the Gulf war vaccines.

[8] See supra note 5, p. 1.

[9] Ibid.

[10] Ibid.

[11] Letter from Anthony M. Lutrell, vice president, Quality Assurance, BioPort Corp., to Dr. Michael Gilbreath, Joint Program Office for Biological Defense, DOD, Jan. 8, 1999 (in subcommittee files).

[12] Major William Terry, "Tracking Troops' Anthrax Shots," (with charts), ArmyLINK News, March 1999.

[13] Ibid.

to be given to service personnel.[14] An anthrax vaccine website was also created.[15] A physician reviewed the AVIP program plans.[16]

In March 1998, at the request of the regional commander, 48,000 troops assigned to the Persian Gulf area began the vaccination series. On May 18, 1998, Secretary Cohen pronounced the four conditions fulfilled and approved the total force program, which began in September with troops in Korea.[17]

DOD cited several factors to support the conclusion the anthrax vaccine is both safe for widespread use and effective against the most likely anthrax threat:

1) FDA approval and monitoring of the vaccine;
2) vaccine usage since approval;
3) assured production capacity;
4) independent medical review;
5) supplemental vaccine testing; and,
6) vaccine tests in animals.[18]

FDA APPROVAL OF THE VACCINE

The AVIP uses the only anthrax vaccine licensed for manufacture in the United States. Anthrax Vaccine Absorbed [AVA] was approved as safe in 1970 based on animal studies and one study of wool workers exposed to indeterminate levels of cutaneous (through skin) and airborne anthrax spores. The disease primarily infects grazing animals and the vaccine has been used since 1970 by some veterinarians, livestock workers, and researchers at risk from exposure. The approved immunization process requires a fixed schedule of six injections over 18 months and an annual booster. The vaccine does not contain live anthrax bacteria, but challenges the immune system to mount a response to filtered elements of the killed bacteria absorbed into an adjuvant.[19]

Subsequent FDA review of the studies in 1985 concluded the vaccine was safe, "fairly well tolerated," and effective against cutaneous anthrax, but that data from both human and animal tests was insufficient to support a finding of efficacy with regard to airborne exposure.[20] In analyzing the benefit/risk ratio of classifying the old vaccine as compliant under new FDA standards, the expert panel concluded, "This vaccine is recommended for a *limited, high-risk of exposure population* along with other industrial safety measures designed to minimize contact with potentially contaminated material. The benefit-to-risk assessment is satisfactory *under the prevailing circumstances of use."*[21] (Emphasis added).

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[14] Department of Defense, AVIP tri-fold brochure, "What Every Service Member Should Know About Anthrax" (undated) (in subcommittee files).

[15] Department of Defense website on Anthrax Vaccination Immunization Program, http://www.anthrax.osd.mil.

[16] Letter from Dr. Gerard N. Burrow, Special Advisor to the President for Health Affairs, David Page Smith Professor of Medicine, Professor of Obstetrics and Gynecology, Yale University School of Medicine, to DOD Undersecretary Rudy de Leon, Feb. 19, 1998 (in subcommittee files).

[17] Steve Bowman, *Department of Defense Anthrax Vaccination Program* (98–873F), Congressional Research Service report (updated), Oct. 28, 1998, p. 2.

[18] Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DOD, NSVAIR anthrax hearing (I), p. 9 .

[19] The FDA-approved immunization schedule: Day 1, 2 weeks, 4 weeks, 6 weeks, 6 months, 12 months, and 18 months. An adjuvant is an ingredient that modifies or enhances the effectiveness of the drug or treatment.

[20] Federal Register, 21 CFR Part 610, Dec. 13, 1985, p. 51058.

[21] Ibid.

The sole producer of the vaccine is the Michigan Biologics Products Institute [MBPI], formerly the Michigan Public Health Department. Since licensure in 1970, FDA monitoring of the vaccine consisted of collecting adverse reaction data and conducting intermittent manufacturing plant inspections.

While detailed information on inspection activities prior to 1990 is not readily available, FDA regulatory scrutiny of the manufacturer has been increasing since then. The Lansing, MI, facility has been cited repeatedly by the FDA for quality control deficiencies and "numerous significant deviations from the Federal Food, Drug, and Cosmetic Act, FDA's regulations and the standards in MBPI's license." [22] In March 1997, the FDA warned MBPI that steps would be taken to revoke production licenses, including anthrax vaccine, unless immediate actions were taken to correct longstanding deficiencies.[23] In March 1998, the plant was closed for $1.8 million in renovations and a $15 million expansion funded by DOD.[24] Vaccine production resumed in May 1999, but neither the renovated facility nor any newly produced vaccine lots have been approved by the FDA.[25]

Deviations from good manufacturing practices can affect vaccine safety and effectiveness. FDA will not permit the release of vaccines not documented to meet approved potency, sterility, and stability levels. Based on concerns over the impact of production process errors on vaccine quality, BioPort quarantined 11 lots of anthrax vaccine. Additional lots are being held pending resolution of questions about potency testing that arose during the supplemental review.[26]

Under FDA regulations, stockpiled lots must be tested for potency at predetermined intervals. Potency tests are done using guinea pigs by comparing the survival rates of animals vaccinated with the test lot(s) against those vaccinated with a previously manufactured control or "reference" lot. Potency test failures during the DOD supplemental testing program have raised questions regarding the validity of test procedures and the selection of reference lots.[27]

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[22] *DOD's Mandatory Anthrax Vaccine Immunization Program for Military Personnel,* 106th Cong., 1st sess., p. 58 (1999) (Subcommittee on National Security, Veterans Affairs, and International Relations hearing of Apr. 29, 1999, No. 106–26) [hereinafter "NSVAIR anthrax hearing (II)"] (testimony of Dr. Kathryn Zoon, Director, FDA Center for Biologics Evaluation and Research).

[23] Center for Biologics Evaluation and Research, FDA, "FDA Warns Michigan Biological Products Institute of Intention to Revoke Licenses," No. D0382, Mar. 11, 1997.

[24] *Department of Defense's Sole-Source Anthrax Vaccine Procurement,* 106th Cong., 1st sess., p. 8 (1999) (National Security, Veterans Affairs, and International Relations Subcommittee hearing of June 30, 1999) [hereinafter "NSVAIR anthrax hearing (III)"] (testimony of Louis J. Rodrigues, Director, Defense Acquisitions Issues, National Security and International Affairs Division, U.S. General Accounting Office).

[25] DOD news briefing, Monday, Dec. 13, 1999 (available at http://www.defenselink.mil and in subcommittee files).

[26] "Medical Readiness: DOD Faces Challenges in Implementing Its Anthrax Vaccine Immunization Program," (GAO/NSIAD–00–36) U.S. General Accounting Office, Oct. 22, 1999, p. 13. See also, Department of Defense Joint Program Office—Biological Defense, "Investigation of Supplemental Potency Testing" JPO–0855 (undated) (in subcommittee files). See also, prepared statement of BG Eddie Cain, Joint Program Manager, Joint Program Office for Biological Defense, NSVAIR anthrax hearing (II), p. 68.

[27] Letter from Joseph S. Little, Contracting Officer, Department of the Army to Fuad El-Hibri, BioPort Corp., Sept. 23, 19989 (in subcommittee files).

ASSURED PRODUCTION CAPACITY

MPBI was purchased in September 1998 by the BioPort Corp., a new company formed by private investors, including former Joint Chiefs Chairman Adm. William J. Crowe. The next month BioPort was awarded a DOD contract valued at $29 million to produce anthrax vaccine for the AVIP.[28] The contract (DAMD17–98–C 8052) provides for a 1 year base period and 2 option years. The contract provides for a full-term, fixed price, fixed annual quantity because "the Government currently requires all the AVA [anthrax vaccine absorbed] that BioPort can produce." Under the agreement, BioPort will receive progress payments at various stages of the anthrax vaccine production process.

On August 5, 1999, DOD announced the contract had been "restructured" to increase the price by $24.1 million, including $18.7 million of advance payments.[29]

This contract, and earlier contracts with MPBI and MDPH, were accompanied by a justification and authorization for other than full and open competition (sole source). The sole source procurement was authorized because "Michigan Biologics Products Institute [MBPI] is the only organization in the U.S. with a Food and Drug Administration [FDA] license to manufacture AVA" and "[d]ue to the time and expense required to produce a licenced product, investing in alternate manufacturers is not considered to be an effective way of meeting the Government's requirements."[30] DOD also indemnified MBPI/BioPort against liability arising from "the risks of adverse reactions, or the failure to confer immunity against anthrax . . ."[31]

Potential liability resulting from adverse events was a major issue for the anthrax vaccine manufacturer even when the vaccine was used by only a few hundred people each year. In 1986, Secretary of the Army John Marsh, Jr., authorized indemnification of the State of Michigan Department of Public Health, which would not provide the vaccine without indemnification due to "the possibility that persons vaccinated may develop anaphylaxis or some unforeseen reaction of serious consequences, including death."[32]

In 1992, Secretary of the Army Togo West, Jr., approved a request to indemnify the anthrax vaccine manufacturer, the Michigan Biologics Product Institute [MBPI], against all liability arising from:

> the unusually hazardous risks associated with potentially severe adverse reactions and the potential lack of efficacy of the AVA. These concerns stem from: a) the *limited use of the vaccine to date,* i.e., tests prior to approval of the

[28] Department of Defense (1998) Award/Contract: U.S. Army Medical Research ACQ Activity—BioPort Corp., DAMD17–98–C–8052, Sept. 17, 1998.

[29] Department of Defense media release, "DOD Announces Contract Restructuring," Aug. 5, 1999 (in subcommittee files).

[30] Joseph S. Little "Justification and Approval for Other than Full and Open Competition," Anthrax Vaccine Absorbed, DAMD17–97–0014 (JPO 0836) May 20, 1997 (in subcommittee files).

[31] Memorandum of decision, Secretary of the Army Louis Caldera, Authority Under Public Law 85–804 to include an indemnification clause in contract DAMD 17–91–C–1139 with Michigan Biologic Products Institute, Sept. 3, 1998 (in subcommittee files).

[32] Memorandum of decision, Secretary of the Army John O. Marsh, authority under 50 U.S.C. 1431–1435 (Public Law 85–804) to include an indemnification clause in contracts or purchase orders with the State of Michigan, Feb. 27, 1986 (in subcommittee files).

vaccine by the Food and Drug Administration are on *too small a scale to permit accurate assessment of types and severity of adverse reactions (only widespread use can provide this assessment);* and b) insufficient experience in mass immunization programs to truly evaluate the efficacy of the vaccine. Moreover, there is no way to predict whether the pathogen against which the vaccine may be used will be sufficiently similar to the pathogen used in tests to ensure vaccine efficacy.[33] (Emphasis added).

In 1998, Secretary of the Army Louis Caldera again authorized indemnification of MBPI because "the size of the proposed vaccination program may reveal unforwarned idiosyncratic adverse reactions."[34] The contracting officer justified the later indemnification request, in part, because, "Since 1990, approximately 600,000 doses have been issued from MBPI's stockpile. The limited use of AVA to date versus the large number of doses that are being stockpiled and subject to use may expand the data base to a point where the statistical significance of a predicted adverse reaction may become a reality."[35]

Following the Gulf war, and prior to adoption of the DOD immunization policy in 1993, and the mandated AVIP in 1998, Pentagon officials considered and rejected alternative anthrax vaccine production sites.[36] Instead, an acquisition strategy was adopted focusing solely on the MBPI/BioPort vaccine.[37]

VACCINE USAGE AND SAFETY

DOD literature says the anthrax vaccine "has been safely and routinely administered in the United States to veterinarians, laboratory workers, and livestock handlers for more than 25 years."[38] Testimony at the March 24 hearing indicated between 100 and 300 civilians may receive the vaccine each year. Since approval, and prior to the AVIP, fewer than 68,000 doses had been distributed apart from stocks used in Operation Desert Storm.[39]

As with any vaccine, anthrax inoculation can cause adverse health events in some individuals, ranging from soreness or swelling at the injection site (local reactions) to fevers, chills, muscle aches, and anaphylaxis[40] (systemic reactions). Local reaction may be mild, moderate, or severe enough to require medical attention. Systemic reactions are generally considered clinically more signifi-

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[33] Memorandum of decision, Secretary of the Army Togo West, Jr., authority under Public Law 85–804 to include an indemnification clause in contract DAMD17–91–C–1139 with the Michigan Biologic Products Institute [undated] (in subcommittee files).

[34] See supra note 31.

[35] Joseph S. Little, Contracting Officer, "Contracting Officer's Request for Authorization for Indemnification Under Authority of Public Law 85–804," Oct. 8, 1997, p. 3 (in subcommittee files).

[36] BG Eddie Cain, "Procurement of the Anthrax Vaccine-Single Source Versus Additional Site," DOD information paper, JPO 0920, Oct. 19, 1998 (in subcommittee files).

[37] BG John C. Doesberg, "Acquisition Strategy for the Procurement of Anthrax Vaccine Adsorbed," Joint Program Office for Biological Defense, JPO 0120, Feb. 1, 1997 (in subcommittee files).

[38] See supra note 14.

[39] Prepared statement of Dr. Kathryn Zoon, Director, FDA Center for Biologics Evaluation and Research, NSVAIR anthrax hearing (II), pp. 52–53.

[40] Anaphylaxis is one form of hypersensitivity to a drug or antigen. Anaphylactic shock is an often severe, sometimes fatal, physical reaction characterized by respiratory symptoms, fainting, swelling, and itching.

cant. Reactions may increase in severity after successive injections.[41]

The AVA has been described as a relatively crude, imprecisely characterized vaccine, and estimates of reaction rates vary widely.[42] According to the FDA-approved AVA product labeling, 30 percent of vaccine recipients can be expected to suffer mild local reactions, 4 percent will incur moderate local reactions and less than 0.2 percent will experience systemic reactions.[43] In 1994 and 1995, DOD considered the need for a new anthrax vaccine "based on the reactogenicity of the current vaccine."[44]

To avoid adverse reactions, the vaccine should not be given to those who experienced a severe reaction to a previous dose or to those with acute respiratory disease or an active infection. Immune compromised persons (i.e., HIV infected) may not respond to the vaccine. It is not recommended for pregnant women or for those under 18 or over 65 years of age.[45]

The Army Anthrax Vaccine Immunization Plan directs medical personnel to report severe adverse reactions (resulting in hospitalization or more than 24 hours lost from duty) through the Vaccine Adverse Events Reporting System [VAERS] administered by the Department of Health and Human Services [HHS].[46] Within HHS, VAERS is a joint project of the Centers for Disease Control [CDC] and the Food and Drug Administration [FDA].[47] VAERS guidance recommends recording any clinically significant symptoms occurring subsequent to vaccine administration, whether or not a causal relationship has been established between the vaccine and the adverse reaction.[48]

The Army Medical Surveillance Activity also receives copies of VAERS forms from all the uniformed services and produces a quarterly report for the U.S. Army Medical Command.[49] The Army Surgeon General has requested the assistance of the HHS Vaccine Injury Compensation Program in evaluating all anthrax-related VAERS data.[50]

The AVIP convened a clinical conference in May 1999 to discuss anthrax issues, including adverse events. Col. Renata Engler, M.D., chief, Allergy-Immunology Department, Walter Reed Army Medical Center, presented data from ongoing research and case studies

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[41] Michigan Biologic Products Institute, "Anthrax Vaccine Absorbed: How Supplied, References, Description, Clinical Pharmacology, Indications and Usage, Contraindications, Warnings, Precautions, Adverse Reactions, Dosage and Administration," FDA License No. 99, Rev. February 1998 (in subcommittee files).

[42] Phillip Brachman and Arthur Friedlander, *Vaccines,* 2d ed., pp. 729–739, Philadelphia, WB Saunders (1994).

[43] See supra note 41.

[44] LTC George W. Anderson, Jr., memorandum "Minutes of the FDA meeting of May 5, 1994 Concerning Production and Purification of PA from Delta Stern–1 (pPa102) CR4," U.S. Army Medical Research Institute on Infectious Diseases, May 19, 1994 (in subcommittee files).

[45] See supra note 41.

[46] Gen. William W. Crouch, U.S. Army Vice Chief of Staff, memorandum "Army Anthrax Vaccine Immunization Program Plan," Apr. 29, 1998, p. 3 and annex C (in subcommittee files).

[47] FDA Center for Biologics Evaluation and Research, "Vaccine Adverse Events Reporting System [VAERS]" available at http://www.fda.gov.cber/vaers/faq.htm.

[48] Ibid.

[49] See supra note 46, p. C–7.

[50] *Anthrax Vaccine Adverse Reactions,* 106th Cong., 1st sess. (1999) (subcommittee on National Security, Veterans Affairs, and International Relations hearing of July 21, 1999) [hereinafter "NSVAIR anthrax hearing (IV)"] [The subcommittee hearing has not yet been printed. Page numbers in this and subsequent references to statements at this hearing refer to individual prepared written statements or the unofficial transcript, held in subcommittee files.] (prepared statement of Gen. Robert Claypool, pp. 13–14).

showing higher adverse reaction rates in women.[51] Also discussed at the conference was the Army Surgeon General's proposed longitudinal cohort study to assess near-term and long-term health effects of the anthrax vaccine.[52]

To convey important information about medical exemptions and adverse reactions, the Army implementation plan directs commanders and medical staff to provide recipients "adequate information on the vaccine, its safety, its benefits, and the need for adherence to the immunization schedule prior to the first anthrax vaccination."[53] The other service implementation plans contain identical or similar requirements.

On April 1, 1999, VAERS data (1990 to 1999) contained 101 reports of adverse events associated with anthrax inoculation, 14 of which were considered serious.[54] In May 1999, DOD reported a total of 123 VAERS filings with FDA, but included only 65 of those in the caculation of an adverse reaction rate of 0.007 percent of 890,888 vaccinations given to date. According to DOD, only 11 VAERS reports "met strict reporting requirements."[55]

INDEPENDENT MEDICAL REVIEW

A review of the AVIP plans, and of basic literature on the anthrax vaccine, was conducted by Dr. Gerard N. Burrow, of the Yale University School of Medicine.[56] According to Dr. Burrow,[57] he conducted his review over 3 months, read materials provided by DOD, and interviewed Pentagon officials responsible for designing and implementing the program. On February 19, 1998, in a four page letter, he concluded, "The anthrax vaccine appears to be safe and offers the best available protection against wild-type anthrax as a biological warfare agent." The letter contains two paragraphs on safety and efficacy. Regarding the safety of the vaccine stockpile, all of which was manufactured under conditions cited by FDA as deficient, Dr. Burrow pointed to the DOD supplemental testing program, and the fact that "FDA directed MBPI to do a comprehensive review to demonstrate that deviations in biologic product lines did not impact anthrax vaccine quality and integrity. The results of this review should be available in the near future."[58] Regarding efficacy of the vaccine, the letter recites usage figures since approval in 1970 and cites the conclusion of an unpublished DOD study that

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[51] Col. Renata Engler, M.D., USA, Chief, Allergy and Immunology Department, Walter Reed Army Medical Center, "Presentation-Anthrax Immunization: Challenges for the Future," *Department of Defense Conference for Biological Warfare Defense Immunizations,* Fort Detrick, MD, May 25–27, 1999 (in subcommittee files).

[52] Department of the Army, Office of the Surgeon General, "Memorandum for Conference Participants," Apr. 16, 1999, p. 2 (in subcommittee files).

[53] See supra note 46 p. C–5.

[54] Testimony of Dr. Kathryn Zoon, Director, FDA Center for Biologics Evaluation and Research, NSVAIR anthrax hearing (II), p. 55.

[55] Department of Defense, briefing slide, "Anthrax Vaccine Adverse Events-Vaccine Adverse Event Reporting System [VAERS] Military—Week Ending May 21, 1999" May 28, 1999 (in subcommittee files).

[56] See supra note 16.

[57] In an Apr. 16, 1999 telephone conversation with subcommittee staff, Dr. Burrow said his charge was a general review of the program, and that as an internist, he has little experience with vaccines. His primary recommendation was the use of focus groups of military personnel to determine appropriate communication strategies.

[58] See supra note 16.

"unit effectiveness could best be preserved through the use of predeployment vaccination." [59]

In a letter to the subcommittee in response to a request to testify on his review of the program, Dr. Burrow wrote:

> Unfortunately, I do not believe I can make a significant contribution to the work of your Committee. I chaired the Institute of Medicine Committee that reviewed the Defense Department program for clinical care of Gulf War veterans in active service and interacted with personnel in the Office of Health Affairs. The Defense Department was looking for someone to review the program in general and make suggestions, and I accepted out of patriotism. I was very clear that *I had no expertise in Anthrax* and they were clear that they were looking for a general oversight of the vaccination program.
>
> I visited the Pentagon on a number of occasions, talked with a variety of people in and out of government and presented my report which you have to the Secretary on March 2, 1998. *I had no access to classified information.* . . .[60] (Emphasis added).

SUPPLEMENTAL TESTING

To address concerns over the age and quality of stockpiled vaccine, DOD undertook an effort to re-test the product before use. A contractor was retained to conduct supplemental testing of vaccine lots, all of which had been manufactured in an aging production facility, and some of which had been approved by the FDA for use beyond the initial expiration date.

Mitretek Systems Inc., reviewed vaccine production records and observed additional testing conducted by BioPort personnel.[61] Of the 31 vaccine lots [62] subjected by DOD to supplemental testing, 18 remained unavailable as of July 1999 due to unresolved purity, potency, or sterility issues.[63]

Some involved in the program opposed supplemental testing as redundant and likely to cause more problems than it solved by establishing a self-imposed vaccine safety standard in addition to FDA lot-release criteria.[64] Their concerns were validated when the supplemental testing program appears to have overwhelmed the MBPI/BioPort testing capabilities, producing anomalous results and delaying the program.[65] Once the testing problems became apparent, vaccine lots not technically in the stockpile when the AVIP was announced were not subjected to the supplemental assays under the rationale the FDA was requiring the same tests for lot

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[59] Ibid.

[60] Letter from Dr. Gerard N. Burrow, Yale University School of Medicine, to Representative Christopher Shays, Apr. 26, 1999 (in subcommittee files).

[61] See supra note 17, p. 3.

[62] Each lot contains approximately 200,000 doses of vaccine.

[63] See supra note 26, p. 13.

[64] Dr. Michael Gilbreath, information paper, JPO 0364, Feb. 4, 1998 (in subcommittee files); prepared statement of Dr. Robert C. Myers, Chief Operating Officer, BioPort Corp., NSVAIR anthrax hearing (II), pp. 83–84.

[65] Ibid. (Gilbreath information paper).

release.[66] All the lots submitted for supplemental testing had also undergone the same FDA lot release protocols.

ANIMAL DATA ON EFFICACY

DOD's determination the vaccine affords protection against virtually all strains of airborne anthrax spores rests primarily on studies of vaccinated animals (guinea pigs, rabbits, and monkeys) challenged with various strains of the disease.[67] But widely varied results within and between animal species suggest variable modes of protection not necessarily correlated to antibody levels stimulated by the vaccine.[68] Without a proven model in animals that is known to correlate to protection in humans, animal data remains only suggestive.

Vaccine-acquired anthrax immunity may also be limited or overwhelmed when the subject is challenged with variant anthrax strains.[69] A report by the Senate Committee on Veterans' Affairs concluded that:

> data suggests that the vaccine can protect humans against inhaled anthrax but to date there is inadequate information to judge how well it works, particularly against weaponized anthrax, which could cause exposure to greater concentrations of anthrax than has occurred among workers exposed on the job.[70]

In response to questions regarding the efficacy of the vaccine against antibiotic resistant or genetically altered anthrax strains, DOD said

> The current US-licensed anthrax vaccine is considered to be highly effective against naturally occurring strains of anthrax, including antibiotic resistant strains. The development of genetically engineered organisms using anthrax or any other biological warfare agent is a potential threat that must be evaluated carefully. We are not aware, however, of any information to suggest that these modified strains have been used in any context other than the research laboratory.[71]

When one U.S. laboratory studying the release of anthrax at Sverdlovsk implied the Russian mixtures of anthrax strains might overcome the protection afforded by the anthrax vaccine, DOD persuaded the author "to correct the press release to make it more accurate." The modification stated, in part, "there is no experimental

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[66] Letter from Secretary of Defense William Cohen to Representatives Shays (CT), Gilman (NY), Kelly (NY), Souder (IN), Ose (CA), and Talent (MO), Sept. 30, 1999, attachment p. 1 (in subcommittee files).

[67] Testimony of Dr. Sue Bailey, DOD Assistant Secretary for Health Affairs, NSVAIR anthrax hearing (I), p. 11.

[68] Prepared statement of Dr. Meryl Nass, NSVAIR anthrax hearing (II) pp. 108–111.

[69] Ibid.

[70] *Report of the Special Investigation Unit on Gulf War Illnesses,* Senate Committee on Veterans' Affairs, 105th Cong., 2d sess., Sept. 1998, S. Rpt. 105–39, p. 122. See aslo, "Is Military Research Hazardous to Veteran's Health?-Lessons Spanning Half a Century," staff report prepared for the Committee on Veterans Affairs, U.S. Senate, p. 11, 103rd Cong., 2d sess., S. Rpt. 103–97, Dec. 8, 1994.

[71] See supra note 66.

data or evidence to suggest that such a mixture is resistant to the FDA-licensed anthrax vaccine used by the US military." [72]

OPPOSITION TO THE AVIP

Some have refused the vaccine. Active duty personnel have been disciplined under service-specific policies for refusing a lawful order. Reservists and National Guard members have resigned or transferred to units or "non-mobility" positions which do not require the vaccine. The DOD does not collect uniform records on refusals, but media reports indicate more than 300 service men and women have refused to take the shot.[73]

Hearing testimony and correspondence from Reservists and National Guard members suggests up to 30 percent of some units would resign or seek to transfer due to the anthrax program.[74] Their concerns focus on the lack of systematic, long-term studies on anthrax vaccine health effects.[75]

Safety is also an issue for some because the anthrax vaccine is one of the exposures under study by the National Academy of Sciences' Institute of Medicine [IOM] pursuant to the Persian Gulf War Veterans Act of 1998, enacted as Title XVI of the 1998 Omnibus Appropriations Act, Public Law 105–277. The law directs IOM to review associations between illnesses and wartime exposures that warrant a presumption of service-connection for sick Gulf war veterans.[76] That study is ongoing.

Efforts to meet Secretary Cohen's four preconditions to AVIP implementation, intended to address likely reservations about the program, have only served to intensify concerns: [77]

1. Problems with supplemental testing underscore vaccine safety and production issues. The failure to test all lots produced before the plant closed suggests to some the promise of supplemental testing was not fulfilled.

2. The prerequisite communication effort engenders resentment and mistrust as simplistic DOD attempts at education and risk communication portray very limited vaccine use as "routine" [78] and attack those with legitimate questions as

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[72] Ibid. Nor is there data demonstrating the vaccine is effective against altered or mixed anthrax strains.

[73] "Vaccine Refused by 23 Aircraft Carrier Sailors," Associated Press, Mar. 11, 1999 (in subcommittee files). The reported number of vaccine refusers has remained fairly stable in public reports, between 200 and 300, for some months.

[74] *Impact of the Anthrax Vaccine Program on Reserve and National Guard Units,* 106th Cong., 1st sess., p. 57 (Subcommittee on National Security, Veterans Affairs and International Relations hearing, Sept. 29, 1999) [hereinafter "NSVAIR anthrax hearing (V)"] [The subcommittee hearing has not yet been printed. Page numbers in this and subsequent references to statements at this hearing refer to individual prepared written statements or the unofficial transcript, held in subcommittee files.] Testimony of Capt. David Panzera; testimony of Tech. Sgt. William Mangieri, NSVAIR anthrax hearing (V), p. 58) see also, testimony of Capt. Thomas Rempfer, NSVAIR anthrax hearing (I), p. 110; testimony of Maj. Redmond Handy, NSVAIR anthrax hearing (I), pp. 102–102. DOD does not collect data on refusals or resignations attributable to the vaccine. An informal survey of Reserve and Guard units shows more than 700 current or likely departures due to the AVIP. The survey can be found at: http://www.dallasnw.quik.com/cyberella/Anthrax/Chron—Info.html, pp. 12–13.

[75] Testimony of Col. Redmond Handy, NSVAIR anthrax hearing (I), p. 91; prepared statement of Ms. Randi Martin-Allaire, NSVAIR anthrax hearing (II), p. 171; prepared statement of Sgt. Michael Shepard, NSVAIR anthrax hearing (II), p. 193; testimony of Major Cheryl Hansen, NSVAIR anthrax hearing (V), p. 31.

[76] Public Law 105–277, title XVI.

[77] Letter from Representativess Benjamin Gilman (NY), et. al. to Defense Secretary William Cohen, July 20, 1999, p. 1 (in subcommittee files).

[78] See supra note 14.

"paranoics"[79] and simple-minded victims of Internet propaganda.[80]

3. Delays in posting data to the tracking system reduce its value as a real time indicator of medical readiness and increases tolerance of deviations in the FDA approved inoculation regimen.[81]

4. Contrary to subsequent DOD characterizations, the promised outside, expert, scientific review of the program was only very general in nature.[82]

Others question the necessity of the program, asking whether it betrays a lack of confidence in deterrence and other force protection elements, and suggesting a vaccine program makes anthrax attack more, not less, likely.[83]

HEARINGS AND LEGISLATIVE PROPOSALS

On March 24, 1999, the Subcommittee on National Security, Veterans Affairs, and International Relations held the first of five hearings on the Department of Defense [DOD] Anthrax Vaccination Immunization Program [AVIP] entitled, "The Anthrax Immunization Program," the hearing examined the effectiveness and efficiency of the AVIP as a medical force protection measure, a record-keeping initiative and long term procurement. The subcommittee heard testimony from Dr. Sue Bailey, Assistant Secretary for Health Affairs, U.S. Department of Defense, accompanied by, Lt. Gen. Ronald R. Blanck, U.S. Army; Rear Admiral Todd Fisher, Deputy Surgeon General U.S. Navy; Lt. Gen. Charles H. Roadman II, U.S. Air Force; Capt. Thomas Rempfer, Connecticut Air National Guard; Maj. Russell Dingle, Connecticut Air National Guard; Pfc. Stephen M. Lundbom, U.S. Marine Corps; Attorney Mark Zaid; Col. Redmond Handy, Member Reserve Officer Association; and Lorene K. Greenleaf.

On April 29, 1999, the subcommittee held a hearing on the AVIP entitled, "DOD's Mandatory Anthrax Vaccine Immunization Program for Military Personnel." The purpose of this hearing was to examine the vaccine's safety and effectiveness against an aerosolized biological weapons attack. Individuals who testified disputed the Department of Defense claim the vaccine is unquestionably safe for force wide use. Some who testified are experiencing serious illnesses they associate with the anthrax vaccine. Testimony was received from Kwai-Cheung Chan, Director, Special Studies and Evaluations Section, National Security and International Affairs Division, General Accounting Office; Dr. Katherine Zoon, Director, Center for Biologics Evaluation and Research, Food and Drug Administration; Dr. Michael Gilbreath, Medical Project

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[79] Lt. Gen. Ronald Blanck, "Ignore the Paranoics: The Vaccine is Safe," Army Times, Feb. 2, 1999, p. 12.

[80] Douglas J. Gilbert, American Forces Press Service, "Anthrax Vaccine Called Effective Force Protection," DefenseLink, Nov. 5, 1998 (in subcommittee files); Washington Times, "Anthrax Shots Drive Air Force Veteran From Service," Oct. 13, 1999, p. 18; PBS New Hour, "Anthrax Vaccine," Oct. 21, 1999 (comments of Gen. Blanck) (transcript in subcommittee files); Col. Guy Strawder, "AVIP Director's Newsletter" (in subcommittee files).

[81] Bradley Graham, "Anthrax Shots Missing Targets?" Washington Post, Sept. 29, 1999, p. A27.

[82] See supra note 60 and accompanying text.

[83] Testimony of Capt. Thomas Rempfer, NSVAIR anthrax hearing (I), pp. 40–41; testimony of Maj. Russell Dingle, NSVAIR anthrax hearing (I), p. 49.

Manager, Joint Program Office for Biological Defense; Dr. Robert Myers, Chief Operating Officer, BioPort Corp.; Dr. Meryl Nass; David Churchill; Randi Martin-Allaire; Roberta Groll; and Michael Shepard.

On June 30, 1999 the subcommittee held a hearing entitled, "Department of Defense's Sole Source Anthrax Vaccine Procurement." The primary focus was to examine AVIP acquisition strategies and procurement activities pursued by the Department of Defense to purchase the vaccine. Issues examined included the technical and financial ability of BioPort to supply the vaccine at the contracted price, and the effect of management problems on the safety and the quality of the vaccine produced. Testimony was given by Louis J. Rodrigues, Director, Defense Acquisition Issues, National Security and International Affairs Division, General Accounting Office; David Oliver, Jr., Principal Deputy Under Secretary of Defense for Acquisition and Technology, Department of Defense; and Fuad El-Hibri, chief executive officer, BioPort Corp.

On July 21, 1999, the National Security Subcommittee held its fourth hearing on the AVIP. Entitled, "Anthrax Vaccine Adverse Reactions," the hearing focused on the program's willingness to recognize and ability to treat adverse reactions to the vaccine in military personnel. Issues discussed included the extent the main adverse event surveillance system used by DOD, the joint FDA/CDC Vaccine Adverse Event Reporting System [VAERS], under-reports adverse events and adverse vaccine reactions. Testifying at this hearing were CPT Michelle Piel, USAF; LT Richard Rovet, USAF; SGT Robert Soska, USA; CPT Jon Richter, USAR; Kwai-Cheung Chan, Director, Special Studies and Evaluations Section, National Security and International Affairs Division, General Accounting Office; MG Robert Claypool, Deputy Assistant Secretary for Health Operations Policy, Department of Defense accompanied by, RADM Michael Cowen, Deputy Director for Medical Readiness, Joint Staff, Department of Defense; COL Renata Engler, Chief, Allergy-Immunology Department, Walter Reed Army Medical Center; and Dr. Susan Ellenberg, Director, Division of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research, Food and Drug Administration.

The subcommittee held its fifth hearing on the AVIP on September 29, 1999 entitled, "Impact of the Anthrax Vaccine Program on Reserve and National Guard Units." The hearing examined the implementation of the AVIP in reserve component units and the impact of the program on retention, readiness, and morale. Testifying at the hearing were Lt. Col. Thomas Heemstra, Indiana Air National Guard; Maj. Cheryl Hansen, Air Force Reserves; Capt. David Panzera, New York Air National Guard; Tech. Sgt. William Mangiere, New York Air National Guard; Charles Cragin, Acting Assistant Secretary for Reserve Affairs, Department of Defense, accompanied by, Maj. Gen. Paul Weaver, Jr., Director, Air National Guard, Department of Defense; Col. Frederick Gerber, Director, Health Care Operations, Office of the Army Surgeon General, Department of Defense; and Col. James Dougherty, Air Surgeon, National Guard Bureau, Department of Defense.

In the first session of the 106 Congress, two bills were introduced regarding the anthrax vaccine program:

Representative Walter Jones (NC) introduced H.R. 2543 on July 16, 1999. Entitled, "The American Military Health Protection Act," the bill would instruct the Department of Defense to make the anthrax vaccination immunization program voluntary for all members of the Armed Forces until the FDA has approved a new anthrax vaccine for humans or the FDA has approved a new, reduced course of shots for the current anthrax vaccine. This bill was referred to the Committee on Armed Services.

Representative Benjamin Gilman (NY), introduced H.R. 2548 on July 19, 1999, cosponsored by Representatives Sue Kelly (NY) and Bob Filner (CA). H.R. 2548 would suspend further implementation of the Department of Defense anthrax vaccination program until the vaccine is determined to be safe and effective through a study by the National Institutes of Health. The Department of Defense Anthrax Vaccination Moratorium Act was referred to the Committee on Armed Services and to the Committee on Commerce.

The fiscal year 2000 Defense Appropriations Act (H.R. 2561) contained a provision directing the Comptroller General to report on: effects on morale, retention and recruiting; the civilian costs and burdens associated with adverse reactions for members of the reserve components; adequacy of long and short term health monitoring; assessment of the anthrax threat, including but not limited to foreign doctrine, weaponization, quality of intelligence, and other biological threats. DOD was directed to contract with the National Research Council to conduct studies on: vaccine adverse events and adverse reactions, particularly among women; vaccine efficacy against inhalation anthrax; correlation of animal models to safety and efficacy in humans; research gaps; and other matters.

III. DISCUSSION

FINDINGS

1. The AVIP is well-intentioned but over-broad response to the anthrax threat. It represents a doctrinal departure overemphasizing the role of pre-exposure medical intervention in force protection

DOD bases the scope of AVIP on the scope of the threat, and the perceived need for additional, individual force protection to meet that threat. Threat assessment requires objective and subjective analyses of U.S. vulnerability, enemy capacity, and enemy intentions. "A threat analysis, the first step in determining risk, identifies and evaluates each threat on the basis of various factors, such as its capability and intent to attack an asset, the likelihood of a successful attack, and its lethality."[84]

Since the King of Athens poisoned his enemy's wells in 600 BC and Alexander the Great hurled diseased animal corpses over the walls of a besieged city, ground forces have been vulnerable to casualties caused by natural or pernicious exposure to chemical and

[84] *Combating Terrorism—Threat and Risk Assessments Can Help Prioritize and Target Program Investments,* U.S. General Accounting Office, GAO/NSIAD–98–74, April 1998 p. 3.

biological pathogens.[85] But in the absence of proven capability and intent to use biological weapons, vulnerability alone does not constitute a validated threat for purposes of determining appropriate and effective countermeasures.

Appropriately, much of the information regarding the BW capabilities and intentions of potential adversaries, and even allies, is classified. As a result, most public descriptions of the anthrax threat focus on the general vulnerability of unprotected forces to anthrax attack, the general ease and availability of anthrax production and the likely lethality of a successful anthrax attack.

According to various unclassified DOD statements, more than 10 countries "have, or are developing, a biological warfare capability."[86] Those nations are: China, Iran, Iraq, Israel, Libya, North Korea, South Korea, Syria, Taiwan, and Russia. Other public lists also include Egypt, Cuba, Japan, and the former Soviet states in Eastern Europe that may have inherited bio-warfare capabilities.[87] For purposes of the AVIP, "The high threat areas validated by our intelligence community for the potential use of anthrax as a biological weapon of mass destruction includes [sic] Korea, Israel, Jordan, Kuwait, Saudi Arabia, Bahrain, Qatar, Oman, UAE, and Yemen."[88] Anthrax is not seen as a threat in the Balkans.[89]

Other descriptions of the anthrax threat focus on the relative ease of acquisition, mass production, and weaponization of the stable, long-lasting anthrax microbe. According to DOD, production of biological warfare agents does not require specialized equipment or advanced technology. Biological agents are more potent and efficient than chemical weapons, and can be delivered through a variety of means. Legitimate uses (i.e., vaccine manufacture) for "dual use" production technologies make counter-proliferation strategies difficult to implement successfully.[90]

Secretary Cohen told Members, "Anthrax poses a clear and present danger to our armed forces. It is the weapon of choice for germ warfare because it is easy to weaponize and is as lethal as the Ebola virus. At least seven potential adversaries have worked to develop the offensive use of anthrax."[91]

In testimony before a subcommittee of the House Armed Services Committee, Deputy Secretary of Defense John Hamre said, "Currently, at least 10 nation states and 2 terrorist groups are known to possess, or have in development, a biological warfare capability."[92]

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[85] Dr. Stephen C. Joseph, Assistant Secretary of Defense for Health Affairs, "Biological Warfare—Information Memorandum" (undated) p. 2 (in subcommittee files).

[86] DOD information paper,"DOD Biological Warfare Threat Analysis," Dec. 15, 1997, p. 1. See also, *Proliferation: Threat and Response,* Department of Defense, November 1997.

[87] Office of Technology Assessment, U.S. Congress, "Proliferation of Weapons of Mass Destruction: Assessing the Risks," p. 65, OTA–15C–559, August 1993 (in subcommittee files). Notably included among those nations are United States allies who, it must be presumed, pose less danger to U.S. forces than nations currently opposing U.S. policy goals.

[88] See supra note 66, attachment p. 13.

[89] Ibid.

[90] See supra note 86. The release of deadly chemical sarin gas in Tokyo by the Aum Shinrikyo cult highlighted the terrorist, and by implication, the military threat posed by chemical and biological weapons. But subsequently acquired information regarding the cult's unsuccessful attempts to use biological agents is seen by some as a counter to the argument those agents are not technically challenging to produce and deploy.

[91] See supra note 66.

[92] Prepared statement of John J. Hamre, Deputy Secretary of Defense, submitted to the Subcommittee on Military Personnel, House Committee on Armed Services, p. 2, Sept. 30, 1999.

DOD testimony to the subcommittee portrayed the threat similarly: "As identified by the chairman of the Joint Chiefs of Staff, anthrax is a major threat to our troops. Anthrax is the primary biological warfare threat faced by U.S. forces. More than 10 countries, including Iraq, have or are suspected of developing this biological warfare capability. Anthrax is the biological weapon most likely to be encountered because it is highly lethal, easy to produce in large quantities, and relatively easy to develop as a weapon." [93]

The AVIP tri-fold brochure describes the threat as follows:

> Biological weapons are maintained by several countries around the world. Use of these weapons could cause widespread illness among unprotected military forces.
> Anthrax is the biological weapon most likely to be encountered because it is:
> - Highly lethal
> - Easy to produce in large quantities
> - Relatively easy to develop as a weapon
> - Easily spread over a large area
> - Easily stored and dangerous for a long time [94]

Clearly, DOD has determined the threat is real and imminent, and has concluded it would be irresponsible not to deploy an available countermeasure to protect the lives and fighting capability of U.S. forces.[95]

But similar statements on the threat have been made by DOD for many years. According to GAO testimony, "The nature and magnitude of the military threat of biological warfare [BW] has not changed since 1990, both in terms of the number of countries suspected of developing BW capability, the types of BW agents they possess, and their ability to weaponize and deliver those BW agents. Inhalation anthrax is considered by DOD to be the primary BW threat because of its lethality, ease of production, and weaponization." [96]

According to unclassified briefing materials assessing the anthrax threat, anthrax stocks and weaponized anthrax have been confirmed only in Southwest Asia. A stock of anthrax has been confirmed in Northeast Asia. Capacity to produce and weaponize anthrax elsewhere (South Asia or transnational) is suspected but unconfirmed.[97]

Assessment of the Iraqi threat concludes that substantial anthrax production capacity exists but exceeds the ability to weaponize. While Iraq appears likely to be able to launch a BW attack using AL HUSSEIN ballistic missiles, aircraft delivery is seen as less likely due to United States and Coalition air superiority.[98]

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[93] Prepared statement of Dr. Sue Bailey, DOD Assistant Secretary for Health Affairs, NSVAIR anthrax hearing (I), p. 8.
[94] See supra note 14.
[95] Prepared statement of Dr. Sue Bailey, DOD Assistant Secretary for Health Affairs, NSVAIR anthrax hearing (I), p. 13.
[96] Prepared statement of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Affairs Division, U.S. General Accounting Office, NSVAIR anthrax hearing (II), p. 12.
[97] DOD, briefing slide entitled, "Anthrax Threat," Apr. 20, 1998 (in subcommittee files).
[98] DOD, briefing slide entitled, "Assessment," Apr. 20, 1998 (in subcommittee files).

So Saddam would be "unlikely to use WMD unless he perceives regime's survival at stake." [99]

So the threat remains tactically limited and regional. The AVIP is universal.

Several factors appear to have fueled the 1997 decision to launch a mandatory, force-wide program to address a long acknowledged, regionally-based threat.

After the Gulf war, the Department of Defense undertook what is now characterized as "a detailed, deliberative process" [100] over more than 3 years that culminated in the conditional decision to implement a mandatory, force-wide anthrax immunization program. "After a three year study, the Department has concluded that the vaccination is the only safe way to protect highly mobile U.S. military forces against a potential threat that is 99 percent lethal to unprotected individuals." [101]

That study was conducted, for the most part, behind closed doors. However, the documentation provided to the subcommittee by DOD [102] describes a process more predetermined than deliberative, as the obvious operational benefits of passive, pre-exposure protection (versus cumbersome protective masks and suits), and the Iraqi threat, drove the decision to use the only vaccine currently available.[103]

In November 1993, DOD Directive 6205.3 set out a broad policy supporting immunization research, development, testing, acquisition and stockpiling of vaccines against current and emerging biological warfare threats. The directive required immunization only of "designated" or "programmed" personnel against agents "for which suitable vaccines are available, in sufficient time to develop immunity before deployment to high threat areas. . . ." [104]

With regard to anthrax, DOD conducted research and program planning to develop an "improved anthrax vaccine" [IAV] that would generate immunity against the known threat in a reasonable time. According to a DOD Operational Requirements Document [ORD], the need for an improved vaccine was identified in the Mission Needs Statement [MNS] for medical defense against chemical and biological warfare agents in August 1994 and in the MNS for Department of Defense biological defense in August 1992.[105]

The mission profile for the improved vaccine called only for inoculation of deployed and rapid deployment units "based on intelligence estimates of the potential for use of specific BW agents against U.S. forces. . . . Other military personnel will be vaccinated prior to departure to BW threat areas. An accelerated im-

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[99] Ibid.

[100] Prepared statement of Dr. Sue Bailey, Assistant Secretary of Defense for Health Affairs, NSVAIR anthrax hearing (I), p. 8.

[101] Letter from Sandra K. Stuart, Assistant Secretary of Defense (Legislative Affairs) to the Honorable Christopher Shays (CT), p. 1, Dec. 15, 1997.

[102] Letter from Representative Christopher Shays, chairman, Subcommittee on National Security, Veterans Affairs, and International Relations, House Committee on Government Reform to Secretary of Defense William Cohen, May 12, 1999 (in subcommittee files).

[103] Department of Defense, information paper, "DOD Biological Warfare Force Protection," Dec. 15, 1997, p. 2 (in subcommittee files).

[104] See supra note 7, p. 2.

[105] Department of Defense, "Operational Requirements Document [ORD] for Improved Anthrax Vaccine," Oct. 2, 1995, p. 1 (in subcommittee files).

munization program will be conducted under certain alert or mobilization conditions."[106]

Shortcomings of the currently licensed vaccine were seen as the "serious logistical obstacles, especially for reserve forces" posed by the approved six-shot schedule and reports that suggest "this vaccine may not provide universal protection against all anthrax strains."[107] Minimum standards for the improved vaccine included generation of a protective immune response within 14 days of administering three inoculations.

Briefing materials produced by the U.S. Army Medical Research Institute of Infectious Disease [USAMRIID] in 1994 listed the following problems with the current vaccine:

Prolonged immunization schedule
Reactogenicity:
Systemic reactions: 0.7–1.3%
Significant local reactions: 2.4–3.9% (5.9%)
Vaccine components completely undefined in terms of characterization and quantitation of the PA, and other bacterial products and constituents present
Significant lot-to-lot variation in the PA immunogen content
Human trials with similar but not identical vaccine showed protection against cutaneous anthrax but insufficient data to show efficacy against inhalation anthrax
Made from spore-forming strain requiring dedicated production facility[108]

Minutes of a May 1994 USAMRIID meeting addressed "the Army's need for a new Anthrax vaccine. This need is based on reactogenicity of the current vaccine, the desire to make a vaccine with defined and well characterized components, and the need to produce a vaccine which does not require a BL–3[109] containment for production or a dedicated production facility, since *B. anthracis* is a spore former."[110]

Iraq's 1995 declarations to the United Nations Special Commission [UNSCOM] described "a substantial BW program"[111] including 8,000 liters of anthrax, 6,000 of which Iraq claimed to have weaponized in missile warheads, aerial bombs, rockets, remote-control aircraft and agricultural sprayers mounted on planes and helicopters.[112] At the same time, DOD interest in an improved anthrax vaccine diminished sharply. Reservations about the suitability of the old vaccine were put aside once it was made the centerpiece of the proposed immunization effort.

The vaccine program is just one element of the Joint Biological Warfare Defense concept encompassing:

- detection and warning
- individual (masks, suits) and collective protection (sealed command and control facilities)

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[106] Ibid., p. B–1.
[107] Ibid., p. 2.
[108] U.S. Army Medical Research Institute of Infectious Diseases [USAMRIID], briefing slide, "Problems with Current MDPH Vaccine," (undated) (in subcommittee files).
[109] Bio-Safety Level 3, the second most stringent of the four levels of controls to protect persons handling infectious agents. For a description of current bio-safety standards see: http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4s3t.htm.
[110] See supra note 44, p. 1.
[111] See supra note 85, p. 5.
[112] Ibid.

- medical (vaccines) countermeasures to prevent disease
- contamination avoidance
- decontamination [113]

Treaties, anti-proliferation regimes, as well as the prospect of tactical and nuclear retaliation, are also meant to deter use of chemical and biological weapons.

These are meant to be parts of an "integrated and overlapping *systems approach* to BW defense"[114] in which both military and medical considerations dictate a hierarchy of force protection measures emphasizing contamination avoidance and physical protection over medical intervention and decontamination. One statement of chem/bio defense doctrine ranks force protection strategies as follows:

> . . . The most effective and singularly most important prophylaxis in defense against biological warfare agents is physical protection. Preventing exposure of the respiratory tract and mucous membranes . . . to infectious and/or toxic aerosols through use of a full-face respirator will prevent exposure, and should, theoretically, obviate the need for additional measures. Chemical protective masks effectively filter biological hazards.
>
> . . . All medical prophylactic modalities described should be viewed only as secondary (i.e., backup), and are not be relied upon as primary protective measures. Agent exposures near the source of dissemination will be high, and likely to overwhelm any medical protective measure.[115]

The AVIP makes medical prophylaxis a primary aspect of force protection and CBW deterrence. In testimony, the DOD Assistant Secretary for Health Affairs put the proposition quite directly: "Our greatest and prime biological enemy today is anthrax. And our strongest weapon against anthrax is vaccination."[116] The Navy's Deputy Surgeon General added:

> We are fortunate to have a time tested, safe and effective vaccine to provide an important element of the body armor needed to defend our personnel against weaponized anthrax. Anthrax has now joined other immunizations received by our Service men and women to protect against disease threats just as important as wearing a gas mask or carrying a rifle when on the battlefield.[117]

The Air Force Surgeon General expressed a similar rationale: "In addition to the potential human cost, mass casualties would degrade our military mission, military capability and mission accomplishment. We would not send people into battle without helmets

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[113] Ibid., p. 7.
[114] DOD, *Medical Defense Against Biological Material,* (undated) p. 1.
[115] Ibid. The section on Prophylaxis and Therapy continues: "The precise efficacy of available medical countermeasures has, of course, never been evaluated in actual field circumstances, but is largely inferred from laboratory studies on nonhuman primates. While these extrapolations may be inexact, they strongly support the efficacy of vaccines and drugs at some agent dose." (Emphasis in original).
[116] Testimony of Lt. Gen. Charles H. Roadman, Surgeon General, USAF, NSVAIR anthrax hearing (I), p. 17.
[117] Testimony of R.Adm. Todd Fisher, Deputy Surgeon General, USN, NSVAIR anthrax hearing (I), p. 17.

and weapons. So we should also provide the best armor against biological dangers that we can. That armor is immunization." [118]

But some service members see an important difference between the physical body armor worn in battle, which can be removed, and medical prophylaxis, which cannot. "The body armor that our Department of Defense refers to is perceived by many service members as 'tin foil armor.'" [119]

Primary reliance on medical intervention may also undermine confidence in other elements of the force protection hierarchy. One hearing witness asked if the vaccine might not "create a facade of force protection" provoking an adversary to even more lethal chem/bio or conventional attack.[120] He noted:

> These foundations of force protection rely on a credible willingness to use force. This resolve won the Cold War and it won the Gulf war. Abandoning this time tested doctrine and emphasizing the inevitability of biological attack to advocate a defensive anthrax vaccination policy may inadvertently result in legitimizing biological warfare.[121]

The vaccine policy also reflects a lack of confidence in current force protection equipment. Physical barriers, effective against all toxins and microbes if used properly and in time, are now viewed as "likely to remain only partially effective for the foreseeable future." [122] Protective suits and masks "degrade individual operating capabilities and force effectiveness . . ." [123] The purpose of the current doctrine on bio/chemical defense "is to maintain combat operations unencumbered by contamination and the wearing of the protective gear." [124]

Even this doctrinal reliance on the primacy of medical protection does not necessarily demand the universal, pre-deployment inoculation that characterizes the AVIP. Throughout the policy deliberation process, the option was considered to hold vaccines in stockpiles and defer actual immunization until mobilization to a threat area.[125] As late as September 1997, decision memoranda to the Under Secretary of Defense contained a recommendation to: "Maintain the planning guidance for total force immunization as a contingency plan, ready for finalizing, coordination, and approval at the appropriate time based on: (a) resolution, in conjunction with the FDA, of facility production issues; and/or (b) changes in the validated anthrax biological warfare threat." [126]

The decision to launch the force-wide, mandatory immunization program, despite well documented misgivings about the vaccine and the capacity of the vaccine manufacturer, seems to have been driven by a genuine concern to avoid casualties, a military requirement for theoretically uniform protection within deployed units, an

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[118] Testimony of Lt. Gen. Charles H. Roadman, II, Surgeon General, USAF, NSVAIR anthrax hearing (I), p. 18.
[119] Testimony of Captain Thomas Rempfer, NSVAIR anthrax hearing (I), p. 40.
[120] Ibid.
[121] Ibid.
[122] See supra note 85, p. 11.
[123] Ibid.
[124] See supra note 103.
[125] Dr. Edward D. Martin, et. al., Acting Assistant Secretary of Defense (Health Affairs), Department of Defense, "Memorandum for Deputy Secretary of Defense—Anthrax Vaccination Implementation Plan—ACTION MEMORANDUM," p. 1, Sept. 19, 1997 (in subcommittee files).
[126] Ibid., p. 2.

expansive view of demands on U.S. troop mobility, and the daunting logistics of the chosen vaccine.

"Why is it essential that the anthrax immunization be mandatory? Military commanders have the responsibility to ensure the health and safety of their troops and to carry out their mission responsibilities. Anthrax is a serious threat. We have a safe and efficacious vaccine. To not use the vaccine constitutes a failure to protect our troops and a risk to carrying out military missions."[127] According to DOD, "We are morally obligated to provide the best protection we are capable of providing to our troops—in the case of protection against anthrax, there is a vaccine to provide individual immunity to this biological warfare agent."[128] According to Dr Bailey, "Like other vaccines that are required to prepare military personnel for deployment, the anthrax vaccine is mandatory."[129]

But the anthrax vaccine requirement differs from general military immunization and chemoprophylaxis policy in two significant respects. Other inoculations are required pursuant to medical, not military command authority,[130] and they are required primarily to maintain and protect the health of personnel from naturally occurring diseases or pathogens endemic to specific duty or deployment areas. Although the threat of natural anthrax "remains a significant problem in numerous countries throughout Africa, the Middle East, Europe and Asia,"[131] the general military immunization policy contains no reference to the anthrax vaccine.

When asked how the United States program compared to the approach of allied forces, such as Great Britain which began a voluntary program, or Israel which appears to rely primarily on antibiotic treatments, the Pentagon responded, "DOD does not base its policies on those of our allies or coalition partners."[132] Because "our Armed Forces must be prepared to conduct successful military operations worldwide at a moments [sic] notice," DOD believes the "mandatory AVIP is clearly in our best interests and strongly supports our national security and military strategies."[133]

But there will be exceptions. A July 1999 Defense Threat Reduction Agency policy on anthrax immunization says:

> Deploying civilian employees who decline to participate in the DTRA-AVIP will be required to execute a "Statement of Informed Declination" attesting to the Agency's offer of anthrax immunization and the individual's decision to decline. By signing this statement, the employee acknowledges and willingly assumes the enhanced medical risk associated with travel to affected regions without receiving the recommended vaccinations. Hence, his/her deployment to these regions in support or mission requirements will not necessarily be precluded. This statement will become

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[127] Prepared statement of Dr. Sue Bailey, Assistant Secretary of Defense for Health Affairs, NSVAIR anthrax hearing (I), p. 10.
[128] DOD, *Public Affairs Talking Points,* p. 1, Dec. 15, 1997.
[129] Prepared statement of Dr. Sue Bailey, Assistant Secretary of Defense for Health Affairs, NSVAIR anthrax hearing (I), p. 10.
[130] Department of Defense, *Medical Services—Immunizations and Chemoprophylaxis,* Army Regulation 40–562, NAVMEDCOMINST 6230.3, AFR 161–13, CG COMDTINST M6230.4D, Oct. 7, 1988.
[131] See supra note 105, p. 1.
[132] See supra note 66, p. 14.
[133] Ibid.

a part of the individual's permanent Occupational Health Record.[134]

One of the primary reasons for the mandatory AVIP is the perceived need for consistent levels of force protection within and between deployed units to guarantee military effectiveness. Field commanders need to know the capabilities of their members. But even the force-wide, mandatory anthrax vaccine program is unlikely to meet that need. DOD concluded, but cannot prove, that individual antibody response to the vaccine equals protection from anthrax attack. That is, DOD believes the more anthrax-fighting antibodies produced, the more medical "body armor" has been acquired. Animal studies suggest this may be the case for some species, but no correlate has been developed to permit extrapolation of this conclusion to humans.[135]

In any event, DOD does not test military personnel for antibody levels to determine the extent to which members of a unit may have acquired protection against anthrax. Uniform protection is also unlikely because individual immunological response to the vaccine can vary substantially due to a variety of factors, including gender, and contemporaneous administration of other vaccines or medicines.[136] Nevertheless, DOD concludes enrollment in the AVIP equals protection for purposes of satisfying the need for uniform force protection.[137]

And, the very factors cited by DOD as necessitating universal AVIP coverage may actually work against that goal. Rapid mobility and the mixture of active and reserve forces mean individuals bring variable levels of protection to their assignments, depending on the number of shots taken to date and their individual immune system response. Some people don't respond to the vaccine at all.[138] So, beyond the general proposition that vaccinated individuals are likely to have some protection against some level of attack, the AVIP will not assure a commander that a unit is uniformly or even substantially protected. In tactical terms, the protection afforded by vaccination would be needed only during the time between detection and the order to deploy individual and collective physical protective measures (suits, masks, tents, et cetera). Better detection capability, improved masks and a battlefield doctrine to deploy protective measures earlier could limit or eliminate the need even for that small window of protection provided by the vaccine.

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[134] Defense Threat Reduction Agency, *Policy Memorandum 99–22,* July 23, 1999, p. 2 (in subcommittee files).

[135] Prepared statement of Kwai-Cheung Chan, NSVAIR anthrax hearing (II), p. 17.

[136] Testimony of Col. Renata Engler, Chief, Allergy-Immunology Service, Walter Reed Army Medical Center, NSVAIR anthrax hearing (IV), p. 173.

[137] See supra note 46, p. 1.

[138] Investigational New Drug [IND] application for anthrax vaccine adsorbed [AVA] submitted by Michigan Biologic Products Institute, Lansing, MI, Sept. 20, 1996, pp. 28–29 (in subcommittee files).

2. The AVIP is vulnerable to supply shortages and price increases. The sole-source procurement of a vaccine that requires a dedicated production facility leaves DOD captive to old technology and a single, untested company. Research and development on a second-generation, recombinant vaccine would allow others to compete

DOD has built a force-wide program on the narrowest possible industrial base.

According to GAO, "The most critical component of the program, an adequate supply of vaccine, is threatened by testing delays and possible loss of production capability."[139] Moreover, GAO found "DOD's plans for maintaining an adequate supply of vaccine are optimistic . . . and assume that FDA will grant approval of tested lots in less time than in the past."[140] Despite the possibility of further delays or a recurrence of financial problems at BioPort, "DOD does not have a formal contingency plan to deal with such possibilities."[141]

When DOD launched the AVIP, subject to the Secretary's four conditions including supplemental testing, MBPI/BioPort held 40 lots of vaccine, roughly the equivalent of 8 million doses, or enough vaccine to provide 1.3 million people the full six-shot regimen (assuming all lots were used before the expiration of original or extended label dating). But problems in the supplemental testing program delayed or precluded release of 18 lots.[142] GAO found:

> In summary, as of June 23, 1999, only 713,000 doses in the stockpile were available for use, and more than half of them—about 416,000 doses—will expire in February and April 2000. On the basis of DOD's estimates of doses required per month, the 713,000 doses would sustain phase 1 of the program through December 1999.[143]

But even that delayed schedule may be optimistic. FDA inspectional findings on the renovated facility contain a number of observations repeated from the February 1998 inspection.[144] FDA considered those earlier findings "significant" and took issue with DOD officials characterizing cGMP matters as mere "bookkeeping difficulties" in public statements.[145] If problems with the renovated facility are determined to be significant enough to bar release of vaccine lots produced since May 1999,[146] DOD could face severe shortages.

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[139] See supra note 26, p. 12

[140] Ibid., p. 5.

[141] Ibid.

[142] Ibid., p. 13.

[143] Ibid., p. 15; including an estimated 3-month supply already delivered to the field at the time of this estimate, GAO concluded the program could be sustained at best through March 2000.

[144] FDA Form 483, Nov. 15–23, 1999 (in subcommittee files). See also, Stars and Stripes, "Cohen Defends Mandatory Anthrax Shots After Ordering FDA-Related Suspension," p. 1, Dec. 20, 1999.

[145] E-mails between Food and Drug Administration and Department of Defense dated Aug. 31–Sept. 1, 1999 (in subcommittee files).

[146] Production of consistency lots began in the renovated and expanded BioPort facility in May 1999. Data on consistency lots is submitted to FDA to validate the production process. Other lots have also been produced by BioPort in the expanded facility, but use of those at risk lots depends on FDA approval of the facility license supplement, an amendment to the license regarding the potency test and approval of test data on each lot.

Because resumption of vaccine production has been delayed longer than anticipated by plant renovations and efforts to meet FDA compliance requirements, implementation of phase II of the AVIP, scheduled to begin in early 2000, has been delayed "in the range of 6 to 12 months." [147]

In addition to production problems and delays, BioPort may not be a reliable financial partner in the vaccine enterprise. At the subcommittee's request, the General Accounting Office [GAO] examined the structure and status of the financial relationship between DOD and BioPort.[148] They reviewed the contract documents, proposals and analyses done in connection with DOD procurement of the anthrax vaccine.[149]

Only 9 months after entering into the agreement, BioPort's ability to perform under the contract was in doubt.[150] In June 1999, the Defense Contract Audit Agency [DCAA] completed an audit of BioPort's financial condition and reached a similar conclusion.[151] According to GAO, estimates contained in BioPort's business plan and contract proposal have proven highly optimistic.[152]

As a result, BioPort had to request emergency assistance from DOD and major modifications to the contract.[153] In order to remain able to produce vaccine for the AVIP, BioPort sought and received an advance payment of $10 million, a significant per-dose price increase and DOD permission to sell up to 300,000 doses each year on the open market, despite the fact those doses would be produced using government furnished equipment under the DOD contract.[154] DOD also authorized BioPort's sale of up to 70,000 doses from the vaccine produced under the prior contract but either released or deemed never part of the stockpile.[155]

This early, extraordinary relief was necessary because production delays reduced estimated income. And, the procurement had to be done by means of a fixed price contract because neither side to the

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[147] Dr. Sue Bailey, Department of Defense news briefing, Dec. 13, 1999, p. 2 (available at: http://www.defenselink.mil) (in subcommittee files).

[148] Letter to David Walker, Comptroller General, U.S. General Accounting Office from Representative Christopher Shays, chairman, Subcommittee on National Security, Veterans Affairs, and International Relations, House Committee on Government Reform, May 13, 1999 (in subcommittee files).

[149] *Contract Management—Observations on DOD's Financial Relationship with the Anthrax Vaccine Manufacturer,* prepared statement of Louis J. Rodrigues, Director, Defense Acquisition Issues, National Security and International Relations Division, GAO, GAO/T–NSIAD–99–24, June 30, 1999.

[150] Testimony of Louis J. Rodrigues, Director, Defense Acquisition Issues, National Security and International Affairs Division, U.S. General Accounting Office, NSVAIR anthrax hearing (III), p. 4.

[151] Defense Contract Audit Agency, report No. 2261–97G21000018, Department of Defense, Sept. 24, 1997 (in subcommittee files).

[152] Prepared statement of Louis J. Rodrigues, Director, Defense Acquisition Issues, National Security and International Relations Division, GAO, NSVAIR anthrax hearing (III), p. 7.

[153] DOD briefing slides, "BioPort Contract—Anthrax Vaccine," June 2, 1999 (in subcommittee files). See also, BioPort Corp. media release, "Anthrax Vaccine Manufacturer Calls for Fair and Reasonable Cotract," June 30, 1999 (in subcommitee files).

[154] Testimony of David R. Oliver, Jr., Principal Deputy Under Secretary of Defense for Acquisition and Technology, NSVAIR anthrax hearing (III), p. 65.

[155] Testimony of David R. Oliver, Jr., Principal Deputy Under Secretary of Defense for Acquisition and Technology, NSVAIR anthrax hearing (III), pp. 64–65. See also, DOD briefing slides, "Anthrax Vaccine Absorbed Information Brief," June 4, 1999 (in subcommittee files). The briefing contained the following points: "Ms. Spector advised that doses in the inventory that have been paid for cannot be used by BioPort for Private/Foreign Sales" and "Release doses from stockpile for private sales—JPO/OSD action (very political)."

contract knew what it actually cost to produce the vaccine.[156] In its transition from a state-owned facility to a private enterprise, MBPI/BioPort has not fully implemented promised cost control and cost accounting systems to support a more appropriate cost-reimbursement procurement.

GAO also found the dependent relationship between DOD and BioPort unusual and risky. While sole-source procurements for vaccines may be common, those producers usually have other product lines generating income from other customers. In this case, problems with the production and delivery of the one vaccine put the corporation in an extemely bad financial position.[157]

One vaccine producer operating a single production site also points to security risks. GAO observed, "But if we are relying upon this vaccine as part of the backbone of our defensive biological program, the question of vulnerability to a single site becomes an issue. If you made a decision with respect to that vulnerability that led you to want to have an alternative site, then we probably should be looking at establishing a second source." [158]

Following the Gulf war, and prior to adoption of the DOD immunization policy (1993) and the mandated AVIP (1998), Pentagon officials considered and rejected alternative anthrax vaccine production sites.[159] Instead, an acquisition strategy was adopted focusing solely on the MBPI/BioPort vaccine.[160]

Since 1993, DOD has focused almost exclusively on the older, FDA approved vaccine, to the exclusion of development work on newer, recombinant vaccine formulations. Not surprisingly, DOD market surveys detected little interest by other pharmaceutical or biologics companies in producing the older anthrax vaccine under a licence from MBPI. So it appears DOD's sole source justification may be self-validating, in that there is only one AVA producer because the single largest vaccine customer has decided to deal with only one producer.

Other manufacturers would be more likely to express an interest in recombinant vaccine production because it can be done more safely and efficiently than older vaccine formulation methods involving live bacteria. But DOD decided not to emphasize recombinant anthrax vaccine development due to the lengthy (6 to 8 years) development and approval time, and potential high costs.

Yet, had DOD officials elected to pursue second-generation anthrax vaccine development aggressively 6 years ago, they would be nearing completion on a newer, purer anthrax vaccine. BioPort's current financial demands, and the company's power to hold the AVIP hostage in the future, appear to undermine DOD's determination the MBPI/BioPort acquisition strategy would prove more affordable than new vaccine development.

One legal review of the BioPort contract sole source justification suggested DOD add a reference to ways competition might be increased by utilizing alternative technologies to produce the anthrax

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[156] Testimony of Louis J. Rodrigues, Director, Defense Acquisition Issues, National Security and International Relations Division, GAO, NSVAIR anthrax hearing (III), p. 28.
[157] Ibid., p. 16.
[158] Ibid., p. 15.
[159] See supra note 36, p. 1.
[160] See supra note 37.

vaccine. The suggestion was not incorporated in the final document.[161]

It appears the choice of the MBPI vaccine for use in the AVIP may also have been premised on DOD and the manufacturer obtaining FDA approval to reduce the lengthy shot course from six shots over 18 months, to just two or three inoculations over 6 weeks. DOD developed a detailed program to gain approval for a shortened AVA shot course due to problematic levels of systemic (0.7 to 1.3 percent) and significant local reactions (2.4 to 3.9 percent) associated with the prolonged immunization schedule.[162] An Investigational New Drug [IND] application was filed on September 20, 1996 at the FDA to study a reduced anthrax vaccine shot course, but design of a definitive comparison study has never been submitted.[163]

So now, having foregone opportunities to improve or diversify anthrax vaccine production capacity, both DOD and BioPort are in a fiscal squeeze. Having made a substantial investment in MBPI and BioPort, DOD now faces hard, costly choices between sustaining the sole FDA licensed manufacturer of the anthrax vaccine, which may prove inadequate, and/or embarking on the establishment and licensure of another. In future budgets, DOD must consider to fund "developing a second source to BioPort or developing a different approach to solve the anthrax problem and don't take that money and put it against solving another bio-threat. . . ." [164]

While these alternatives are being reviewed, the mandatory force-wide program to provide protection against what DOD characterizes as the pre-eminent biological warfare threat is on a very uncertain procurement footing. Without more extraordinary DOD assistance, BioPort appears financially incapable of capitalizing and sustaining a highly technical, heavily regulated manufacturing process. The same financial pressures that hindered MBPI's ability to comply with FDA good manufacturing practices could also continue to affect BioPort's capacity to produce a safe and effective product on schedule.

3. The AVIP is logistically too complex to succeed. Adherence to the rigid schedule of six inoculations over 18 months for 2.4 million members of a mobile force is unlikely, particularly in reserve components. Using an artificial standard that counts only shots more than 30 days overdue, DOD tolerates serious deviations from the Food and Drug Administration [FDA] approved schedule

No other vaccine required by DOD for force health or combat protection demands so complex an administration schedule.[165] The

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[161] Elizabeth Arwine, Legal Advisor, "Legal Review of Justification and Approval [J&A];" Michigan Biologic Products Institute [MBPI], Jun. 3, 1997, p. 1 (in subcommittee files). See also, Joseph S. Little, "Response to JAG Comments," Department of Defense memorandum for record, June 4, 1997 (in subcommittee files).

[162] See supra note 108.

[163] Letter from Melinda K. Plaisier, Interim Associate Commissioner for Legislative Affairs, Food and Drug Administration to Representative Christopher Shays, chairman, Subcommittee on National Security, Veterans Affairs, and International Relations, House Committee on Government Reform, Mar. 15, 1999 (in subcommittee files).

[164] Testimony of David R. Oliver, Jr., Principal Deputy Under Secretary of Defense for Acquisition and Technology, NSVAIR anthrax hearing (III), p. 69.

[165] See supra note 130.

FDA approved inoculation regime is six shots over 18 months, with a subcutaneous injection of AVA to be given as follows:

#1—start of series
#2—2 weeks later
#3—1 month after start of series
#4—6 months after start of series
#5—1 year after start of series
#6—18 months after start of series.
Booster—annually after completion of initial series.[166]

The ability to track immunizations and meet this schedule was one of Secretary Cohen's four preconditions to the AVIP. But even the Secretary of Defense received his fourth inoculation 3 weeks before it was due.[167]

In an effort to comply with the elaborate timetable, DOD administers a three-tiered recordkeeping system. Each inoculation should be recorded on the individual service member's shot record.[168] Data recorded should include the date and AVA lot number. The same data is also entered into one of the service branch medical systems.[169] Finally, the service branch systems periodically forward inoculation data to the Defense Enrollment Eligibility Reporting System [DEERS], a pre-existing facility modified to serve as an interim access point for centralized AVIP data. In the future, DOD plans to centralize AVIP data using an upgrade of the Composite Health Care System now under development.[170]

This system was designed to address problems with medical recordkeeping encountered during Operation Desert Shield, Desert Storm, and in Bosnia.[171] However, while GAO found some improvements in vaccination records, a sampling of AVIP tracking at four locations discovered varying levels of discrepancies between paper and electronic data. According to GAO:

> Inconsistency in dates could lead to vaccinations being given off-schedule and to inaccurate readiness reports. Inconsistent or missing lot information could hinder investigations, should concerns arise over a specific lot. Also, information that is not recorded in paper records makes it difficult to address adverse reactions needing immediate care or determine the validity of subsequent claims for disability compensation.[172]

GAO also found use of DEERS data more limited than anticipated. "DEERS was envisioned as a major source of reports on program implementation. However, concerns about the timeliness and accuracy of data in DEERS have cause service representatives to rely on interim, service-specific tracking systems, and other systems to track and report vaccination information."[173] Specific concerns centered on duty station data, found in some cases to be up-

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[166] See supra note 41.
[167] E-mail from Col. Fred Gerber dated Sept. 1, 1998 (in subcommittee files).
[168] Form #PHS–731, Department of Defense (in subcommittee files).
[169] Service-specific subsystems: the Army MEDPROS, Navy SAMS and R–STARS, Air Force MITS.
[170] See supra note 26, p. 10.
[171] Ibid., p. 20.
[172] Ibid., p. 21.
[173] Ibid., p. 22.

dated only 6 to 9 months late.[174] This severely limits the utility of DEERS as a tool to generate unit compliance or readiness reports, since the database often does not reflect current unit membership. Readiness estimates based on AVIP tracking data are "still suspect," according to an internal DOD document.[175]

The difficulties of tracking anthrax vaccinations in the active force are compounded in reserve component units,[176] given changing unit memberships and monthly training schedules unlikely to match the inoculation regime. This difficulty was anticipated,[177] but DOD acknowledged in testimony that compliance with the FDA inoculation schedule in reserve component units was lower than in the active force due to less frequent drill schedules and timing of access to military medical facilities for purposes of receiving the vaccine.[178]

As the logistical challenges of vaccine compliance increase, so do the risks of deviations from the approved schedule. While the effect of schedule deviations is another unknown element of the AVIP, DOD concludes "the greater the deviation the less certain the protective effect in humans."[179] Nevertheless, "DOD set a timeliness goal of vaccinating 90 percent of all service members no more than 30 days after their vaccinations are due. . . ."[180] DOD reports meeting that goal.[181]

On August 4, 1999, the subcommittee requested data on vaccine regimen compliance in all reserve component units then enrolled in the vaccine program. The DEERS reports provided to the subcommittee contained shot records on 32,681 individuals who had received one or more inoculations prior to July 31, 1999. Almost half (15,625) the individuals listed were overdue to receive an inoculation. In some cases, entire units had missed the schedule by a month or more. A summary of the data follows:

Branch/Res. Comp	# Enrolled	# Overdue	% Overdue
AFReserves	8931	2954	33
AIRNG	9246	2482	27
ArmyNG	2441	1443	59
ArmyReserves	5802	3661	63
MCReserves	2730	1967	72
USNReserves	3531	3118	88[182]

The Air Surgeon, Col. James Dougherty, disputed the accuracy of the DEERS data. In an e-mail reacting to a media report of poor

[174] Ibid.
[175] E-mails from Maj. Guy Strawder dated Feb. 17, 1999 (in subcommittee files).
[176] Reserve components consist of Army, Navy, Air Force, and Marine reserve units as well as Army and Air National Guard units. Reserve units are elements of the national military. National Guard units are state militias unless federalized.
[177] See supra note 108.
[178] Prepared statement of Charles L. Cragin, Acting Assistant Secretary for Reserve Affairs, DOD, NSVAIR anthrax hearing (V), pp. 5–7; testimony of Charles L. Cragin, NSVAIR anthrax hearing (V), p. 150.
[179] Memorandum on "Policy Deviation from Anthrax Vaccine Immunization Schedule" from the Department of Defense dated Sept. 11, 1998, p. 1 (in subcommittee files).
[180] See supra note 26, p. 24. See also, testimony of Charles L. Cragin, Acting Assistant Secretary for Reserve Affairs, DOD, NSVAIR anthrax hearing (V), p. 150.
[181] Department of Defense, "Anthrax Vaccine Immunization Program Quarterly Review," Jan. 22, 1999, p. 9 (in subcommittee files).
[182] Letter and accompanying computer diskette from Charles L. Cragin to Representative Christopher Shays dated Aug. 23, 1999 (in subcommittee files).

compliance in a Connecticut Air National Guard unit, he said "all the data are inaccurate" because the DEERS system is updated weeks after shots are actually administered.[183] DOD also said the data showing overdue inoculations was inflated due to the inadvertent inclusion of Individual Ready Reserve forces, service members who are separated from military service but available for call-up.[184] Nevertheless, according to an internal DOD document, readiness estimates based on AVIP tracking data are "still suspect." [185]

If the centralized tracking system cannot provide a real-time picture of the inoculation status of the entire force, or individual units, it fails to meet the operational standard set by the Secretary as a condition of AVIP implementation.

The data provided to the subcommittee by DOD also showed most reserve component members receive the first three inoculations on schedule, with compliance deviations occurring with regard to subsequent shots.[186] That may not be entirely inadvertent. DOD documents contain the statement "Soldiers with 3 or more vaccinations are Protected." [187] The DOD position that "functional protection" [188] is provided after only three of the six required inoculations sets a deployability standard against which reserve component commanders are measured. Once members of a unit have received three shots, there appears to be little incentive to press for further compliance with an increasingly unpopular program.

There is little scientific evidence to support the theory that three shots protect as well as six. DOD expended significant time and resources in 1994 and 1995 on plans and programs to demonstrate the safety and efficacy of a shorter anthrax inoculation regime, and a different route of administration. An Investigational New Drug [IND] application was filed to guide further animal studies and clinical trials in humans. But the effort appears to have all but abandoned when planning for the AVIP began. Support for the FDA application to reduce the shot course seems to have been redirected to vaccine acquisition and AVIP logistics.

In September 1999, the Director of the FDA Center for Biologics Evaluation and Research, Dr. Katherine Zoon, wrote to Dr. Sue Bailey, Assistant Secretary of Defense for Health Affairs regarding data showing significant deviations from the AVA administration routine:

> . . . Because we are unaware of any data demonstrating that any deviation from the approval intervals of doses found in the approved labeling will provide protection from anthrax infection, we strongly recommend that the An-

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[183] E-mails from James Dougherty dated Sept. 1, 1999. (in subcommittee files)

[184] Testimony of Charles L. Cragin, Acting Assistant Secretary for Reserve Affairs, NSVAIR anthrax hearing (V), p. 104 (in subcommittee files).

[185] See supra note 175.

[186] See supra note 182.

[187] See supra note 134, p. 2, and e-mails from Department of Defense personnel dated Feb. 17–Apr. 14, 1999 (in subcommittee files); If the manufacturer of a pharmaceutical or biologic product advised patients or physicians that half the FDA approved dosage or administration regimen was as effective against the labeled indication, it would be a serious violation of FDA regulations.

[188] See supra note 134, p. 2.

thrax Vaccine Immunization Program follow the FDA approved schedule.[189]

Prior to the administration of each shot, medical personnel are directed to provide information on the vaccine and the program, and to inform each recipient regarding the health factors that should exclude a person.[190] Exclusionary factors include severe reaction to a previous shot, active infection, pregnancy, current immuno-suppression.[191] Service members should also be informed regarding the identification and reporting of adverse health events suffered subsequent to inoculation.[192]

But GAO found medical staff and service members were not well informed about reporting adverse events and found more than 40 percent of those sampled had not received information on how to report vaccine related adverse events.[193] Testimony by service members reflected the GAO findings.

Ms. Randi Martin-Allaire, a civilian employee of the Michigan Air National Guard told the Subcommittee, "I was on antibiotics at the time I received my fourth injection, and was never asked if I was on any type of medication or antibiotics." [194] Her colleagues described similar miscues and confusion over the standards for identifying and treating vaccine adverse reactions.[195]

Service members report AVIP information and briefings seem designed to persuade, not educate. The inability of Air Force briefers to answer service members' questions led one commander to suspend the vaccination program until the Air Force Surgeon General personally intervened.[196] Vaccine recipients also report mass inoculations during which no questions regarding current health status are asked and no VAERS forms made available.[197]

The AVIP is made more complex by the need to address growing resistance to the vaccine, specifically in reserve component units. The impact of the AVIP on retention in reserve component units could be significant. Informal surveys by service members suggest the Air National Guard may suffer air crew attrition of 30 percent or more.[198] To date, the Defense Department has not acknowledged any unusual pattern of resignations attributable to the AVIP.[199]

It is not clear where the Department might look to discern such a pattern. DOD collects no centralized data on refusals or resignations attributable to the vaccine program. Some service members also said unit commanders openly discouraged attribution of resignations or transfers to the AVIP.[200] An Air Force Reserve Interim Anthrax Policy forbids the approval of transfer requests

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[189] Letter from Dr. Katherine C. Zoon to Dr. Sue Bailey dated Sept. 29, 1999 (in subcommittee files).
[190] See supra note 46, p. C–5.
[191] See supra note 41.
[192] Department of Defense, "Clinical Practice Guidelines for Managing Adverse Events After Anthrax and Other Vaccinations," Nov. 15, 1999 pp. 1–2. (in subcommittee files).
[193] See supra note 26, pp. 24–26.
[194] Prepared statement of Randi J. Martin-Allaire, NSVAIR anthrax hearing (II), p. 170.
[195] Prepared statement of Roberta Groll, NSVAIR anthrax hearing (II), pp. 176–179; and prepared statement of David Churchill, NSVAIR anthrax hearing (II), pp. 183–188.
[196] Debra Funk, "Air Guard Unit Delays Anthrax Inoculations," Air Force Times, July 5, 1999, p. 29.
[197] E-mails and meeting notes (in subcommittee files).
[198] See supra note 74.
[199] Testimony of Maj. Gen. Paul Weaver, Director, Air National Guard, DOD, NSVAIR anthrax hearing (V), p. 118.
[200] E-mails (in subcommittee files).

made by anyone scheduled or directed to begin the anthrax immunizations.[201]

GAO was critical of this lack of monitoring to determine the effectiveness of the AVIP communications effort.[202] Without data on refusals, "it is difficult to better target educational efforts and address emerging concerns. These problems need to be resolved *if the program is to succeed* in vaccinating the entire force against anthrax."[203] (emphasis added)

To address the logistical challenges of the current immunization schedule, and to reduce the number of exposures to a "reactogenic"[204] vaccine, DOD developed a detailed program to gain approval for a shortened AVA shot course, but FDA approval has not been pursued.

4. Safety of the vaccine is not being monitored adequately. The program is predisposed to ignore or understate potential safety problems due to reliance on a passive adverse event surveillance system and DOD institutional resistance to associating health effects with the vaccine

Based on data gathered during limited occupational use since licensure, the AVA can be considered nominally safe. But the vastly expanded use of the vaccine for a new purpose requires a proactive approach to emerging safety issues. That approach is not now a part of the AVIP.

As with any vaccine, anthrax inoculation can cause adverse health events in some individuals, ranging from soreness or swelling at the injection site (local reactions) to fevers, chills, muscle aches, and anaphylaxis[205] (systemic reactions). Local reaction may be mild, moderate, or severe enough to require medical attention. Systemic reactions are generally considered clinically more significant. Reactions may increase in severity after successive injections.[206]

More inoculations mean more reactions. An immunization program using a vaccine requiring six shots and annual boosters should be prepared to deal with some number and variety of adverse health effects. Despite having been licensed for almost 30 years, the vaccine had not been widely used prior to the Gulf war.[207] As noted previously, lack of adequate medical record-keeping prevents systematic study of that cohort for health effects possibly associated with the anthrax vaccine and other medicines and toxins. The vaccine is being studied as a potential factor in Gulf war veterans' illnesses.[208] As GAO noted, "The long term safety of the vaccine has not yet been studied."[209]

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[201] Command Anthrax Policy, U.S. Air Force Reserve, June 22, 1999 (in subcommittee files).
[202] See supra note 26, p. 35.
[203] Ibid.
[204] See supra note 108.
[205] Hypersensitivity to a drug or antigen. Anaphylactic shock is an often severe, sometimes fatal, physical reaction characterized by respiratory symptoms, fainting, swelling, and itching.
[206] See supra note 41.
[207] Prepared statement of Kathryn C. Zoon, Ph.D., NSVAIR anthrax hearing (II), pp. 52–53.
[208] See supra note 1.
[209] Prepared statement of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Relations Division, GAO, NSVAIR anthrax hearing (II), p. 11.

The AVA has been described as a relatively crude, imprecisely characterized vaccine, and estimates of reaction rates vary widely.[210] According to the FDA-approved AVA product labeling, 30 percent of vaccine recipients can be expected to suffer mild local reactions, 4 percent will incur moderate local reactions, and less than 0.2 percent will experience systemic reactions.[211] In 1994 and 1995, DOD considered the need for a new anthrax vaccine "based on the reactogenicity of the current vaccine."[212]

In April 29, 1999 testimony[213] before the subcommittee, the General Accounting Office [GAO] summarized studies of anthrax vaccine reactions, finding rates of systemic reactions ranging from 0.05 percent to 48 percent. (Table 1, below).

Table I: Reactions to Licensed Anthrax Vaccine Reported in Various Studies

Study	Type of Reporting	Number Vaccinated (or doses)	Local reactions (percent)		Systemic reactions (percent)	
			Mild	Moderate/Severe	Mild	Moderate/Severe
IND	Active/Passive	3,984 [a]	6–20 [b]	1–10 [b]	None [b]	0.05 [b]
Pittman (1997)	Active	508	16	5	29 [c]	14
TAMC (1998)	Active	536	Not Addressed	Not Addressed	43 [d]	5
DOD (Current monitoring)	Passive	223,000 [e]	[e]	[e]	[e]	[e]

[a] This number represents the number of study participants who received the first dose of the licensed vaccine.

[b] These figures represent the percentage of people who experienced this type of reaction during the study, even if they had previously been inoculated with the Merck vaccine.

[c] This figure also includes persons who had reactions of "unknown" severity.

[d] This figure represents the frequency of the most common side effect, myalgia.

[e] DOD testified that as of Mar. 16, 1999, more than 223,000 service members have been immunized. There had been 42 reports on adverse effects submitted to the FDA and CDC. Only seven service members required hospitalization or experienced loss of duty for more than 24 hours.

In later testimony, GAO also observed:

> In addition to reporting to VAERS, DOD has conducted three efforts to actively collect data on adverse reactions after service members received the anthrax vaccine. Data from these efforts show that women reported twice the rate of adverse reactions than men for both local (e.g. swelling) and systemic (e.g. malaise and chills) reactions. In addition, a higher proportion of women than men reported making an outpatient medical visit after a vaccination, and more than twice the percentage of women reported that they missed one or more duty shifts after their vaccinations than did men.[214]

Captain Michelle L. Piel believes she suffered an adverse reaction to the anthrax vaccine. Fatigue, dizziness, joint pain and severe cold-like symptoms following her first two inoculations resulted in the loss of flight status. When she suggested submitting

[210] Ibid., p. 16.

[211] See supra note 41.

[212] "Minutes of FDA Meeting of 5 May 94 Concerning Production and Purification of PA from Delta Sterne," Department of the Army, May 19, 1994, p. 1.

[213] Prepared statement of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Relations Division, GAO, NSVAIR anthrax hearing (II), p. 16.

[214] Prepared statement of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Relations Division, GAO, NSVAIR anthrax hearing (IV), p. 3 (in subcommittee files).

a report to VAERS, she testified, "My request met reluctance."[215] Because her symptoms did not fall within the range of expected vaccine reactions, doctors as Dover Air Force Base did not associate her illness to the AVA. She concluded, "This is a major reason why adverse events from the anthrax vaccine are underreported."[216] She added,"It didn't make sense to me. I was too sick to fly. I was too sick to get another shot. But my illness wasn't reportable on a VAERS form?"[217]

When others at Dover suspected health effects might be linked to the vaccine, efforts to report a trend "were met with resistance and discouragement from within Dover's medical community."[218] According to Capt. Piel, "It took 6 months to reach the right, highly specialized doctors to begin to diagnose my immune system problems."[219]

At the reaction rates cited by the U.S. Army Medical Research Institute of Infectious Diseases [USAMRIID],[220] the anthrax vaccine program, when implemented across the entire 2.4 million member force, could produce 31,200 systemic reactions and up to 93,600 severe local reactions. Recently, the Army Surgeon General conceded that, "Systemic events occur in 5 to 35 percent of anthrax-vaccine recipients."[221] At the range of systemic reactions found by DOD in the Tripler Army Medical Center active surveillance study, the AVIP could generate over 1 million systemic reactions, many thousands of which will require medical management and treatment.[222]

Given that prospect, it might have been expected by service members that an integral part of the AVIP would be highly sensitive active and passive surveillance systems to "permit accurate assessments of types and severity of adverse reactions"[223] because "only widespread use can provide this assessment."[224] That was one factor which lead DOD to indemnify the vaccine manufacturer against the "unusually hazardous risks" of vaccine production.[225]

To better quantify those risks, and to detect adverse reaction trends early, the program design could have included detailed medical protocols on screening, vaccine administration, and adverse events. The AVIP could have assembled and trained a multi-disciplinary network of health professionals to manage the anticipated adverse event caseload. It could have provided each recipient with a simple, one page vaccine information sheet on adverse events and drug inter-actions of the type routinely provided with childhood vaccines. The AVIP could have designed and initiated the con-

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[215] Prepared statement of Capt. Michelle L. Piel, NSVAIR anthrax hearing (IV), p. 3 (in subcommittee files).
[216] Ibid.
[217] Ibid.
[218] Ibid.
[219] Ibid., p. 4.
[220] See supra note 108.
[221] Letter from Lt. Gen. Ronald R. Blanck to Mark Zaid dated Dec. 10, 1999, p. 1 (in subcommittee files).
[222] See supra chart at note 213.
[223] See supra note 33.
[224] Ibid.
[225] Ibid.

trolled, cohort studies only now being discussed to learn more about reaction rate differences by age and gender.[226]

The AVIP does not include those safety elements.

Instead, the program now relies primarily on an adverse event surveillance and reporting system known to understate the nature and extent of health effects associated with vaccine administration. Access to immunologists and allergists is limited geographically. Not until 1 year after the program began did DOD update briefing materials to include information on reporting adverse events and revise program regulations to make reporting requirements more inclusive, clarify patient and provider responsibilities, and explain how to process a Vaccine Adverse Event Reporting System [VAERS] form. Only in July 1999 did DOD distribute draft clinical guidelines that outline clinical protocols, pre-treatments, specialty referral processes, contraindications, categorizations of local and systemic reactions, and associated treatment algorithms.[227]

According to GAO testimony, studies have shown passive systems sometimes capture only 1 percent of adverse events temporally or causally related to use of a medical device or vaccine. Reports also vary in quality and utility due to inconsistencies in identifying and interpreting health effects as vaccine related. A passive system is useful as a "sentinel" to alert clinicians to unexpected events.[228] "It does not tell you how often, with what severity, or does not establish causality. The limitations are very well accepted." [229]

Because passive systems are voluntary, the data generated are subject to a self-selection bias, in that trends in volunteered data cannot be extrapolated as if representative of an entire cohort or population. As a result, information from a passive reporting system, like VAERS, is not an appropriate source of data for use in generating adverse reaction rates.

Nevertheless, AVIP reports and DOD public statements portray the ratio of VAERS reports to inoculations given as an adverse reaction rate.

> In presenting reaction rate data, program and DOD officials have shown reactions reported to VAERS as a percentage of all vaccinations. They did so in several briefings to GAO and congressional staff, in prepared testimony, and on the program's Internet site. However, according to FDA guidance, incidents in the VAERS database reflect a temporal, not necessarily a causal, relationship with vaccination and thus should not be used to calculate the incidence of reactions.[230]

GAO found, "This is misleading because of potential underreporting of events to VAERS, and the potential for overstating the reac-

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[226] Deborah Funk, "Military Officials Order Study to Determine Vaccine's Safety, Long-term Side effects," Army Times, July 12, 1999, p. 12.

[227] Prepared statement of Maj. Gen. G. Robert Claypool, Deputy Assistant Secretary for Health Operations Policy, DOD, NSVAIR anthrax hearing (IV), p. 12 (in subcommittee files).

[228] Testimony of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Relations Division, GAO, NSVAIR anthrax hearing (IV), p. 125 (in subcommittee files).

[229] Testimony of Dr. Shushil K. Sharma, Special Studies and Evaluations Section, National Security and International Relations Division, GAO, NSVAIR anthrax hearing (II), p. 25.

[230] See supra note 26, p. 32.

tion rate because reports sent to VAERS are not confirmed to be causally linked to the vaccination."[231] The potential for over-reporting is limited, however, by DOD screening of VAERS reports before inclusion in quarterly AVIP figures. In this regard, GAO concluded, "Thus, DOD does not have reliable information on the extent of adverse reactions."[232]

Even if useful to gauge short term reactions, passive reporting systems are also unlikely to capture long term or chronic health effects or syndromes, since providers and vaccine recipients do not generally associate an illness with an event far removed in time.[233] But many service members are concerned over possible long term health effects of the anthrax vaccine, alone or in combination with other treatments and exposures.[234] According to GAO, "A primary reason for dissatisfaction with information about long-term side effects appears to be that research has not been done to address the topic. According to program officials, such studies have recently been discussed but are not yet funded or underway."[235]

The AVIP's strict VAERS reporting requirements of hospitalization or more than 24 hours absence from duty limit the scope of any safety surveillance to severe, short term reactions. This overly narrow interpretation of adverse event data could result in DOD missing the types and severity of adverse reactions only widespread use would otherwise reveal. The "statistical significance of a predicted adverse reaction"[236] will only become apparent if the statistics are permitted to capture the full range of available data.

A system already known for underreporting can be made even less reliable in the hands of an institutional culture resistant, even hostile, to reports attributing ill health to the anthrax vaccine. Air Force Lieutenant Richard Rovet, while serving as Health Care Integrator for the Flight Medicine Clinic at Dover AFB, noted a number of individuals reporting potentially vaccine-related symptoms: dizziness, ringing in the ears, joint pain, muscle aches, memory impairment, fatigue, numbness, prolonged fever and chills, localized and persistent rashes.[237] He said there was significant confusion in the field regarding reportable reactions "especially in regard to what constitutes systemic reaction."[238] Lt. Rovet testified medical providers saw the issue of identifying vaccine reactions "politically sensitive and like to avoid it."[239]

That resistance reduces what few incentives already motivate military personnel to report sick. Particularly when complaining of symptoms of unknown origin, a service member risks the label "malingerer" or "depressed."[240] If seeking care seems a dead end,

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[231] Ibid.
[232] Ibid.
[233] Prepared statement of Dr. Meryl Nass, NSVAIR anthrax hearing (II), p. 107.
[234] Prepared statement of Capt. Michelle L. Piel, NSVAIR anthrax hearing (IV) (in subcommittee files); prepared statement of Capt. Jon Richter, NSVAIR anthrax hearing (IV) (in subcommittee files); and e-mails sent to the subcommittee (in subcommittee files).
[235] See supra note 26, p. 32.
[236] See supra note 30.
[237] Prepared statement of Lt. Richard Rovet, NSVAIR anthrax hearing (IV), p. 2 (in subcommittee files).
[238] Testimony of Lt. Richard Rovet, NSVIAR anthrax hearing (IV), p. 25 (in subcommittee files).
[239] Ibid.
[240] Prepared statement of Capt. Michelle L. Piel, NSVAIR anthrax hearing (IV) p.3 (in subcommittee files).

"why risk your flying status if you are just suffering some of the mild symptoms of joint pain or you feel a little bit tired? Why should you go to the doctor if you feel you can continue to operate an airplane? And that is why people don't come forward." [241]

An Air Force Reservist, Capt. Jon Richter, also suffered chronic symptoms he attributed to the vaccine. While he came forward, he testified there is little incentive for others do so. "I was encountering more of my squadron mates who were vaccinated that said they too had experienced various reactions, including tinnitus, dizziness, muscle and joint pain, and, in one case, gray-outs. However, most were attempting to keep it low profile and did not readily discuss these matters for fear of reprisal." [242] "Word travels fast. Morale is at an all time low. People are trigger shy about coming forward with their symptoms. There is an air of fear and distrust prevalent throughout." [243]

A reluctance to acknowledge vaccine related health effects could also block access to the immunologists and allergists experienced in the diagnosis and treatment of adverse reactions. This can be a more acute problem for National Guard and Reserve members whose level of access to military medicine, particularly specialists, for vaccine matters is uncertain. Witnesses at the subcommittee's April 29 hearing from the Michigan Air National Guard described a difficult and time consuming process to gain access to medical personnel with relevant expertise.[244]

According to the Dr. Renata Engler, Chief Immunologist at the Water Reed Army Medical Center, and a consultant to the AVIP, "Vaccine administration is serious business and deserves more care and training of those who deliver the service." [245] One critical issue, she said, "is that stakeholders who understand the clinical issues have NOT been represented in the organizational policy development." [246] "There is a problem that the organization does NOT have a forum for experienced, ongoing clinical input into the many problems that surround immunization delivery and adverse reaction management." [247] (Emphasis in original).

Those problems include recognition of potentially life-threatening hypersensitive reactions, use of pre-treatments to mitigate vaccine reactions and the criteria to be applied to determine temporary or permanent medical exemption, or waiver, from the AVIP. At the first DOD conference on biological warfare immunizations, held in May 1999, Dr. Engler made a presentation on the clinical challenges posed by the AVIP. She summarized several case studies of those who had suffered adverse reactions to the anthrax vaccine, with data from Walter Reed Army Medical Center, data from Dr. Hoffman's study in Korea, and patient profiles from Dover AFB.[248] In her slide presentation, she noted a "fear of military medical es-

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[241] Testimony of Capt. Michelle L. Piel, NSVAIR anthrax hearing (IV), p. 59 (in subcommittee files).
[242] Testimony of Capt. Jon Richter, NSVAIR anthax hearing (IV), p. 38 (in subcommittee files).
[243] Ibid, p. 41.
[244] Prepared statement of Roberta Groll, NSVAIR anthrax hearing (II), pp. 176–179; prepared statement of Randi Martin-Allaire, NSVAIR anthrax hearing (II), pp. 167–171; and prepared statement of David Churchill, NSVAIR anthrax hearing (II), pp. 183–188.
[245] E-mails from Col. Renata Engler dated Dec. 4, 1998 (in subcommittee files).
[246] E-mail from Col. Renata Engler dated Dec. 15, 1998 (in subcommittee files).
[247] Ibid.
[248] See supra note 51, pp. 3–7.

tablishment" and concluded the AVIP message should be, "Every service member deserves the same quality of care as ANY OTHER PATIENT: investigate problems proactively & objectively, validate suffering, knowledge base and unknowns. Vaccines are drugs & NOT 100% safe." [249]

Regarding the availability of medical deferrals and waivers, Dr. Engler asked, "Should medical waivers become a punitive event? . . . Do we want rigid administrative guidelines that polarize and antagonize service members with problems? Can we acknowledge risk & include choice of affected AD in final disposition? Does every service member have to be immunized or is there room for a benefit risk ratio discussion?" [250]

Room for that discussion may be limited. The risk/benefit decision underlying the AVIP can conflict with the clinician's duty to weigh the risks and benefits to the individual patient. In an e-mail exchange with Col. Fred Gerber, operational head of the AVIP, Dr. Engler posed the following example:

> A rash within 2 hours of the vaccine could represent an increased risk for life threatening anaphylaxis with next dose—if you ignore this and do not handle it appropriately and a subsequent dose results in significant harm, you are outside the standard of care and would NOT be excused by the "active duty" blanket. Our specialty has worked with this type of patient and achieved successful and safe subsequent vaccination but this requires expertise and very carefully prepared informed consent. ETHICALLY, you cannot expose a soldier to a medical treatment if he/she is at increased risk for harm from it and yes we do waiver people for serious vaccine reactions from future reactions and they continue on active duty for the most part. Anthrax brings unique urgency to the scenario and a group discussion on these issues with an ethicist is crucial.[251] (Emphasis in original).

Col. Gerber, while disclaiming any purview over clinical issues, was unwilling to acknowledge that safety considerations might need to overcome the AVIP imperative in some number of cases:

> Not sure I agree with what you've presented Renata. If . . . she had a rash within 2 hrs of shot #1 . . . [w]hy would that exempt her from getting rest of series and going to Korea? Who should go in her place? Those become the issues. Korea is one of the two AVIP Phase I High Threat Areas . . . everyone is at increased risk for exposure to anthrax there. By your algorithm, when we get to Phase II of the AVIP, new soldiers coming into service would be put out of service because of an adverse reaction to anthrax . . . what about an adverse to any of the other 17 immunizations? . . . Call it like you see it, but I wouldn't quickly exempt soldiers from worldwide assignments who have rashes, pain, swelling, etc. Let's face it, AVA is one of many soldiers have to take. The more exotic

[249] Ibid., p. 12.
[250] Ibid.
[251] See supra note 245.

> vaccines are yet to come. . . . Does a rash in 2 hours mean you can't get any more immunizations without additional clinical follow-up/eval? I'm not sure it does.[252]

Concerns about the short and long term safety of the anthrax vaccine are legitimate. It is disingenuous for DOD to say 30 years of use have seen no serious short-term or chronic adverse health effects associated with the vaccine. For most of that time, no one was looking.

The short-term adverse reaction rates contained in the FDA-approved labeling were derived from data gathered during testing of an earlier, less reactogenic anthrax vaccine. FDA only established the Vaccine Adverse Event Reporting System in 1990. That passive surveillance system, while useful to detect sentinel events or clusters for further study, understates the extent of reactions. Limited use of the vaccine since licensure has yielded limited information that suggests higher reaction rates, particularly in women.[253]

Since the AVIP began, DOD has undertaken two active follow-up surveys of vaccine recipients, one in Korea and another at Tripler Army Medical Center, Hawaii. The results of both studies indicates both local and systemic reactions at generally higher rates than described in the product labeling. According to GAO, "The data gathered in Korea also show that after the first two shots, more than twice the proportion of women than men reported systemic reactions of fever, malaise, or chills than did men."[254] The Tripler survey also demonstrates gender differences in reported reactions.[255]

Service members' concerns about the impact of manufacturing process lapses on vaccine quality and safety are well placed. For biological products, the process is the product. "[Q]uality cannot be guarantees from final tests on random samples but only from a combination of in-process tests, end-product tests, and strict controls of the entire manufacturing process."[256] At BioPort, and its predecessor the Michigan Biologics Products Institute, those controls were found to be less than strict.

The long-term safety of the licensed vaccine has not been studied.[257] It is of little comfort to service members that no other vaccines have been subject to any post-licensure longitudinal study. Unlike more modern vaccines, the AVA was approved before animal toxicity studies were even required. As a result, "studies have not been performed to evaluate the effect of AVA on carcinogenesis, mutagenesis or impairment of fertility. Animal reproduction studies have not been conducted with AVA. Neither is it known whether AVA can cause fetal harm when administered to a pregnant woman or whether it can affect reproductive capacity."[258]

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[252] E-mails from Col. Fred Gerber dated November 17, 1998 (in subcommittee files).
[253] "Anthrax Vaccine: Safety and Efficacy Issues," (GAO/NSAID–00–48) U.S. General Accounting Office, Oct. 12, 1999, pp. 1–7.
[254] Ibid., p. 3.
[255] Ibid., p. 4.
[256] Prepared statement of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Affairs Division, GAO, NSVAIR anthrax hearing (II), p. 13.
[257] Ibid., p. 11.
[258] See supra note 138, pp. 87–88.

It is unlikely the current anthrax would be approvable under modern regulatory standards for the safety and efficacy of biological products. It seems unlikely BioPort will be able to achieve and sustain modern manufacturing standards for safe vaccines.

5. Efficacy of the vaccine against biological warfare is uncertain. The vaccine was approved for protection against cutaneous (under the skin) infection in an occupational setting, not for use as mass protection against weaponized, aerosolized anthrax

Uncertainties about safety might be more readily accepted if there were no questions about the effectiveness of the anthrax vaccine. Safety risks would be tolerable if the benefits were unquestioned. But there are questions. The proposition that the AVA will provide effective protection against the most likely form of weaponized anthrax, aerosolized spores in significant quantities, is unproven.

And, until there is an anthrax attack, the proposition must remain unproven. The industrial settings in which anthrax was a threat have all but disappeared.[259] It would be unethical to expose human test subjects to a lethal agent. So, based on proven efficacy against indeterminate levels of cutaneous exposure in an industrial setting, it can only be assumed the vaccine provides equivalent protection against high levels of inhalation exposure.

That assumption is supported by data from tests on vaccinated animals who survive aerosol challenge. But different survival rates between animal species, and between anthrax strains, raise more questions than the vaccine answers about the actual physiological mechanism of protection. Without a way to correlate animal data to human protection (i.e., PA antibody titers), efficacy of the vaccine may never be more than suggested or inferred.

According to GAO:

> Studies on the efficacy of anthrax vaccine have been limited to a study of the efficacy of the earilier version for humans and studies of the efficacy of the licensed vaccine for animals. The only study of the efficacy of the vaccine for humans was performed by Brachman, using the original vaccine. The Brachman study claimed that the vaccine gave 93 percent (and a lower confidence limit of 65 percent) protection against anthrax penetrating the skin. It found that the number of individuals who contracted anthrax by inhalation was too low to assess the efficacy of the vaccine against this form. There has been no specific study of the efficacy of the licensed vaccine in humans. Rather, its efficacy in humans has been inferred from other data, including a reduction in the incidence of anthrax following immunization of at-risk individuals and from animal experiments.[260]

All the DOD animal studies support the view that the licensed vaccine can protect some animals against exposure to some strains

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[259] Only research and testing facilities now present an occupational setting posing a danger of anthrax exposure.

[260] Prepared statement of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Affairs Division, GAO, NSVAIR anthrax hearing (II), pp. 16–17.

of anthrax either by inoculation or inhalation. But animal species differ in susceptibility.[261] In testimony submitted to the subcommittee, Dr. Meryl Nass summarized the available data from animal studies of anthrax vaccine efficacy. "One can see varying survival rates from 0–100% depending upon the strain of anthrax used and possibly other parameters of the experiment. Survival rates in guinea pigs varied from 23% to 71% when they were exposed to inhaled anthrax."[262] Studies in mice showed survival rates between no higher than 10 percent.[263]

In concluding the current vaccine is effective against aerosol challenge, DOD relies primarily on studies using rhesus monkeys. "These animal studies showed that the FDA-approved anthrax vaccine provided greater than 95% protection against high-dose aerosol challenge with anthrax in the monkey model. Human antibody response to the FDA-licensed vaccine provides further suggestive evidence that the FDA-licensed anthrax vaccine will protect against inhalation anthrax."[264]

But, according to GAO, "several studies have shown no direct comparison of immunity in humans to that in monkeys."[265] In fact, the one immunized monkey that died in the DOD studies "had a low antibody titer similar to other monkeys that lived following a lethal aerosol challenge."[266]

One study comparing the efficacy of a live spore vaccine to a PA-based vaccine, like the AVA, concluded, "Immunization with cell-free preparations which contained components of that anthrax toxin did not provide adequate protective response against some challenge isolates of *B. anthracis.* The fact that the spore vaccine provided protection against all isolates tested suggests that other antigens may play a role in active immunity."[267]

DOD resists that suggestion because confidence in the efficacy of the current anthrax vaccine in humans, against all known strains, depends heavily on the conclusions 1) that the antibody response to the one antigen, PA,[268] protects against the toxic mechanism of all natural anthrax, and 2) that the antibody response in animals correlates to a similar protective response in humans.

The lack of an immunological correlate of protection against anthrax limits the extent of efficacy claims that can be made about the current vaccine, and it poses a profound challenge to the studies needed to approve an improved vaccine or a shorter AVA shot course. In describing the challenges to demonstration of efficacy for proposed changes in the dose and use of the current anthrax vaccine, DOD noted:

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[261] See supra note 253, p. 8.
[262] Prepared statement of Dr. Meryl Nass, NSVAIR anthrax hearing (II), p. 108.
[263] Ibid., p. 110.
[264] Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DOD, NSVAIR anthrax hearing (I), p. 11.
[265] U.S. General Accounting Office, Correspondence to Representative Steve Buyer from Kwai Cheung-Chan, "Summary of GAO's Findings on the Safety and Efficacy of the Anthrax Vaccine," (GAO–NSIAD–00–54R), Nov. 4, 1999, p. 3.
[266] See supra note 138, p. 90.
[267] Stephen F. Little and Gregory B. Knudson, "Comparative Efficacy of Bacillus anthracis Live Spore Vaccine and Protective Antigen Vaccine against Anthrax in the Guinea Pig," Infection and Immunity, May 1986, vol. 52, No. 2, p. 511.
[268] Protective antigen [PA] is one of three proteins involved in the mechanism of anthrax toxicity.

> Presently there are no precise serological or other immunological correlates of protection to enable conclusions to be drawn from immunization studies in man. The extrapolation from animal studies to humans likewise is seriously complicated by this fact. . . .
> The demonstration in some animal models that protection with the present vaccine varies across challenge strains further complicates studies and limits the breadth of efficacy claims that can be made.
> To date, no animal or other potency test has been demonstrated to be well correlated with protection of humans. *The potency test required for the present vaccine*[269] *has not been well correlated to efficacy in humans and it is doubtful that it can be.* (Emphasis added).
> It has recently been stated that the antigenic components of the licensed vaccine are not well defined and that there is lot to lot variation in the level of protective antigen. Because of these points, efficacy studies will likely have to include multiple lots to demonstrate consistency of protection.[270]

Regarding efficacy, one author of an anthrax vaccine study wrote, "My concern is not the long-term health effects of this vaccine, but rather that it is not efficacious against all strains of *B. anthracis.* If I were the scientific director of an offensive BW program for a government hostile to the U.S., I would direct my investigators to repeat this experiment, screening a larger number of *B. anthracis* isolates until a strain was isolated that would kill immunized animals, and then use that vaccine resistant strain as the stock for producing spores to be used in filling BW submunitions." [271]

Genetically engineered anthrax strains could also defeat the current vaccine if the resulting organism caused disease in new ways. Reports that Russian scientists successfully inserted genes into a virulent anthrax strain were received by DOD with some skepticism. Col. Gerald Parker, then-commander of USAMRIID, was quoted as saying the claims needed to be evaluated "to learn whether the advance is theoretical or practical, and whether it could sidestep the American anthrax vaccine." [272] Taking a more skeptical approach to threat assessment than DOD uses with regard to natural anthrax, Col. Parker added, "It's one thing to do this in the lab. But its a whole different thing to produce it in large quantities to be used as a weapon. That would be very difficult." [273]

Concerns about the efficacy, and by implication the necessity, of the vaccine are legitimate given the extent of unproven, unknown, and perhaps unknowable, aspects of the protection afforded. The vaccine almost certainly could be overwhelmed by a high-dose aerosol exposure. Immunized troops near an initial release point could

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[269] The current potency test uses guinea pigs.
[270] See supra note 138, p. 45 (presentation slide entitled, "Challenges to Demonstration of Efficacy for the Proposed Changes in Dose and Use of Anthrax Vaccine," included in supporting documentation to MBPI IND application) (in subcommittee files).
[271] Memorandum from Gregory B. Knudson to Representative Christopher Shays dated May 8, 1999, (in subcommittee files).
[272] William J. Broad, "Gene-Engineered Anthrax: Is It a Weapon?" New York Times, Feb. 14, 1998 (in subcommittee files).
[273] Ibid.

still suffer significant casualties. The vaccine may have diminished effect against highly virulent strains, or combinations of strains. The vaccine may provide no protection against genetically engineered anthrax.

RECOMMENDATIONS

1. The force-wide, mandatory AVIP should be suspended until DOD obtains approval for use of an improved vaccine

The anthrax vaccine program is not sustainable in its present form. Due to the lack of assured production, AVIP phase II has already been delayed. Confidence in the quality of the vaccine stockpile is low and the capacity to procure sufficient new production remains highly doubtful. The program should be suspended while contingency plans for allocation of available vaccine are formalized and research is conducted to obtain a safer, more effective vaccine.

Signaling an awareness the anthrax immunization effort was on weak conceptual and logistical footing from the start, Secretary Cohen announced four preconditions to the start of the program: supplemental vaccine testing, an adequate tracking system, completed implementation and communication plans and an independent scientific review. Those were appropriate. Had they been more scrupulously addressed, the AVIP might be a very different, much better program.

The military anthrax immunization program should have been conditioned on completion of the same level of research and testing required of other battlefield systems. We would not ask U.S. forces to fight using rifles designed in the 1950's. We should not ask them to rely on 1950's era medical technology, when modern science has the capacity to produce an improved vaccine. Much has changed in the biologics industry since the AVA was first approved in 1970. As evidenced by FDA inspectional findings in 1998 and 1999, not enough has changed at the vaccine production facility to bring it into full compliance with modern manufacturing standards. It is doubtful the AVA would be approved by the FDA today.

As additional assurance the anthrax immunization program is as safe as possible, DOD should test the vaccine for toxicity, mutagenicity, carcinogenicity and reproductive effects in animals. The current AVIP should be suspended while those studies, and other steps recommended by the subcommittee, are undertaken.

The AVIP should be suspended because it lacks an essential element in a medical program: trust. However well-intentioned, the anthrax vaccine effort is viewed by many with suspicion. It is seen as another chapter in a long, unhappy history of military medical malfeasance in which the healing arts are corrupted to serve a lethal purpose.

The fundamental rationale for the AVIP—that something, even an old, questionably effective vaccine, is better than nothing—gives little comfort to those who daily see their forebears and colleagues grow sicker from radiation testing, Agent Orange, and Gulf war illnesses. If the noble experiment fails, if the vaccine ultimately causes more casualties than weaponized anthrax, many men and women in uniform do not believe their Government will acknowledge their sacrifice or treat their wounds.

Trust must be earned. It can be earned only with a degree of candor and openness that has not been the hallmark of the AVIP to date. While claiming a new awareness of the need for effective risk communication, the Pentagon still reverts to absolutist declarations, heavy handed propaganda, and *ad hominem* attacks whenever the risks of the anthrax vaccine are communicated too effectively or persistently. In a culture based on a chain of command and the power to compel, attempts at persuasion and education often devolve into intimidation. Labeling opponents "paranoics"[274] and ridiculing the intelligence or courage of those with legitimate questions[275] are not the methods of modern risk communication.

Nowhere is DOD's failure to communicate the relative risks and benefits of the AVIP more obvious than in reserve component units. The bulk of vocal resistance to the AVIP has arisen in the few Reserve and National Guard units included in phase I. Those service members have more options than active duty personnel. If they conclude the anthrax vaccine poses more risk than benefit to their civilian and military careers, they can resign, or seek a transfer to a non-mobility position. Many have done so.

DOD appears to be in denial on this issue, ignoring clear signs the anthrax program is having, and will certainly have, a substantial impact on retention and morale in reserve component units. At the subcommittee's September 29, 1999 hearing on the subject, Maj. Gen. Paul Weaver, Director, Air National Guard, testified there had been "one known refusal documented."[276] Previously, the subcommittee had received testimony and correspondence from several members of Air Guard units who had refused the vaccine, more than one of whom were in the hearing room when Gen. Weaver made that statement.

Principal Deputy Assistant Secretary of Defense (Reserve Affairs) Charles Cragin testified the impact of the AVIP on retention was "negligible"[277] despite having been given information just days before that more than half the air crew in one unit has submitted resignations attributable directly to the anthrax program.[278] At the same hearing, Mr. Cragin conceded "the Department's efforts to inform and educate reserve personnel about the anthrax protection program were not initially as robust as they should have been."[279]

Until much more is known about the true impact of a mandatory vaccine program on retention, readiness, and morale in the most voluntary sector of the all-volunteer U.S. armed forces, the AVIP should be suspended.

Rather than risk long term health impairment, some service members would be willing to consider the vaccine-preventable risk of anthrax among the inherent, unavoidable risks of military service. They do not have that option, an opportunity to assume risk

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[274] See supra note 79.
[275] See supra note 80.
[276] Testimony of MG Paul Weaver, Director, Air National Guard, NSVAIR anthrax hearing (V), p. 119.
[277] Prepared statement of Charles Cragin, Acting Assitant Secretary for Reserve Affairs, NSVAIR anthrax hearing (IV), p. 3.
[278] Letter (with attachments) from Charles Cragin to Representative Christopher Shays, attachment p. 1, Oct. 21, 1999. (in subcommittee files).
[279] Prepared statement of Charles Cragin, Acting Assitant Secretary for Reserve Affairs, NSVAIR anthrax hearing (IV), p. 4.

made available to essential civilian employees of the Defense Threat Reduction Agency.[280]

Others view this force protection effort as an untested medical solution to a purely mechanical problem—contamination prevention and avoidance—better solved by physical rather than pharmacological technology. With regard to the anthrax vaccine, DOD appears to accept more unknowns and greater technological risks than would be tolerated in any combat weapon system. As a result, some service members are not convinced this "commander's program" is for their long-term protection as much as for battlefield convenience and the preservation of short-term mission capability while under anthrax attack. Suspension of the AVIP would allow DOD to focus more attention and resources on development and deployment of chemical defense doctrine, tactics, detection capability as well as individual and collective protection equipment effective against all threats.

The subcommittee makes no recommendations regarding the status of those service members who left the armed forces voluntarily, or as the result of disciplinary actions, due to the anthrax vaccine program. Just as each service branch, operating under the Uniform Code of Military Justice, determined its own approach to vaccine refusals, each should determine through its own processes what appeals, if any, might be available in the event the AVIP is restructured or suspended.

2. DOD should accelerate research and testing on a second-generation, recombinant anthrax vaccine

Despite the "clear and present danger"[281] posed to U.S. troops by anthrax as a biological weapon, DOD considers development of an improved anthrax vaccine "an unfunded requirement."[282] Had that requirement been addressed more aggressively after the Persian Gulf war, the 8 to 10 year development, testing and FDA approval process now posited by DOD as an potential barrier to a new vaccine could have already been breached.

Although an improved vaccine based on recombinant technology may not necessarily have better safety characteristics than the current vaccine,[283] it would address two other problems plaguing the AVIP. Production of a second vaccine, at a second site, would diversify the industrial capacity to support so critical a program, making vaccine supplies more abundant and more secure from attack. And, because recombinant techniques do not require extensive dedicated facilities, capital costs can be allocated across more than one product, increasing the likelihood other manufacturers would compete for DOD contracts.

The second generation vaccine studied by DOD was also more consistently characterized in terms of PA content than the AVA.[284] Lot-to-lot consistency would address one challenge noted by DOD

[280] See supra note 134.

[281] See supra note 66, p. 1.

[282] Testimony of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Affairs Division, GAO, NSVAIR anthrax hearing (IV), p. 100.

[283] Testimony of Col. Renata Engler, Chief, Allergy and Immunology Department, Walter Reed Army Medical Center, NSVAIR anthrax hearing (IV), p. 155.

[284] Prepared statement of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Relations Division, GAO, NSVAIR anthrax hearing (IV), p. 13.

to demonstrating efficacy of a vaccine that cannot be tested in humans.[285] It would also give commanders greater confidence that vaccinated troops, to the greatest extent possible, have achieved a more uniform level of protection.

David Oliver, Principal Deputy Under Secretary of Defense for Acquisition and Technology, said in testimony that DOD would be reviewing procurement options with regard to a second AVA production site versus a new vaccine. He suggested, however, that funds spent on an improved anthrax vaccine would limit funds available to address other bio-threats.[286] That trade-off puts anthrax on a par with other biological agents in terms of threat, when in fact DOD considers anthrax the pre-eminent bio-threat. Budgets estimates for the Joint Vaccine Acquisition Program [JVAP] indicate DOD anticipates procurement of limited, deployment-contingent stocks of vaccines against other biological weapons, making anthrax the only agent targeted for universal immunization. Improving the medical prophylaxis against the primary threat should be a DOD funding priority.

DOD concedes, "In the case of anthrax vaccine, the current FDA-licensed vaccine is not ideal. The vaccine was developed in the 1950's and 1960's by the state-of-the-art procedures at that time, and licensed in 1970. Advances in biotechnology and genetic engineering may enable improvements in the vaccine that allow fewer doses or use of highly purified protective antigen. The DOD scientists are pursuing both of these objectives. A highly-purified recombinant protective antigen vaccine has shown efficacy in animal models." [287]

But DOD is unwilling to wait for the research, development, and FDA approval processes,[288] even though DOD believes "within a year we will get FDA approval for reduced dose based on the science." [289]

To address the domestic bioterrorism threat, the Department of Health and Human Services' National Institute of Allergy and Infectious Diseases formed a working group to develop and test a second generation anthrax vaccine, and the Institute has funded some research. DOD should support those efforts.

With regard to an improved anthrax vaccine, the American Public Health Association adopted a policy statement in November 1999 urging DOD to "delay any further immunization against anthrax using the current vaccine or at least to make immunization voluntary" [290] and to convene a commission of military and non-military public health experts to review safety and efficacy evidence for the current vaccine, attempt to determine when an improved vaccine might be available, and make recommendations about continuation of the current program.[291] Their recommenda-

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[285] See supra note 108.
[286] Testimony of David R. Oliver, Jr., NSVAIR anthrax hearing (III), pp. 68–69.
[287] Department of Defense, "Information About the Anthrax Vaccine and the Anthrax Vaccine Immunization Program," prepared by the AVIP Agency, Jan. 25, 2000, pp. 12–13 (available at: http://www.anthrax.osd.mil) (in subcommittee files).
[288] Ibid.
[289] Testimony of Col. Fred Gerber, Director, Health Care Operations, Office of the Army Surgeon General, NSVAIR anthrax hearing (V), p. 153.
[290] "Anthrax Immunization," American Public Health Association, policy statement No. 9930, Nov. 10, 1999.
[291] Ibid.

tions were based on the concern "that mandatory immunization with a vaccine of unproved efficacy when an improved vaccine may soon be available, is contrary to public health principles and may adversely effect the acceptance of voluntary or mandatory immunization programs in which there is good evidence of efficacy and safety. . . ." [292]

3. DOD should pursue testing of the safety and efficacy of a shorter anthrax inoculation regimen

A shorter shot course could reduce the cost of the immunization program, simplify delivery logistics, and lower the incidence of adverse reactions.

According to GAO testimony, "No studies have been done to determine the optimum number of doses of the anthrax vaccine." [293] The original inoculation schedule of three doses was based on a regimen developed using animals in the early 1950's. However, three people who received three doses of a weaker formulation of the vaccine became infected after exposure to anthrax. The number of doses was then arbitrarily increased to six, the number used in the only human efficacy study published in 1962, and thus the number approved by FDA.[294]

Even if a prolonged, multi-shot regimen is necessary to generate an initial immune response, the annual booster may be unnecessary. GAO noted:

> In November 1971, the Division of Biologics Standards, NIH, noted an apparent increase in reports of adverse reactions after individuals received booster shots. The Division considered it advisable to reevaluate the need for annual boosters and possibly the amount of the booster dose. Although the record is unclear as to whether or not NIH requested a reevaluation, to date, no such reevaluation has been done.[295]

The 1993 DOD Directive on biological warfare defense mandates immunization "against validated biological warfare threat agents, for which *suitable* vaccines are available, in sufficient time to develop immunity before deployment to high threat areas. . . ." [296] (Emphasis added). For this purpose, "suitable" should not just mean FDA approved, but demonstrably as safe and effective as possible for the intended military use. A vaccine that takes 18 months, and annual boosters, to confer immunity should not be considered suitable under the policy.

In 1995, the Joint Program Manager for Biological Defense reported, "The immunization schedule of 6 shots over 18 months has stopped the approval process for an annual immunization program against this high threat biological warfare agent. Moreover, it has

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[292] Ibid.
[293] Testimony of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Affairs Division, GAO, NSVAIR anthrax hearing (IV), p. 97.
[294] Prepared statement of Kwai-Cheung Chan, Director, Special Studies and Evaluation Section, National Security and International Affairs Division, GAO, NSVAIR anthrax hearing (IV), p. 5.
[295] Ibid., p. 6.
[296] See supra note 7.

been used by critics to question the relevance of the biological defense [BD] vaccine program to the DOD." [297]

If the time to develop immunity could be reduced substantially, use of the anthrax vaccine would be safer and could be targeted far more effectively to forces deploying to high threat areas.

Based on animal studies and research into the immunological response to the vaccine in humans, DOD concludes most persons acquire the bulk of whatever protection is achieved after two or three shots.[298] DOD documents assert that three inoculations provide functional protection, and the services' AVIP implementation plans set as "desirable" the goal that "all personnel assigned to high threat areas receive their first three shots prior to deployment." [299] In the interest of reducing adverse reactions, particularly in persons whose immune systems have already mounted a complete response to the vaccine, DOD should put its belief in the efficacy of a reduced shot course to the test of rigorous scientific trials.

To the extent those efficacy studies were put aside due to the lack of a correlates of human immunity, that challenge will have to be overcome in any event as DOD attempts to develop and deploy other vaccines against other bio-threats. That work might as well be done in support of a safer vaccine against the primary biological warfare threat, anthrax.

In terms of increased safety, there is also some evidence an intramuscular injection would produce fewer side effects and adverse reactions than subcutaneous administration. DOD expended significant time and resources in 1994 and 1995 on plans and programs to demonstrate the safety and efficacy of a shorter anthrax inoculation regime, and a different route of administration, but appears to have all but abandoned those efforts when planning for the AVIP began. Support for the FDA application to reduce the shot course seems to have been redirected to vaccine acquisition and AVIP logistics.

4. DOD should enroll all anthrax vaccine recipients in a comprehensive clinical evaluation and treatment program for long term study

DOD only recently began "to design a set of studies to better evaluate the long term safety of the anthrax vaccine . . . to conform with present-day, post-marketing practices." [300] While employing active surveillance techniques, these will be cohort studies because "[i]t would be labor-intensive, cost-prohibitive, and would not conform to civilian expectations for us to use this in all 2.4 million service personnel whom we will administer the vaccine to." [301] According to Gen. Claypool, DOD will also use linked databases to

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[297] Col. John C. Doesburg, Joint Program Manager for Biological Defense, memorandum on "Urgent Requirement for Integrated Command Support to Revise the Immunization Schedule for Anthrax Vaccine" (JPO 0045) from the Department of the Army, Nov. 17, 1995 (in subcommittee files).

[298] Testimony of Maj. Gen. Robert Claypool, Deputy Assistant Secretary for Health Operations Policy, NSVAIR anthrax hearing (IV), p. 179; Arthur M. Friedlander, Philip R. Pittman, and Gerald W. Parker, "Anthrax Vaccine: Evidence for Safety and Efficacy Against Inhalational Anthrax," the Journal of the American Medical Association, Dec. 8, 1999, vol. 282, No. 22, pp. 2104–2106.

[299] See supra note 46, p. 1, sec. 1(a)(8).

[300] Testimony of Maj. Gen. Robert Claypool, Deputy Assistant Secretary for Health Operations Policy, NSVAIR anthrax hearing (IV), p. 108.

[301] Ibid.

conduct active surveillance of vaccine recipients, using DEERS and "the large medical database residing at a tri-service defense medical surveillance system here in the National Capital region of the Walter Reed installation." [302]

But these steps, coming more than 1 year after AVIP implementation, are not enough to monitor the impact of the vaccine program on military health. Having missed the opportunity to study the large cohort of service members who received the AVA during Operations Desert Shield and Desert Storm, DOD has an obligation to reach beyond "civilian expectations" to evaluate the safety of this vaccine.

Particularly for members of reserve component units, access to primary care and specialists at military facilities can be limited. According to DOD, adverse events after the anthrax vaccine are "line of duty illnesses." [303] Therefore,

> a member of the Reserve Component may present themselves for initial treatment and evaluation at any military treatment facility, after vaccination during a period of duty. The member will be examined and provided necessary medical care. Once treatment is rendered or the individual's emergent condition is stabilized, a Line of Duty and/or Notice of Eligibility status will be determined by the member's unit, as required. No treatment beyond that justified to stabilize the condition or emergency is authorized until Service connection is validated.

But requiring an immediate determination of service-connection for vaccine related health effects means many short term, and most long term, adverse reactions will not be monitored by DOD physicians. The causal attribution of health effects to inoculations is difficult, becomes more difficult over time, and remains unlikely in a military program institutionally resistant to any suggestion the vaccine is not safe. Service members should not bear the burden of proof the vaccine caused their ill-health subsequent to inoculation. The process of proving service-connection has frustrated Gulf war veterans' efforts to obtain accurate diagnoses, effective treatments, and fair compensation for their unexplained illnesses. It should not be repeated in the AVIP.

Enrollment of every vaccine recipient in a clinical evaluation and treatment protocol would allow DOD to capture a unique and valuable data set for use in their longitudinal studies, avoiding disputes over cohort selection bias and other methodological issues. The evaluation and treatment program could also be the vehicle for assembly of the multidisciplinary teams envisioned by Dr. Engler [304] to develop and implement clinical protocols and maintain a consistent standard of care in the AVIP. It would also help assure service members the vaccine program, as a medical force protection effort, has as its primary purpose the protection of the health of the force.

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[302] Ibid., p. 109.

[303] Dr. Sue Bailey, "What Everyone Needs to Know about the Anthrax Vaccine" quarterfold brochure, Department of Defense, Nov. 1, 1999, p. 3 (in subcommittee files).

[304] E-mails from Col. Renata Engler dated Dec. 4–8, 1998 (in subcommittee files).

5. While an improved vaccine is being developed, use of the current anthrax vaccine for force protection against biological warfare should be considered experimental and undertaken only pursuant to FDA regulations governing investigational testing for a new indication

Under FDA regulations, use of an FDA-approved product in an unapproved way, or for an unapproved purpose, can only be undertaken pursuant to clinical trial protocols contained in Investigational New Drug [IND] applications.[305] IND protocols must be approved by an Institutional Review Board charged to monitor the scientific credibility and ethical soundness (i.e., patient protections) of the trial. FDA must agree the trial proves the product is safe and effective for the proposed use. Informed consent must be obtained from persons enrolled in IND drug or vaccine trials.

If DOD proposed to use the anthrax vaccine against a disease or indication not currently described in the FDA-approved product labeling (i.e., high blood pressure), an IND application would be required. If DOD proposed to alter the FDA-approved AVA inoculation regimen (i.e., by eliminating one or more of the six shots), and IND would be required.

Despite the fact the vaccine was approved as safe and subsequently deemed effective only against cutaneous anthrax infection, DOD asserts use of the FDA-approved AVA as prophylaxis against weaponized, inhalation anthrax does not constitute an off-label use against a new indication because "[w]hile the package insert for this vaccine is nonspecific as to the route of exposure, DOD has long interpreted the scope of the license to include inhalation exposure, including that which would occur in a biological warfare context."[306]

While some in DOD may have interpreted the scope of MBPI's FDA license to include inhalation anthrax by implication, others proceeded as if explicit labeling for the indication would be necessary. Throughout development of the anthrax policy that eventually became the AVIP, some in DOD interpreted FDA regulations as requiring approval of both a reduced number of inoculations and the new indication. A 1995 memo states:

> The use of a reduced schedule to protect service members from aerosol exposure to anthrax can only legally be done if the FDA licenses the vaccine for that specific schedule and indication. . . . Obtaining FDA license approval for a specific immunization schedule change and for a labeled indication change (aerosol challenge) must provide data that establish safety of two doses of the vaccine given at 0 to 4 weeks since this schedule does not mimic the current schedule of 0, 2 and 4 weeks. More extensive problems exist in demonstrating vaccine efficacy against an aerosol challenge.[307]

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[305] 21 CFR Part 312.

[306] Letter from Dr. Stephen C. Joseph to Dr. Michael A. Friedman dated Mar. 4, 1997 (in subcommittee files).

[307] Micheal J. Gilbreath, Ph.D., "Is the current Anthrax vaccination regimen necessary?" Department of Defense information paper (JPO 0044), Nov. 10, 1995, pp. 1–2.

In September 1996, the vaccine manufacturer, MBPI, submitted an IND application which said, "The ultimate purpose of this IND is to obtain a *specific indication for inhalation anthrax* and a reduced vaccination schedule."[308] (Emphasis added). Briefing slides produced by USAMRIID in October 1997 reference two separate objectives to be met in a supplement to the AVA license:

- Supplement to AVA license to reduce the number of immunizations and change the route of immunization.
- Supplement AVA license to explicitly include inhalational anthrax as an indication.[309]

Since 1997, the *Department of Defense Nuclear/Biological/Chemical [NBC] Defense—Annual Report to Congress* has referred to medical CBW countermeasures proven safe because they have "been widely used to treat other medical conditions."[310] The report cites pyridostigmine bromide, the botulinum toxoid vaccine, both used for CB prophylaxis only pursuant to INDs, and the anthrax vaccine. But DOD's interpretation of the current AVA labeling rests on the conclusion there is but one indication—anthrax infection acquired by any means. Against what "other medical condition" was the anthrax vaccine used to prove its safety?

When DOD asked the FDA to concur with the implicit inclusion of inhalation anthrax in the current product labeling, the response was affirmative but tepid. FDA Lead Deputy Commissioner Michael Friedman wrote:

> While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert does not preclude this use. The original efficacy trail clearly showed that the vaccine conferred a high level of protection against cutaneous exposure. None of the 5 inhalation cases in this trial occurred in Anthrax Vaccine recipients, but these data alone are insufficient to allow definitive statistical conclusions. Results from animal challenge studies have also indicated that pre-exposure administration of Anthrax Vaccine protects against inhalation anthrax.
>
> Therefore, I believe your interpretation is not inconsistent with the current label.[311]

It was on this basis DOD proceeded to design the AVIP without informed consent procedures, or an informed consent waiver, and without other elements of a clinical trial such as consistent data gathering and detailed health outcome monitoring.

DOD was aware of the extensive problems confronting the effort to prove vaccine efficacy for the new indication, most notably that ". . . no animal or other potency tests has [sic] been demonstrated

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[308] See supra note 138, p. 1.

[309] Department of Defense, "Supplemental to AVA License" USAMRIID presentation slides, Oct. 28, 1997 (in subcommittee files).

[310] *Department of Defense Nuclear/Biological/Chemical [NBC] Defense—Annual Report to Congress,* March 1999, pp. 3–3 to 3–4; *Department of Defense Nuclear/Biological/Chemical [NBC] Defense—Annual Report to Congress,* February 1998, pp. 3–4 to 3–5; *Department of Defense Nuclear/Biological/Chemical [NBC] Defense—Annual Report to Congress,* March 1997, pp. 3–4 to 3–5.

[311] Letter from Dr. Michael A. Friedman to Dr. Stephen C. Joseph dated Mar. 13, 1997 (in subcommittee files).

to be well correlated with protection of humans."[312] DOD conducted, and plans to continue, studies attempting to validate an animal model so findings can be extrapolated to humans.

In launching the AVIP, DOD did not confront those problems but sidestepped them by concluding use of the vaccine to prevent anthrax infection, however acquired, would not require an IND as long as the approved inoculation schedule was followed. So the AVIP's cumbersome logistics, additional costs, and increased risk of adverse reactions all flow directly from an unwillingness to do the research and testing to develop a better vaccine or improve the safety and efficacy of the current AVA.

That research and testing will have to be done in any event. In 1997 DOD told Congress:

> DOD complies with all Food, Drug and Cosmetic Act requirements. The Food and Drug Administration [FDA] requires large-scale field trials in human subjects to demonstrate efficacy of drug and biologicals prior to licensure. There are, however, legal and ethical constraints that preclude such efficacy studies for NBC countermeasures. Field studies of efficacy cannot be performed, since exposure to most NBC agents does not usually occur naturally. Moreover, the high lethality and/or toxicity of NBC agents also makes it unethical to expose human subjects in controlled efficacy studies usually required by the FDA for product licensure (e.g., test of effectiveness of the product against the threat in humans). For these reasons, *many NBC countermeasures are likely to remain in an Investigational New Drug [IND] status, requiring their administration under provisions of an approved protocol and with written informed consent* from their service members. In contingency situations, DOD may request a waiver of informed consent from the FDA. DOD continues to work with the FDA to seek alternative methods for demonstrating safety and efficacy of NBC medical countermeasures and to obtain their licensure.[313] (emphasis added)

Given the predicted likelihood NBC vaccines will be available only in IND status for some years to come, DOD will need to develop the capacity to conduct broad-based clinical trials and effectively communicate risk/benefit assessments through informed consent processes. In the interests of deploying a safer, presumably more effective vaccine against the pre-eminent biological warfare threat, DOD should be willing to develop that capacity now. Instead, DOD has chosen to address the primary threat with a dated, secondary countermeasure with substantial unknowns regarding quality, safety, and efficacy.

In prescribing the vaccine, DOD is engaging in the practice of medicine. "It is true doctors can use drugs off label. It is never true

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[312] See supra note 307, p. 2. The memo continues, "The potency test required for the present vaccine has not been well correlated to efficacy in humans." The current potency test uses guinea pigs. Tests challenging different animal species with a range of anthrax strains showed the vaccine provides varied levels of protection. Against some strains, vaccinated guinea pigs and mice suffered 100 mortality. In DOD studies using nonhuman primates (rhesus monkeys) between 88 and 100 percent of the vaccinated animals survived.

[313] See supra, note 310, 1998 report, p. 3–4.

they can do so without informed consent of the patient . . . You are not immunized from getting informed consent." [314] If DOD were to concede administration of AVA against inhalational battlefield exposure is an off label use, informed consent would be required. The AVIP could be transformed, for most, into a voluntary program, with limited mandatory usage of the vaccine possible only pursuant to a carefully monitored informed consent waiver.

In a statement submitted to the subcommittee, the Association of American Physicians and Surgeons asserted:

> A distinction must be made between treatment and experimentation. It may be asserted that anthrax vaccine (unlike pyridostigmine bromide as used in the Gulf War or anti-botulinum vaccine) constitutes "treatment," or that it is not experimental because of being declared safe and effective by FDA. . . . In fact, the anthrax vaccine was licensed by the FDA before efficacy studies were required. Its efficacy against inhalational anthrax has been questioned. . . . British epidemiologist suggested that troops be publicly randomized to receive active vaccine or placebo, clearly implying that many consider the vaccine to be experimental.[315]

The AAPS recommended a careful examination of the medical ethics involved in military, and civilian, vaccination efforts, noting the entire point of informed consent in combat is "not to prevent soldiers from obtaining whatever protection may be afforded them by an investigational agent that has not been adequately tested, but rather, it is to give them the choice of whether they think the 'protection is worth the risks of adverse effects.'" [316]

Although DOD's track record administering INDs or informed consent waivers is not exemplary,[317] current procedural safeguards, adopted since the Gulf war, provide far more protection to service members receiving investigational products than the AVIP now provides.

In November 1997 the subcommittee proposed, and the full Government Reform and Oversight Committee approved, an oversight

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[314] Testimony of Arthur Caplan, Ph.D., *Force Protection: Improving Safeguards for Administration of Investigational New Drugs to Members of the Armed Forces,* 106th Cong., 1st sess. (1999), unofficial transcript, p. 77 (subcommittee on National Security, Veterans Affairs and International Relations hearing of Nov. 9, 1999) (in subcommittee files).

[315] Submitted statement of Dr. Jane M Orient, executive director, Association of American Physicians and Surgeons, NSVAIR anthrax hearing (I), p. 119, citing the European Journal of Epidemiology 4:12–19, 1998 and Ness AR, Harvey I, Gunnell D, Smigh GD: "All troops sent to Gulf should be randomized to receive anthrax vaccination or placebo." British Medical Journal 316:1322, 1998.

[316] Ibid. (quoting Grodin MA, Annas GJ: Journal of the American Medical Association 277:712–713, 1997).

[317] In 1990, DOD requested authority to administer IND products, pyridostigmine bromide and botulinum toxoid vaccine, to certain military personnel. DOD also requested a waiver of informed consent requirements in connection with the use of those products by the armed forces. The FDA granted the DOD requests under the terms of an interim rule establishing the procedures and conditions under which informed consent waivers could be obtained by DOD. But DOD did not meet the conditions FDA placed on the waivers, failing to provide information to individual service members about the IND products and failing to keep the medical records necessary to fulfill the protocols and capture data about the safety of the drugs. Despite some improvements in medical recordkeeping, DOD's next use of an IND vaccine showed similar problems. In 1997, the General Accounting Office observed "nearly one fourth of the soldiers who received an investigational tick-borne encephalitis vaccine before deploying to Bosnia did not have this information noted in their files." ("Defense Health Care: Medical Surveillance Improved Since Gulf War, but Mixed Results in Bosnia," [GAO/NSIAD–97–136] U.S. General Accounting Office, May 13, 1997, p. 33.)

report on Gulf war veterans' illnesses containing 18 findings and 18 recommendations.[318] Among them was the finding that "[t]he FDA was passive in granting and failing to enforce the conditions of a waiver to permit use of PB by DOD" and the recommendation that "FDA should grant a waiver of informed consent requirements for the use of experimental or investigational drugs by DOD only upon receipt of a Presidential finding of efficacy and need." [319]

Legislation reflecting that recommendation was introduced in both chambers of Congress.[320] The 1999 Defense Authorization Act contained provisions, codified at 10 U.S.C. 1107(f), implementing the recommendation by strengthening notice requirements and by requiring a Presidential authorization for any waiver of informed consent.

In view of the new statutory provision, FDA on October 5, 1999 revoked the 1990 interim final rule and issued a new regulation to govern DOD compliance with IND conditions and informed consent waivers.[321]

On September 30, 1999 the White House issued Executive Order 13139 establishing the procedures by which the President would comply with the new law.[322] The Executive order says "[w]aivers of informed consent will be granted only when absolutely necessary" and only upon a written determination by the President that obtaining consent is not feasible, is contrary to the best interest of the service member or is not in the interest of national security. In the event a waiver is granted, the DOD Secretary must notify Congress and publish a notice in the Federal Register. No waiver may last more than one year. Waivers may be renewed based on a new, fully documented request." [323]

The statute establishes clear U.S. policy that waiver of informed consent in military operations is deemed appropriate and necessary under certain circumstances. The statute, the FDA interim rule and Executive Order 13139 describe, and limit, those circumstances and attempt to ensure any decision to use IND drugs or vaccines without informed consent is as open as possible, supported by sufficient information and authorized at the highest level.

The new regime for waiving informed consent requirements appears far more rigorous and transparent than the system employed under the original interim rule. The statute is very explicit in describing the information that must be provided to each individual service member being given an IND drug or vaccine. The written information must include a clear statement the substance is investigational, the reason the drug or vaccine is considered necessary, information regarding possible side effects and drug interactions, and any other information FDA may require as part of the IND protocol.

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[318] *Gulf War Veterans' Illnesses: VA, DOD Continue to Resist Strong Evidence Linking Toxic Causes to Chronic Health Effects,* 2d report by the Committee on Government Reform and Oversight, House Report 105–388, Nov. 7, 1997, pp. 3–6.

[319] Ibid.

[320] H.R. 4035, 105th Cong., 2d sess.; S. 2057, 105th Cong., 2d sess.

[321] Federal Register, 21 CFR Parts 50 and 312, Oct. 5, 1999, p. 54180.

[322] Executive order of Sept. 30, 1999, "Improving Health Protection of Military Personnel Participating in Particular Military Operations" No. 13139, the White House, Washington, DC.

[323] Ibid.

That is more clinically useful information than the AVIP now routinely conveys. Consistently providing balanced risk/benefit assessments in an IND setting would also move DOD closer to its stated goal of more effective risk communication. According to an article linked to the DOD AVIP website:

> People are different. One size does not fit all when it comes to explaining risk. Some prefer short, simple messages about a vaccine's benefits and risks.8,12,68 These people, presumably a majority of the population, will be satisfied with the summary information comprising the Vaccine Information Sheets [VISs] published by the Centers for Disease Control and Prevention. Others want more detailed information. Some will scour the literature to explore every fact they can find. The goal of risk communication involving vaccines should be informed consent.68 True consent to vaccination is only possible if the individual has received all the information he or she wants and understands that information. Then an informed vaccine decision can be made. Providing this information demonstrates respect for the individual. From the clinician's perspective, the consent process can be part of the efforts to identify contraindications to vaccination (e.g., severe hypersensitivity, immunodeficiency).[324]

The FDA "believes that exceptions from the informed consent requirement should apply rarely and only when sufficient additional protections are provided to the military personnel affected." [325] The agency also expresses the view that DOD should pursue drug development through normal regulatory procedures, despite the obvious difficulty of acquiring efficacy data regarding chemical and biological warfare exposures. In the future, requests for informed consent waivers must be accompanied by a history and projected time line for full scale development of the drug or vaccine in question.[326] No more waiting until the eve of war to shortcut a process that could have been underway for months or years.

Under the new law, only the President may waive prior consent requirements, and only after certifying in writing that obtaining consent is not feasible, is contrary to the best interest of the service member, or is not in the interest of national security. With regard to the first two justifications, the President must apply the standards and criteria used by the FDA for waivers. Those standards and criteria are detailed in the new FDA interim rule. To meet them, the Secretary of Defense must document for the President all the scientific data, threat assessment, lack of alternatives, and conditions under which the IND product will be used.

The FDA regulation strengthens the role of the Institutional Review Board [IRB] in approving and monitoring the IND protocols for which waivers are granted. IRBs are panels charged with assuring that clinical trials have legitimate scientific goals and that pro-

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[324] Department of Defense, "Anthrax Vaccine Immunization Program" at Internet page http://www.anthrax.osd.mil/ citing John D. Grabenstein and James P. Wilson, "Are Vaccines Safe? Risk Communication Applied to Vaccination," Hospital Pharmacy, Vol. 34, No. 6, pp 713–729 (available at http://www.anthrax.osd.mil/SCANNED/ARTICLES/grabedocs/vaccines.htm).

[325] See supra note 321 p. 51484.

[326] Ibid.

tocols protect human subjects. Under the regulation, an IRB must review all aspects of the proposed IND and waiver. Significantly, the IRB must include at least three members who are not employees of the Federal Government. This should add some element of independent review to DOD waiver requests. The rule also requires detailed certifications from DOD regarding recordkeeping systems, medical staff training, and communication of benefits and risks.

The Executive order of September 30, 1999 mirrors the FDA regulation in many respects, requiring the DOD Secretary to support a waiver request with written justification, rationale, and proof of IRB review. The Assistant to the President for National Security Affairs and the Assistant to the President for Science and Technology must also review the request. After approval of a waiver, the Eexecutive order requires monitoring and periodic reports on compliance with IND protocols and waiver conditions.

These more explicit and elaborate procedures address many of the problems noted in the execution of the Gulf war waivers. If applied rigorously, those safeguards could also form the basis for a mandatory anthrax vaccine program for certain deployed forces, Special Forces, or other elements determined by the President to warrant vaccination in the interests of national security. The remainder of the force could choose to enroll in an IND protocol [327] or assume the risks of biological warfare not addressed by individual and collective protection, detection, battle tactics and deterrence.

In July 1999, the Air Force Times editorialized it was time to "Stop Mandatory Anthrax Inoculations" because the manufacturer appeared unreliable, and because:

> More research is needed to understand the long-term risk of using the anthrax vaccine. And now, long after initiating the vaccination program, the Pentagon is finally planning such a long-term study of the vaccine's health effects. That's good, but until those risks are understood, the Pentagon should proceed with caution—not reckless abandon.[328]

The editorial concluded "the risks of the vaccine are outweighed by the risk of contracting anthrax" [329] and advised service members to take the shots. "But in the absence of empirical evidence proving the vaccine's long-term safety, the troops should be given the chance to decline. Give them the information they need to make wise, informed decisions for themselves. Let those who decline live with what they consider a reasonable risk." [330]

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[327] Open protocols could be established for the on-going trial of a reduced vaccine regimen or a trial of a purer vaccine.

[328] "Stop Mandatory Anthrax Inoculations," Air Force Times, Army Times Publishing Co., Jul. 12, 1999, p. 44.

[329] Ibid.

[330] Ibid.

DISSENTING VIEWS OF HON. HENRY A. WAXMAN, HON. ROD R. BLAGOJEVICH, HON. TOM LANTOS, HON. MAJOR R. OWENS, HON. ELEANOR HOLMES NORTON, HON. ELIJAH E. CUMMINGS, HON. DANNY K. DAVIS, HON. JOHN F. TIERNEY, HON. HAROLD E. FORD, JR., AND HON. JANICE D. SCHAKOWSKY

We agree with many points set forth in the report. We submit dissenting views, however, because we disagree with the report's primary recommendations regarding whether to suspend the Department of Defense [DOD] program and reclassify the anthrax vaccine as "experimental."

I. ASSURED PRODUCTION AND CAPACITY

We agree that the anthrax program is vulnerable to supply shortages. Because the producer has been unable to obtain the Food and Drug Administration [FDA] approval to reopen its renovated production facility, no source of anthrax vaccine currently exists. Without a guaranteed supply, DOD will continue to experience difficulty meeting the demand it has created through its program to vaccinate all 2.4 million service members.

We also agree that the program is vulnerable to price increases. Within a year of agreeing to produce anthrax vaccine for DOD, the producer and DOD renegotiated the terms of the contract. The producer obtained advance payments, a price increase, and permission to sell on the open market, despite DOD's need for the vaccine. Explanations about the foreseeability and need for this renegotiation were unsatisfactory.

Although we acknowledge that DOD enters into exclusive contracts as a regular course of business, we agree that accelerating research and testing on a second-generation, recombinant anthrax vaccine may encourage competition and enhance production stability. One potential benefit of such a vaccine is that it could be produced in various facilities rather than a single, dedicated facility. In addition to enhancing competition, diversifying the source of anthrax vaccine could reduce security risks at production sites.

II. COMPLEXITY OF PROGRAM

The anthrax vaccination program is logistically complex. The FDA-licensed shot regimen requires six shots over a period of 18 months and a booster shot annually thereafter. The report correctly raises serious concerns about DOD's ability to perform successfully this regimen for certain members of its force. For example, it is difficult for DOD to deliver timely shots to Reserve and Guard service members who report for duty less frequently than active duty members.

We also agree that DOD's "timeliness goal" of vaccinating 90 percent of service members within 30 days after vaccinations are due

is insufficient. Under this standard, the first three vaccine inoculations—which FDA requires in 2-week intervals—instead could be delivered on the same day and still be considered "timely." We note that FDA wrote to DOD in September 1999 expressing concern with potential deviations from the approved schedule.[1]

If DOD continues the vaccination program, we recommend that DOD take measures to improve the administration of its program. We note that DOD has accomplished significant improvements, such as the utilization of the Defense Enrollment Eligibility Reporting System to combine service-based record systems into one central repository. In addition to upgrading these recordkeeping systems through the Composite Health Care System, we recommend that DOD revise its timeliness standard from 1 month to a window of days.

III. SAFETY MONITORING

We agree that vaccine safety could be monitored more thoroughly and comprehensively. The report acknowledges that, "[a]s with any vaccine, anthrax inoculation can cause adverse health events in some individuals . . .." The report also points out that, at the rates of adverse reactions cited by DOD, implementation across the entire force could produce thousands of systemic and local reactions. Although only a small percentage of these would require extended treatment or hospitalization, we agree that aggressively managing this anticipated caseload must be a priority for DOD.

The report suggests that the program may not be capable of performing adequate monitoring because of DOD's "institutional resistance to associating health effects with the vaccine." The subcommittee heard from several service members who relayed accounts of inappropriate behavior by DOD personnel. Although the subcommittee did not verify the prevalence or accuracy of these accounts, we do not doubt that such actions inevitably occur, whether or not officially sanctioned. While we disagree that DOD is incapable of performing adequate safety monitoring, we believe DOD should meet a higher standard. We recommend several measures to raise DOD's performance.

As part of its safety monitoring program, DOD relies on the Vaccine Adverse Event Reporting System [VAERS]. Under this system, FDA collects reports of symptoms temporally related to the receipt of the anthrax vaccine. DOD requires its physicians to file VAERS reports only if such reactions result in hospitalization or the loss of 24 hours of work. Although DOD physicians are permitted to file VAERS reports in cases below this threshold, it appears this is seldom done. We recommend that DOD require its physicians to file VAERS reports for all adverse events that result in hospitalization, any amount of missed duty, or any other negative health effects considered relevant by service members or their physicians.

The subcommittee also heard from several service members who claimed they were never told about VAERS forms or were unable to access them. DOD has been proactive in this regard by, in addition to taking other steps, placing on its website a direct link to the on-line FDA VAERS form. To augment this effort, we suggest

[1] Letter from Dr. Katherine C. Zoon to Dr. Sue Bailey (Sept. 29, 1999).

that DOD consider distributing paper copies of VAERS forms with each dose of anthrax vaccine administered.

IV. VACCINE SAFETY

The report does not conclude that the anthrax vaccine is unsafe. The report states that the vaccine "may be as safe as many other approved products" and "can be considered nominally safe." In their appearances before the subcommittee and committee, officials from the General Accounting Office [GAO] never stated that they believed the vaccine is unsafe. Instead, both the committee report and GAO argue that the vaccine's safety has not been demonstrated sufficiently to date.

FDA testified on several occasions before the subcommittee and the full committee that the agency believes the vaccine is safe. On April 29, 1999, FDA stated, "[w]e believe anthrax vaccine is a safe and effective vaccine for the prevention of anthrax disease."[2] At a later hearing, FDA officials reported that "FDA continues to view the anthrax vaccine as safe and effective for individuals at high risk of exposure to anthrax, when used in accordance with the approved labeling."[3] At another hearing, FDA officials explained why they believe the vaccine is safe:

> Our confidence in this vaccine, like all vaccines, is based upon four components: first—the review of manufacturing and clinical trials and subsequent clinical laboratory experience with the vaccine; second—ongoing inspections of the manufacturing facility; third—our lot release requirements; and fourth—our ongoing collection and analysis of adverse event reports. So far, the data gathered from VAERS reports on anthrax vaccine do not signal concerns about the safety of the vaccine.[4]

Without additional information to the contrary, we are not in a position to overturn FDA's judgment. Unlike FDA officials, we have little or no medical expertise. In our opinion, the report's criticism of a lack of studies demonstrating safety is insufficient to overturn FDA's findings based on the vaccine's 30-year history.

In addition, we fear the report's expectations for the safety of a new generation vaccine may be overly optimistic. The report recommends that DOD suspend its program only until it obtains "approval for use of an improved vaccine." Yet the recombinant vaccine envisioned by the report may be no safer than the existing version. The report concedes that "an improved vaccine based on recombinant technology may not necessarily have better safety characteristics than the current vaccine," but it offers no further explanation.

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[2] *Anthrax (II): Safety and Efficacy of the Mandatory Vaccine,* Hearing before the Subcommittee on National Security, Veterans Affairs, and International Relations, House Committee on Government Reform, 106th Cong., 1st sess. (Apr. 29, 1999) (testimony of Dr. Katherine Zoon, Director, Center for Biologics Evaluation and Research).

[3] *Anthrax Vaccine Adverse Reactions,* Hearing before the Subcommittee on National Security, Veterans Affairs, and International Relations, House Committee on Government Reform, 106th Cong., 1st sess. (July 21, 1999) (testimony of Susan S. Ellenberg, Ph.D., Director, Division of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research).

[4] *Defense Vaccines: Force Protection of False Security?* Hearing before the House Committee on Government Reform, 106th Cong., 1st sess. (Oct. 12, 1999) (testimony of Dr. Katherine Zoon, Director, Center for Biologics Evaluation and Research).

We would encourage further safety research on a new anthrax vaccine. In addition, we agree with the report's recommendation to pursue testing of the safety and efficacy of a shorter anthrax inoculation regimen. We also agree with the report's emphasis on continued testing for intramuscular injections, which may reduce reaction rates generally and address proportionally higher reaction rates among women.

V. CLASSIFICATION OF THE VACCINE AS "EXPERIMENTAL"

With respect to reclassification of the vaccine, we also defer to FDA's opinion that DOD's current use of the anthrax vaccine should not be considered "experimental." On November 3, 1999, Representatives Burton, Shays, Gilman, and Jones wrote to FDA essentially proposing the report's recommendation to reclassify the vaccine as "experimental" and conduct investigational new drug [IND] testing.[5] The rationale for this argument was that FDA had approved the vaccine for use against "cutaneous" infection (through the skin) during occupational use, but not against "inhalation" infection (through the lungs) during wartime.

In a November 26, 1999, response, FDA found no basis for this proposal.[6] FDA corrected a misconception that the vaccine is licensed only for use "by a limited population of individuals at risk for cutaneous exposure to anthrax."[7] FDA also stated that "use of the vaccine for protection against both cutaneous and inhalation anthrax exposure is not inconsistent with the labeling."[8] Addressing the proposal directly, FDA stated:

> There is presently no basis for concluding that the anthrax vaccine, a licensed product, when used in accordance with current labeling, should be used pursuant to an IND application or, as requested in your letter, that FDA "place the anthrax vaccine back under IND status."[9]

VI. RECOMMENDATION TO SUSPEND THE PROGRAM

Whether to suspend the vaccination program is a decision that must be made by security experts based on the most complete information relevant to all risks and benefits. These factors are sometimes unquantifiable; indeed, some are unknowable and will remain so until ultimately tested in combat. Because the report is not based on classified information regarding the likelihood of an anthrax attack, it provides insufficient information to overturn DOD's decision to pursue the vaccination program.

The report recognizes that "[t]hreat assessment requires objective and subjective analyses of U.S. vulnerabilities, enemy capacity, and enemy intentions." The report also acknowledges that "much of the information regarding the BW [biological weapons] capabilities and intentions of potential adversaries, and even allies, is classified." Yet the report bases its conclusions only on unclassified information. Members received no classified information at the full

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[5] Letter from Representatives Burton, Shays, Gilman, and Jones to Dr. Jane E. Henney (Nov. 3, 1999).
[6] Letter from Melinda K. Plaisier to Representative Walter B. Jones (Nov. 26, 1999).
[7] Id. at 2.
[8] Id.
[9] Id. at 3.

committee level, and the subcommittee had no closed hearings in which it could consider such information.

As a result, the report's conclusions—that "the threat remains tactically limited and regional" and that the program "is designed to reach far beyond those at risk"—do not reflect DOD's full judgment about the actual extent of the threats involved. The report states that "DOD has determined the threat is real and imminent, and has concluded it would be irresponsible not to deploy an available countermeasure to protect the lives and fighting capability of U.S. forces." Without additional information to the contrary, we defer to DOD's conclusion.

VII. KEVIN EDWARDS

At the committee meeting to consider this report, Representative Dan Burton, chairman of the Committee on Government Reform, raised the case of Kevin Edwards. He began his statement by displaying photographs of Mr. Edwards's bruised body. He then said:

> We have spoken to many individuals who have been ill for a very, very long time. One example is Mr. Edwards of North Carolina. I want you to look at these pictures. I think these pictures will show what can happen when there really is a bad reaction or an adverse event. Mr. Edwards has what appears to be third degree burns on much of his body but in fact, it is a condition that developed after receiving the anthrax vaccine.

Subsequent investigation by the minority does not substantiate Mr. Burton's allegations. While Chairman Burton attributed Mr. Edwards's illness to the anthrax vaccine, he failed to disclose that Mr. Edwards's case had been considered by the Anthrax Vaccine Expert Committee. Although the Privacy Act protects Mr. Edwards's medical records, the findings of the Expert Committee were fundamentally different from Chairman Burton's conclusions.

Exhibit 1 to these views is a letter from Representative Henry A. Waxman, ranking minority member, that sets forth additional details related to Mr. Edwards's case.[10]

HON. HENRY A. WAXMAN.
HON. ROD R. BLAGOJEVICH.
HON. TOM LANTOS.
HON. MAJOR R. OWENS.
HON. ELEANOR HOLMES NORTON.
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HON. DANNY K. DAVIS.
HON. JOHN F. TIERNEY.
HON. HAROLD E. FORD, JR.
HON. JANICE D. SCHAKOWSKY.

[10] Letter from Representative Henry A. Waxman, ranking minority member, to Representative Dan Burton, chairman (Mar. 17, 2000) (exhibit 1).

March 17, 2000

The Honorable Dan Burton
Chairman
Committee on Government Reform
2154 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Burton:

At last week's Committee meeting to consider the anthrax report, you spotlighted the case of Kevin Edwards of North Carolina. You began your statement by displaying photographs of Mr. Edwards's bruised body. You then said:

> We have spoken to many individuals who have been ill for a very, very long time. One example is Mr. Edwards of North Carolina. I want you to look at these pictures. I think these pictures will show what can happen when there really is a bad reaction or an adverse event. Mr. Edwards has what appears to be third degree burns on much of his body but in fact, it is a condition that developed after receiving the anthrax vaccine.

Your display of Mr. Edwards's photos took me and other Democratic members by surprise. Although Mr. Edwards developed his symptoms in 1998, his case was never presented at any of the seven hearings before the Subcommittee or Committee. You also did not give me or other Democratic members any advance warning of your intention to introduce Mr. Edwards's case just moments before voting on the report. As a result, I was unable to respond to your allegations during the meeting.

Since the meeting, however, my staff has investigated the case of Mr. Edwards. What we have learned casts doubt on your assertions.

We have learned that the Anthrax Vaccine Expert Committee recently analyzed Mr. Edwards's case. This interagency group, which consists of medical experts drawn largely from outside government, was established to examine conditions reported in the Vaccine Adverse Event Reporting System that might be related to the anthrax vaccine. The Expert Committee reviewed substantial documentation from Mr. Edwards's medical file and, although the Privacy Act protects Mr. Edwards's medical records, I understand the Committee's conclusions conflict fundamentally with your assertions. I also have been advised that — as chairman of a full committee — you could have obtained a copy of the Committee's findings regarding Mr. Edwards's case if you had sought one.

According to news reports, Mr. Edwards was diagnosed with Stevens Johnson Syndrome (SJS). In investigating this illness, my staff obtained information from the SJS Foundation that indicates that this condition can be caused by almost any drug, including over-the-counter drugs. We also learned that a preliminary Department of Defense analysis indicates that the prevalence of SJS and related sicknesses among service members has declined over the past few years and has continued to decline since the implementation of the anthrax vaccine program. Whether or not you agree with these findings, they seem inconsistent with your supposition that the anthrax vaccine caused his condition.

This case also conflicts with a statement you made at a May 27, 1999, hearing on dietary supplements. You argued then that government descriptions of adverse events should include disclaimers and additional information "so that people can realize that this might be an isolated case that might be related to something else that they were taking at the same time." You further said, "What we need is good information so the American people can make good decisions, and the Congress as well." Unfortunately, your use of Mr. Edwards's case does not meet this standard.

I am pleased that the Subcommittee was able to investigate the Department of Defense anthrax vaccine program in a fair and even-handed manner, and I hope you will consider amending the Committee record as necessary to ensure that it is accurate with regard to Mr. Edwards's case.

Sincerely,

Henry A. Waxman
Ranking Minority Member

cc: Members of the Committee on Government Reform

SUPPLEMENTAL VIEWS OF HON. BERNARD SANDERS

The chairman of the Subcommittee on National Security, Veterans Affairs, and International Relations is to be commended for the extremely thorough hearings he has held leading up to this report. He is also to be commended for the extremely well documented report, itself, and the decisive recommendations contained therein. All of these recommendations are fully supported by the testimony presented to the subcommittee—testimony which raised serious questions about the anthrax vaccine, its manufacturer, and the Department of Defense's [DOD] vaccination program.

As the report documents, the anthrax vaccine is of questionable efficacy and safety. DOD's mishandling of the vaccination program has exacerbated these concerns. Questions about efficacy have been compounded by the failure of DOD to administer the six shot regimen in accordance with the FDA-approved vaccination schedule. Safety concerns have been heightened by DOD's failure to track and record adverse reactions. Moreover, DOD's refusal to even acknowledge the concerns raised by members of the armed services has created significant morale problems among active service members, as well as National Guard and Reserve forces.

DOD also must shoulder the blame for failing to pursue a more effective and safe vaccine against anthrax. Had DOD acted immediately after the Persian Gulf war to find an alternative; a safer, more effective vaccine would be available now.

Against this backdrop of DOD mismanagement and stonewalling, some service members have refused to be vaccinated against anthrax. As a result, service members have been disciplined, including being discharged from the armed services. While I fully understand the need for the military to insist on compliance with lawful orders, DOD cannot escape its own responsibility for the refusal of its members to take the vaccine.

The subcommittee's report expressly "makes no recommendation regarding the status of those service members who left the armed forces voluntarily, or as the result of disciplinary action, due to the anthrax vaccine." Some have questioned whether the order to take the vaccine itself is lawful. The subcommittee did not set out to answer that question and the testimony it received was not adequate to resolve it.

DOD's position is buttressed by the Food and Drug Administration's [FDA] view that DOD's anthrax program does not represent an off-label use. However, given the documented failure of DOD to administer the vaccine in accordance with the FDA's approved schedule, DOD's insistence on deploying service members before the six shot regimen is complete, and the insufficiency of scientific evidence to support claims of efficacy against weaponized anthrax, it is not clear that the FDA's position would pass muster under the

Administrative Procedures Act's "arbitrary, capricious or contrary to law" standard.

This ambiguity and the well documented DOD mishandling of its anthrax vaccine program argues strongly that, at a minimum, DOD should exercise extreme leniency in its treatment of service members who have refused to take the anthrax vaccine, including removing derogatory findings and comments in service records, reversing reductions in rank and pay, and permitting the re-enlistment of members who have been discharged.

If DOD accepts the subcommittee's recommendation—as it should—to recategorize its anthrax program as being in Investigational New Drug status then future disciplinary proceedings will be unnecessary because service members will only receive the vaccine after providing their informed consent.

If there is one thing that the subcommittee learned from its review of DOD's anthrax vaccination program it is that the trust of many service members has been severely shaken. Acceptance of the recommendations in the subcommittee's report and reversal of prior disciplinary actions will go a long way toward rebuilding the trust of service members in the DOD and would be in the best interest of our Nation's armed forces.

HON. BERNARD SANDERS.

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