DOD'S MANDATORY ANTHRAX VACCINE IMMUNIZATION PROGRAM FOR MILITARY PERSONNEL

HEARING

BEFORE THE

SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS, AND INTERNATIONAL RELATIONS

OF THE

COMMITTEE ON GOVERNMENT REFORM

HOUSE OF REPRESENTATIVES

ONE HUNDRED SIXTH CONGRESS

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DOD'S MANDATORY ANTHRAX VACCINE IMMUNIZATION PROGRAM FOR MILITARY PERSONNEL

THURSDAY, APRIL 29, 1999

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS, AND INTERNATIONAL RELATIONS,
COMMITTEE ON GOVERNMENT REFORM,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:05 a.m., in room 2247, Rayburn House Office Building, Hon. Christopher Shays (chairman of the subcommittee) presiding.

Present: Representatives Shays, Mica, Souder, Terry, Tierney, Allen, and Schakowsky.

Also present: Representative Metcalf.

Staff present: Lawrence Halloran, staff director and counsel; Robert Newman and Marcia Sayer, professional staff members; Jonathan Wharton, clerk; David Rapallo, minority counsel; and Ellen Rayner, minority chief clerk.

Mr. SHAYS. I would like to call this hearing to order.

The plan to immunize 2.4 million men and women against weaponized anthrax raises legitimate concerns about the safety and efficacy of the current vaccine when used for that purpose on that many people. To address those questions, we asked the General Accounting Office [GAO], to examine the data, supporting safety and efficacy claims and to gauge the impact of good manufacturing practice deviations on vaccine quality.

Their preliminary findings will be discussed today. Based on the GAO study and other information obtained in the course of the subcommittee's investigation, the anthrax vaccine immunization program [AVIP], seems a very broad undertaking built on a very narrow foundation. The one study of safety and efficacy in humans, which was conducted among textile workers in the late 1950's, tested a different vaccine formulation than the one subsequently approved by the Food and Drug Administration [FDA], and used in the AVIP.

Using data on one vaccine to support the approval of another is problematic, particularly when there is no direct marker or correlate of human protection to use in comparing the two vaccines.

Lack of a surrogate for anthrax immunity also means efficacy tests outcomes in animals cannot be extrapolated to humans. The fact that vaccinated monkeys survived exposure to inhaled anthrax

longer than guinea pigs or mice suggests, but does not prove, some vaccine protection in man.

Later studies of the FDA-licensed vaccine also show wide variations in adverse reaction rates, suggesting safety issues that may become apparent as usage grows from 200 or 300 people each year to several hundred thousand. There have been no studies of long-term health effects.

Poor DOD recordkeeping prevented any systematic health surveillance of the 150,000 Gulf war troops who took the vaccine. Last year, Congress directed the National Academy of Sciences to study the association between Gulf war veterans' illnesses and wartime exposures, including the anthrax vaccine.

So it may be premature to conclude that the vaccine is as safe and effective for use in a global protection effort as it might be for use by a few thousand mill workers and veterinarians.

Other factors relied upon by DOD to support vaccine safety and efficacy findings have been inflated to better match the scope of the AVI program. DOD relies heavily on FDA approval of the vaccine and FDA regulation of the manufacturer as an indicia of the vaccine's safety and quality. But we now know that approval was based on another vaccine in another time for use in another setting against a different route of exposure.

FDA inspection reports portray an uncharacteristically passive regulator tolerating numerous serious and persistent violations for years at the Michigan production plant, now owned by the BioPort Corp.

The DOD witness at our previous hearing pointed to the "independent review of the health and medical aspects of the overall program by Dr. Gerard Burrow of Yale University Medical School," but his report entailed no independent analysis of safety and efficacy data.

In a recent letter to the subcommittee, Dr. Burrow clarifies that mischaracterization of his work, saying his charge was only "general oversight of the vaccination program."

The AVIP confronts many active-duty, reserve, and national guard members with agonizing personal and professional choices. They deserve answers to their questions about the effectiveness and wisdom of this mandatory, invasive forced protection program. They deserve to know the vaccine chosen to meet the preeminent biological threats is as well tested and technologically advanced as the best weapons systems.

They need to be assured claims of AVIP safety are based on more than exaggerated interpretations of inconclusive data, and they need to be assured claims of AVIP effectiveness are based on more than wishful thinking about monkeys.

At this time, I would like to call on our colleague Ms. Schakowsky to see if you have any statement. OK? And Mr. Terry.

I would invite our guest to the committee and invite Mr. Metcalf if he would like to make a statement.

[The prepared statement of Hon. Christopher Shays follows:]

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Statement of Rep. Christopher Shays
April 29, 1999

The plan to immunize 2.4 million men and women against weaponized anthrax raises legitimate questions about the safety and efficacy of the current vaccine, when used for that purpose, on that many people.

To address those questions, we asked the General Accounting Office (GAO) to examine the data supporting safety and efficacy claims, and to gauge the impact of Good Manufacturing Practice (GMP) deviations on vaccine quality. Their preliminary findings will be discussed today.

Based on the GAO study, and other information obtained in the course of the Subcommittee's investigation, the AVIP seems a very broad undertaking built on a very narrow foundation.

The one study of safety and efficacy in humans, conducted among woolen mill workers in the late 1950s, tested a different vaccine formulation than the one subsequently approved by the Food and Drug Administration (FDA) and used in the AVIP. Using data on one vaccine to support the approval of another is problematic, particularly when there is no direct marker or correlate of human protection to use in comparing the two vaccines. Lack of a surrogate for anthrax immunity also means efficacy test outcomes in animals cannot be extrapolated to humans. The fact that vaccinated monkeys survive exposure to inhaled anthrax longer than guinea pigs or mice suggests, but does not prove, some vaccine protection in man.

Later studies of the FDA licensed vaccine also show wide variations in adverse reaction rates, suggesting safety issues that may become apparent only as usage grows from two or three hundred people each year to several hundred thousand.

There have been no studies of long term health effects. Poor DoD record keeping prevented any systematic health surveillance of the 150,000 Gulf War troops who took the vaccine. Last year, Congress directed the National Academy of Sciences to study the association between Gulf War veterans' illnesses and wartime exposures, including the anthrax vaccine.

So it may be premature to conclude the vaccine is as safe and effective for use in a global force protection effort as it might be for use by a few thousand mill workers and veterinarians.

Other factors relied upon by DoD to support vaccine safety and efficacy findings have been inflated to better match the scope of the AVIP program. DoD relies heavily on FDA approval of the vaccine and FDA regulation of the manufacturer as indicia of vaccine safety and quality. But we now know that approval was based on another vaccine, in another time, for use in another setting, against a different route of exposure. And FDA inspection reports portray an uncharacteristically passive regulator, tolerating numerous, serious and persistent violations for years at the Michigan production plant, now owned by the BioPort Corporation.

The DoD witness at our previous hearing pointed to the "independent review of the health and medical aspects of the overall program" by Dr. Gerard Burrow of Yale University Medical School. But his report entailed no independent analysis of safety and efficacy data, and in a recent letter to the Subcommittee, Dr. Burrow clarifies that mischaracterization of his work, saying his charge was only "general oversight of the vaccination program."

The AVIP confronts many active duty, reserve and national guard members with agonizing personal and professional choices. They deserve answers to their questions about the effectiveness and wisdom of this mandatory, invasive force protection program. They deserve to know the vaccine chosen to meet the preeminent biological threat is as well-tested and technologically advanced as any weapons system. They need to be assured claims of AVIP safety are based on more than exaggerated interpretations of inconclusive data. And they need to be assured claims of AVIP effectiveness are based on more than wishful thinking about monkeys.

We welcome the testimony of all our witnesses this morning as we continue our oversight of the anthrax vaccine program.

Mr. METCALF. I would. Thank you, Mr. Chairman.

I want to thank the chairman and other members of the subcommittee for allowing me to participate in this hearing and express my concerns regarding the safety and effectiveness of the anthrax vaccine. I am deeply grateful that you have been willing to conduct this examination of the Department of Defense's anthrax vaccine immunization program for all military personnel.

I have two outstanding Navy bases in my district. The men and women assigned to carry out the missions of Naval Station Everett and Naval Air Station Whidbey Island are some of our Nation's finest. I want for them the very best in protection, training, equipment, and every advance of science and medicine that is at our disposal.

I understand the grave concerns which have been the catalyst for the anthrax immunization program. I must question, however, the decisions that have been made resulting in the current program. From the time this program was announced, I have had serious reservations.

It is my understanding that we have one source for the anthrax vaccine, and that single source has had significant problems with FDA violations. I also understand that the anthrax vaccine currently being used to vaccinate our active-duty force was produced prior to renovations that are under way at the production facility.

The scientific research upon which FDA based its approval was not conducted to assess protection against a weaponized version of anthrax. Furthermore, the current vaccine was never intended for widespread general use but rather for a very small, targeted population.

The monitoring system for reporting problems has been woefully inadequate.

Those are just a few of the facts that cause me to question the wisdom of this accelerated service-wide program.

I would like to make the committee members aware of the recently published GAO investigation that I requested regarding the presence of squalene antibodies being found in the blood of some sick Gulf war-era veterans.

I asked the GAO to determine if there was any possibility that veterans had received an adjuvant formulation containing squalene and to evaluate the validity of the independent research being reported. In their response, the GAO revealed the depth of research that had been conducted using experimental squalene adjuvant formulations by both the Department of Defense and National Institutes of Health.

It also confirmed that the independent research is based on sound scientific principles. The integrity of the findings convinced the GAO that this issue needs to be pursued aggressively.

There are many troubling questions that have been raised as a result of GAO's squalene study. Many of you may have seen the investigative articles currently in the press. There have been even suggestions that there could be a relationship to the anthrax vaccine.

I don't know what we will find, but I do know that we have a moral obligation to those who are suffering to stay the course until this mystery is solved.

On behalf of the extraordinary active-duty personnel and veterans in my district, I want to thank you, Mr. Chairman, for the efforts of this committee. You have provided desperately needed leadership on this issue. Your quest for accountability and the truth is an example to all of us.

I am confident that our military force will be stronger as a consequence of this examination of the anthrax vaccine program.

I look forward to working with you on this.

Mr. SHAYS. Thank you. It is nice to have you here.

Let me just get some housekeeping out of the way.

I ask unanimous consent that all members of the subcommittee be permitted to place any opening statement in the record and that the record remain open for 3 days for that purpose. And without objection, so ordered.

And I ask further unanimous consent that all witnesses be permitted to include their written statements in the record. And without objection, so ordered.

At this time, I would like to call our first witness. His name is Mr. Kwai Chan, Director of Special Studies and Evaluations, National Security and International Affairs Division, General Accounting Office [GAO].

Thank you. And I believe you are accompanied by Dr. Sushil Sharma. And I will swear in both of you, but, Mr. Chan, I think you are the only one who will be giving testimony.

Mr. CHAN. Yes.

[Witnesses sworn.]

Mr. SHAYS. Note for the record that both have responded in the affirmative.

Mr. Chan, what we are going to do is, we are going to have a green light for 5 minutes, we are going to roll it over for another 5 minutes.

Mr. CHAN. OK.

Mr. SHAYS. And your testimony, obviously, is very important because it sets the stage for the rest of the hearing. So I want to make sure you say everything you need to say.

So, if you are ready, let's begin.

STATEMENT OF KWAI CHAN, DIRECTOR OF SPECIAL STUDIES AND EVALUATIONS, NATIONAL SECURITY AND INTERNATIONAL AFFAIRS DIVISION, GENERAL ACCOUNTING OFFICE, ACCOMPANIED BY SUSHIL K. SHARMA, ASSISTANT DIRECTOR

Mr. CHAN. Thank you, Mr. Chairman and members of the subcommittee and Congressman Metcalf. It is, indeed, my pleasure to be here today. Before I present to you our findings on the safety and efficacy of the vaccine, which we conducted at your request, I want to introduce my colleague, Dr. Sharma, and also I want to acknowledge my staff, Dr. Howard Deshong and Mr. George Bogart in helping me to prepare this testimony.

Let me first discuss the context. As you know, controversy has surrounded the anthrax immunization program since DOD began vaccinating the first of 2.4 million active-duty and reserve members. Some have questioned the safety and efficacy of the vaccine, especially after they learned about the numerous problems FDA

found during the inspection of the Michigan facility. Some Gulf war veterans believe that their illnesses might have been caused by anthrax vaccines that they received during the war.

Let me turn to our results. With regards to safety, I have three findings to report. First, the short-term safety of a vaccine was obtained from data collected for licensing and data on subsequent use. The interpretation of pre-licensing data was complicated by a switch from one vaccine to another while the study was under way.

Second, after licensing, this vaccine has been used by a small number of individuals, unlike other vaccines. This number is too small to detect rare and serious adverse events. In the 1970's, FDA did not have an adverse-effect reporting system in place for vaccines. From the available data, we can say that the reported numbers are based on how closely you monitor individuals who receive this vaccine.

As shown in table one on page 7 of my statement—you see a table there—which says that if you do not follow individuals closely after they receive the vaccine, like in a passive system, the number of significant adverse events are significantly lower. And when you monitor individuals closely, then the number rises significantly, this means that the adverse-event reporting system is really dependent on the data you collect, and on the way you collect the data.

Third, the long-term safety of the vaccine has not yet been studied, and, therefore, one cannot conclude that there are no known long-term effects.

In summary, then, concerning vaccine safety, studies have been performed to examine the safety of both original vaccine and the licensed vaccine. These two vaccines were made using different processes and have different data to support their safety.

While these studies identify varying rates of adverse reactions depending on the data-collection mechanism, be they passive or active, they did not question the safety of the vaccine. The long-term safety of the vaccine had not been studied.

With regard to the efficacy of the vaccine, I have three findings to report. First, the only human efficacy study conducted was done on the earlier vaccine, not the licensed vaccine. This study on efficacy was done in 1962 by Brachman. The study demonstrated efficacy against cutaneous anthrax but not inhalation anthrax, which is the current military threat.

In the 1980's, the military collected efficacy data on animals specific to inhalation anthrax. All these studies have supported the view that in those models the vaccine can protect against some anthrax strains, but not all.

Work using monkeys conducted in 1996 show for the first time that non-human primates could be protected against inhalation anthrax. However, in both the guinea pig and the monkey studies, protection did not correlate with the level antibodies to protective antigen [PA].

More recent work done in 1998, by the military, came to the same conclusion, "It is unknown what immune mechanisms are important in specific resistance to anthrax. Without a specific and measurable immune correlate of protection, extrapolation of protec-

tion data to show that the vaccine is effective for humans, is of questionable value."

Taking all the evidence into account, it is likely that the vaccine does give some protection. But to what extent, against what amount of anthrax, against which strains, and how long protection last are not known.

In summary, on efficacy, I can say that studies on efficacy of the original and licensed vaccines have been limited to a study of the efficacy of original vaccines for humans and studies of the efficacy of the licensed for animals.

The study on the original vaccine concluded that the vaccine offered protection against cutaneous anthrax. The studies on the licensed vaccine focus on the efficacy of vaccines in protecting animals against inhalation anthrax. These studies, while showing some positive results, may not be extrapolated to humans.

DOD is planning to conduct such correlating studies.

With regards to FDA's inspection of the Michigan facility, we found that until 1993 FDA inspectors did not inspect the part of the facility where anthrax vaccine was made because they were not immunized with anthrax vaccine.

The 1996 and 1998 inspection by FDA of the MBPI facility is one of a series that through the years have been problematic. The Michigan facility has received warning letters and notice of intent to revoke their facility license.

FDA's inspection of the Michigan facility found a number of deficiencies, which fall into two categories. Those that, although serious, might affect only one or a limited number of batches that were produced when the deficiency was extant and those of generic nature that could compromise the safety and efficacy of any or all batches.

The manufacturing plant is currently closed for renovation.

Mr. Chairman, this concludes my remarks.

[The prepared statement of Mr. Chan follows:]

United States General Accounting Office

GAO

Testimony

Before the Subcommittee on National Security, Veterans' Affairs, and International Relations, Committee on Government Reform, House of Representatives

For Release on Delivery
Expected at
10:00 a.m., EST
Thursday,
April 29, 1999

MEDICAL READINESS

Safety and Efficacy of the Anthrax Vaccine

Statement of Kwai-Cheung Chan, Director, Special Studies and Evaluations, National Security and International Affairs Division

GAO/T-NSIAD-99-148

Mr. Chairman and Members of the Subcommittee:

We are pleased to be here today to discuss the results of our ongoing examination of the safety and efficacy[1] of the anthrax vaccine, which is being done at your request. My testimony presents preliminary findings on (1) the short- and long-term safety of the vaccine, (2) the efficacy of the vaccine, and (3) problems the Food and Drug Administration (FDA) found in the vaccine production facility in Michigan that could compromise the safety, efficacy, and quality of the vaccine. We plan to issue the final report on our review this fall.

As you know, concerns have been raised about the Department of Defense's (DOD) anthrax immunization program since the Department began vaccinating the first of 2.4 million active duty and reserve members. For example, some Gulf War veterans are suffering from unexplained illnesses that they believe might have been caused by anthrax vaccines that they received during the war. Also, some active duty military personnel expressed concerns regarding the safety and efficacy of the anthrax vaccine after the FDA found problems during the inspection of the facility that was manufacturing the anthrax vaccine. With this background, I will discuss our results.

[1] Safety means relative freedom from harmful effects to persons affected directly or indirectly by a product that has been prudently administered, taking into considerations the character of the product in relation to the condition of the recipient at the time. Efficacy is not an absolute term. It is a measure of a product's ability to produce a given response. An effective vaccine will provide a certain degree of protection for a certain period of time.

RESULTS IN BRIEF

The anthrax vaccine being given to U.S. military personnel was licensed in 1970. Before the vaccine was licensed, the vaccine and the manufacturing process were changed, creating a similar vaccine, produced by the Michigan Department of Public Health (MDPH), which was the one eventually licensed.[2] The safety study conducted before licensing used both the original vaccine and MDPH vaccine. Knowledge to date about the safety of the vaccine includes the results of the original study and a 1998 DOD study of 500 vaccine recipients. While these studies identified varying rates of adverse reactions, they did not question the safety of the vaccine. The long-term safety of the vaccine has not yet been studied.

Prior to the time of licensing, no human efficacy testing of the MDPH vaccine was performed. However, a study was done on the efficacy of the original vaccine. This study concluded that the vaccine provided protection to humans against anthrax penetrating the skin. In the 1980's, DOD began testing the efficacy of the licensed vaccine on animals, focusing on its protection against inhalation anthrax. DOD recognizes that correlating the results of animal studies to humans is necessary and told us that it is planning research in this area.

[2] The original license for the production of anthrax vaccine was issued to MDPH. In 1995, the licensed facility changed its name to the Michigan Biologic Products Institute. In 1998, the licensed facility was sold, and its name was change to BioPort. The term MDPH will be used to refer to the licensed facility throughout this testimony.

Careful control of the manufacturing process is essential to ensure the quality of the product. The FDA inspections of the facility where the licensed vaccine was manufactured uncovered numerous problems. The facility received warning letters from FDA, including one in March 1997stating its intent to revoke the facility's license. The facility closed its plant in 1998 and is now being renovated. FDA requires the manufacturer to meet specifications for sterility, stability, purity, and potency. In addition to the lot release testing required by FDA, DOD is conducting supplemental testing of each lot from this plant before distributing the vaccine.

BACKGROUND

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.

The original anthrax vaccine was developed by George Wright in the 1950s and first produced on a large scale by Merck. After a 1962 study on the vaccine's effects in mill workers, its manufacturing process was changed, and the Michigan Department of Public Health (MDPH) took over as the vaccine's producer. This

changed vaccine was licensed in 1970 by the Division of Biologics, National Institute of Health, to be manufactured by MDPH.

Vaccines have three distinguishing features that contrast with those of chemical drugs. First, either they have no clearly chemically defined composition, or simple chemical analysis is insufficient for effective characterization. Second, proper evaluation of them (qualitatively or quantitatively) is usually done by measuring their effects *in vivo* (in the living organism). Finally, quality cannot be guaranteed 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.

VACCINE SAFETY

Studies have been performed to examine the safety of both the original vaccine and the licensed vaccine. These two vaccines were made using different processes and have different data to support their safety. While these studies identified varying rates of adverse reactions, they did not question the safety of the vaccine. The long-term safety of the vaccine has not yet been studied.

Data on Safety of the Original Vaccine

A study on the original vaccine's safety was done by Philip Brachman and published in 1962.[3] Brachman reported on 379 subjects that received this vaccine. About 35 percent had local reactions, a figure that varied during the inoculation series. Some recipients developed more severe edema that extended to the mid-forearm or wrist. Two individuals had systemic reactions in addition to the edema. The researchers actively collected data on adverse reactions to the vaccine, and the study concluded that individual reactions to the vaccine were relatively minor.

Data on Safety of the Licensed Vaccine

After the original vaccine was developed, MDPH was granted a license for a similar vaccine that differed from the original vaccine in three ways. First, the manufacturing process changed when MDPH took over. Second, the strain of anthrax that Merck used to grow the original vaccine was changed, and another strain was used to grow the MDPH vaccine. Finally, to increase the yield of the protective antigen (which is believed to be an important part of the vaccine's protective effects), the ingredients used to make vaccine were changed from the original vaccine.

Four safety studies have been done that include the licensed vaccine. The results of those studies are presented in Table 1. The Center for Disease Control

[3] P.S. Brachman et al., Field evaluation of a human anthrax vaccine, American Journal of Public Health, vol. 52 (1962), pp. 632-645.

collected data on the Investigational New Drug (IND) study, DOD collected data for both the Pittman study and the Tripler Army Medical Center (TAMC) Anthrax Survey, and DOD is currently collecting reports on adverse events. The number of adverse reactions appears to depends, in part, upon whether the mechanism for monitoring reactions is active or passive. (Active monitoring means that the vaccine recipients are contacted to ascertain any adverse reactions after vaccine administration; passive monitoring means that the onus is on the vaccine recipients to report any adverse reactions after vaccine administration.) None of the studies questioned the vaccine's safety.

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]	.05[b]
Pittman (1997)	Active	508	16	5	29[c]	14
TAMC (1998)	Active	536	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 March 16, 1999, more than 223,000 service member 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.

VACCINE EFFICACY

Studies on the efficacy of the original and the licensed vaccines have been limited to a study of the efficacy of the original vaccine for humans, and studies of the efficacy of the licensed vaccine for animals. The study on the original vaccine concluded that the vaccine offered protection against anthraxpenetrating human skin. The studies on the licensed vaccine focused on the efficacy of the vaccine in

protecting animals against inhalation of anthrax. These studies, while showing some positive results, may not be extrapolated to humans. DOD is planning to conduct such correlating studies.

Human Efficacy Study

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.

Because the vaccine used in the Brachman study was different from the licensed vaccine, additional data were submitted to the Division of Biologics, Department of Health, Education, and Welfare (HEW), to support the license application for the MDPH vaccine. In a February 1969 memorandum, an HEW committee concluded that based on the data, the assumption of efficacy appeared speculative. Similarly, a 1991 Army document noted that "it would be scientifically incorrect to assume that this (*licensed*) vaccine would be totally efficacious under different circumstances, that is, beyond the parameters of the study design." Thus, assuming that the epidemiological evidence from the original vaccine is applicable to the licensed vaccine, we can concludethat the licensed vaccine is efficacious against cutaneous exposure but that testing still needs to be

conducted on inhalation anthrax. In the absence of a specific study, efficacy of the licensed vaccine for 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.

Animal Efficacy Studies of Licensed Vaccines

Beginning in the late 1980's, DOD began studying the efficacy of vaccines on animals, using guinea pigs, rabbits, and monkeys. All of these studies support the view that in these animals, the licensed vaccine can protect against exposure to some strains of anthrax either by inoculation or inhalation. It is clear, however, that animal species differ in their susceptibility. Studies of guinea pigs show that some anthrax strains are more or less resistant to vaccines for humans (both the U.S. and United Kingdom versions) but are protected by the live spore veterinary vaccine.[4]

Research using monkeys showed for the first time that monkeys could be protected against aerosol exposure.[5] However, in both the guinea pig and monkey studies, protection did not correlate with levels of antibodies to a protective antigen. Several studies have shown no direct comparison of immunity in humans to that in monkeys. Study findings suggest that "the importance of various

[4] P.C.B Turnbull, et al., Development of antibodies to protective antigen and lethal factor components in humans and guinea pigs and their relevance to protective immunity, Infectious Immunology, vol. 52 (1988) pp.356-363.

specific immune mechanisms against inhalation anthrax may vary in different animal species or . . . the ability of the licensed human vaccine to stimulate cell-mediated immunity may be greater in some species than others." A 1998 study comes to the same conclusion and emphasizes the need for further studies. In animals, the lack of correlation of protection with antibodies to protective antigen has some important consequences.

DOD recognizes the importance of establishing a correlate of immunity in humans. Recently, it has sought to develop a serologic correlate of immunity in an animal model to use for humans.

VACCINE MANUFACTURING PROCESS

The quality of a vaccine is closely linked to its manufacturing process, which must be rigorously controlled to ensure that batches of vaccines produced on different occasions are of reproducible and consistent quality. In general, quality is achieved by applying the current good manufacturing practice. This process is not static but involves manufacturers and regulators in a continuing process of assessment and upgrades as scientific progress, technical development, and experience help to identify deficiencies and make improvements possible. Such principles also apply to the facilities and equipment in which products are manufactured.

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[5] B.E. Ivins, et al., Efficacy of a standard human anthrax vaccine against Baccillus anthracis aerosol challenge in rhesus monkeys, in "Proceedings of the International Workshop on Anthrax,

Accordingly, vaccine production is very highly regulated to ensure that the products are of consistent quality and safe and effective for the purpose(s) for which regulatory approval was granted. Until 1993, FDA inspectors did not inspect the MDPH facility where the anthrax vaccine was made. According to FDA, access was not granted because its inspectors had not been vaccinated against anthrax.

FDA's inspections of the MDPH facility found a number of deficiencies. The deficiencies that FDA identified in its February 1998 inspection fall broadly into two categories: those that, although serious, might affect only one or a limited number of batches that were produced when the deficiency was extant and those of a generic nature that could compromise the safety and efficacy of any or all batches. DOD had also identified deficiencies during a March 1992 inspection, including the absence of stability studies. In 1998, MDPH closed its plant, which is now being renovated. DOD has directed that supplemental testing be done on the lots of vaccine in the current inventory.

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Mr. Chairman, this concludes my statement. I will be happy to answer any questions you may have.

(713030)

Salisbury Medical Bulletin, Special Supplement no. 87 (1996) pp.125-126.

Mr. SHAYS. Would you repeat your last sentence. I was——

Mr. CHAN. Yes.

Mr. SHAYS. Make your last point.

Mr. CHAN. The manufacturing plant is currently closed for renovation.

Mr. SHAYS. Right, but before that.

Mr. CHAN. Yes.

Mr. SHAYS. I just want to be clear on the dates. That is what I was asking my staff. The plant was not inspected until when, thoroughly, by FDA?

Mr. SHARMA. The FDA inspectors were visiting the plant and the process has changed over time, but they were not able to enter the facility where they were manufacturing the——

Mr. SHAYS. Dr. Sharma, I am going to have you get a separate microphone, if you can. I am sorry. I should have asked you to do that before. I apologize to our official reporter.

Yes. You can pull it down and put it in front of you please. Does it reach?

There you go. Thank you, Jonathan.

Mr. SHARMA. FDA inspectors had been inspecting the manufacturing facility at routine intervals. However, while they looked at other components of the GMP, they did not enter the manufacturing facility because they were told that they were not immunized.

The first evidence that we found from FDA records was in 1996, when they were told, essentially, that they were immunized and they could enter the facility, and which point in time they uncovered numerous problems.

Mr. SHAYS. So are we basically saying the anthrax portion was never fully inspected until 1996?

Mr. SHARMA. That is correct. The other components of the anthrax production were looked at, at routine intervals such as, you know, where they have the labeling——

Mr. SHAYS. No. I understand. OK.

Let me start out first by, Mr. Chan, talking about safety. I just want to follow the flow of these questions. So you have responded in part, but I want to make sure I am focused on it.

How different is the licensed vaccine from the earlier version used in the study?

Mr. CHAN. The original vaccine was developed in the 1950's by Dr. Wright in Fort Detrick, as I remember. And, the actual license vaccine, MDPH at the time, the Michigan Department of Public Health, was granted a license for a similar vaccine. But I think we found at least there were three differences from the original vaccine.

First, the manufacturing process changed when MDPH took over, and second, the strain of anthrax that Merck used—this is the original license, I mean the original vaccine was produced by Merck. The strain of anthrax that Merck used to grow the original vaccine was changed, and another strain was used to grow the MDPH vaccine.

And finally, to increase the yield of the protective antigen [PA], the ingredient to make the vaccine was changed from the original vaccine.

So, I think we see three different changes made.

Mr. SHAYS. Do you consider the safety data on the earlier vaccine relevant to the questionable safety of the licensed vaccine? I mean, how relevant is this issue?

Mr. CHAN. I think it is relevant and also is important to understand, back in the 1970's, when the requirement for licensure was purely based on safety. I think that the way that it was done, and later on maybe FDA can expand on this, it is based on the comparison of level of antibody generated, by the two different vaccines.

Mr. SHAYS. Excuse me a minute. I should be timed, Jon. Sorry. I am sorry. Make your last point again, please.

Mr. CHAN. I am saying that I think the only possible similarity that was produced is really based on the antibody reaction to PA that was generated using the two different vaccines. So, in a way, on the current standard, they are clearly two different vaccines.

Mr. SHAYS. OK. What basis did you find for the DOD statement that no known long-term side effects are associated with the anthrax vaccine?

Mr. CHAN. Well, I think maybe the statement by itself is misleading because in a way I don't believe and we have not found any studies on long-term effects. So if you did not collect the data, certainly there will be no known side effects.

Mr. SHAYS. When you say you didn't find it, could you just elaborate. I mean, do they exist? Did you make requests of DOD and others?

Mr. CHAN. Yes, we have. Yes.

Mr. SHAYS. And they were not able to provide you any data that would have shown you these studies.

Mr. CHAN. Right. We explain that they need to be actively monitoring those people to really determine that, and I may also say that on other vaccines, such monitoring was not done either. But for them to say that there are no long-term side effects, we cannot find any studies to support that statement.

Mr. SHAYS. At all?

Mr. CHAN. No.

Mr. SHAYS. OK. Did you find any toxicology studies on the vaccine in animals?

Mr. CHAN. You want to expand on that?

[Mr. Chan speaks to Mr. Sharma.]

Mr. SHARMA. No, not from the earlier work. These were not the requirement——

Mr. SHAYS. I am going to ask you to speak a little closer to the microphone, and a little more slowly, if you would, Doctor.

Mr. SHARMA. It is my understanding, based on the review of DOD documents that they provided to us, a need for such work was suggested in 1996, or around that period, but to the best of our knowledge, such studies has not been conducted.

Mr. SHAYS. Did you find any animal studies to evaluate any reproductive effects of the vaccine?

Mr. SHARMA. No.

Mr. CHAN. No.

Mr. SHAYS. Now, you explained the chart that you had.

Mr. CHAN. Yes.

Mr. SHAYS. But I am to basically infer that if they didn't have followup, then they didn't have reports. But if they had followup,

then there were serious side effects associated with the vaccine. Is that correct?

Mr. CHAN. What we are saying is the following. If you have an active data-collection mechanism, that means actually monitor people you can see that both the Pittman study and also the Tripler study, TAMC, the numbers are numerically much higher.

Mr. SHAYS. OK, now the Pittman study shows 29, and the other study shows 43. Is that 43 out of 536 and 29 out of—oh, this is the percent?

Mr. CHAN. The percent. Yes.

Mr. SHAYS. Now, we are saying that 29 percent had side effects. Is that correct?

Mr. CHAN. Systemic, mild side effects, yes.

Mr. SHAYS. They were fairly mild, and 43 percent had mild side effects in the other study. In Great Britain, it is voluntary?

Mr. CHAN. Yes, it is.

Mr. SHAYS. In France, they don't do it. Their force protection is through protective gear.

Mr. CHAN. Yes.

Mr. SHAYS. In the United States, it is mandatory. In Great Britain, it is voluntary. And in France they don't do it.

Now, in Great Britain we learned that you could improve the anthrax vaccine. In other words, this is an old vaccine that we have now.

Mr. CHAN. Yes, sir.

Mr. SHAYS. And that there would be, they claim, less side effects. But if you did that, wouldn't you have to do a new study to determine if this next-generation vaccine were safe and effective and so on?

Mr. CHAN. Yes, you do.

Mr. SHAYS. So basically what we have is we have a 1950's vaccine, or a 1960's vaccine that could be improved.

Mr. CHAN. Sixties. Approved in 1970. Yes.

Mr. SHAYS. If we did the work to improve it, it would take some time, but then we would have to obviously test it.

Mr. CHAN. Correct. As I understand it, first of all, this vaccine, as you know, was licensed in the 1970's. And so improvement can come in many different ways, one of which is really the reduction of number of doses that is required.

Mr. SHAYS. OK.

Mr. CHAN. The six doses plus the booster.

Mr. SHAYS. Let me just indulge the committee just for two more questions. And let me ask you: Why six shots?

Mr. CHAN. Well, we don't know why either. We understood from the beginning that in animal studies, only three shots were required to be done. But in the Brachman study, six shots were imposed. And from then on, it became sort of de facto, the number of shots required were six.

I might add that the Department of Defense is interested in looking and examining why six shots, and could they, in fact, reduce the second of the six shots.

Mr. SHAYS. Well, let me ask you: Why—what is the claim for the six shots? There has to be some basis for it.

Mr. CHAN. I do not believe there is a scientific basis for it, except the Brachman study, of which they selected the six shots dose as the regimen they adopted.

Mr. SHARMA. If I may just add to it. I think the way we understand is, the original experiments that were done on mice used the three shots. And then, in the human studies, subsequently, when three shots were used, they found three cases that were infected with anthrax. Two of them had complete series. In one DOD document that they provided to us, it was stated that the investigator arbitrarily decided to change it to six shots.

And that was the basis for the six shots series. We have not found any other evidence, and that is because there is really no relationship between the level of immunity and the protection. So it is not based on any scientific basis that I know of.

Mr. SHAYS. Well, we will ask our other witnesses.

And last, does the six-shot anthrax increase or decrease the safety of the vaccine?

Mr. CHAN. The safety of the vaccine?

Mr. SHAYS. Yes. In other words, if you take six—we are talking efficacy and we are talking safety—but in terms of if you do it six times, is it safer or less safe? We don't know? We do know?

Mr. SHARMA. Well, we do know that each time you take shots you have more pain. So the more shots you are going to give, you are going to experience more adverse events—at least the probability increases. And this is one of the very strong limitations of the current vaccine. The schedule is too long and heavy on the recipients without any scientific evidence of its needs.

Mr. SHAYS. Thank you. I appreciate the committee's indulgence. And Ms. Schakowsky.

Ms. SCHAKOWSKY. Thank you, Mr. Chairman.

Has the current vaccine ever been studied in humans to determine its protection against inhalation anthrax?

Mr. CHAN. No it hasn't.

Ms. SCHAKOWSKY. And are you aware of any other vaccines that have been licensed by the Food and Drug Administration without efficacy data to support the intended use in humans?

Mr. CHAN. I am not aware of that.

Mr. SHARMA. No. I have FDA credentials of this.

Mr. CHAN. Yes.

Ms. SCHAKOWSKY. Oh, OK. So you just——

Mr. CHAN. We are not aware of that.

Mr. SHARMA. We are not aware of this.

Ms. SCHAKOWSKY. OK. I am wondering if you are—if you do know if the results of the efficacy studies in animals then can be extended and extrapolated to reach conclusions about the efficacy in humans?

Mr. CHAN. Well, what we found was that if you use the measure, the so-called antibody, to the PA in animals, that different response in terms immuno-degenecity by species; that is, what we find is that there is no direct correlation to the higher the level antibody implies that you are more likely to be protected among the animals. Although, the best one is really with the monkeys. They are pretty good in terms of that relationship.

We do not have a scientific way to link between animals to humans in terms of a correlation. How does protection correlate in terms of the level antibody to protect the antigens that are there, to the antibody.

So, in a way, DOD is, and certainly CDC, are interested in pursuing and, examining this issue because that would be a real help to science and development of vaccines in the future.

Ms. SCHAKOWSKY. The passive monitoring that DOD is doing now, is there any active monitoring going on at all?

Mr. CHAN. Yes. In the table, you find the TAMC, 1998, the Tripler, so-called, is active monitoring. This is something that they are doing now, with a small number of vaccinated individuals.

Ms. SCHAKOWSKY. Are these all DOD studies? Is that what you are saying? First of all, mine says page 6 and then it has——

Mr. CHAN. I am sorry.

Ms. SCHAKOWSKY. There are four columns.

Mr. CHAN. Yes.

Ms. SCHAKOWSKY. DOD is at the bottom, and it says current monitoring, and it says passive, 223,000.

Mr. CHAN. That is right.

Ms. SCHAKOWSKY. Are any of those other studies DOD studies or are they all?

Mr. SHARMA. They are all DOD studies.

Ms. SCHAKOWSKY. They are all DOD studies?

Mr. CHAN. Yes.

Ms. SCHAKOWSKY. OK. I see.

So, what we are finding here is that passive studies in terms of determining any kind of reactions at all seem to be fairly—not results are reported? Is that what you are saying?

Mr. CHAN. The result in DOD, the current monitoring, the last column you find——

Ms. SCHAKOWSKY. I am looking at the last column, the passive monitoring.

Mr. CHAN. Yes, right. And you find that, the level of so-called reported adverse events is very low in the nature of 0.006 to 0.007.

And the intent of this table is to show that, depending on how you gather your information, you end up with different kinds of numbers.

Ms. SCHAKOWSKY. OK.

Mr. CHAN. So, in a small way, the Tripler, the TAMC, data, which is also being collected by DOD as well, is an active way to reach and find out, are there adverse events, which is something that DOD is pursuing.

Mr. SHARMA. Let me add to—I think it is very well known that the VAERS, which is the system that apparently is in place under FDA—strictly dependent upon the individuals physicians or healthcare providers to report. It has been well agreed that it is a signal system; that is, it tells you that something is happening with this vaccine. It does not tell you how often, with what severity, or does not establish causality. The limitations are very well accepted.

Mr. SHAYS. Excuse me 1 second. We don't usually have this problem. Are we able to turn it down a little bit?

I am sorry, Dr. Sharma.

Jonathan, we are keeping you busy today, buddy.

Why don't we do this. Why don't you keep talking and we will just ignore the red light, I am sorry to interrupt you.

Mr. SHARMA. I think the VAERS system has, as you know, a lot of advantages, but if it is used as a basis to determine absolute numbers, then it is, you know, certainly very misleading. And that is what we are trying to convey. This is a vaccine which, up until 1991, when it first was used on a large scale of 150,000 people during the Gulf war, that was our first opportunity to learn about how this vaccine works on large numbers. But we lost that opportunity. And for the first time, now, we have another opportunity to learn about this vaccine. However, if you are going to rely your safety information based on a passive system, and present that as an absolute number, you will be under-reporting the adverse events.

Ms. SCHAKOWSKY. No. When we do polls to determine public opinion, we also have a degree of accuracy. I am wondering in these other studies, when we talk about, for example the Pittman study, where we had 29 percent saying they had a mild reaction, 14 percent severe or moderate, to what degree of accuracy can we—what can we say in terms of——

Mr. SHARMA. These are absolute numbers. You know, it is not like in that particular cohort 29 percent experienced that. There is no confidence interval. It is actually——

Ms. SCHAKOWSKY. No. I understand that, but were these, the number vaccinated, the 500 and—the sample, the universe. Was that selected in any kind of scientific way?

Mr. CHAN. This is a group that they have. It is not a randomly selected sample. So as a result, the confidence level cannot be provided. I mean, it could be done that way.

Ms. SCHAKOWSKY. We don't have any studies that are done that way so that we can——

Mr. CHAN. If you want to achieve generalizability, no. We don't have that. A passive system, potentially, could have that because if everybody provided information, then you end up with a census data without sampling. But if people are not encouraged to provide events that they believe are attributable to vaccine and go through the system of reporting, then you will have a very low rate of reporting, as a result.

If you want to do an active monitoring, you can do it by selecting a sample of a few thousand people, and monitoring them over time. The only question is that with vaccine is it difficult, to detect rare events and disease or illness out of this small samples?

Unlike polls, it is always one or zero. But to capture a single event that may occur in a very rare way, then it is difficult. And so you have that conflict.

Mr. SHARMA. I think this is a very important point. One of the rare events, Gullain-Barre syndrome, for example, about 1 in 100,000 people, when DOD currently started using this vaccine, and after it was used in about 150,000 people, they had 1 case. So there are these rare events that, even if you monitor a population but if it is small, the likelihood of seeing those events is very, very small, even in the active monitoring system.

Ms. SCHAKOWSKY. So what is the best way then for us to determine accurately the side effects, the safety hazards?

Mr. SHARMA. There are a number of models one could use, and I think in our discussion with CDC they had provided and discussed with DOD some several options. But let me just talk to you about how it is currently being done by some of the newer vaccines.

One, with Merck, varicella vaccine, they had voluntarily decided to followup 100,000 individuals who are receiving this vaccine for over—at least a start—10 year period. For another vaccine, CDC, under contract, is following about the same number of individuals in four HMO settings. And DOD has an excellent opportunity to monitor because they are all in the system. And there are a number of ways one could do that. And I am sure they are aware of it and would be able to comment on that.

Mr. CHAN. I think what we are saying is that if they want to do it, it can be done, without greatly disturbing the system, the way it is right now.

Ms. SCHAKOWSKY. Thank you.

Mr. SHAYS. I would like to call Mr. Terry, but I just want to verify one thing on your chart.

Mr. CHAN. Yes.

Mr. SHAYS. Basically, in the Pittman study, 43 percent had either mild or more severe reaction when you monitored. In the TAMC—and that stands for what, TAMC?

Mr. CHAN. Tripler.

Mr. SHAYS. OK. Right, Army Medical Corps.

They had 48 percent when they monitor it.

Mr. CHAN. Yes.

Mr. SHAYS. And now the DOD—current monitoring—they have none. Are they, in fact, monitoring? Can we even put the word "current" monitoring? Or is that being a little disingenuous?

Mr. CHAN. Well, they have the VAER system, as we said.

Mr. SHAYS. They have a what?

Mr. CHAN. The VAER system, the passive system where people can send in a form.

Mr. SHAYS. So, do they give out the forms?

Mr. CHAN. We have another study looking into that to see how effective that is.

Mr. SHAYS. OK.

Mr. CHAN. But, nevertheless, it is still a passive system.

Mr. SHAYS. So we don't really even know what kind of monitoring it is, if at all.

Mr. CHAN. If you look at footnote E here, it basically shows that right now they are experiencing out of 223,000 vaccines you have 42 reports and so on.

Mr. SHAYS. No, but my point is they are not basically monitoring.

Mr. CHAN. Well, that is what we call data collection is passive. You wait for people to come in and tell you rather than actively go——

Mr. SHAYS. OK. I don't call that monitoring, with all due respect.

Mr. CHAN. Oh. OK. I am sorry.

Mr. SHAYS. No. You can call it that. I don't call it that.

Mr. CHAN. OK.

Mr. SHAYS. Mr. Terry.

Mr. TERRY. Thank you, Mr. Chairman. Some of my questions are in regard to the Michigan production facility. I am reading your

statement, for the record and listened to your opening statement and I just need to clarify a little bit of a timetable because it raises some red flags with me.

In your statement, you say that the DOD had inspected the facility, or at least did an inspection in 1992, where it found just a generic statement of deficiencies, including the absence of stability studies. My question is, just to verify the timetable, that study occurred by the DOD in 1992?

Mr. CHAN. That is correct.

Mr. TERRY. And then, in 1993, the FDA tried to do an inspection and was turned away because they weren't, they didn't have their immunizations. So the inspection didn't occur until 1996. Is that a correct timeline so far?

Mr. SHARMA. Yes. I want to qualify it. This is inspection of the manufacturing plant. The FDA has been inspecting very regularly and systematically documenting problems with other components of the production facility. And these problems were very systemic and persistent.

Mr. TERRY. OK. But they didn't get the opportunity to get into the plant to do the physical inspection until 1996?

Mr. SHARMA. Yes.

Mr. TERRY. And that raises my point here. Some red flags were put up in 1992; more should have been put up in 1993, but yet they continued to manufacture and use the vaccine. Correct?

Mr. SHARMA. That is correct.

Mr. TERRY. Until recently, when they, I guess, voluntarily have closed down the plant for "renovation"?

Mr. CHAN. Right. When we say, inspect the facility, we mean the anthrax production facility because BioPort produces other vaccines as well.

Mr. TERRY. Right, and that is what I am focusing on.

Mr. CHAN. And so——

Mr. TERRY. Well, we aren't having a hearing on those others.

Mr. CHAN. I understand. But what I am saying is that FDA had been inspecting them without entering into that particular production site and observing basic systemic problems in terms of the processing for the other stuff as well. So they were noticing those kinds of issues as well.

Mr. TERRY. That is part of my point. We had some of these red flags popping up, but yet we went through from 1992 until sometime after 1996 but they were still manufacturing.

Mr. CHAN. Right.

Mr. TERRY. Right there that raises a concern with me, but the issue then is the safety of the end product. Do the deficiencies that were found then by the FDA in any way affect the safety or the potency of the vaccine?

Mr. CHAN. As we stated in terms of vaccine, because it is biologic, it is important that you need to make sure safety is built into the process itself and not just the end product tests. Right now, we are really talking about the end-product test. And DOD had imposed on further supplemental testing after FDA had passed or released a lot.

So they are doing an extensive listing.

Mr. TERRY. OK. So I guess——

Mr. SHAYS. Could the gentleman just yield a second?

Is the answer yes to the question?

Mr. TERRY. Yes. That is what I was going to followup with, Chris. I am still not sure if we, if I learned that the safety of the product was jeopardized by these deficiencies. Who are you to trust?

Mr. CHAN. I do not know.

Mr. TERRY. All right.

Mr. CHAN. I can't answer that. But I can tell you that off the lots that have been produced so far, I believe 31 lots—maybe I'll get the numbers incorrectly—but 8 of those lots have been released and supplementary testing has been done by DOD to release it for vaccination.

And my understanding is that of those remaining lots, as many as 20 lots have been quarantined for further testing. So, it is possible to examine those lots that are going through further testing to determine where the problems lie in terms of the process. That means you go backward to find it. That is possible.

I am not sure that has been done. To examine where did it fail. It could be filtration, it could be something else. But nevertheless, I cannot answer the question as to whether they are safe or not.

Mr. TERRY. Well, you had mentioned the lots. I think we could spend a few more minutes dissecting your answer to that, but are there lots that were quarantined? Is this pursued by the FDA?

Mr. CHAN. Our understanding is the lots had not passed for release, and have not been supplementary tested by—testing had not been done. So it is awaiting for further testing.

Mr. TERRY. Thank you, Mr. Chairman. My time is up.

Mr. SHAYS. Thank you very much. I'm sorry, Mr. Allen you have the floor.

Mr. ALLEN. Thank you, Mr. Chairman. Couple of questions. Have there been any studies of the potential effects of the anthrax vaccine when used in combination with other vaccines or other drugs? Any studies that—and a little bit of background. In hearings that this committee held on the effects of Gulf War Syndrome, one of the—you always hesitate to say it—conclusions, but one of the views was that it was a combination of different kinds of chemicals that might be responsible for the various maladies described collectively as the Gulf War Syndrome.

And so, what I am wondering is, it's one thing to test an anthrax vaccine all by itself, but it seems to me that typically our service men and women get a variety of different vaccines. And I would be interested in knowing whether there is any potential for interaction of the anthrax vaccine with others that we should take account of?

Mr. SHARMA. To the best of my knowledge, there is one unpublished DOD study, which looked at the interaction effect with botox and anthrax——

Mr. ALLEN. Between, what was the first?

Mr. SHARMA. The botulism toxide vaccine and anthrax. And I will be very happy to provide you for the record our review of that study.

Mr. ALLEN. OK. Good. I would appreciate receiving that. The other, in the GAO report, you mention the Brachman study claimed that the vaccine gave 93 percent protection against an-

thrax penetrating the skin, but indicated that the tests on humans with respect to inhalation are—there are too few cases to come to any conclusion.

And in your report, on the next page here, it says that you conclude that testing still needs to be conducted on inhalation anthrax, and you go on to mention some animal studies. How do you do that? How would you do it? What kind of study could be designed or should be designed to determine the efficacy of vaccine against exposure to anthrax by inhalation?

Mr. CHAN. Well, in fact DOD is pursuing studies to examine whether there is a correlate—that means define the ingredient that provides protection. They do believe that in animal studies, the protective antigen plays a major factor, but it is not the only factor. So they are looking for other means to examine that, as I understand they are pursuing now in their own research.

Mr. ALLEN. Other means besides animal studies? Or——

Mr. CHAN. No. Looking at animal studies and see how it may be correlated to the human response.

Mr. ALLEN. I see. OK. Thank you very much.

Mr. SHAYS. Thank you. I think it is Mark Souder. I think you are next.

Mr. SOUDER. I am sorry, I read through your testimony. I'm sorry I missed the testimony and the first part of the questions. Are the side effects with this vaccine fairly typical for this serious of vaccine? In other words, the 43 percent in the one study even to have mild, that seemed pretty high, although other studies were lower.

Mr. CHAN. Well, I caution, first of all, that the analysis had not been done whether in fact it is directly related to the vaccination itself. So that needs to be done, and then try to attribute it to the vaccine. And then I think one can draw the conclusion whether it is really caused by the vaccination.

Mr. SOUDER. Would that be true of other studies of vaccines, however those——

Mr. CHAN. Yes, you need to do that because there could be other reasons why it is causing the problem. But those are the kind of observations you would expect. But the degree, in terms of numbers and so on, it appears to be high.

Mr. SOUDER. What about when it says "moderate or severe." What does that mean? In other words, is it—I saw one reference to fevers and chilling, or how frequent is that? Does it mean you are debilitated? That you can't ever recover? That you are more prone—you said in your statement that we don't know the long-term impact.

Mr. SHARMA. This is very typical of, you know, most bacterial vaccines. You do recover, and what it—the difference between really mild and moderate and severe is discomfort and how it really impacts your functioning. And when you are talking about mild to moderate, this number is high. And, but also you have to recognize this is a very old vaccine, and I think it will be very appropriate for you to ask a PA, what their comment or reaction would be if a newer vaccine would show these numbers. Would it be acceptable to them?

I think they will be a much better position to address the issue.

Mr. SOUDER. Thank you for doing that question for us. [Laughter.]

I see in the testimony of Dr. Zoon that is coming there is a discussion in her testimony about the anthrax vaccine used on livestock workers, and it said that from this manufacturer, that between 1991 and present, 1.2 million doses were distributed. Have you ever looked at that as to—that's a pretty big universe to see whether there are any side effects in that industry.

Mr. SHARMA. Well, let me comment. I think there are two things. We have to make a distinction between the old vaccine and the licensed vaccine or the original vaccine. As far as we know, for the licensed vaccine, post-licensure, approximately 60,000—2,000 doses per year were distributed on average. But we have no information how many individuals were vaccinated. So even if you assume every shot went into a human body, we are talking about over 30 years period, approximately about 60,000 individuals at best.

However, in our discussion with scientists at Fort Detrick, the estimates of the number of people who may have received this vaccine over a 30-year period, range from somewhere between 200 to about 2,000, at the most. And we don't know who those individuals are. There has been no followup. No systematic followup has been done.

So we really—I don't know, you know, the context of, I have not reviewed FDA testimony, but, you know, you have to make a distinction between the old vaccine and the new vaccine.

Mr. SOUDER. If there was any kind of systematic pattern of at least beyond mild, to moderate, would that not have likely shown up? In other words, in health journals and so on with the distribution.

Mr. SHARMA. If the vaccine use is on a very large number of people, you would expect some adverse reactions. But again, you have to recognize the number of people prior to 1998 that were the target group for this vaccine were small. But in general, we would—I would agree with you, if there was somebody who just dropped dead or if a very serious event occurred, it would have been reported.

Mr. SOUDER. The symptoms that you described seemed like they could also become confusing. In other words, depending on the delay, you could be uncertain of the symptoms. Could that also make for a reporting problem?

Mr. CHAN. Yes. That is why you need to gather information first and minimize the screening process of what you believe to be vaccine-related or not, examine those, and pull out the ones it is not and try to examine further. That is why I am saying there are a number of steps. In here, we are just showing the immediate reaction of the number of adverse events. And I have to qualify those numbers.

Mr. SOUDER. So there could be many people who don't think it was related to the vaccine and, in fact, it was. Or there could be people in some of these studies who thought it was the vaccine and it wasn't because we haven't gone——

Mr. CHAN. That's right. If you have things such as swelling, edema, around the vaccinated site, and you are going to attribute

to the vaccine, but other reactions such as fever, you may not be able to attribute to it. Yes.

Mr. SOUDER. Thank you.

Mr. SHAYS. Just a small point. You were reading ahead to FDA's testimony. Most of the doses, I make an assumption, after 1991 were not with livestock workers. It was really the war in the Gulf, I believe.

I think you will find that most would be that way, and maybe we will have the FDA clarify that. But that is from their statement on page 11. It is a minor point. But for many years, we didn't have that many people taking the vaccine until the war in the Gulf.

Mr. Mica.

Mr. CHAN. Oh, I see. Now I understand. The numbers I was a little surprised by.

Mr. SHAYS. Yes. No, the statement basically says from 1974 until 1989, approximately 68,000 doses were distributed.

Mr. CHAN. I see.

Mr. SHAYS. In 1990, approximately 268,000 doses were distributed. Between 1991 and the present, we understand that approximately 1.2 million doses were distributed.

Mr. CHAN. All right.

Mr. SHAYS. But we will have that clarified.

Mr. CHAN. I understand.

Mr. SHAYS. Mr. Mica.

Mr. MICA. Thank you, Mr. Chairman. Just a couple of questions. It is my understanding that the only study of the efficacy of the vaccine was performed by the Brachman study?

Mr. CHAN. Yes, sir.

Mr. MICA. And it is also my understanding that the study gave the vaccine a 93 percent protection against anthrax penetrating the skin. It said a lower confidence level of 65 percent. Can you explain this lower confidence limit, a 65 percent in this study?

Mr. CHAN. I think they had one case of cutaneous anthrax after they received the vaccine. And you have to forgive if I am incorrect with the numbers. Out of a total possible expected number of 13.5 or so, and so if you look at that then the actual protection turned out to be 92.5 percent.

Now, since it is a small sample, they determine what is the uncertainty of that number. And so they end up with the expectation of 92.5 percent protection but with a lower limit of, as low as 60-some-odd percent.

Mr. MICA. Well, I also found——

Mr. CHAN. That's against cutaneous anthrax.

Mr. MICA. Your report found the number of individuals who contracted anthrax by inhalation was too low to assess the efficacy of the vaccine against this form. So, my concern is that we don't have that many experiences with human studies. They are fairly limited, and from the information and analysis you have conducted, I am wondering if, again, this forced vaccination is that effective. Do you feel it is that effective and should be continued?

I mean, just basically, based on the reports and the studies that have been done.

Mr. CHAN. Well let me answer the first question about why do we say that it is a small number.

When the test was done—the study was done—and published in 1962, it was supplied to four different mills.

Mr. MICA. Right.

Mr. CHAN. And the only inhalation anthrax that occurred was in mill A, where there were five of them occur, all in a span of 2 months or so. OK?

And the understanding at the time was that since in the mill itself the air quality was poor, that everybody was exposed to inhalation anthrax. And what the data actually showed, aside from the small number, that anthrax epidemic occurred in one plant and no place else. This would suggest that whatever level of air quality that they were exposed to, including those who did not get vaccinated, end up with inhalation anthrax.

And out of the 1,400, if I remember correctly, some 870 did not get complete vaccinations. So what I am saying is that for that period, a year and a half or so, 5 cases out of 870 people did not end up with inhalation anthrax.

So that is the rate you end up with even if you are unprotected.

Mr. MICA. But what this boils down to, I'm trying——

Mr. CHAN. I am sorry.

Mr. MICA. I am trying to get a simple determination, you know, based on the experiments that have been done, the testing of this vaccination. Of course, some of it, as you have said, is in a different setting against different exposures.

The basic question here is, we have several millions of potential folks that may be vaccinated in the future with this, is it that effective? Or are we going through this giving some sort of false security because it may not protect them?

Mr. CHAN. Well, potentially, you could. In our statement we state that we believe in fact that it does provide some protection, although the problem, as we discussed before, is about the correlation between animal and human in responding to the challenge.

Mr. MICA. But there hasn't been enough human testing to determine that under different circumstances. Is that correct?

Mr. CHAN. Yes.

Mr. MICA. And based on the reactions the folks have had, do you think people should have an opportunity to opt out? Should this be mandatory?

Mr. CHAN. I think you are asking a policy question. That's the DOD——

Mr. MICA. Well, no. OK, if you have your kid who is going to serve in the military or you, based on what you know, you have studied this, you are a scientist and have had scientists look at this, would you recommend that folks have the opportunity to opt out? Or are we using our service men and women as guinea pigs in a big experiment that we are not sure really works?

And also, a concern that I have is that you give them some false sense of security.

Mr. CHAN. I am hoping that we all, hopefully, in this hearing we end up agreeing with what the data tell us. And the decision of whether one is vaccinated should be based on a balance between the risk and possible benefits. You are asking a question, does this vaccine have a for the lack of a better word is, have a lot of limitation?

Mr. MICA. I am sorry.

Mr. CHAN. A lot of limitation, in the sense that it requires a number of shots over a long period of time. So when you ask the question of forced vaccination—mandatory vaccination, an issue—is if you need an 18-month lead time to fully vaccinate, it is hard for the commander to say I know precisely who is going to go where in the future with the understanding potentially anybody could be there in the future.

And then the second question is that this is really the only solutions they have, potentially. So when will you go?

The third thing I would say is that there are other possible alternatives because vaccination is not the only way to defend against BW agent. You can put masks on; you can basically take antibiotics. Those are other possibilities, and generally we know that, for example, over the next couple of years, both Department of Defense as well as Department of Energy are spending up to $200 million in terms of detecting both chemical and biological agents, which will help you to speed up the time in detection and respond to an attack.

I am not sure I can answer your question in the very precise way.

Mr. MICA. Are you ready to be vaccinated?

Mr. CHAN. If you tell me exactly where to go next year, sir, I would tell you that. As a private citizen, I don't see that threat to myself or my family, but if, in fact, I need to go to a place where I do know the country has this, then I would consider that.

But let me also say there is research done where they examine post-exposure treatments of people, using antibiotics, possibly with this vaccine that, is licensed, there are some promising results with animal studies. So those are other options I can have.

And certainly, as the chairman suggests, that we can also pursue the second-generation vaccine.

Mr. MICA. Thank you. Thank you, Mr. Chairman.

Mr. SHAYS. Thank you. Mr. Metcalf, do you have a question or two?

Mr. METCALF. Yes, I do. Thank you, Mr. Chairman.

Mr. Chan, as a result of your concurrent investigations of anthrax and squalene antibodies, have any suspicions been raised about a potential connection between the two? And if so, could you discuss this.

Mr. CHAN. I do not know the connection scientifically. I do know that there are soldiers out there who had called us, both Dr. Sharma and myself, with this concern. As you know, our study basically took the positions that we believe DOD should do some research to examine if indeed a valid assay can be developed to determine the presence of the squalene. I think that would really clear up a lot of issues.

Mr. METCALF. Thank you. That sort of coordinates with my request for the DOD to do an in-depth investigation on this. If the DOD acted on GAO's squalene report recommendation, do you believe that this would allay the suspicions about a connection between squalene as a presence in a vaccine and the Gulf war illnesses?

Mr. CHAN. Well, I think developing a valid assay is just the first step of that. If in fact we find that it cannot be validated, then clearly the associations cannot be pursued. But if in fact you can validate it, indeed you find an antibody, I think a whole set of new questions would be raised.

Mr. METCALF. Thank you.

Mr. SHAYS. Thank you. I just have a clarification of a question that Mr. Terry asked, and that is in regards to the process. My understanding is that the process is important when you are developing a vaccine, and I am going to read what you said.

You said, vaccines have three distinguishing features that contrast—this is on page 4 of your testimony—that contrast with those of chemical drugs. First, either they have no clear chemical-defined composition or simple chemical analysis is insufficient for effective characterization. Second, proper evaluation of them, qualitatively or quantitatively, is usually done by measuring their effects in the living organism. Finally, quality cannot be guaranteed from final tests on random samples but only from a combination of in-process tests and production tests and strict controls of the entire manufacturing process.

Isn't it a fact that when you are dealing with biologicals, the process is a very important element to determine both the safety and effectiveness of the vaccine that you are developing?

Mr. CHAN. I believe the integrity of the process is a necessary condition, but it is not sufficient to guarantee quality.

Mr. SHAYS. It is not, but you can take the inverse.

Mr. CHAN. Yes, sir.

Mr. SHAYS. And you can question the quality, and, therefore, you have to raise gigantic concerns about whether the vaccine should be used. Isn't that true?

Mr. CHAN. I think that raises the question. Yes.

Mr. SHAYS. Yes, it does. And just this other point with the Brachman study.

Mr. CHAN. Yes.

Mr. SHAYS. This was in 1955 and 1959, published in 1962. It was in a wool mill. Isn't the problem, we don't know how they were, at what levels they were exposed? We don't know if there was any exposure. We make an assumption that in a wool mill there is going to be some exposure, but don't know what level. It could have been the entire time, it could have been none or minimal exposure to anthrax. Isn't that correct?

Mr. CHAN. Yes, that is my one comment I made about inhalation anthrax. The uniqueness of the timing when it all occurred in one place, in one short period of time when epidemic occur, it does not suggest that the other plants have problems with air quality with anthrax spores around.

Mr. SHAYS. Well, that means something to you. I want to put it in my words, and then tell me if I am inaccurate here.

Mr. CHAN. Yes.

Mr. SHAYS. In my words, we have no control of the threat. First we don't know if the threat was the same to those who had the vaccine and to those who didn't have the vaccine. That is one point.

But the other point is we don't know what level the threat was. The entire time, there could have been minimal exposure. I mean, there could have been there could not have been. Isn't that correct?

Mr. CHAN. Yes, it is.

Mr. SHARMA. Let me just answer. We had a meeting on this issue with Dr. Brachman. And we raised this issue, that was there any environmental monitoring done. And his reply was no. In those days, the standards were very different. And then we raised this issue, how do you know that if no disease occurred it was because bales were not contaminated. And he did say to us, that this was one of the very fundamental problems in his study. He did not envision this problem in those days.

But as we discussed, he agreed, that there was no environmental monitoring. They were equating absence of disease with the efficacy of the disease. Indeed, the only time they checked for the contaminant of the bales was when the epidemic occurred. And they did find the bale was contaminated. But they did not look for every single bale that these mills were receiving whether or not——

Mr. SHAYS. And we don't know what level of contamination——

Mr. SHARMA. No. There was no monitoring at all.

Mr. SHAYS. So let's—I could make a summation: One, there was practically none or that there was some, and so this vaccine protects against low-level exposure but that if you had exposure, this study would be meaningless.

I mean, I can infer that?

Mr. CHAN. Well, yes. I think, what you might be looking for is sort of a dose response relationship: How many doses you—I believe, in fact, that, you know, with protective antigens, you cannot protect a person ultimately in the sense that you can always overwhelm your immune system by having enough spores and so on. So there is a limit here in terms of the level of protection.

That is why I think it is important to have the self-protection, mask and all the other things that helps. It is really sort of like giving you the first breath. Because if you just sit there and keep on breathing this stuff, you get overwhelmed and can be in trouble as a result.

Yes, you are right. And you are raising a question which we did not, could not address with Brachman's study because we don't know what the level of exposure was, and we really do not know if at higher levels whether the vaccinated individual would be protected or not. I think that is a question.

Mr. SHAYS. When you say we, you mean generically we, including Mr. Brachman?

Mr. SHARMA. That is correct.

Mr. CHAN. Including him. Yes.

Mr. SHAYS. And that is not a criticism of him when he did his study, but it is a criticism of applying this 1950's study to potentially vaccinating 2.4 million Americans who will be ordered and who are being ordered to take it.

Ms. Schakowsky.

Ms. SCHAKOWSKY. I just had one question. I was reflecting, Dr. Sharma, on your response to the chairman's question about how we got to six doses. And you said, essentially, that some individual arbitrarily, I think was your word, decided on six doses. I want to go

back to that just for a minute. So we have nothing to show that there is any correlation between this six—these six doses and the efficacy of it, the levels of protection. And nor do we know how this may impact on adverse reactions on the safety—do we know anything about four versus six or one versus six or anything?

Mr. SHARMA. You have asked two questions. And the first question is about the multiple dose schedule: We do know that there is a pending IND with FDA which is looking at a reduced-dose schedule. However, one of the problems is we don't know what the level of immunity means in terms of the protection.

There is some animal data that DOD has collected that looks promising, but what they need to do is to do the bridging studies which shows what is the relationship between the level of immunity and protection. And then if they could develop those correlates, then you can overcome this hurdle of, which is the second question, that is how do you extrapolate those results to humans. And that has not been done.

Now, with regard to your second questions on what is the relationship between number of dosages and adverse events, I don't remember exactly, but, yes, there is one place where I have seen on anthrax vaccine where they had looked at the adverse events by number of shots. And they do increase with the frequency of the dose.

Mr. CHAN. I think, if I may answer the question a little differently, I think if in fact one can have an IND whereby one can reduce the six shots to even three shots, it would be a tremendous tactical advantage logistically in terms of applying these vaccines, the current licensed vaccine. Because that would mean, instead of requiring 18 months for a full regimen of shots, it would be reduced to 4 weeks.

So the surgeon general of the Army, you know, have been trying to figure out how best to do that. I think they are initiating a study to examine that. And it is significant in that sense.

Ms. SCHAKOWSKY. I just want to say that what we don't know is just so overwhelming. And in your answer—in your testimony, it says several studies have shown no direct comparison of immunity and humans to that in monkeys, and the bridging, as you call it, studies that haven't been done and the studies of dosage and how they relate to protection and safety—it is just dramatic, I think.

Thank you.

Mr. SHAYS. I think we are ready to get to the next panel. Mr. Chan, I appreciate your statement, and I also appreciate your frank answers to our questions. Thank you, and Dr. Sharma.

Mr. CHAN. Thank you.

Mr. SHAYS. And obviously, I appreciate the panel No. 2 and No. 3 for their patience as well.

So at this time, I would call Dr. Katherine Zoon, Director, Center for Biologics Evaluation and Research, Food and Drug Administration, more commonly called FDA, accompanied by Mr. John Taylor, Senior Adviser for Regulatory Policy from FDA. And then we have General Eddie Cain, Joint Program for Biological Defense, Department of Defense, and Dr. Robert Myers, chief operating officer for BioPort Corp.

Welcome them to come and, if you could remain standing just so I could swear you in. As you know, we swear in all of our witness who testify.

Now, let me ask as well. Is there anyone else who might assist you, who you might prefer to answer the question? If they are here, I would prefer they stand up as well so we don't have to swear them in again.

So if they are here, if there is anyone who might—even if you end up not doing it, it is probably better to just get sworn in. That helps us out. And then we will identify you for our recorder if, in fact, you respond to a question.

And if you would, raise your right arms please.

[Witnesses sworn.]

Mr. SHAYS. Thank you. I recognize all the individuals who stood up as responding in the affirmative. I think it is very important for all of our—we have three people testifying, Dr. Zoon, also General Cain and Dr. Myers, for you to feel that you can give a full statement. And also I have no problem with you responding to anything you have heard. You have been very gracious in listening to the testimony. And you may disagree with it, and you may have some very helpful facts that would allay some of our fears as well.

So, we will start out with Dr. Zoon, then we will go to General Cain, and then we will go to you, Dr. Myers. And I am going to do a 5-minute clock. I am going to switch the clock again another 5 minutes. And we will see if that gives you enough time.

So, at this time, Dr. Zoon.

STATEMENTS OF KATHRYN ZOON, DIRECTOR, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION; GENERAL EDDIE CAIN, JOINT PROGRAM FOR BIOLOGICAL DEFENSE, DEPARTMENT OF DEFENSE; ROBERT MYERS, CHIEF OPERATING OFFICER, BIOPORT CORP.; AND JOHN TAYLOR, SENIOR ADVISER FOR REGULATORY POLICY, FOOD AND DRUG ADMINISTRATION

Dr. ZOON. Thank you, Mr. Chairman.

Mr. Chairman, members of the committee, and Mr. Metcalf, if he comes back, I am Dr. Kathryn Zoon, Director of the Center for Biologics Evaluation and Research at the Food and Drug Administration. I appreciate the opportunity to discuss the safety and efficacy of the anthrax vaccine currently manufactured by BioPort Corp.

Mr. Chairman, we are aware that some people question the safety and efficacy of the anthrax vaccine. Let me be clear, we believe that for persons at high risk, the licensed anthrax vaccine is safe and effective for the prevention of the often-fatal anthrax disease.

Our confidence in this vaccine is based upon four components. First, the clinical trials and subsequent clinical laboratory experience with the vaccine. In this case, the Brachman trial and the CDC trial, which I will discuss.

Second, ongoing inspections of the manufacturing facility based on our CGMP requirements. Third, our lot release requirements, which are another layer of protection, and fourth, our surveillance of adverse event reports that serve as an early warning system.

We continue all our efforts in all four categories of these areas to help assure that only safe and effective products are on the market.

Anthrax is a highly infectious disease caused by spores of a bacterium known as bacillus anthracis. Untreated cutaneous anthrax infection has a mortality rate of approximately 20 percent. Inhalation anthrax has a mortality rate of 80 to 90 percent or higher.

Mr. Chairman, the only known effective prevention against anthrax disease is the anthrax vaccine. The Centers for Disease Control and Prevention data on reported cases in the United States indicate a decline from 130 cases per year at the beginning of the century, to zero cases per year in recent years. Use of the anthrax vaccine to immunize people at risk of exposure along with vaccination of animals against anthrax has likely contributed to a favorable decline in anthrax infections.

I will describe the historical efficacy data for you. During the 1950's, Philip Brachman and his colleagues conducted a single-blinded clinical trial involving workers in four mills in northeastern United States. Mill workers were at risk because they routinely handled anthrax-infected animal materials. By comparing the completely vaccinated population versus the placebo population, the authors of the study calculated a vaccine efficacy level of 92.5 percent.

On April 14, 1966, CDC submitted an investigational new drug application for the anthrax vaccine to the Division of Biological Standards, which at that time was part of the National Institutes of Health. Under this IND, the Michigan Department of Public Health manufactured most of the lots of investigational vaccine prepared in a similar, but not identical, manner to the vaccine used in the Brachman study.

Data submitted to the Division of Biological Standards under this IND describe CDC's experience with approximately 7,000 study participants, including textile workers and laboratory workers. On November 10, 1970, the Division of Biological Standards granted a license to the Michigan Department of Public Health for the production of anthrax vaccine.

The data submitted by CDC met the provisions of the Public Health Service Act, which require evidence of safety, purity and potency. After the Division of Biological Standards was transferred from NIH to FDA, a panel review was initiated to verify whether existing data supported the safety and efficacy of biological products. The panel on review of bacterial vaccines and toxoids evaluated all safety and efficacy from the CDC and Brachman trials.

The panel recommended that anthrax vaccine manufactured by the Michigan Department of Public Health be classified as a category one product, meaning it was considered safe, effective and not misbranded.

As the panel concluded, it would be virtually impossible to conduct an efficacy study today as the incidence of naturally occurring anthrax in humans is low and sporadic in occurrence. The safety data base developed by CDC under the IND, however, would be considered a reasonable pre-licensure data base to evaluate such a product today.

The population that has been immunized to date represents individuals who are considered to be at risk for exposure. Approximately 7,000 patients were vaccinated during the CDC clinical trials. While it is not possible to accurately report the precise number of people vaccinated between 1974 and 1989, approximately 68,000 doses were distributed. This is sufficient to vaccinate about 11,000 people.

Deviations from current good manufacturing practices have recently been documented during inspections of the anthrax vaccine manufacturing facility. CGMP's are only one of the several safeguards to assure product quality. Our surveillance includes information from testing and review of manufacturing records, which showed lots of product available for distribution are safe and effective for immunizing individuals at risk.

The anthrax vaccine is subject to lot release. The lot-release program helps assure product safety by providing a quality-control check on product specifications. Each product lot of anthrax vaccine undergoes thorough testing, including purity, potency, identity, and sterility. Manufacturers may release lots only after this testing is documented and reviewed by the FDA.

FDA uses the vaccine adverse-event reporting system, VAERS, to track adverse-event reports possibly associated with licensed vaccines. Any person, including a patient, can file an adverse-event report. Reporting adverse experiences associated with anthrax vaccine is voluntary for healthcare providers and mandatory for the manufacturer. A report does not indicate that the vaccine caused the adverse event, but only that the event occurred soon after the vaccine administration.

From the time VAERS started operating in 1990, until April 1st, 1999, 101 reports of adverse experiences have been received regarding the anthrax vaccine. Of these, 87 were non-serious and 14 were considered serious events. As the number of people immunized with vaccine increased, the number of adverse-event reports may also increase.

Data from the VAERS system can serve as a useful tool in identifying potential problems with the vaccine. Thus far, the reports received on the anthrax vaccine do not signal concerns about the safety of the vaccine.

Mr. Chairman, let me state clearly that we are confident that for persons at high risk, the licensed vaccine is safe and effective for the prevention of anthrax—disease.

I can assure you that FDA will remain vigilant in its oversight.

I appreciate the subcommittee's interest in this very important topic, and I will be happy to answer any questions.

Thank you.

[The prepared statement of Dr. Zoon follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

STATEMENT

BY

KATHRYN C. ZOON, Ph.D.

DIRECTOR

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE SUBCOMMITTEE ON NATIONAL SECURITY,
VETERANS AFFAIRS, AND INTERNATIONAL RELATIONS

COMMITTEE ON GOVERNMENT REFORM

U.S. HOUSE OF REPRESENTATIVES

APRIL 29, 1999

FOR RELEASE ONLY UPON DELIVERY

Introduction

Mr. Chairman and Members of the Committee, I am Dr. Kathryn Zoon, Director, Center for Biologics Evaluation and Research, Food and Drug Administration (FDA or Agency). I appreciate the opportunity to discuss the safety and efficacy of the anthrax vaccine, currently manufactured by BioPort, Corporation. As the Committee requested, I will explain FDA's Memorandum of Understanding (MOU) with the Department of Defense (DOD). I will describe events at the time of approval of the vaccine and our experience since then. Lastly, I will describe the compliance history of BioPort Corporation. Let me start by briefly explaining the MOU with DOD.

Memorandum of Understanding with Department of Defense

On May 21, 1987, FDA entered into the current MOU with DOD. This replaced the previous MOU signed in 1974. The 1987 agreement established procedures to be followed by DOD and FDA regarding the investigational use of drugs, biologics and medical devices. The MOU affirms that clinical testing of new drugs will be done in accordance with applicable regulations concerning Investigational New Drug Applications (INDs) and Institutional Review Boards (IRBs).

The MOU addresses the possibility of a need for expedited review of an IND by FDA to meet DOD requirements concerning National defense considerations. Under the MOU, DOD is responsible for classifying medical research and development as it relates to information that may be made public under Freedom of Information Regulations. It should be stressed that this agreement, however, does not allow DOD to perform research on humans without submitting an IND and it requires DOD to comply with all FDA regulations.

Background

Anthrax is a highly infectious disease caused by spores of a bacterium known as *Bacillus anthracis*. These spores resist destruction and may be present in the soil for decades, occasionally infecting grazing animals that ingest the spores. Goats, sheep and cattle are examples of animals that may become infected. Human infection may occur by three routes of exposure to anthrax spores: cutaneous, gastrointestinal, and pulmonary. Skin contact with live infected animals, or with the hide, hair or bones of an infected animal may lead to infection of a person's skin, known as cutaneous anthrax infection. This is the most common manifestation of anthrax in humans, accounting

for more than 95 percent of cases. Eating undercooked or raw infected meat can cause gastrointestinal anthrax infection. Breathing in airborne spores may lead to pulmonary anthrax, also known as inhalation anthrax.

Experience has shown that inhalation anthrax has a very high mortality rate, with estimates ranging from 80 percent to 90 percent or higher. Untreated cutaneous anthrax infection is associated with a death rate estimated to be approximately 20 percent.

Inhalation anthrax infection has two phases. During the first phase, which occurs within one to five days after inhalation of the spores, the patient has influenza-like symptoms, such as a cough, malaise, fatigue and mild fever. Several days later these symptoms may subside, but are rapidly followed by the second, more severe stage of disease. During the second phase, the patient experiences sudden onset of severe respiratory distress, and sometimes chest pain accompanied by fever. Chest x-rays may show fluid in the lung. Within a day, septic shock and death will likely occur.

The only known effective prevention against anthrax is the anthrax vaccine. Treatment of cutaneous anthrax infection involves administration of antibiotics. In the case of pulmonary anthrax infection, therapy has been of limited benefit, except when given immediately after exposure.

Prior to use of the anthrax vaccine, cases of human anthrax infection in the United States were much more prevalent. According to data from the Centers for Disease Control and Prevention, (CDC) there were approximately 130 reported cases of anthrax infection per year at the start of this century. In the past decade, there have been years with no reported cases of human anthrax infection in the United States. It is difficult to assess exactly how much of this dramatic reduction is due to the vaccine, but immunization with the anthrax vaccine of people at risk, along with vaccination of animals against anthrax, have likely contributed to this favorable decline. Elsewhere in the world, human anthrax cases continue to be reported, especially in countries with predominately agricultural economies.

History of the Anthrax Vaccine

Clinical trials on the anthrax vaccine were conducted by Philip S. Brachman et al. during the 1950's[1]. This controlled field study involved workers in four mills in the northeastern United States that processed imported animal hides. This selected population was at risk because the mill workers routinely handled anthrax-infected animal materials. Prior to vaccination, the yearly average number of human anthrax infection was 1.2 cases per 100 employees in these mills.

For this trial, employees who had not previously contracted anthrax were selected and divided into two groups. The groups were balanced with regard to their age, length of employment, department at the mill, and the particular job they performed. The trial was a single-blinded study, where the participants were not told whether they received the vaccine or placebo. Individuals who did not participate in the controlled study [because they were ineligible (i.e. had a history of prior anthrax) or chose not to receive the injections] were also monitored for

[1] Philip S. Brachman, M.D., Herman Gold, M.D., Stanley A. Plotkin, M.D., F. Robert Fekety, M.D., Milton Werrin, D.V.M., F.A.P.H.A., and Norman Ingraham, M.D., F.A.P.H.A.

anthrax. These individuals were referred to as the observational group.

During the trial, 26 cases of anthrax infection were reported at the mills - five inhalation and 21 cutaneous. Of the five inhalation cases, two individuals had received the placebo, while three individuals were in the observational group. Four of the five people who developed inhalation anthrax died. No cases of inhalation anthrax occurred in vaccine recipients. Of the 21 cutaneous cases, 15 individuals had received the placebo, three individuals were in the observational group, two individuals were partially immunized and one individual was fully immunized. Based upon a comparison between the populations completely vaccinated versus the populations receiving placebo, the authors calculated a vaccine efficacy level of 92.5 percent.

On April 14, 1966, CDC submitted an IND for the anthrax vaccine to the Division of Biologics Standards, which was then part of the National Institutes of Health (NIH) and later transferred to FDA. The method of preparing this vaccine was similar, but not identical, to the vaccine used in the Brachman et al. study. The vaccines in both studies

were based on the immunity induced by the protective antigen (PA). Persons receiving the vaccine made by the two different methods demonstrated similar peak immune responses (antibody concentration) following the initial three doses.

Textile employees and laboratory workers were immunized under this IND. A number of lots of investigational vaccine used by CDC under this IND were manufactured by the Michigan Department of Public Health (MDPH).

The data submitted to the Division of Biologic Standards described the CDC's experience with approximately 16,000 doses of anthrax vaccine from four lots manufactured at MDPH. These MDPH lots were administered to approximately 7,000 study participants.

For the four MDPH lots used for vaccinations, reported local reactions at the immunization site ranged between 3 percent to 36 percent of the initial series of doses, and 3 percent to 33 percent of the booster doses, depending on the lot. Reported mild reactions were 3 percent to 20 percent of all doses. Reported moderate local reactions were 1 percent to 3 percent of doses. Severe reactions

were reported for less than 1 percent of doses. Systemic reactions were reported in four cases during the five-year reporting period. These reactions included fever, chills, nausea and general body aches, and were reported to have been transient.

The Division of Biologics Standards determined that the data submitted by CDC supported licensure of the vaccine. On November 10, 1970, the Division of Biologics Standards issued a product license to MDPH to manufacture anthrax vaccine.

Approved labeling for the anthrax vaccine states that immunization with this product is recommended for individuals who may come in contact with animal products that may be contaminated with *Bacillus anthracis* spores; and for individuals engaged in diagnostic or investigational activities which may bring them in contact with *Bacillus anthracis* spores. It is also recommended for persons at high risk, such as veterinarians and others handling potentially infected animals.

The approved labeling also states that anthrax vaccine is to be administered subcutaneously (injected under the

skin). After the initial dose of 0.5ml, further doses of 0.5ml are administered at two weeks, four weeks, six months, 12 months and 18 months, with yearly boosters thereafter.

The Panel Review

The Public Health Service Act, under which biologicals such as vaccines were licensed, required evidence of safety, purity and potency. After the Division of Biologic Standards was transferred from NIH to FDA, expert panels were assigned to review information on biological products, including vaccines that had been on the market prior to the transfer. The review was initiated in order to verify whether existing data supported the safety and efficacy of marketed biological products.

Biological products were divided into one of six categories. FDA assigned responsibility for initial review and recommendation for all products in these six categories to separate independent advisory panels of outside scientific experts, collectively known as the Advisory Review Panel. The Advisory Review Panel also was charged with advising FDA, in the form of a report, on

classification of these products into one of the following categories: Category I - safe, effective and not misbranded; Category II - unsafe, ineffective or misbranded; Category III - insufficient information, further testing required.

Based upon their review of available data, the Advisory Review Panel recommended that the anthrax vaccine manufactured by MDPH be classified as a Category I product and that appropriate licenses be continued based upon substantial evidence of safety and effectiveness of this product. The safety data from the CDC trials and the efficacy data from the Brachman et al. trials were the basis for these findings. These findings were published in the *Federal Register* on December 13, 1985.

Today, it would be difficult to repeat the efficacy studies. This is because there are no evident populations in the United States where prophylactic vaccine protection against natural exposure to anthrax could be evaluated in a clinical field trial, such as was done in the Brachman et al. study. Specifically, the incidence of naturally occurring anthrax in humans is low and sporadic in occurrence, making identification of a trial target

population difficult. Likewise, it would be unethical to perform challenge/protection studies in humans. In addition, human immunogenicity and safety data would be required. The safety database obtained by CDC under the IND would be considered a reasonable pre-licensure database to evaluate a safety study today.

Post-Marketing Experience

Since licensure in November 1970, the anthrax vaccine has been used by livestock workers, veterinarians, lab workers and researchers who are at risk for infection. The manufacturer provided FDA the following information regarding distribution. From 1974 to 1989, approximately 68,000 doses were distributed. In 1990, approximately 268,000 doses were distributed. Between 1991 and the present, we understand that approximately 1,200,000 doses were distributed.

It is not possible to give a precise number of persons who received the vaccine prior to use in Operation Desert Storm and Operation Desert Shield. We estimate that approximately 7,000 patients received approximately 16,000 doses of the vaccine during clinical trials conducted by

the CDC. In addition, between 1974 and 1989, our files show approximately 68,000 doses were distributed. This is sufficient to vaccinate about 11,000 people with the full six-dose regimen of the currently approved anthrax vaccine. It is possible that some doses distributed were not used, or that some individuals did not receive the full course of the vaccine. Thus, it is not possible to accurately report the precise number of people vaccinated between 1974 and 1989.

According to the CDC, from 1962 to 1974, 27 cases of anthrax occurred in the "at-risk" populations in the United States. Of those, 24 cases occurred in unvaccinated individuals, one case after the person had been partially immunized with one dose of the vaccine and two cases after individuals had been partially immunized with two doses of the vaccine. No documented cases of anthrax were reported for individuals who have received the recommended six doses of the vaccine.

Vaccine Adverse Event Reporting - Anthrax

With regard to safety data, FDA and CDC jointly operate a system called the Vaccine Adverse Event Reporting System

(VAERS). FDA uses this system to track adverse events possibly associated with licensed vaccines. Reporting of adverse events associated with the use of anthrax vaccine is voluntary for individual healthcare providers. The vaccine manufacturer, however, must report to FDA all reports of adverse events of which they are aware.

The report of an adverse event to VAERS is not documentation that a vaccine caused the event, only that the event occurred soon after the vaccine was administered. Doctors and other healthcare providers are encouraged to report serious or unexpected adverse events following vaccination, whether or not they believe that the vaccination was the cause of the adverse event. Since it is difficult to distinguish a coincidental event from one truly caused by a vaccine, the VAERS database contains events of both types.

It should be emphasized that adverse event reports can be made by a health care professional, a patient or anybody else. If a patient's physician does not file a VAERS report, the patient can do so. FDA encourages individuals to report to VAERS any clinically significant adverse event occurring after the administration of any vaccine licensed

in the United States. Reports to VAERS may be made in writing or by calling a toll-free number, 1-800-822-7967. Reporting instructions are available on the Internet at www.fda.gov/cber/vaers.html.

From the time the VAERS system started operating in 1990 until April 1, 1999, there have been 101 reports of adverse events associated with use of the anthrax vaccine reported to the VAERS system. Of those, 87 were non-serious events and 14 were considered serious events. Non-serious events include the following symptoms: injection site edema (swelling with fluid in tissue), injection site hypersensitivity, rash, headache and fever.

Of the 11 serious reactions reported during the current anthrax vaccination program, most individuals have recovered. Three patients were hospitalized for injection site reactions. One individual experienced a more widespread allergic reaction. One individual was hospitalized with a confirmed case of aseptic meningitis nine days after vaccination. Another individual experienced Gullain-Barré syndrome within 24 hours of the third dose. He was unable to walk for nine days. He gradually recovered and had symptom resolution within five

months of the vaccination. Three weeks after receiving the vaccine, another individual experienced bipolar disorder and has not recovered.

It should be emphasized, once again, that it is not always possible to attribute a cause and effect relationship between a reported event and a vaccination. With the exception of injection site reactions, all of the adverse events noted above do occur in the absence of immunization.

While the data gathered from the VAERS system can serve as a useful tool in spotting potential problems, the data gathered from the VAERS reports on anthrax vaccine, thus far, do not signal concerns about the safety of the vaccine. As more people receive the vaccine, the numbers of adverse events reported will increase.

Lot Release

Because of the complex manufacturing processes for most biological products, each product lot undergoes thorough testing for purity, potency, identity, and sterility. Manufacturers may release lots only after this testing is documented. FDA may require lot samples and protocols

showing results of applicable tests to be submitted for review and possible testing by FDA. In this case, the manufacturer may not distribute a lot of the product until FDA's Center for Biologics Evaluation and Research releases it. The lot release program is part of our multi-part strategy that helps assure product safety by providing a quality control check on product specifications. The anthrax vaccine is subject to lot release.

Michigan Biologics Product Institute / BioPort Corporation

The BioPort Corporation facility in Lansing, Michigan is the only manufacturer licensed by FDA to manufacture anthrax vaccine. Originally, the facility was operated by the Michigan Department of Public Health. In 1996, the facility became known as the Michigan Biologics Products Institute (MBPI), an entity controlled by the State Government of Michigan. Currently, the facility is known as BioPort Corporation based upon the September 1998 transfer of ownership from MPBI to BioPort Corporation.

FDA has inspected this facility on many occasions during the past decade, identifying a number of deficiencies requiring correction. In particular, FDA conducted an

inspection of MBPI in November 1996. During that inspection, FDA investigators documented numerous significant deviations from the Federal Food, Drug, and Cosmetic Act, FDA's regulations and the standards in MBPI's license. Based upon the documented deviations, FDA issued a Notice of Intent to Revoke Letter (NOIR) to MBPI in March 1997. The NOIR letter did not mandate the closure of the facility or lead to seizure of finished product. The letter, however, did state that if MBPI's corrective actions proved to be inadequate, they would run the risk of having their license revoked.

MBPI responded to the NOIR with a "Strategic Plan for Compliance" presented to FDA in April 1997. This plan called for the periodic submission of data to FDA that would serve as evidence of MBPI's progress towards achieving compliance with FDA's regulations. Under the plan, FDA would review this data and then monitor MBPI's progress through follow-up inspections. In February 1998, FDA conducted a follow-up inspection of the MBPI facility to evaluate MBPI's compliance with its strategic plan.

The February 1998 inspection disclosed significant deviations from FDA's regulations. These deviations

included, but were not limited to, the manufacture of the anthrax vaccine. In addition, the inspection resulted in a request by FDA that MBPI quarantine 11 lots of anthrax vaccine held in storage, pending review of additional information to be submitted by BioPort regarding the lack of investigations into possible problems with potency, sterility and particulate matter. These lots are still in quarantine, and will remain in quarantine until the company submits required information to the Agency. FDA noted that MBPI had made progress in achieving its compliance goals, but additional work remains in order to correct the deviations related to the manufacture of the anthrax vaccine.

Pursuant to its purchase of the MBPI facility in September 1998, BioPort agreed to abide by the strategic plan and other commitments for corrective actions made by the management of MBPI.

It should be noted that MBPI halted production of anthrax vaccine sublots in January 1998 to begin a comprehensive renovation of the anthrax production facilities. No anthrax vaccine has been produced since BioPort became owner of the facility.

In its most recent inspection of BioPort Corporation in October 1998, FDA found continuing improvement. FDA believes that the products not quarantined by BioPort are safe and effective for the labeled indications. FDA found that the firm had made progress toward meeting objectives under its strategic plan in bringing the facility into full compliance. Based on BioPort's progress to date, FDA is hopeful that the company will continue to demonstrate improvement. Further FDA inspections should verify BioPort's compliance with regulations for the manufacture of all products, including anthrax vaccine. We will continue to work closely with BioPort to ensure that the goals outlined in their strategic plan are met.

Conclusion

Mr. Chairman, we believe anthrax vaccine is a safe and effective vaccine for the prevention of anthrax disease - an often-fatal disease. Our confidence in this vaccine, like all vaccines, is based upon four components: first - the 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 of adverse event reports. We will continue our efforts in all four of these areas, with the anthrax vaccine and all vaccines, to assure that only safe products are on the market.

I appreciate the Subcommittee's interest in this very important topic and would be happy to answer any questions.

Mr. SHAYS. Thank you very much.

General Cain. Thank you.

General CAIN. Chairman Shays and other distinguished committee members, I am honored to appear before your committee today to address the production and supplemental testing of the Department of Defense, the DOD's, vaccine program. I am Brigadier General Eddie Cain, Joint Program Manager of the Joint Program Office for Biological Defense, and I have served in this position since June 1998.

I have provided the committee with a more detailed written version of my testimony that I would like to submit for the record. Today, I will address the specific questions raised in your letter to Secretary Cohen that are in my area of responsibility.

The Joint Program Office of Biological Defense plays a major role in force protection with DOD by providing detection equipment and medical products to all service members. One aspect of my mission is to provide centralized program management for the advance development and production of all DOD biological defense vaccines, including anthrax vaccine.

This responsibility includes licensing, testing, and stockpiling these biological defense vaccines. As was stated during the March 24th hearing, anthrax is a major biological warfare threat faced by our armed forces. More than 10 countries, including Iraq, have or are suspected of developing a 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 weaponize. If anthrax is used as a biological weapon, disease will most likely occur by inhalation of anthrax spores. Death is the usual outcome once clinical symptoms appear regardless of any post-exposure treatment.

Death from anthrax, however, is preventable by immunization with the licensed vaccine, thereby enhancing force protection. On a personal note, I have received four of the six shots, and I can tell you that I have no reservation about taking the vaccine, and I have had no adverse reaction.

Protection of the total force against anthrax was initiated by Secretary Cohen in December 1997. One of the conditions required before implementation of the immunization plan was that supplemental testing had to be accomplished to assess sterility, safety, potency, and purity of the vaccine lots in the stockpiles. The FDA has previously released all lots in the stockpile. DOD, however, for added assurance, directed the Joint Program Office to contract the Michigan Biological Products Institute, now BioPort, to conduct supplemental testing on all lots of anthrax vaccine in the DOD stockpile.

Whereas, BioPort conducts the actual testing, Miretek Systems Inc., a DOD contractor, provides independent oversight of this testing. Miretek staff observes all aspects of the supplemental testing and provides a written report to the Joint Program Office on the acceptability of the testing and test results.

The Joint Program Office then reviews all data prior to releasing any lot for shipment and use. Only those lots in the original stockpile that have passed supplemental testing have been approved for use for immunization.

Supplemental testing began in January 1998. As of April 1999, eight lots have passed all supplemental testing requirements. Detail status of the remaining lots is outlined in my written testimony.

I will now discuss the anthrax vaccine production facility, which is the only FDA licensed manufacturer in the world. Before implementation of the immunization plan and the November 1996 inspection, a DOD task force evaluated the anthrax vaccine capabilities at the facility. It was determined that the facility would require substantial renovation to meet production and FDA regulatory requirements.

Let me reiterate that the decision to renovate the facility was made before the 1996 FDA inspection. Production was stopped in January 1998 to begin the renovations. The physical aspects of the renovation were completed in January 1999. Completion of the renovation also requires validation of the manufacturing equipment and the production process. The process validation includes producing several lots of anthrax vaccine for review by the FDA.

We expect new vaccine to be available by January 2000.

With respect to current vaccine availability, there is sufficient anthrax vaccine to support the Secretary of Defense anthrax immunization program through December 1999. Beyond 1999, both the remaining doses in the stockpile and new vaccine produced in the renovated facility will ensure that DOD has sufficient doses to meet force-protection requirements.

In conclusion, anthrax vaccine is a key element in protecting service members against a lethal threat of anthrax. The DOD will continue to work with BioPort and the FDA to ensure there is a sufficient supply of safe and effective anthrax vaccine.

Mr. Chairman, this concludes my statement. Although I did not address your question regarding adverse reaction reports, I have included a statement in my written testimony from the Office of the Surgeon General regarding this topic.

I am ready to address any questions that may fall in my responsibility at this time.

[The prepared statement of General Cain follows:]

RECORD VERSION

STATEMENT BY

BRIGADIER GENERAL EDDIE CAIN

JOINT PROGRAM MANAGER

JOINT PROGRAM OFFICE FOR BIOLOGICAL DEFENSE

FALLS CHURCH, VIRGINIA

BEFORE THE

NATIONAL SECURITY, VETERANS AFFAIRS AND
INTERNATIONAL RELATIONS SUBCOMMITTEE

COMMITTEE ON GOVERNMENT REFORM

FIRST SESSION, 106th CONGRESS

ANTHRAX VACCINE IMMUNIZATION PROGRAM (AVIP)

APRIL 29, 1999

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BIOGRAPHY

BG EDDIE CAIN

JOINT PROGRAM MANAGER
JOINT PROGRAM OFFICE FOR BIOLOGICAL DEFENSE

Brigadier General Cain was born in Steens, Mississippi, on April 1, 1948. Upon completing ROTC and educational courses of study at Jackson State University in 1971, he was commissioned a Second Lieutenant in the U.S. Army Chemical Corps and awarded a Bachelor of Science degree in Chemistry.

His assignments include: Commander, HHC, Rocky Mountain Arsenal; Commander, 588th (Heavy) Maintenance Company, Giessen, Germany; Chemical Officer, 2nd Brigade, 8th Infantry Division and 2nd Brigade, 1st Cavalry Division; Aide-de-Camp, DCG, 5th Army; Readiness Group Advisor, Fort Sill, OK; Executive Officer, 2nd Chemical Battalion (Smoke); Operations Officer, 13th Corps Support Command; Division Chemical Officer, 1st Cavalry Division (Hvy Mech); Politico-Military Affairs Officer, Office of the Secretary of Defense; Commander, 23rd Chemical Battalion, EUSA, Korea; Deputy Commander, USA Material Destruction Agency; Commander, USA Chemical Activity, Pacific (Johnston Island) and III Corps Chemical Officer.

Brigadier General Cain's military education includes the U.S. Army Chemical Corps Officer Basic and Advanced Courses. He is also a graduate of the U.S. Army Command and General Staff College and a 1993 graduate of the U.S. Army War College.

Brigadier General Cain was promoted to BG on 2 October 1998.

Brigadier General Cain's military awards and decorations include the Legion of Merit (1st Oak Leaf Cluster), Defense Meritorious Service Medal, Meritorious Service Medal with 4 Oak Leaf Clusters, Army Commendation Medal, Army Achievement Medal, Air Assault Badge, the Office of the Secretary of Defense Badge and while he was Commander of the U. S. Army Chemical Activity Pacific, the unit was awarded the Army Superior Unit Award.

He is married to the former Fredia Jean Webb of Woodville, Mississippi. They have two children: a son, Eddie D'Andra, and a daughter, Trina Laketha.

BG EDDIE CAIN

Introduction

Chairman Shays, Representative Blagojevich and Distinguished Committee Members, I am honored to appear before your Committee today to address the production and supplemental testing of the Department of Defense's (DoD) Anthrax Vaccine.

I am Brigadier General Eddie Cain, Joint Program Manager of the Joint Program Office for Biological Defense (JPOBD). I have served in my present position since June 1998.

The JPOBD provides centralized program management for the advanced development and production of all DoD biological defense (BD) vaccines. Major areas of responsibility include the development, licensing, stockpiling and testing of BD vaccines.

Background

Anthrax is a major biological warfare threat faced by United States forces. More than ten countries, including Iraq, have or are suspected of developing a 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 due to the stability of its spore stage. If anthrax is used as a biological weapon, disease will most likely occur by inhalation of anthrax spores. Death is the usual outcome once clinical symptoms appear regardless of any post-exposure treatment. Death from anthrax, however, is preventable by immunization with the licensed vaccine.

The responsibilities for funding, management and oversight of the DoD Anthrax Vaccine contracts were assumed by the JPOBD in 1995 from the U.S. Army Medical Research and Development Command (USAMRDC), currently the U.S. Army Medical Research and Materiel Command, headquartered at Fort Detrick, Maryland.

Memoranda of Understanding (MOUs)

The Committee requested that DoD address the purpose and operation of any past or current MOUs between DoD and the Food & Drug Administration (FDA). I am not aware of any MOUs between DoD and FDA that specifically deal with the licensed Anthrax Vaccine. Since 1987 there have been two general MOUs between DoD and FDA. The first MOU, "Investigational Use of Drugs, Antibiotics, Biologics, and Medical Devices by the Department of Defense", was signed in May 1987. This MOU formalized agreements that DoD would comply with Federal regulations for DoD sponsored clinical research as pertains to 21 CFR 312 or 21 CFR 812. FDA agreed to special expedited review for DoD requirements to meet national defense conditions including stockpiling considerations for future use. FDA also agreed to maintain a cadre of personnel who have appropriate security clearances if research projects involve potential security issues. The second MOU, "Quality Assurance Support for Medical Materiel Having Military Application", was signed in June 1991. The latter MOU formalized the relationship and defined the responsibilities of USAMRDC and FDA to each other during the research, development and pre-marketing acquisition of medical materiel for military application. This MOU expired June 1997.

Supplemental Testing

As you know, the Secretary of Defense (SECDEF) announced in his December 15, 1997 press release that the Anthrax Vaccine Immunization Program (AVIP) would start only after several conditions were met. One of those conditions was "supplemental testing to assure sterility, safety, potency and purity of the vaccine". FDA had previously released these anthrax vaccine lots for use. DoD, however, for added assurance directed JPOBD to contract with BioPort, formerly Michigan Biologic Products Institute (MBPI), to conduct supplemental testing, with external oversight, on all lots of anthrax vaccine in the DoD stockpile.

The supplemental testing is based on tests required by FDA for lot release, and provides an added level of confidence in the potency and purity of the anthrax vaccine in our

stockpile. BioPort has performed, and continues to perform supplemental testing on all licensed lots of anthrax vaccine that were in DoD's original stockpile. Mitretek Systems Inc. performs independent oversight and provides a quality assurance function for DoD within the BioPort production facility. Mitretek's staff observes all aspects of the supplemental testing and provides a written report to JPOBD on the acceptability of the testing and test results. JPOBD reviews all data prior to releasing any lot for shipment and use.

Supplemental testing began in January 1998, and originally was scheduled for completion in November 1998. As of April 1999, eight licensed lots have passed all supplemental testing requirements. JPOBD has approved these eight lots for use.

During the conduct of supplemental testing BioPort and Mitretek Systems Inc. identified an inconsistency in the control values in potency assays conducted in June and September 1998. Based on this inconsistency, JPOBD suspended supplemental testing and sent a "Tiger Team" of subject matter experts to help resolve the problem. Corrective action is being implemented. We expect to resume testing within six months and do not anticipate any impact on the immunization plan.

Manufacturing Facility

In support of DoD Directive 6205.3, "DoD Immunization Program for Biological Warfare Defense", dated November 26, 1993 and in anticipation of the SECDEF announcement to immunize the total force, JPOBD evaluated the anthrax production capabilities and determined that it would require renovation to ensure it would meet FDA regulatory requirements. JPOBD initiated discussions with the manufacturer in the summer of 1996 to shut down the production line for renovation. The final feasibility study was completed in May 1997. Cost estimates and design work were started, and construction in a number of ancillary areas was initiated in 1997. Production line operations were suspended in January 1998 so that production line renovation could begin.

The physical aspects of the renovation were completed in January 1999 on schedule. Completion of the renovation also requires validation of the manufacturing equipment and the production process. The process validation includes producing consistency lots of anthrax vaccine for review by FDA. We expect this to be completed by January 2000.

Stockpile

There is sufficient anthrax vaccine to support the immunization plan through December 1999. As of 15 April 1999, doses available for immediate use include one undistributed lot that has completed supplemental testing along with four additional lots recently released by FDA. These latter four lots are not part of the original DoD stockpile and did not undergo supplemental testing because lot release data were recently completed and submitted to FDA for review and approval.

No lots are under mandatory quarantine. Twenty-one lots of the original stockpile are voluntarily quarantined by BioPort pending resolution of supplemental testing or FDA regulatory issues. JPOBD is working closely with BioPort to resolve these issues prior to making any lots available for DoD use.

Adverse Reactions

The Anthrax Vaccine Immunization Program (AVIP) Office, Office of the Army Surgeon General, provided the following information:

"The safety of the vaccine is the most closely scrutinized aspect of the entire Anthrax Vaccine Immunization Program, or AVIP. We monitor very closely for trends and events that may indicate problems and we have an immunization tracking system that can readily allow us to analyze these problems by unit, by lot, or by location.

"Since DOD began the AVIP during the National Command Authorities directed contingency OPERATION Desert Thunder in March of 1998, DOD submitted 49 individual

VAERS-1 Forms, representing the vaccine adverse events from over 810,000 individual vaccination events in more than 260,000 Service Members, representing a 0.006% incidence rate. Only 8 of these 49 Vaccine Adverse Event Reporting System Forms indicated a requirement for either hospitalization or loss of duty for more than 24 hours. Of these 49 reports, 26 are characterized as local hypersensitivity reactions. This includes local erythema or redness at the site of vaccination, a subcutaneous nodule or knot under the skin, tenderness, and perhaps swelling. Of these 26 local reactions, 9 were classified as mild-local redness at the injection site (1-2 centimeters in diameter); 10 were classified as moderate-local redness (greater than 1-2 centimeters but less than 5 centimeters in diameter) and perhaps a subcutaneous nodule; 7 were classified as severe local reactions-redness exceeding 5 centimeters in diameter or perhaps swelling at the site which, in some cases, actually extends to the lower forearm. It is important to note and compare that other US National vaccines with similar components and constituency, such as tetanus toxoids and typhoid for example, have nearly identical adverse events associated with their use. The remaining 23 of 49 adverse events are classified as systemic reactions. Systemic reactions range from hives, muscle and joint pain, nausea, fever, and chills. Again, these rare adverse events are commonly cited in the medical literature with many other vaccines. In fact, you should note systemic reactions occur with greater incidence with the Mumps, Measles and Rubella Vaccine, Hepatitis B Vaccine, and Diphtheria, Tetanus and Pertussis Vaccines, effectively given as part of our National vaccination programs. One US Navy sailor experienced a more serious systemic reaction after his third vaccination referred to as Guillian-Barre Syndrome (GBS). The etiology of this syndrome is still unknown, although it has been associated with recent infectious disease and vaccinations. The CDC reports that the vast majority, 95 percent of patients with GBS, do not report receiving any vaccine in the weeks prior to developing symptomatically. GBS gained some notoriety during the 1976 national vaccination against swine influenza and was found to increase the rate of GBS slightly less than one case per one hundred thousand vaccinations. Subsequent influenza vaccines prepared from other virus strains have not been clearly associated with an increased frequency of GBS. More recent studies suggests the rate may be as low as 1-3 cases per 1,000,000 people vaccinated. The possible risk of developing GBS following immunization is so small, however, that it is difficult to study and accurately estimate.

"The 49 VAERS events outlined for you represent all reports submitted through our reporting system within all Department of Defense Military Treatment Facilities. The FDA implemented their vaccine adverse event reporting system, commonly referred to as VAERS, in November of 1990. VAERS is the responsibility of the Division of Biostatistics and Epidemiology in the Center for Biologics Evaluation and Research. It is also monitored at the CDC by the National Immunization Program, Vaccine Safety and Development Activity. Since 1990, only 101 adverse events have been reported to the FDA as temporally associated to the anthrax vaccine. These reports come from disparate sources and may actually be submitted directly by any individual suffering an adverse event. Since this is a passive surveillance system, this open approach encourages the submission of any and all events that may represent a significant trend. The FDA cites that only 9 of these 101 reports represent a serious event. Serious events are defined by the FDA as those that are life-threatening, result in a chronic illness or condition, or require hospitalization. The FDA assesses that none of these events are causally related to the anthrax vaccine and do not represent a sentinel trend in adverse health effects associated with the vaccine. All adverse events reported within the DoD have resolved and all have returned to duty.

"It is also important to distinguish the difference between adverse events and side-effects associated with the vaccine. While our system does not discourage reporting any VAERS temporally associated with the vaccine, many of those reports submitted represent side-effects. Any case that results in either loss of duty for more than 24 hours or hospitalization must be reported through the DoD as an adverse event. Conversely, side-effects do not effect either duty performance or any other activity of daily living. The history on the use of this vaccine in the United States, which was licensed more than 28 years ago, suggests that the side effects associated with its use are minimal. The product insert for the vaccine cites that as many as 30-percent of recipients will experience a mild, local reaction. The clinical data submitted to the FDA when the vaccine was first licensed in 1970 estimated 16-percent or less would experience a mild local reaction, as few as 4-percent would experience a moderate local reaction, and less than 1-percent would have a serious local reaction including swelling at the site of inoculation that may extend down the

extremity. Less than 1-percent of the study group experienced any type of systemic reaction. Studies on reactions and side-effects by the US Army Medical Research Institute for Infectious Diseases, USAMRIID, conducted from 1977 to 1996 validates the earlier reports and the low reactogenicity of this vaccine.

"All the members of the AVIP collective team-the Surgeons General, the Joint Program Office, the Joint Staff, and the Assistant Secretary of Defense for Health Affairs, have endeavored to continuously monitor the health of our people to protect against any adverse health effect. Under the direction of the Army Surgeon General, Tripler Army Medical Center launched an internal survey of more than 600 assigned clinicians to closely evaluate every conceivable side effect that had any temporal correlation to the anthrax vaccination. We encouraged the survey participants to report any side-effects, irrespective of the degree of severity, to develop an accurate projection of the vaccine's effect on the service member's health and the degree to which it impaired his duty performance. Less than 5-percent sought medical care for side-effects after any of the first three doses, and most of these side-effects, according to the principal investigator, were determined to be from illness not related to the vaccine. Only 3 VAERS were reported from the population, none of which required hospitalization. This survey will continue, with no established endpoint, until we have sufficient data to confirm the historical rates associated with this vaccine.

"The Army Surgeon General, acting on behalf of the Executive Agent, has also requested the assistance of an external review panel to analyze each of the reported VAERS. Presently, the Vaccine Injury Compensation Program (VICP), from the Department of Health and Human Services is evaluating 100% of all VAERS received by the FDA related to the anthrax vaccine. The VICP has met three times now and reviewed 59 of the 84 reported VAERS. Their recommendation is for, "no change in the current DoD anthrax immunization program except to initiate observational studies, preferably with a control group, as soon as possible.

"The Army Surgeon General has proposed a longitudinal, cohort study to assess both near-term and long-term reactions. This item will be discussed at a clinical conference scheduled for May 1999. Attendees include clinicians from all Services, the Armed Forces Epidemiological Board, the CDC, and the Center for Bioterrorism at Johns Hopkins University.

"Mr. Chairman, Representative Blagojevich, Distinguished Committee Members, Force Health Protection is the concept embedded in Joint Vision 2010 which not only identifies how we will manage battlefield casualties in the next millennium, but how we must leverage our medical resources to maintain a healthy and fit force, and prevent casualties throughout the operational spectrum. The AVIP epitomizes this paradigm by using superior technologies to add another dimension of protection against emerging threat of anthrax as a biological weapon of mass destruction. Leveraging the superior technologies of the future, this program provides a template for managing all health readiness metrics and ensures a hyper-fit force that will be preeminent in any form of conflict. We continue to monitor the safety of this program to ensure and protect our most valued asset-the individual soldier, sailor, airman and marine. "

Conclusion

Anthrax vaccine is a key element in protecting service members against the lethal threat of anthrax. DoD is working with BioPort, the only licensed anthrax vaccine manufacturer to ensure there is a supply of this safe and effective vaccine.

Mr. SHAYS. Please summarize that Surgeon General's report.

General CAIN. In summary, Mr. Chairman, the surgeon general just concluded that it is safe and effective—that the vaccine is safe and effective.

Mr. SHAYS. That is a real summary. [Laughter.]

I was hoping for a little meat in there, a little detail. Are you prepared to give anything more than that summary?

General CAIN. I am not at this time.

Mr. SHAYS. Dr. Myers.

Dr. MYERS. Mr. Chairman and distinguished committee members, my name is Dr. Bob Myers, and I am the chief operating officer of BioPort Corp. And thank you for making my stay here in Washington as pleasant as possible.

I am proud to come before you today and tell you about our experiences as the manufacturer of the first and only routinely used defense vaccine in our country. I am pleased to have this opportunity to personally assure you of our vaccine's safety and effectiveness. Indeed, this vaccine, instead of being criticized, should be welcomed as a safe and effective counter to biological warfare in today's highly threatening global environment.

I have worked for the lab since 1978, when it was owned by the Michigan Department of Public Health. I have been involved in, largely directed, the manufacture of all doses of anthrax vaccine being used in the Department of Defense, by the Department of Defense in its anthrax vaccine immunization program.

Let me be clear at the outset. I don't set policy; I make vaccines. And I am totally committed to providing the very best protection possible against the anthrax threat. BioPort has worked closely with the FDA to license and manufacture a quality vaccine, and we are working closely with the DOD to build and test a stockpile of vaccine that meets their important force-protection requirements.

As you have heard this morning, anthrax is by far the most likely bio-weapon we will face in the near future. The vaccine has been produced in Michigan since the mid-1960's, when the Federal Government came to the Department of Public Health and asked them to develop and produce an anthrax vaccine which was badly needed in the textile industry as well as to protect laboratory workers studying anthrax.

The Michigan lab had a long and outstanding history as one of the leading vaccine developers in the country, had an excellent working relationship with the CDC and the DOD, and last, but by no means least, they were willing to do the work on a vaccine that would protect people against anthrax at a time when there was no interest.

While the anthrax vaccine was licensed in 1970 on the basis of efficacy already presented to you today by FDA, and this was before I started working at the lab, I routinely review information relating to its safety and effectiveness. So I note the efficacy of BioPort's vaccine was confirmed in 1985 by an expert panel, which found that from 1962 to 1974 no cases—let me repeat, no cases—occurred in fully vaccinated individuals despite continued cases in unvaccinated mill workers.

The FDA panel concluded that the anthrax vaccine is safe and effective.

And let me just point out by example here, in way of answering some questions that may arise—I will start out by saying yearly deaths for the United States for 6 or 7 years, 1990, one; 1991, three; 1992, one; 1993, three; 1994, six; 1995, four; 1996, four.

None of these deaths occurred in vaccinated individuals, and the vaccinated individuals receive either three or five doses. Now, the example that I am describing is an example that is not anthrax, but rabies.

We give fives doses of rabies after exposure. Do we know we need to have five doses? No, but when the studies were done, five doses worked. If you don't get vaccinated for rabies, you die after you have been exposed.

Five doses of DTP are given to children between the ages of birth and 5. Would four doses work? While there is some evidence to show that for newer vaccines, perhaps four doses would, and you wouldn't need a fifth.

Why are there six doses for anthrax vaccine? Because six doses work to stop disease, and there haven't been incidences of disease that are large enough since then to study.

Mr. SHAYS. Let me just make sure I am clear on that. Are you saying in general, Dr. Myers, that six doses is the norm for all vaccines?

Dr. MYERS. No I am not. I am saying that five doses for rabies vaccine post exposure works. Nobody wants to take a risk at cutting that back to four. Five doses of DTP are given between birth and 5 years of age. There is some evidence to show that the fifth dose may not be needed, but it is still given. And we know that six doses of anthrax vaccine worked in clinical studies, and since the incidence is so small, no additional studies have been done. Six works; we stay with six.

Mr. SHAYS. Let me just let you continue, and then I will have you come back.

Dr. MYERS. Thank you.

Mr. SHAYS. Thank you. I am sorry I interrupted you.

Dr. MYERS. Thank you.

The FDA and DOD have already spoken to adverse events that have been reported to them. And my written testimony fully covers this topic as well.

I would like to make several additional comments. Let me describe a study that you may not be familiar with. It is a study of about 400 individuals whose reactions were actively solicited after three doses—for each of three doses: Redness, any, 21 percent. Soreness, any, 68 percent. Swelling, any, 11 percent. Arthralgia, any, 16 percent. Fatigue, any, 33 percent. Headache, any, 37 percent. Headache, severe, 2.8 percent. Rash, any, 5.2 percent. Rash, severe, none. Fever, 99.5 degrees Fahrenheit or greater, 2.26 percent.

Seems like a rather high reaction rate. Listen carefully. What is striking is that this was part of a study done with one of the most recently licensed FDA vaccines, a vaccine licensed to protect against lyme disease. But most striking, the reaction rates I just described to you were from the placebo group, not the vaccine.

If you actively solicit reaction rates to injected vaccines, because they use needles, they break the skin, they break nerve fibers, they

create inflammation. You will have side reactions. Most will be local. Some will be severe. Generalized reactions can also occur.

I have personally had many doses of the vaccine over the years, more than you, General Cain, and have had nothing worse than the sore arm experienced by many others. If the anthrax vaccine were available for my wife, my children, and my grandson, I would have absolutely no reservation in administering the vaccine to them, including my eldest daughter who is of child-bearing age.

One of the ways the safety and efficacy of vaccines are ensured is through periodic inspections of manufacturing facilities to determine if they are operating in accordance to their license and according to good manufacturing practices.

Our labs have been inspected at least 48 times since 1969, including several recent inspections that reported serious deviations of GMP's. BioPort takes this matter very seriously.

I would like to point out that contrary to the testimony of the GAO, the manufacturing facility was inspected in January 1993. That is the anthrax manufacturing line. It is not a plant. It is not even a building. It is a floor in a building at a campus that has about 20 buildings, most of them two stories or more.

This facility, on the basis of that inspection, was approved in July 1993. Two inspections in 1998, one in February and the other in October, concentrated heavily on the anthrax vaccine, the lots in the stockpile, and related GMP issues. We expect another inspection this summer as part of the FDA's review of our renovated anthrax facility that many have already discussed this morning.

After the February 1998 FDA inspection, we voluntarily quarantined, as a precautionary measure, 10 lots previously released by the FDA. An 11th lot had been quarantined before the inspection. These lots will remain in quarantine until any outstanding issues are resolved to the satisfaction of BioPort and the FDA. If satisfactory resolution is not obtained, the lots will be rejected.

In conclusion, the anthrax vaccine being provided to our troops is safe and effective. It's a typical vaccine. It is not the exception. BioPort is fully committed to making safe and effective vaccine. I am greatly concerned about the unsubstantiated comments made by those who, for whatever reason, are opposed to this important protection against one of the most serious biological threats in the world today.

The anthrax vaccine is an essential component of force protection in our military, and we at BioPort are committed to providing the men and women who serve our country with the highest quality vaccine.

Thank you for the opportunity to be here today. I would be happy to answer any questions you might have.

[The prepared statement of Dr. Myers follows:]

Testimony of Dr. Robert C. Myers
Chief Operating Officer, BioPort Corporation
Lansing, Michigan

Presented to the Subcommittee on National Security, Veterans Affairs, and International Relations

April 29, 1999

INTRODUCTION AND BACKGROUND

Chairman Shays, Representative Blagojevich and distinguished committee members, my name is Dr. Bob Myers and I am the Chief Operating Officer of BioPort Corporation.

I am proud to come before you today to tell you about our experiences as the manufacturer of the first and only routinely used defense vaccine in the country. I am pleased to have this opportunity to personally assure you of our vaccine's safety and effectiveness. Indeed, this vaccine, instead of being criticized, should be welcomed as a safe and effective counter in today's highly threatening global environment.

I have worked for the lab since 1977, when it was owned by the Michigan Department of Public Health, later known as the Michigan Biologic Products Institute (MBPI). I have been involved in the manufacture of all doses of the anthrax vaccine being used by the Department of Defense (DoD) in its Anthrax Vaccination Immunization Program (AVIP).

Let me be clear at the outset. I don't set policy. I make vaccines. And I am totally committed to providing the very best protection possible against the threat of anthrax. BioPort has worked closely with the FDA to license and manufacture a quality vaccine and we're working closely with the DoD to build and test a stockpile of vaccine that meets their important force protection requirements.

Anthrax is a very real threat that is virtually always fatal. Anthrax is also considered a low-tech bioweapon — it's easy to get, it's easy to grow, and it's not too difficult to weaponize. As a result, anthrax is by far the most likely bioweapon we will face as we move into the new millennium.

Testimony of Robert C. Myers
April 29, 1999

That anthrax is a potential bioweapon has long been known — long before the recent resurgence of concern on the likely use of bio-weapons by terrorists or aggressor nations. The National Centers for Disease Control (now the CDC) and the DoD came to the Michigan Department of Public Health some 35 years ago and asked them to develop and produce an anthrax vaccine. They asked the Michigan group for three reasons:

- First, Michigan had a long and outstanding history as one of the leading vaccine developers in the country.
- Second, Michigan had an excellent working relationship with the CDC and the DoD as a well-respected, highly reliable, pre-eminent biologics lab.
- Last but by no means least, the Michigan Department of Public Health was *willing* to work on a vaccine that would protect people against anthrax at a time when no one else would. We stepped up to the plate when we were needed, and worked in tandem with scientists from Fort Detrick and the Public Health Service to develop an improved, safe and more highly effective anthrax vaccine during the years 1965-1970.

EFFICACY OF ANTHRAX VACCINE

The anthrax vaccine was first licensed by the FDA in 1970. At that time, it was badly needed in the textile industry, as well as to protect laboratory workers studying anthrax. In fact, the only time anthrax vaccine was tested for efficacy in controlled trials in humans was in four textile mills in the northeastern United States. That vaccine — less potent but very similar to ours — was tested from 1955 to 1959 in these textile mills because anthrax occurred regularly in mill workers — especially in mills processing imported goat hair. (On average, 1.2 cases of anthrax, mostly cutaneous, were reported per 100 employees per year.)

In that study, the vaccine was determined to be 93 percent effective against cutaneous anthrax. Twenty-one cases of cutaneous anthrax were reported — 18 in people who either received the placebo or no vaccine, two cases in people who had received three doses of vaccine with 5-13 months elapsing since the last dose, and one case in which the individual had received two doses of the vaccine with less than two weeks elapsing since the last dose.

Although the cases of inhalation anthrax were insufficient in number to obtain a measure of efficacy, five cases did occur during the study -- none in fully vaccinated individuals.

Four of the five individuals died. This single, controlled trial of vaccine efficacy was the basis of efficacy upon which the federal government licensed the anthrax vaccine in 1970.

The efficacy of Bioport's vaccine was confirmed in 1985 by an expert FDA panel, which found that from 1962 through 1974, NO cases — let me repeat, NO CASES— occurred in fully vaccinated individuals despite continued cases in unvaccinated mill workers. The FDA concluded that there was sufficient evidence that the anthrax vaccine is safe and effective under its licensed conditions.

Because it would be unethical to conduct placebo-controlled human studies, the only available method to show the effectiveness of the vaccine today is through animal studies. While several studies in guinea pigs about ten years ago found mixed results in the vaccine's ability to protect against some strains of anthrax, recent studies in rhesus monkeys and rabbits have proven that our vaccine is highly effective in preventing inhalational anthrax, even with so-called vaccine resistant strains. In those studies, groups of monkeys were protected against anthrax aerosol challenges at doses between 100 and 1000 times the amount lethal to unvaccinated animals, up to two years after being given only two doses. The superior effectiveness that has been demonstrated in these studies is the basis for the current work under an approved Investigational New Drug (IND) application aimed at reducing the number of doses required.

Finally, Dr. Arnold Kaufmann, a highly regarded epidemiologist who followed anthrax infection in the United States for the CDC and is now retired, in April of 1998 stated the following: "To the present date, I am unaware of any person who has developed any form of anthrax after receiving either two doses of the current vaccine with seven or more days elapsing since the last dose, or three doses of the current vaccine, regardless of time elapsed since the third dose." We are also unaware of occurrence of any anthrax in vaccinated individuals, but a few cases of cutaneous anthrax continue to occur sporadically in the U.S. in people who have not received the vaccine.

SAFETY OF ANTHRAX VACCINE, INCLUDING ADVERSE EVENTS

Certainly the safety of a vaccine must be assured. Yet anthrax vaccine is a perfect example of a safe vaccine that is still being unfairly criticized. It baffles me that someone going to the Middle East would actually refuse protection against a disease that is

virtually always fatal. You get inhalation anthrax, you don't get better. You die. Vaccines given by injection don't get any safer than the anthrax vaccine. The side effects — a sore arm, an occasional slight fever — occur less frequently than they do with common childhood vaccines like DTP (diphtheria-tetanus-pertussis) and MMR (measles-mumps-rubella).

As a requirement for licensure, the safety of our anthrax vaccine was studied between 1965 and 1970 under an approved IND, sponsored by the CDC. During that five-year period, some 16,500 doses of anthrax vaccine were administered. This included the initiation of vaccination of at least 4,000 individuals and the administration of approximately 6,500 booster doses. Reactions and rates of reactions identified in those studies served as the basis for the discussion of reactions now found in the prescribing information for anthrax vaccine.

These reactions to our anthrax vaccine — which, by the way, are common reactions to ANY injected vaccine — are as follows:

- Mild reactions — consisting of a small red area (half an inch to less than an inch) plus slight local tenderness — occur in approximately 30 percent of recipients. This reaction usually occurs within 24 hours and begins to subside by 48 hours. Occasionally, the redness increases to up to about two inches in diameter. Local reactions tend to increase in severity by the 5th injection and then may decrease in severity with subsequent doses.
- Moderate local reactions, which occur in four percent of recipients of a second injection — are defined by an inflammatory reaction greater than five cm (approximately two inches) in diameter. This area may itch. Subcutaneous nodules (little lumps) — the result of inflammation — may occur at the injection site.
- More severe local reactions are even less frequent than moderate reactions and consist of extensive swelling of the forearm in addition to the local inflammatory reaction. ALL local reactions have been reversible.
- Systemic reactions have occurred in less than 0.2 percent of recipients and include malaise and lassitude. Chills and fever have been reported in only a few cases. (You should know that both recombinant hepatitis B vaccines currently on the market report systemic reactions at least five times as often as is reported for the anthrax vaccine.)

Between licensure in 1970 and May 1994, adverse events reported to the Michigan Labs from the 65,000 doses distributed were few in number. The adverse events reported were similar in nature to those found during clinical trials of the vaccine and none were associated with chronic or permanent local or systemic effects. Through May 1994, no reports of adverse events were received by the Michigan Labs during or after the Persian Gulf conflict. No reports of adverse events were received by Michigan in any of the four yearly reporting periods beginning in April 1994 and ending in April 1998. Since that time BioPort has received directly two reports of adverse events and is now processing a report from a Michigan National Guardsman, concerning reactions in 12 individuals.

Additionally, BioPort is aware of 101 adverse events reported through the Vaccine Adverse Event Reporting System (VAERS). The VAERS reports run from November 1990 through now. Of the 101, only 9 were classified as serious. Serious adverse events for any vaccine are defined as those that are life-threatening, result in a chronic illness or condition, or require hospitalization. It is my understanding that the FDA has assessed that none of these 9 events were caused by the anthrax vaccine and do not represent any trend in adverse health effects associated with the vaccine. From the 49 adverse events reported to VAERS by the DoD, the most serious was in a young man who developed Guillian-Barre Syndrome, temporally associated with his third dose of anthrax vaccine. We are informed that this individual fully recovered. I am also told that all others have been resolved and all individuals have returned to duty. I am sure the GAO, FDA and the DoD have more to say about the safety profile of the anthrax vaccine in their testimonies.

I personally have had many doses of the vaccine over the years and have had nothing worse than the sore arm experienced by many others. If the anthrax vaccine were available for my wife, children and my grandson, I would have absolutely no reservation in administering it to them, including to my oldest daughter who is of childbearing age.

FDA COMPLIANCE AND RELATED MATTERS

Our records show that our labs have been inspected by the FDA and its predecessor, the Division of Biological Standards of NIH, at least 48 times since 1969. Each inspection focused on one or more of three manufacturing activities: bacterial vaccines and toxoids, viral vaccines, or plasma derivatives. Examined during each of these inspections were elements common to the manufacturing of all products at our site, including the manufacture of anthrax vaccine. Such common elements included: policies and

procedures, recordkeeping, analytical laboratories, quality control practices, raw materials handling, filling and packaging, and storage, warehousing and distribution.

The purpose of these inspections is to determine if we are operating according to our license and according to current Good Manufacturing Practices (GMP). Recent inspections and accompanying detailed establishment inspection reports are largely a matter of public record.

It's no secret that we and others in the biologics industry have had some pretty negative findings from the FDA inspections in recent years. Just before that string of inspections, in January 1993, the anthrax vaccine manufacturing facility was inspected and a renovation to the facility was subsequently approved in July of 1993. Contrary to some reports, that's not so very long ago. Most recently:

- In 1994, we received a rigorous inspection of our plasma derivatives operation, that included several serious deviations from GMP.
- In 1995, we received a warning letter following another inspection of plasma operations and rabies vaccine manufacturing.
- A 1996 inspection showed that we had not yet fully implemented the corrections we had promised.
- This inspection was followed, in March 1997, by a "Notice of Intent to Revoke" (NOIR) letter--threatening to initiate proceedings to revoke our license.

Immediately after receiving the NOIR letter, we met with our clients, including the DoD, to rapidly develop and execute a comprehensive plan to resolve FDA concerns about our operation. We formally responded to FDA with our Strategic Plan for Compliance, which we are executing with oversight from the FDA.

Two inspections in 1998, one in February and another in October, concentrated heavily on the anthrax vaccine, the lots in the stockpile and related GMP issues. We expect another inspection this summer, as part of FDA's review of our anthrax vaccine fermentation and purification facility renovation. This renovation, for which planning was initiated in 1996 with construction beginning in early 1998, is now completed and new lots are in production. The release of these new lots will be dependent upon the FDA's approval of the renovated facility.

After the February 1998 FDA inspection, we immediately participated in a conference call, initiated by the FDA, to discuss several of the lots mentioned in the inspection report. As a result of that telephone call, we voluntarily quarantined, as a precautionary measure, 10 lots previously released by the FDA, pending resolution of those issues through our internal investigations and performance of any necessary additional analyses. Six lots were quarantined over concerns about the potency test (FAV018, FAV021, FAV022, FAV023, FAV025, FAV028), three for sterility assurance issues (FAV029, FAV032, FAV035) and one because of a high rejection rate for the presence of particles (FAV016), now known to be inert gasket material. An eleventh lot (FAV026) discussed with the FDA had already been quarantined and rejected by MBPI Quality Assurance for sterility assurance issues. These 10 lots will remain in quarantine until any outstanding issues are resolved to the satisfaction of BioPort and the FDA. If satisfactory resolution is not obtained, the lots will be rejected.

It should be pointed out that when lots are released by the FDA, the DoD has traditionally paid for them, but has not taken possession of the doses in the lot. Rather, the DoD has requested that we store these lots, on-site, creating, over time, a vaccine "stockpile." This is very different than a normal commercial manufacturing situation in which lots are made in accordance with a market forecast and in consideration of the expiration dating period. In that scenario, those lots would be actually administered to recipients on a regular basis. Now, with the AVIP program, manufacturing will be more closely tied to annual forecasts. However, there is a great deal of discussion regarding stockpiling vaccines such as anthrax and smallpox for both civilian and military use. I do not sense that a consensus has been reached across and within federal agencies on how stockpiling can be acceptably achieved in an acceptable and timely fashion.

All 32 lots of the existing vaccine in this stockpile, owned by the DoD but stored by us, were essentially quarantined by DoD as part of Secretary Cohen's announcement of implementation of the program to vaccinate all service personnel. In his December 15, 1997 announcement, the Secretary specified, among other things that each of the lots must be additionally tested (the so-called supplemental testing) by the manufacturer with audit oversight by an independent DoD contractor who would report back to the DoD on the acceptability of each lot. At that time, MBPI agreed to cooperate with the DoD in this effort and began testing the lots. To date, eight lots have been tested and released through this program for distribution in support of the AVIP. Due to the suspension of potency testing in the fall of 1998 because of a greatly increased number of non-valid tests

additional lots were not released. An amendment to our product license to address these non-valid tests and other aspects of the potency test was originally filed several years ago. Since February of 1998, BioPort has worked closely with FDA to achieve approval of this amendment. Additionally, investigations by BioPort and JPO contractors revealed possible causes for the testing difficulties. These difficulties were evaluated and steps have been taken to address them. The test is now functioning as it was originally intended. With this consistent test performance and approval of the potency test amendment, we expect additional lots to be released from the stockpile.

CONCLUSION

No one is more committed to making a safe and effective vaccine than we are. I am greatly concerned about the unsubstantiated comments made by those who, for whatever reason, are opposed to this important protection against one of the most serious and deadly biological threats in the world today. The fact that the senior defense leaders of our country have been inoculated with our anthrax vaccine is an indication of their confidence in its safety, and their belief in its effectiveness and necessity. The anthrax vaccine is an essential component of force protection in our military and we at BioPort are committed to providing the men and women who serve our country with the highest quality vaccine.

Mr. SHAYS. Thank you. Dr. Myers, let me just say, since your company produces the vaccine, that if we ask questions of others and you think something is not stated correctly that even if we did not ask you, I want to make sure that you let us know you want to respond and jump in.

Dr. MYERS. Thank you very much. I will.

Mr. SHAYS. Let me start with you, Dr. Zoon.

Would FDA approve a new anthrax vaccine today based on data from a different vaccine?

Dr. ZOON. FDA would look at the data supplied by the manufacturer and, depending on the data submitted, that possibility exists.

Dr. MYERS. If I could just add to that as a manufacturer? There are many vaccines that are licensed without direct efficacy studies in humans. The rabies vaccine, formerly manufactured by the Michigan Department of Public Health, was licensed in 1998—1988—based on post-exposure-simulation studies not exposure in actual field conditions with known rabid animals.

Mr. SHAYS. OK. I am happy to have you jump in. I just want to pursue the question, and then you are welcome to jump in.

Dr. MYERS. I am sorry.

Mr. SHAYS. Dr. Zoon, is it your testimony that the FDA will approve a new vaccine based on data from a different vaccine? Do they do that?

Dr. ZOON. As I said, Mr. Chairman, we would look at the entire data base——

Mr. SHAYS. No. That is not what I asked. I want you to answer the question. I asked, can you give me examples of other times that you have done that in the past.

Dr. ZOON. We have approved materials in which study was done with another product, which was developed by a different company, and then there were changes during the initial production—major manufacturing changes during the course of the study.

Mr. SHAYS. What was that product?

Dr. ZOON. The product was Avenex.

Mr. SHAYS. And so all the studies were on the old vaccine. And then they were allowed to change it and you approved it based on the studies of the older vaccine?

Dr. ZOON. The pivotal study was done with the original material. Yes.

Mr. SHAYS. OK. There were studies done afterwards, before you——

Dr. ZOON. There were, there were——

Mr. SHAYS. Let me just say something. I don't want you to answer quickly, I want you to speak more slowly because this is your field, not mine. And I don't want to get lost.

Dr. ZOON. Right. OK.

Mr. SHAYS. What I am asking is, did you, before you licensed that product, even though you did the pivotal studies, you said, on an older vaccine, did you continue to do studies on the new vaccine before you approved it?

Dr. ZOON. The material was continued in other clinical studies.

Mr. SHAYS. Before you approved it?

Dr. ZOON. That is correct.

Mr. SHAYS. OK.

Dr. ZOON. However, those studies weren't the pivotal efficacy studies.

Mr. SHAYS. But the bottom line is you still did studies before you approved it.

Dr. ZOON. We did studies—the material was put in humans. Yes.

Mr. SHAYS. OK. And has FDA licensed any other vaccine without human efficacy data, and I think Dr. Myers responded. But I want you to respond.

Dr. ZOON. Has FDA—excuse me.

Mr. SHAYS. Has FDA licensed any other vaccine without human efficacy data?

Dr. ZOON. Efficacy data? I am not prepared to answer that question. I don't have all the information with me today. I would have to go back and look at my records to get back to you on that.

Mr. SHAYS. But none comes to mind. I realize that there may be many. But none comes to mind right now?

Dr. ZOON. To be honest with you, Mr. Chairman, I focused my concentration on anthrax vaccine for this hearing, and I would be happy to go back and check the records for that.

Mr. SHAYS. OK. Did you want to make a comment, Dr. Myers?

[Myers indicates he doesn't.]

Mr. SHAYS. OK. Why did FDA conclude that you needed six shots for anthrax? Dr. Zoon, why did the FDA conclude you needed six shots, not seven, not five, not four. What was the basis, what study was done that showed the six was what you needed to do?

Dr. ZOON. Mr. Chairman, I will answer your question. I wanted to make one clarification for the record, is that the product that I described, Avenex, is a therapeutic, not a vaccine—just to make sure that that is clear.

Mr. SHAYS. OK. Then let's back up. Tell me a vaccine.

Dr. ZOON. I don't have any other examples here right now.

Mr. SHAYS. OK. Is there anyone else in FDA here who could tell me of any vaccine that has been approved by, where a study has been done on one and then approved on another? I would be happy to swear you in. I am not saying it doesn't exist. We just want it on the record.

Ms. GOLDENTHAL. I am Karen Goldenthal.

Mr. SHAYS. Why don't you sit down. And I thank you. And feel free to catch your breath a second. Move that water out of the way, and we are in no rush.

Ms. GOLDENTHAL. I am Karen Goldenthal with FDA.

Mr. SHAYS. And let me request that you leave your name with the recorder.

Ms. GOLDENTHAL. Certainly.

Mr. SHAYS. Thank you. Nice to have you here. Thank you.

Ms. GOLDENTHAL. Thank you, Mr. Chairman. The Merck hepatitis A vaccine underwent a very major manufacturing change between the time of the pivotal efficacy trial and the time of approval. And this involved a scale-up and actually change in the procedure of how the hepatitis A virus was grown. So that is an example that comes to mind. And it actually took the sponsor several years to work out all of the issues with the new manufacturing change.

And then they did a comparison with the material from the efficacy trial.

Mr. SHAYS. Did they do new studies with the new vaccine?

Ms. GOLDENTHAL. You know, I would have to go back at the file and detail to give you that information, but I believe that they did one study where they looked at the immunogenecity of the new material.

Mr. SHAYS. I don't know what that last sentence——

Ms. GOLDENTHAL. The antibody response.

Mr. SHAYS. OK. Thank you.

Mr. SHAYS. Let me just ask two more questions here.

Does the FDA require immune correlate protection in an animal model as the basis for extrapolation of efficacy findings to humans?

Dr. ZOON. Excuse me, Mr. Chairman, can you——

Mr. SHAYS. We are trying to find—I want to know if you have to find a correlate between what you do in an animal versus its impact on a human being.

Dr. ZOON. There are not good animal models for all studies. However, there are a number for many systems, and with vaccines, often animals are used to look at protection and looking for evidence of correlation with protection as well as human data. And when we can do studies in humans, we also look for correlates of protection.

Mr. SHAYS. Do you look for them, or do you actually demand that they exist before you license?

Dr. ZOON. In vaccine trials, you had asked earlier about why six doses. In the field of vaccinology, much of it is determined empirically; that means you pick a regimen, you study the regimen.

[Microphone wires knocked out.]

Mr. SHAYS. Let me just finish my question then. I am sorry.

Dr. Myers, and then I am going to come back for a second round. But if the vaccine is demonstrably safe, why would the company request and receive an indemnification from DOD against the risk of liability due to the possible adverse reactions and failure of the vaccine to convey immunity?

Dr. MYERS. The answer to that is the same reason that there is a National Vaccine Injury Compensation Program now. It is to control tort. In 1985, the——

Mr. SHAYS. Speak slowly. You are going to get your chance to say everything. I just want to——

Dr. MYERS. I want that 20-minute break. [Laughter.]

Mr. SHAYS. Yes, sir.

Dr. MYERS. I am sorry. In 1985, the price of a dose of DTP vaccine went from 15 cents to $11 and above because of the tort activity, the litigation that was uncontrolled and unpredictable. I am happy to say now that the cost of a dose of DTP is much, much less as the Federal Government has very wisely funded a program to adjudicate, deliberate, and pay reasonable award to people injured.

There is no such program for anthrax vaccine.

Mr. SHAYS. OK. But, let me understand. Is it comparable? Why wouldn't you be given the same protection as others? This seems like it is greater protection. I may be wrong.

Dr. MYERS. I would welcome and encourage all vaccines to be included in the National Vaccine Injury Compensation Program, but today they are not. And the anthrax vaccine is not included in that program, federally mandated program.

Mr. SHAYS. You make other products, like tetanus and others for DOD?

Dr. MYERS. That is correct. Not for DOD.

Mr. SHAYS. OK. But do you have—explain to me—do you have that same exemption?

Dr. MYERS. Not from the DOD. We are in the Department of Treasury-administered National Vaccine Injury Compensation Program, and we pay a surcharge; that is, an excise tax, on each dose that is distributed. That funds the program in the case of the rare but possible event that there is injury.

Mr. SHAYS. OK. Working backward, and then obviously, the seller pays the cost. In other words, am I to infer, trying to answer the question for you, that is your testimony in essence if you are under that program, you would just charge the DOD that much more?

Dr. MYERS. I don't have my legal counsel here today, and I think it is a matter for legal counsel to determine whether the choice would be to go with National Vaccine Injury Compensation Program or to continue to pursue indemnification.

Mr. SHAYS. Well, during this break, I will give you a little bit of a homework assignment. If you would just find out why this seems a bit broader, and I would just love to know why. And maybe there is an explanation. And if you would call your counsel and find out the answer to that.

Dr. MYERS. Let me just say—could I complete the answer. At the highest level, this vaccine is getting serious criticism. These hearings have added to that criticism. I think much of that criticism is unfounded.

Mr. SHAYS. It may be.

Dr. MYERS. And I think people would be—anybody who is trying to protect their business would be scared to death of not having indemnification with such loud and unfounded criticism occurring.

Mr. SHAYS. Well, let me just respond to that because there are two sides to every story. This is a mandatory vaccine. This is not voluntary. This is 2.4 million people, not a few hundred, and this committee and others have every requirement to examine the facts. And I asked a very simple question, and I don't think it is a hard question to answer. And in fact, I think you may have answered it. All I want to know, is this unique for this particular vaccine that gives you an added advantage that didn't exist for others and, if so, why? And if it isn't, then the question is a simple answer and on to the next question.

General Cain, maybe you could respond to why you decided to do this.

General CAIN. What was the question?

Mr. SHAYS. Yes. The question is: The DOD decided to basically give BioPort blanket indemnification, hence risk of liability due to the possibility of adverse reaction or failure of the vaccine to convey immunity. And I need to know why DOD decided to do that?

And if you want to think about that and give us an answer when we come back. The question is, have you done it for others as well?

And we will have a 20-minute break. Thank you.

[Recess.]

Mr. SHAYS. I would like to call this hearing to order. I could ask some more questions, but I am just going to kind of make a comment that hopefully puts this hearing in some context.

I chaired the Subcommittee on Human Resources before I chaired this subcommittee, both in Government Reform. And we oversaw FDA. We have done a lot of work, the former committee, on Gulf war illnesses. I candidly have suspicions that raise my concerns, but I will first state, I don't know if in the end the military, the DOD, is correct in, one, having this policy. I will say to you that there are soldiers that have do not want to take this vaccine, General Cain.

So I don't know whether they are correct or not. And when I ask these questions, I think we could be in a conflict and our soldiers could be exposed to anthrax and do I want to be the person that somehow moved our Government to not do this?

So there are questions on both sides. In my mind, the jury is out. Where the jury is not out for me is, that given some of our concerns that this is a mandatory program and not a voluntary one. It would seem to me that until some questions are answered, this should be a voluntary program.

So I will obviously acknowledge to myself and for the record that I believe this should be a voluntary program until some questions are answered and that then the military should be required to convince their men and women that it is in their best interest, and then let the men and women of our forces come to some conclusion.

I will also say that one of my problems is that I did not like how the FDA handled pyridostigmine bromide [PB]—I didn't say it correctly, but I can say PB—and that for the use in the military it was a nerve agent, and it was used and licensed for that. And we used it as a prophylactic, which was not the way it was designed for, and I am critical of FDA for, one, being so lax in what they allow the military to do.

The military was supposed to keep records, and it didn't.

So, yes I have those suspicions that I bring to the table. So, I have questions. Dr. Myers, I have questions that we have only one plant, you are the sole source. I have questions that there may be easy answers to, and then you can feel relaxed and we go on to the next thing.

You know, one is the indemnity, another is, why are we funding the plant. There can be reasons for that. We are not even going to get into that. One thing I can say is that this is not the last hearing. So I don't have to have all my answers now.

But I can say to the FDA, I need to know, because it is unfair for you, Dr. Zoon, for me to expect that you would be able to know other cases where you have handled it the same way. But I have a suspicion that when it comes to the Government, we allow the Government to have one standard and the private sector to have another.

And in my past, I found that to be true. So I want to make sure it is the same standard. And so, would you just explain to me, Dr.

Zoon, when you say if a person is at high risk, the vaccine is safe and effective. Why did you use the word high risk?

Dr. ZOON. Because that is what the package insert labeling recommends it for.

Mr. SHAYS. So, is it not safe and effective for those people who aren't at high risk? So I guess effectiveness is moot, but is it safe?

Dr. ZOON. The vaccine labeling lays out the population for which this vaccine has been recommended. And, in fact, in the labeling, sir, it does say who those populations are. I can review that for you if you would like.

Mr. SHAYS. No. I just need to know the concept of high risk.

Dr. ZOON. Well, high risk was intended as the data showed from the study——

Mr. SHAYS. Why don't you, one, put the document in the record, and then——

Dr. ZOON. The package insert? I would be delighted to.

[The information referred to follows:]

Supplied From Anthrax Vaccine Bottle

HOW SUPPLIED

Anthrax Vaccine Adsorbed is supplied in 5 mL vials containing 10 doses each.

STORAGE

THIS PRODUCT SHOULD BE STORED AT 2 TO 8°C (35.6 to 46.4°F). Do not freeze. Do not use after the expiration date given on the package.

REFERENCES

1. Brachman, P.S., *et. al.* Field Evaluation of a Human Anthrax Vaccine. Amer. J. Pub. Health, *52*:632-645 (1962).
2. Editorial: Vaccine Against Anthrax. Brit. Med. J., *2*:717-718 (1965).
3. Advisory Committee for Immunization Practices. Adult Immunization, Morbidity and Mortality Report, *33*(15):33-34, 1984.
4. Committee on Immunization, *Guide for Adult Immunization, 1985*, Amer. Col. Physicians, Philadelphia, PA (1985).
5. Report of Committee on Infectious Diseases, 19th Edition, Amer. Acad. Pediatrics, Evanston, IL (1982).

These recommendations are prepared by the Michigan Department of Public Health only for the guidance of the physician. They do not replace the experience and judgment of the physician, who should be familiar with the recent pertinent medical literature before administering any biologic product.

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F-483 100/M 2/98 Rev. 2/98

ANTHRAX VACCINE ADSORBED

DESCRIPTION

Anthrax Vaccine Adsorbed is a sterile product made from filtrates of microaerophilic cultures of an avirulent, nonencapsulated strain of *Bacillus anthracis* which elaborates the protective antigen during the growth period. The cultures are grown in a synthetic liquid medium and the final product is prepared from the sterile filtered culture fluid. The potency of this product is confirmed according to the U.S. Food and Drug regulations (21 CFR 620.23): Additional Standards for Anthrax Vaccine Adsorbed. The final product contains no more than 2.4 mg aluminum hydroxide (equivalent to 0.83 mg aluminum) per 0.5 cc dose. Formaldehyde, in a final concentration not to exceed 0.02%, and benzethonium chloride, 0.0025%, are added as preservatives.

CLINICAL PHARMACOLOGY

Anthrax Vaccine Adsorbed is used in man to promote increased resistance to *Bacillus anthracis* by active immunization (1,2).

INDICATIONS AND USAGE

Immunization with Anthrax Vaccine Adsorbed is recommended for individuals who may come in contact with animal products such as hides, hair, or bones which come from anthrax endemic areas and may be contaminated with *Bacillus anthracis* spores; and for individuals engaged in diagnostic or investigational activities which may bring them into contact with *B. anthracis* spores (1-5). It is also recommended for high risk persons such as veterinarians and others handling potentially infected animals. Since the risk of exposure to anthrax infection in the general population is slight, routine immunization is not recommended.

If a person has not previously been immunized against anthrax, injection of this product following exposure to anthrax bacilli will not protect against infection.

CONTRAINDICATIONS

A history of a severe reaction to a previous dose of anthrax vaccine is a contraindication to immunization with this vaccine.

WARNINGS

1. Any acute respiratory disease or other active infection is generally considered to be adequate reason for deferring an injection.
2. Persons receiving cortico-steroid therapy or other agents which would tend to depress the immune response may not be adequately immunized with the dosage schedule recommended. If the therapy is short termed, immunization should be delayed. If the therapy is long termed, an extra dose of vaccine should be given a month or more after therapy is discontinued.

PRECAUTIONS

1. *General:* Epinephrine solution, 1:1000, should always be available for immediate use in case an anaphylactic reaction should occur, even though such reactions are rare.
2. *Carcinogenesis, Mutegenesis, Impairment of Fertility:* Studies have not been performed to ascertain whether Anthrax Vaccine Adsorbed has carcinogenic action, or any effect on fertility.
3. *Pregnancy:* PREGNANCY CATEGORY C. ANTHRAX VACCINE ADSORBED
   Animal reproduction studies have not been conducted with Anthrax Vaccine Adsorbed. It is also not known whether Anthrax Vaccine Adsorbed can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Anthrax Vaccine Adsorbed should be given to a pregnant woman only if clearly needed.
4. *Pediatric Use:* This antigen should be administered only to healthy men and women from 18 to 65 years of age because investigations to date have been conducted exclusively in that population.

ADVERSE REACTIONS

Local Reactions: Mild local reactions occur in approximately thirty per cent of recipients and consist of a small ring of erythema, 1-2 cm in diameter, plus slight local tenderness(1). This reaction usually occurs within 24 hours and begins to subside by 48 hours. Occasionally, the erythema increases to 3 to 5 cm in diameter. Local reactions tend to increase in severity by the 5th injection and then may decrease in severity with subsequent doses.

Moderate local reactions which occur in 4 per cent of recipients of a second injection are defined by an inflammatory reaction greater than 5 cm diameter. These may be pruritic. Subcutaneous nodules may occur at the injection site and persist for several weeks in a few persons. A moderate local reaction can occur if the vaccine is given to anyone with a past history of anthrax infection.

More severe local reactions are less frequent and consist of extensive edema of the forearm in addition to the local inflammatory reaction.

All local reactions have been reversible.

Systemic Reactions: Systemic reactions which occur in fewer than 0.2 per cent of recipients have been characterized by malaise and lassitude. Chills and fever have been reported in only a few cases. In such instances, immunization should be discontinued.

DOSAGE AND ADMINISTRATION

Dosage

Primary immunization consists of three subcutaneous injections, 0.5 mL each, given 2 weeks apart followed by three additional subcutaneous injections, 0.5 mL each, given at 6, 12 and 18 months(1).

If immunity is to be maintained, subsequent booster injections of 0.5 mL of anthrax vaccine at one year intervals are recommended.

Administration

1. Use a separate sterile needle and syringe for each patient to avoid transmission of viral hepatitis and other infectious agents.
2. Shake the bottle thoroughly to ensure that the suspension is homogeneous during withdrawal. The rubber stopper should be treated with an appropriate disinfectant and allowed to dry before inserting the needle.
3. This preparation must be given subcutaneously after cleansing the overlying skin with an antiseptic.
4. Follow the usual precautions to avoid intravenous injection.
5. After withdrawing the needle, the injection site may be massaged briefly and gently to promote dispersal of the vaccine.
6. The same site should not be used for more than one injection of this vaccine.
7. Do not syringe-mix with any other product.
8. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Mr. SHAYS. OK. And then, now, I'm sorry——

Dr. ZOON. And so in that case, the package insert defines some of the high risk population and makes reference to others, but it discusses the issues surrounding the general population, where it is not recommended.

Mr. SHAYS. OK. What is left on the table from the GAO's statement is that basically there has been only one study of human beings. And, one, I need to know if that is in fact true. I think, Dr. Myers, you mentioned a study of 400, which I am not really familiar with, but I don't think that was a study related to licensing.

Dr. MYERS. That is correct, sir.

Mr. SHAYS. OK. But what is—all three of you, General Cain as well—what is your reaction to the fact that basically there is one study but that study involved a wool mill that we don't know, as he said, the environment, we don't know the exposure level of anthrax, the disease, in that environment.

One, do you concur with that?

Dr. Zoon first.

Dr. ZOON. I am sorry, can you repeat the question, sir?

Mr. SHAYS. Yes. I am going to start with you, and I am just going to let Dr. Myers respond.

I want you to respond to the GAO's report. I mean, frankly, if we leave it on the table as it is, it is a pretty strong indictment against the—and I don't think it was intended to be as strong as it was—but in the end, with their response to the questions, they are basically saying they had a study that took place in the 1950's, reported in the early 1960's, and, the Brachman study, that basically had some who were, had the vaccine and some who didn't, and made certain conclusions.

But they made conclusions without knowing the environment and without knowing the exposure to disease. It could, in fact, have been very little exposure. So I just need to let you respond to that.

Dr. ZOON. OK. I would like to just review some of the data that we have. I can't respond to the GAO report because we haven't seen the report. We have just heard this morning, their testimony. We had a meeting prior where some issues were——

Mr. SHAYS. But I want you to respond to their testimony. Let's just respond to their testimony. You have heard them.

Dr. ZOON. OK. I would say there are the Brachman studies and then there are the CDC studies, which are the major studies that we are looking at. In the Brachman study, it wasn't——

Mr. SHAYS. Was that the only one relating to humans?

Dr. ZOON. No. The CDC study and the Brachman study both involved humans.

Mr. SHAYS. OK. And the CDC study was when?

Dr. ZOON. The CDC study began in 1966 and lasted until 19—actually was followed out through probably close to 1974 with some of the followup.

Mr. SHAYS. OK. Why don't you talk about the Brachman study first?

Dr. ZOON. The Brachman study was a controlled field study. It was single-blinded, means that the individuals who received the vaccine and or placebo, did not know which ones they were getting.

And then there was also an observational group that had no treatment.

As was stated, there are four mills in the Northeast in which these studies were done. The incident rate of anthrax back then was about 1.2 cases per 100 employees. So the trial was conducted in that environment.

In looking at the cases of the data from the Brachman study, a number of things were revealed. And as a result of the study—when they looked at the—there were 26 cases of anthrax reported. And, of those, 21 were cutaneous cases; 15 of those cases were in the placebo; one, as stated by the GAO, was in the vaccinated group, and two were in the partially vaccinated group, and three were in the observational group.

Mr. SHAYS. What is the observational group?

Dr. ZOON. The observational group is the group that received no treatment.

Mr. SHAYS. OK. But those with placebo received no treatment but thought they were.

Dr. ZOON. Right. That is correct.

Mr. SHAYS. OK.

Dr. ZOON. So those studies were done in the controlled studies. They monitored adverse events as well as the efficacy to look at the safety and efficacy of the vaccine.

In the CDC study, this——

Mr. SHAYS. Before you go into that, you didn't answer the question.

Dr. ZOON. Well, I am going through the data. I think that is important.

Mr. SHAYS. No. I don't want you to go through the data. I want you now to react to the fact that is it true and is that important that the, we don't know the environment, we don't know the level of disease that they were exposed to. Obviously you can't control——

Dr. ZOON. I think there is a little bit of a difference of opinion on that. Our review of the information in this area, suggests that there was environmental monitoring of some—of a certain degree going on. In fact, Dr. Brachman had published a report on the mill and, regarding an inhalation anthrax outbreak, and we would be happy to submit that paper to the record.

[NOTE.—The information referred to is held in the subcommittee files.]

Dr. ZOON. And in those cases they believe they were looking at what were in the environment in those cases.

Mr. SHAYS. Well, do they know the level of exposure? They don't. I mean, I think I can say that and I am not even a doctor.

Dr. ZOON. Right. I am just telling you what the information is that is available in the literature, and I think while one can never guarantee what the exposure rate is, there was some information and data regarding what was in the environment, and, in fact, those were published.

Mr. SHAYS. Then how do you react to Mr. Chan, I think it was him saying that he spoke with Mr. Brachman—Dr. Brachman—and that the doctor acknowledged that they didn't know the environment?

Dr. ZOON. Yes. I am just saying what information we have available, Mr. Chairman.

Mr. SHAYS. OK. Well you have information that that is what he said.

Dr. ZOON. No. I said that is what was reported in the literature.

Mr. SHAYS. If you found that the environment—that can't assess the environment, does that make you look at the study differently?

Dr. ZOON. I think it would depend on the context of the whole—one of the things when these studies were done, we do know what the case rate was for that environment at that time as a gestalt, which was about 1.2 cases per hundred employees. We also know that——

Mr. SHAYS. Dr. Zoon, you don't know at what level they were exposed. You don't know that.

Dr. ZOON. I personally don't know that. Yes.

Mr. SHAYS. No. But aren't you being a little disingenuous, with all due respect. How would they have determined exposure in 1950?

Dr. ZOON. You have a case rate——

Mr. SHAYS. Is there someone else who can answer the question? I just want it on the record.

It seems to me, what you would have said is, no, we don't know. And it would seem to me that if you don't know what the environment is, then the study isn't as valid. That would seem to me the straightforward answer to the question.

And I don't know, are we playing a game here?

General CAIN. Could I comment?

Mr. SHAYS. Sure.

General CAIN. I think one of the points I have incorrect, and somebody can correct me. It is impossible to do human efficacy testing right now because you have to expose a human to the anthrax virus.

Mr. SHAYS. I am not arguing that we should do that. I am just taking some question as to why we could claim the study should satisfy, because that is what DOD did, that the study should satisfy us because we did it with humans and then when we look at the study in, hopefully, a relatively intelligent way, we raise questions.

And then there should be answers to them.

Dr. MYERS. Mr. Chairman?

Mr. SHAYS. Yes.

Dr. MYERS. Could I comment from a manufacturer's perspective?

Mr. SHAYS. Sure.

Dr. MYERS. Let me give whooping cough as an example. Many times, you don't know——

Mr. SHAYS. Before you give another example, I am just interested in this. And then believe me, you can give—you can say that is true but it is true in a lot of other cases. I just want to establish——

Dr. MYERS. That's true, but it is true in a lot of other cases.

Mr. SHAYS. No, but is it true? Is it true that we didn't know the environment? I just want to establish that point and then we will get on to the next.

Dr. ZOON. Yes.

Dr. MYERS. We knew that goat hair was contaminated with anthrax spores.

Mr. SHAYS. At what level?

Dr. MYERS. I am not sure we knew that level.

Mr. SHAYS. OK. That is fair. And it may——

Dr. ZOON. Right. But——

General CAIN. For me, as a deployed soldier, if I am deployed to an area, and I do know that we have no detection capability to detect or warn at this time, which will tell you to put your mask on. There is nothing out there to tell you. And if I know that in that area there are anthrax spores, the only recourse I have is to have an anthrax vaccine shot.

Mr. SHAYS. Well, I know, that would be the way you see it, but with all due respect, we need to know that this shot will protect at a level that you would be exposed at. We would need to know that.

And it may have been that in this case that the levels were low and, therefore, this vaccine is effective for low levels, but maybe not at the levels, sir, that you would encounter in warfare.

Dr. Zoon, Dr. Myers I am going to let you——

Dr. ZOON. I just wanted to reaffirm that we did have the historical data on the number of cases of anthrax that the employees got at the mills, and that was the historical data base that in which we were comparing the frequency of anthrax. So, while we don't have the exact levels that were in each bale, and the technology probably didn't even exist for that then, we did have the number of cases——

Mr. SHAYS. Let me just interrupt you. That is fine. I am not saying that they didn't do their job. I am just saying then let's put it on the record. That's all.

Dr. ZOON. Yes, but we do have the information, sir, that——

Mr. SHAYS. You have historic data: how many and how much.

Dr. ZOON. Yes. We have historic data that there are 1.2 cases of anthrax per 100 employees.

Mr. HALLORAN. Cutaneous?

Dr. ZOON. I don't have the breakdown, but most of them would be cutaneous.

Mr. SHAYS. Dr. Myers, you have been very patient. Thank you. And I am happy that—when you talked about rabies, it got my interest. So there may be other things that you want to share.

Dr. MYERS. In doing clinical trials for efficacy, I, as a student of those, cannot speak to environmental contamination versus case rate in isolation as a single, as a single item. There are many avenues for the determination of the amount of exposure. A very commonly accepted avenue is the case rate in a population. And that is what was done in this case.

And I was only going to point out, sir, that with whooping cough, we don't know how many organisms our babies breathe when we do tests for whooping cough vaccines. We simply understand the incidence of the disease in the population being studied.

Mr. SHAYS. Right. The only difference I would say to you, is that we are ordering people to take a vaccine who may be at potential high risk if an enemy exposes them to this disease, but we don't

know at what level they would expose us. And I don't think we have any tests that would be able to answer that question.

So I realize we are just——

Dr. MYERS. I appreciate that point. I think it is a matter or policy, and it is probably central to the issue: Should vaccination be mandatory? And I am not going to offer an opinion on that other than to say I believe the vaccine works. And if people are exposed to anthrax by an airborne route, and they are not vaccinated, 9 out of 10 of them will probably die. Some will die even if they are given antibiotic for long-term. On the other hand, if they are vaccinated, I am as confident as we will ever be at this time that most people will survive.

Mr. SHAYS. Let me, before going to John Tierney, would you just elaborate on rabies. You had mentioned it and I interrupted you.

Dr. MYERS. Oh, I had mentioned rabies in that there seems to be some parallels, in fact. If you don't take rabies vaccine after exposure, whether the animal was known rabid or not, and you find out later that the animal was rabid, you will be dead. The disease occurs at a very low rate. As I pointed out in the testimony, one or two deaths, perhaps four deaths, a year. So the contention by the GAO that the disease occurs at such a low rate, therefore you can't tell if it is effective, I guess could be alleged for rabies vaccine, and probably a couple other vaccines as well.

So it seems that, as I listened to the GAO testimony, that the GAO was striving to set apart anthrax vaccine without placing it in context with all other licensed vaccines, with respect to manufacturing, with respect to clinical trials, with respect to post-licensure surveillance, and with respect to the status of the vaccine today.

And last, I would just like to point out that as we grapple with the mandatory immunization issue or policy issue, if you will, for anthrax vaccine, we should also consider the 9 or 10 other vaccines that are given to recruits during basic training and ask the question should those be mandatory as well. And really drill down to the reasons we think they should be mandatory.

There will probably be that there is a reasonable belief that at some point in deployment, or before deployment even, these people will be at risk to diseases that these vaccines protect from. If they get sick, their troop efficiency will be lowered, their unit strength will be lowered. So we vaccinate for hepatitis B for all recruits. These sorts of things.

And I just want to make sure that when we think about anthrax vaccine, we think about it in the context of all vaccines.

Mr. SHAYS. Yes, the only caveat I would say to you is, sir, that—and this is what we will find out—is the vaccines that our soldiers have that aren't anthrax, have had a history of wide use before they became mandatory?

And this is not a subtle difference. And there is wide use now; whereas, before there wasn't.

Dr. MYERS. Could I just make one final comment about that? Most vaccines are licensed on clinical safety trials that aren't that different in magnitude than those done in the 1960's. And it is only after license, and it begins to be used in widespread use that you

may or may not detect those kinds of events that occur at the level of 1 in 1 million or 1 in 3 million.

Now, you are never going to get there with a vaccine if it is never in widespread use, and I'll go back to rabies again. Maybe there are 15,000 post-exposure treatments a year. So you might be looking at 15,000 people. But these people believe strongly in that. Just like anthrax, if you are exposed, you die if you don't get vaccine, just like that. They believe that the benefit of taking five doses, not over a year, but five doses over a 28-day period, day 1, 3, 7, 14, and 21 or 28, far outweigh the risks of developing a lethal disease.

Mr. SHAYS. That is helpful. Thank you. Mr. Tierney.

Mr. TIERNEY. Thank you. I only have one. Dr. Myers, is it—am I accurate in thinking the Department of Defense is now financing the renovation of some of your facilities?

Dr. MYERS. The DOD may want to answer that directly, but the financing of the renovation is largely funded by contractual funds from the DOD.

Mr. TIERNEY. And can you tell me why that is? Why they are funding a private corporate facility?

Dr. MYERS. Well, we are a private corporate facility, but we are not selling hardly any anthrax vaccine in the private sector. Our facility capability for making anthrax vaccine is almost entirely reliant on DOD funds. We are a 6-month-old company. As we move into the private sector, we believe that there are possibilities not only for defense vaccines but our other products as well. And our goal is to become entirely non-reliant on DOD funding for the defense vaccine sector.

In order to do that, we must be healthy.

Mr. TIERNEY. So you are telling me that you think Department of Defense moneys are going into your facilities in order to help you get healthy. I mean, is that——

Dr. MYERS. As long as these moneys are going in and there was what is called, you may be familiar with this term, GFE, Government furnished equipment, there are strict regulations and constraints on the use of that equipment, such that we can't take Government equipment and make, chug out vaccine, if you will, and sell it to the private sector. That is just not legal in this country with GFE.

Mr. TIERNEY. Doctor, you are the chief operating officer of the corporation. Are you also a member of the board of directors?

Dr. MYERS. Yes I am, sir.

Mr. TIERNEY. And are you one of the principals of the corporation?

Dr. MYERS. Will you define principal?

Mr. TIERNEY. Are you one of the owners of the shares of stock in the corporation?

Dr. MYERS. I am a minority shareholder of a company called Michigan Biologic Products Inc. And Michigan Biologic Products Inc. is a minority shareholder of BioPort.

Mr. TIERNEY. Thank you.

General CAIN. Could I comment on that, on DOD perspective?

Mr. SHAYS. Go ahead.

General CAIN. Given that BioPort is the only source available for the anthrax vaccine, it was imperative that DOD maintain their vi-

ability. The SECDEF immunization program, FDA inspections, and privatization mandated that DOD put forth an aggressive effort to maintain industrial capability. In addition to the routine program management functions, DOD, on a short-term basis, is providing resources to assist the manufacturer in achieving full compliance with FDA regulatory requirements.

A few examples include a transition team that assists in development of their strategic plan, a regulatory specialist to oversee the FDA compliance documentation, and a construction engineer that orchestrated renovation of the production line.

As a result of DOD support, there has been marked improvement in the facility, and I am confident that in the near future BioPort will be able to function without our assistance.

Mr. TIERNEY. Thank you.

Mr. SHAYS. Let me ask one point, Dr. Myers, that you were making that I found very interesting. You were suggesting that people had adverse effects in another case where they didn't even have—they were placebos or something?

Dr. MYERS. They were placebos. That is correct.

Mr. SHAYS. It is for the record, and we would look at this. So I just want you to be as precise as possible about it. What are you referring to?

Dr. MYERS. The product insert is public knowledge and I would be happy to put it——

Mr. SHAYS. It's not public knowledge to me, so just put it on the record again.

Dr. MYERS. Yes. In the study, approximately 400 individuals were given three doses of a vaccine.

Mr. SHAYS. Right.

Dr. MYERS. And these individuals were actively solicited for the identification of reactions: Did you have a sore arm? Did you have redness? They do this with a diary or a nurse interview, either in person or by telephone. And you find that even for placebo preparation, for the reason I pointed out, you are injecting something with a needle, you are breaking nerve fibers, you are expanding interconnective—connective tissue within those nerve fibers with that dose.

Mr. SHAYS. You know, when they give us a shot, they never describe it that way. [Laughter.]

Dr. MYERS. I apologize for the detail. [Laughter.]

Mr. SHAYS. But the bottom line to it is, that what?

Dr. MYERS. The bottom line to it is that even with placebo preparations, you have local reactions that are as much as 60 percent. And with general reactions, when asked did you have headache, did you have fatigue, did you have fever, you find that those reaction rates are very high as well, even for preparations that don't contain active vaccine ingredients, the placebo.

Mr. SHAYS. That would seem to—sorry to interrupt you. That would seem to speak to the issue of the monitoring, the active versus passive monitoring. So I would infer that you are suggesting that if someone was—when the Pittman study in 1997 was done and 29 percent said they had a mild reaction and others had more, 14 percent had a more severe, you might—and yet with DOD, there really is very little response, you would suggest that is just the na-

ture of the shot. And if you asked someone right after a shot, they would respond that way.

Dr. MYERS. Yes. And I think there is a further point that I believe in. And that is, just like I know I had a sore arm, because you get a sore arm when you have a vaccine shot into your arm with a needle, that most of the military personnel now understand that. Goodness, they were given vaccines, many vaccines, as basic recruits. They know what an arm feels like after a vaccine, not just anthrax vaccine, but any vaccine.

So probably, it is because they understand the nature of inflammation for a vaccine that is injected that this passive surveillance is so low, not because it is being hidden or they care, or there is a serious problem, it is just that they understand. They are used to getting more shots in the army in basic training than most adults are over several decades. It is no big deal.

Mr. SHAYS. OK. I knew that needed to be put on the record since we have the other issue, and I am happy to have it put on the record. Let me just ask you, General Cain, and then I think we will go to the next panel. And then I will certainly ask any of you to make comments.

Mr. Taylor, I would also say that sometimes someone who sits and just listens to questions ends up with the best answers in the end. [Laughter.]

And so I am going to invite you to make any comment you want at the end as well.

This is to you General Cain, how many lots of anthrax vaccine are awaiting the completion of the supplemental testing?

General CAIN. What was that again?

Mr. SHAYS. How many lots of anthrax vaccine are awaiting the completion of the supplemental testing? If that is an answer——

General CAIN. Eight from 31. So——

Mr. SHAYS. Eight are finished?

General CAIN. Eight are finished.

Mr. SHAYS. Right. And is that a question that you can answer for us, Dr. Myers?

Dr. MYERS. I can answer it.

Mr. SHAYS. OK. You have that. OK. And I also want to know what went wrong with the potency tests. Is that something you want to answer, Dr. Myers?

Dr. MYERS. I can.

Mr. SHAYS. And then, general, when you are ready, you can answer the first question.

Are you prepared to answer that one?

Dr. MYERS. Which one?

Mr. SHAYS. The question is what went wrong with the potency tests. Can you answer that?

Dr. MYERS. Yes.

Mr. SHAYS. OK. Answer it please.

Dr. MYERS. There was an increased level of testing.

Mr. SHAYS. Speak slowly though.

Dr. MYERS. That was required as a result—[laughter as Dr. Myers slows his speech.]

I am having a problem. I guess I am just emphatic. I will try to slow down.

Mr. SHAYS. No. But this is to your advantage, isn't it? To put it on the record?

Dr. MYERS. Yes.

Mr. SHAYS. OK.

Dr. MYERS. During the increased level of testing in the spring of 1998, we found inconsistent results in control vaccine values across several tests with several different dilutions of vaccine. It is a test you know something is not behaving properly when your control vaccine is not behaving properly.

We suspended potency testing, first in the spring of 1998 for a short period of time, and then in the fall of 1998 for a longer period of time while we stepped back to design and evaluate possible sources for the inconsistent results in the potency tests. Those studies have pretty well been completed now. The potency test is behaving again as it should be. And we have assignable causes for the erratic results previously experienced.

Mr. SHAYS. Thank you. So the first question I wanted to ask, how many lots of anthrax vaccine are awaiting the completion of supplementary testing? The other question I wanted to ask is, are lots produced under conditions FDA found in violation being released without supplemental testing?

So who can answer that question?

General CAIN. There are 24, 24 lots right now, that are awaiting supplemental testing.

Mr. SHAYS. OK.

General CAIN. Most of those are, in fact, for potency. The other three, serial D purity, and has been completed in safety. There are three lots that have been quarantined voluntarily by BioPort themselves, 3 of those 24.

Mr. SHAYS. So this last question? The question is, are lots produced under conditions FDA found in violation being released without supplemental testing?

General CAIN. No.

Mr. SHAYS. Your answer is no?

General CAIN. That is no.

Mr. SHAYS. OK. Is that consistent with everybody else's position? Who would be qualified to answer this besides you, General Cain? Dr. Zoon.

Dr. ZOON. Well, once they have passed the lot release testing and are available and have met all the criteria, they are available for distribution.

Mr. SHAYS. So, in other words, your initial concern, once it is dealt with, then they are released?

Dr. ZOON. Yes. As long as there are no other, as was reported earlier, there were some lots in quarantine. And those are currently in quarantine because of some observations that we had on inspection. Those observations that we had on inspection need to be investigated by BioPort. Depending on the outcome of those investigations, those lots may or may not be distributed.

Mr. SHAYS. And then they are reviewed by you before a decision is made?

Dr. ZOON. Yes.

Mr. SHAYS. OK. Any other final——

Dr. MYERS. If I might just add a small point to clarify. When the vaccine is released by the FDA, the DOD pays for the vaccine. So they own it at that point. And we store it onsite for them. The DOD has requested for their vaccine that they already own that supplemental testing be done for 32 lots that were in a stockpile at a point in time. And I just wanted to clarify that is not an activity that is at all directed by the FDA. It is the DOD.

Mr. SHAYS. OK. Got you. Any other comments before we get to the next panel? Mr. Taylor. Dr. Zoon, we will let you go.

Dr. ZOON. Yes, Mr. Chairman, I just want to correct one fact that, for the record, that FDA did do inspections for anthrax prior to 1996. I think Dr. Myers alluded to one, but there were a number of inspections for the anthrax.

Mr. SHAYS. On the site seen all parts of the production—I understand that it is part of the building, but it is certainly contained part of the building. Correct?

Dr. ZOON. Right. We were in the production facility several times. Often, though, there was an active manufacturing going on when we were there, but we were actually in the facilities where the anthrax was manufactured, being manufactured.

Mr. SHAYS. The statistics in the beginning, Dr. Myers, though, you were talking about the FDA being there, not necessarily just for anthrax. Right? We are focusing on anthrax.

Dr. MYERS. Well, what I pointed out in my oral testimony was that in January 1993, not so very long ago, the FDA inspected the second floor of the building that is the anthrax vaccine sublot manufacturing area where fermentation, bacterial culture, and purification is done. That is the isolated part of the facility. They were there, January 1993, because of facility renovation that had recently been completed, which was approved in July 1993.

Mr. SHAYS. And then——

Dr. MYERS. And I am surprised that the GAO didn't have that report.

Mr. SHAYS. OK, but from 1993 to 1996, did the FDA get into the site?

Dr. MYERS. Between 1993 and 1996, did the FDA go to the second floor of this building where the sublots are made?

Mr. SHAYS. Yes.

Dr. MYERS. To my knowledge, they did not during that 3-year period.

Mr. SHAYS. Right. You know, that shouldn't be. Right? I mean——

Dr. MYERS. We, as I said, have received 49 inspections since 19—or at least 48 inspections since 1969. Up until very recently, it has been the agency's position to do one inspection at least once every 2 years for each of three areas: bacterial vaccines and toxoids, viral vaccines, and plasma derivatives.

We have all three types of manufacturing operations; therefore, it could be expected that we would have one and a half or so inspections per year.

Dr. ZOON. If I could just clarify one point, and make one other point. We have had inspectors in there. We have inspectors who were immunized with anthrax vaccine to do the inspection. And they were in there in 1990, looking at it, during the time of Desert

Storm, and also in 1993 to look at both the records and looking at some of the areas in the site.

So I just wanted to make sure that the record was corrected.

Mr. SHAYS. Would you also make sure the record—when did the Army—excuse me, when did the DOD make a determination to have a mandatory policy on anthrax and engage the plant, whether it was mandatory or not? When did that take place? General Cain?

General CAIN. I believe in December 1997.

Mr. SHAYS. And since then, how many times has the plant been inspected?

Dr. ZOON. I didn't hear his comment.

Mr. SHAYS. Since 1997, December 1997.

Dr. ZOON. Oh, I can give you those numbers. Do you have those, John?

Mr. TAYLOR. Yes. The facility has been inspected twice, in February 1998 and in October 1998.

Mr. SHAYS. And, it is not operating now. So——

Mr. TAYLOR. That is correct. It is not operating right now; however, I believe as Dr. Myers alluded to, we will re-inspect the facility, and once they are up and running, they are right now producing consistency lots with the hope that they will resume full production by the end of the year. And obviously, we will go in and make sure that they are producing the vaccine in compliance with our regulations.

Mr. SHAYS. Thank you. Is there anything else that any of you would like to say?

Mr. TAYLOR. Yes, Mr. Chairman, I want to clarify, or address one point that you made after the break. FDA is obviously cognizant and sensitive to the criticism that was leveled against us in regards to the Gulf war. And I can assure you that we are regulating BioPort and the anthrax vaccine the same way we would regulate any other manufacturer. So I just wanted to address that point.

Mr. SHAYS. Thank you.

General, I asked you to do—indemnification. I am trying to think of the question that I asked before I left.

General CAIN. Yes, I think, why we have a blanket indemnification of BioPort. Two reasons. One, if we had not, it would have added 50 more cents per dose for the vaccines.

Mr. SHAYS. Right.

General CAIN. So, from an economic standpoint, it was smart to do it that way. But more importantly, 2 years ago, when we submitted out interest from industry, not a single industry—manufacturer—wanted to get involved unless there were an indemnification clause.

Mr. SHAYS. OK. Fair enough. Was there another question that I asked someone else to check out before the break or was that the only question?

OK. I think that was it. Thank you very much. And——

Did you have something you wanted to say, Dr. Zoon. I am sorry.

Dr. ZOON. Yes. I just wanted to assure the chairman that, as FDA, we believe this vaccine is safe and effective for high-risk individuals, but we are committed to being vigilant, in both the review of activities surrounding this vaccine, and vigilant on monitoring

the adverse event reports. And we will continue to do so to the best job we can.

Mr. SHAYS. Thank you very much. Anything else?

Dr. MYERS. I just wanted to say that I applaud you and your committee for holding these hearings and for allowing me to be here today to speak as the manufacturer. I think it is very important that you listen to the next panel. I think it is very important that we recognize that there are people who suffered ill effects from the Gulf war. I just want to say that I hope that we concentrate on diagnosing their diseases and adequately funding their care, and that we make certain that we not dwell too long because it would be a disservice to them on the issue of anthrax vaccine because I truly believe it is unfounded.

Mr. SHAYS. OK. Thank you very much. And I will assure you that you will always have an opportunity if you hear of a hearing and you want to come back and put something on the record, you are more than welcome. [Laughter.]

Thank you very much.

Dr. MYERS. Thank you, Mr. Chairman.

Mr. SHAYS. This time, I am going to ask Dr. Meryl Nass, physician, Freeport, ME; Ms. Randi J. Martin-Allaire, Eaton Rapids, MI; Ms. Roberta Groll, Battle Creek, MI; Mr. David Churchill, Albion, MI; and Mr. Michael Shepard, Savannah, GA, ask them all to come forward and ask them to remain standing so I can swear them in.

It goes Nass, Martin-Allaire, Groll, Churchill, and Shepard.

[Witnesses sworn.]

Mr. SHAYS. Note for the record that everyone has responded in the affirmative, and one of the advantages of the last panel is—the disadvantage is you have to wait, the advantage is you get to hear other testimony. And I am happy to have you summarize your testimony and speak to the questions that were asked and the answers that were given. Or you can give your testimony, and we are really grateful that you are here. So thank you.

Dr. Nass, we will start off with you. And we will get the clock. One final note, Jonathan is leaving and is going to work for me in Connecticut. He has done a tremendous job for me, but I think that you probably left yesterday mentally with all of these distractions today. [Laughter.]

Dr. Nass.

STATEMENTS OF MERYL NASS, PHYSICIAN, FREEPORT, ME; RANDI J. MARTIN-ALLAIRE, EATON RAPIDS, MI; ROBERTA GROLL, BATTLE CREEK, MI; DAVID CHURCHILL, BATTLE CREEK, MI; AND MICHAEL SHEPARD, SAVANNAH, GA

Dr. NASS. Thank you. To start off, I wanted to clarify some of the statements made earlier about safety. We have several studies that were presented that looked at adverse effects. But those studies only lasted from 7 days to 30 days following vaccinations. So what we had were short-term effects only. And there is a significant amount of data on that. But it really tells us nothing about what we are interested in, which is, is there chronic illness due to anthrax vaccine?

Now, although none of the studies looked into that, one of them, the IND study, which was just done and submitted by Dr. Myers

to FDA, would have been an ideal study to look into long-term effects because they collected blood from service members on at least an every 2-month basis for a period of 2 years, but only inquired about adverse effects over the first 30 days of that study.

Now, when you are wondering what exists that we can look at to try and determine if there is a problem with the vaccine over the long-term, one looks to several cohorts that might be useful. The first, of course, is the workers at Fort Detrick for whom this vaccine was in fact originally developed. There is some obfuscation about this.

But two workers at Fort Detrick died in the 1950's from inhalation anthrax. And it was determined that if Fort Detrick were to continue to do work on offensive biological weapons, they would need to vaccinate their employees so they wouldn't lose them to the diseases they were studying.

And it was for that purpose—this was a high-risk group subject to inhalation anthrax—it was not in any way developed for mill workers or livestock workers who were used as an experimental study group and who were not given the vaccine subsequently. And there was no need for them to have it because they only developed cutaneous anthrax, which is easily treatable with a zero mortality rate with oral antibiotics.

When you look at the Detrick workers, there are actually three studies in existence. These workers were multiply immunized with a number of vaccines. The studies were published in 1958, 1965, I believe, and 1974. They suggest that there were, in fact, some chemical differences in the blood of multiple vaccinees as opposed to controls, suggest that there were some people who developed cancer of the immune system that might have been related to multiple vaccination. But the actual effects of the vaccines were not clear.

Now in the subsequent 25 years, nothing has been published on these employees at Detrick. I don't know whether the Army, for whom they have worked, has done any studies, but this would be very useful to find out.

Another group, obviously, is the Gulf war veterans and the Gulf-era veterans who were non-deployed but vaccinated and whose only exposure was to vaccines, not necessarily only the anthrax vaccine.

No studies have been done in the United States and published that look at the relationship between anthrax vaccine or multiple bio-warfares vaccines and subsequent Gulf war illness. Now there is data that could be examined to look into this question.

I know Han Kang of the VA has this data. He told me about 4 or 5 months ago that he would try to do the correlations but has told me since that he hasn't had the time.

In England, one study has been published, Catherine Unwin, is the first author, and that did show a statistically significant relationship between vaccination for anthrax alone and multiple vaccinations, and then subsequently onset of Gulf war illness. This was British veterans. It was a study based on recall. The British veterans apparently used some British-made anthrax vaccine, and some United States-made.

We really don't—I don't know how much of which they used, but my suspicion is that at least half of what was administered in Eng-

land was the American vaccine. And I think that may be supported by some statements that were made earlier, that suggest that 268,000 doses of United States anthrax vaccine were available at the time of the Gulf war.

Certainly studies that look into this for U.S. veterans are critical. One of the reasons we don't have them is the issue of missing records. I have provided a declassified document that suggests that the Army, in fact, does have some immunization records that have been classified, that might help us to relate anthrax vaccine and Gulf illness.

But so far, no one that I know of has access to this data.

Seventh-Day Adventists, in fact, have been asked to participate in a recent study, out of Fort Detrick again. These folks were vaccinated up until the early 1970's and, as far as I know, they were not looked at since. But late last year, in September and October, they were asked to now provide information about any symptoms or disease they may have been diagnosed with in the interim. And when one looks at the survey, they are being asked about symptoms of Gulf war illness.

So it is very interesting. I guess the military hasn't figured out yet whether the vaccine may contribute to Gulf war illness. As far as I know, they have not publicized the existence of this study, but they are interested in finding out.

Is a new epidemic emerging from the current round of vaccinations? I am sorry to say that this does seem to be the case. Both the features of the illnesses that have been reported to me, and the official military response to these illnesses, echo the plight of ill Gulf war vets who remain today without a defined illness and without meaningful approaches to treatment.

Another issue I would like to just touch on is that of legal questions with regard to this vaccine. One of those is whether the vaccine, the order to vaccinate is a lawful order. And I suggest that it may not be, based on the preconditions that Secretary Cohen stipulated at the time he ordered the anthrax vaccine immunization program, several of which do not appear to have been met.

Second, in my looking at the FDA inspection reports between 1993 and 1998, I see the anthrax line only mentioned in the 1998 report. It wasn't mentioned earlier. And the late 1996 report suggests that the Army was performing the anthrax inspections and, therefore, FDA did not have the responsibility to do so. I am not sure that this is supported by the law, which requires FDA to investigate at least every 2 years, and more often if there are problems. And certainly the problems have been well documented at MBPI, now BioPort.

The third and most interesting legal issue is that of whether the currently licensed anthrax vaccine is the only anthrax vaccine to have been given to service members, and if in fact other vaccines may have contributed to illness. An unlicensed vaccine can only be given to a service member if informed consent is obtained. And I have not met a service member or Gulf war vet who tells me that informed consent was sought from them at the time they were vaccinated.

However, this article, written in 1990 by Ernest Takefuji and Philip Russell, who were both administrators at Fort Detrick, sug-

gests that in fact unlicensed anthrax vaccines were administered to service members. And a letter inquiring about this to DOD last year that Mark Zaid and Pat Eddington wrote got an answer that, in fact, the anthrax vaccine mentioned here is not the same anthrax vaccine as the licensed vaccine that service members are currently receiving, suggesting that at least one other has been given.

Dr. Zoon talked about the VAERS reporting and how this produces information about adverse effects suffered shortly after vaccination. I would submit that this is the weakness of the VAERS system. What one really needs is active surveillance over a long period, of a significant enough number of vaccinees to find out whether there is chronic illness. It just doesn't matter what you find out in the first week or the first 30 days if people get over it.

And we are not doing proper surveillance of vaccines if this is all we focus on.

I provided an addendum to my testimony today which asks the general question, is vaccination a good defense against biological warfare? Even if the vaccine were 100 percent effective against all strains of anthrax, which nobody claims, it still would be a porous defense because an enemy would simply choose another biological agent, one that occurs naturally or one created using genetic engineering.

William Patrick, who formerly headed the offensive program at Fort Detrick, had this to say, "It takes 18 months to develop a weapons-grade biological agent and 10 more years to develop a good vaccine against it."

I submit that it is impossible to produce vaccines that will keep up with the rate of development of new bio-warfare agents, and that vaccines should clearly not be the first line of defense in this or any case against the threat of biological warfare.

Despite the fact that vaccines are unlikely to provide this defense——

Mr. SHAYS. We need to get you to——

Dr. NASS. Thank you. May I have 1 minute? Thanks.

Congress appropriated $322 million in 1997 for the Joint Vaccine Acquisition Program. Its goals are to develop new vaccines for more than 10 known bio-warfare pathogens and administer the vaccine to all U.S. service members. The anthrax program can be regarded as the introduction to this much larger and less well known program.

The FDA has publicly stated that it intends to expedite licensing for these new bio-warfare vaccines.

Are we already embarked on a misadventure that will dwarf the anthrax vaccine program in cost, futility, and medical repercussions? What will it take to call a halt to the current round of vaccinations and, of at least equal importance, what will it take to investigate these illnesses and develop treatment protocols that are serious about getting answers and providing care?

Thank you.

[The prepared statement of Dr. Nass follows:]

Congressman Shays, members of the Committee, thank you for inviting me here today to testify about anthrax vaccinations. My goal in this hearing is to provide you with a different prospective than was provided by the Department of Defense physicians and spokesperson regarding the evidence for safety, efficacy, necessity, and possibly even legality, of the anthrax vaccine immunization program.

I would also like to briefly revisit the subject of vaccinations and their possible role in Gulf War Illness. Finally, I hope to leave you with the question of whether illnesses suffered by servicemembers who have received the vaccine in the last 12 months resemble the illnesses suffered by servicemembers following the Gulf War.

Is the vaccine necessary?

At the last hearing on the anthrax vaccine immunization program, Congressman Shays asked, "Why now?" He was told that the threat has recently increased. Has it?

"We have knowledge that as many as ten nations either have or are suspected to have the capability of chemical and biologic warfare.

> Susan Bailey, M.D., Assistant Secretary of Defense for Health Affairs, August 14, 1998, D.O.D. news briefing

"We have seen the number of nations possessing biological agents increase from four to ten that we know of – there are probably more."

> Dr. Thomas J. Welch, Deputy Assistant to the Secretary of Defense for Chemical Matters
> July 28, 1988, Hearing before the Committee on Governmental Affairs of the U.S. Senate.

The Department of Defense was aware of ten nations with biological weapons in 1988. They are still aware of ten nations in 1999.

A central question is whether the vaccine is effective. Will it really work? If anthrax were to be used, will it protect all our soldiers, or the vast majority of our servicemembers? One must look to the animal data. I have compiled all the published guinea pig and mouse experiments in the following three tables. All were immunized with the vaccine servicemembers are currently receiving, termed MDPH, for the Michigan Department of Public Health which manufactured it. 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. The Ames strain is considered a virulent strain; the Vollum strain, less so.

Guinea Pig
Survival Following Anthrax Spore Injection

Lead Author	Vaccine	#Doses	Anthrax Strain	% Survival Vaccinated	% Survival Control
1986 Little	MDPH	3	Vollum 1B	100%	13%
	MDPH	3	Ames	0	17%
1988 Ivins	MDPH	3	Vollum 1B	67%	0
1988 Turnbull	MDPH	3	Ames/New Hampshire /Penicillin resistant	17%	0
1990 Ivins	MDPH	3	Ames	75%	0
1992	MDPH	3	Ames	100%	0
1994 Ivins	MDPH	2	Vollum 1B	89%	11%
	MDPH	2	Ames	63%	11%

Guinea Pig
Survival after Inhaling Anthrax Spores

Lead Author	Vaccine	# Doses	Anthrax Strain	% Survival Vaccinated	Control
1986 Little	MDPH	3	Vollum 1B	71%	0
1988 Ivins	MDPH	3	Vollum 1B	67%	0
1995	MDPH	2	Ames	23%	0

There is debate about which experimental animals might parallel the human response. One hopes that we are more like guinea pigs than mice, since the best survival rate in mice immunized with the human vaccine and then injected with different anthrax strains was only 10%.

Mouse
Survival Following Anthrax Spore Injection

Lead Author	Vaccine	# Doses	Mouse Strain	Anthrax Strain	% Survival Vaccinated	Controls
1988 Welkos	MDPH	3	A/J	Vollum 1B	0	0
	MDPH	3	CBA/J	Vollum 1B	10%	0
1990 Ivins	MDPH	3	CBA/J	Ames	3%	0
1992 Ivins	MDPH	2	CBA/J Male	Ames	0	0
	MDPH	2	CBA/J Female	Ames	10%	0
	MDPH	2	A/J	Ames	0	0

D.O.D. spokespersons claimed that the guinea pig and mouse data should be ignored because the data from monkeys indicates very high survival rates, approaching 95-100%. The question remains, however, whether monkeys do parallel the human response, and how monkeys will respond to more highly virulent anthrax strains, since the monkey experiments cited by D.O.D. used only the Ames strain of anthrax.

Are monkeys more relevant than guinea pigs in assessing anthrax vaccine effectiveness?

1. Many thousands of guinea pigs have been studied, but only 45 monkeys.

2. The potency studies and safety studies done to release lots at the vaccine manufacturer are all performed in guinea pigs.

3. "Since we lack surrogate markers to compare vaccine efficacy between animals and humans, it is still unknown which animal models, if any, resemble the human response to anthrax vaccine."
   Bruce Ivins, lead anthrax vaccine researcher at Fort Detrick

   "To date, no animal or other potency tests have been demonstrated to be well-correlated with protection of humans. The potency test required for the present vaccine has not been well correlated to efficacy in humans, and it is doubtful that it can be. . ."
   "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."
   Joint Program Office for Biological Defense meeting 20 October 1995.

This brings us to the question of whether the vaccine is effective against all anthrax strains. The data we have just reviewed suggests it may not be.

- "But fortunately for vaccines, it is difficult to surpass or circumvent the effectiveness of the vaccine. We all know you can develop resistance to antibiotics, for instance, but it's much more difficult to circumvent the vaccine . . <u>This vaccine is thought at this point to be effective against all the strains we know about</u>."
  Sue Bailey, M.D., Assistant Secretary of Defense for Health Affairs, August 14, 1998, D.O.D. Press Briefing

- D.O.D.'s experts disagree. Two studies at Fort Detrick, in 1986 and 1998, found that 9 and 27 anthrax strains, respectively, killed at least half the immunized guinea pigs injected with these strains.[1,2] The strains are all naturally occurring, and were isolates from around the world.

- Most of these strains were never tested in monkeys, so no evidence exists that the vaccine will protect monkeys against highly virulent strains.

- D.O.D. had other concerns about the vaccine: "Vaccine-induced protection is undoubtedly overwhelmed by extremely high spore challenge."
  From J-4A01206-91 Joint Staff Action Processing Form 16 August, 1991.

[1] Little, Stephen F. and Knudsen, Gregory B. "Comparative Efficacy of Bacillus anthracis Live Spore Vaccine and Protective Antigen Vaccine against Anthrax in the Guinea Pig." <u>Infection and Immunity</u>, May 1986, p. 509-512.
[2] Fellows, Patricia et al. "Anthrax Vaccine Efficacy Against B. anthracis Strains of Diverse Geographic Origin." Presented at International Anthrax Conference. Sept. 1998.

The following table from Little and Knudsen's publication provides the data on guinea pig survival using a variety of anthrax strains in 1986.

INFECTION AND IMMUNITY, May 1986, p. 509–512
0019-9567/86/050509-04$02.00/0
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Vol. 52, No. 2

Comparative Efficacy of *Bacillus anthracis* Live Spore Vaccine and Protective Antigen Vaccine against Anthrax in the Guinea Pig

STEPHEN F. LITTLE* AND GREGORY B. KNUDSON
U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland 21701-5011

TABLE 1. Histories of isolates used in this study

Isolate	Source and date of isolation
Vollum	Cow; ca. 1944
Vollum 1B	Derived from Vollum
Ames	Cow; Iowa, 1980
Buffalo	Buffalo; Iowa, 1979
17T5	Kudu; South Africa, 1957
NH	Human; New Hampshire, 1957
SK31	Wildebeest; South Africa, 1974
ACB	Human; Ohio, 1952
SK61	Human; California, 1976
SK162	Human; Florida, 1976
VH	Human; South Africa, 1952
V770	Cow; Florida, 1951
C28	South Africa, 1939
307	Human; Hull, 1943
285	Goat; South Africa, 1942
Nebr	Cow; Nebraska, 1978
57	Goat; South Africa, 1946
Albia	Iowa, 1963
1928	Cow; Iowa, 1925
3515	1963
SK102	Pakistan wool; New Jersey, 1976
SK128	Ireland wool; Massachusetts, 1976
SK465	Buffalo; Iowa, 1979
C4080C	Mill; North Carolina, 1978
M36	Derived from Vollum
Vollum 1	South Africa, 1948
TX366295	Cow; Texas, 1983

TABLE 2. Survival of guinea pigs after immunization with PA vaccine or Sterne spore vaccine and i.m. challenge with 1,000 spores of various *B. anthracis* isolates

Challenge isolate[a]	Vaccine efficacy (survivors/total)			
	Expt 1		Expt 2	
	Saline	PA vaccine	Saline	Sterne spore vaccine
Vollum	0/6[b]	6/6	ND[c]	ND
Vollum 1B	1/8	10/10	2/5	8/8
Ames	1/6	0/6	0/6	6/6
Buffalo	1/6	1/6	0/6	5/6
17T5	0/6	1/6	0/6	7/8
NH	0/6	3/9	0/6	6/6
SK31	0/6	3/6	0/6	6/6
ACB	0/6	1/6	0/6	6/6
SK61	0/6	2/6	0/6	6/6
SK162	1/6	2/6	0/6	6/6
VH	0/6	1/6	1/6	6/6

[a] Challenge dose, 10^3 spores i.m.
[b] ND, Not done.

The following table reviews data generated by Fellows, Linscott, and Ivins, in 1998. Twenty-seven strains of anthrax killed 50% or more of immunized guinea pigs, suggesting that strains available throughout the world are sufficiently virulent to defeat the vaccine.

Anthrax Vaccine Efficacy Against *B. anthracis* Strains of Diverse Geographical Origin

Patricia Fellows, Mara Linscott, and Bruce Ivins
Bacteriology Division, USAMRIID, Ft. Detrick

Brucella canis [illegible]

Strain & Origin	VNTR[1]	% Surv[2]	TTD, day[3]
Human Isolates			
ASIL K4539/France	3	6	5
BA1065/Zimbabwe	3	7	4
ASIL K5926/India	5	13	5
ASIL K7938/S. Korea	5	19	4
ASIL K5887/India	4,5,6	25	5
25 Ohio ASB/USA	3	31	5
BA1017/Haiti	4	31	5
BA1022/Pakistan	5	50	5
Other Isolates			
39/South Africa	3	13	7
ASIL K1759/South Africa	5	25	5
BA1024/Ireland	4	44	7
BA1033/South Africa	4	100	NA[4]

Strains were obtained from the Serology Division culture collection with the exception of those with the designation ASIL, which were kindly provided by the Martin Hugh-Jones Laboratory at Louisiana State University, Baton Rouge, Louisiana.

Strain & Origin	VNTR[1]	% Surv[2]	TTD, day[3]
Animal Isolates			
ASIL K7976/Namibia	5	5	5
Ames/USA	4	13	4
ASIL K5091/Norway	5	13	5
ASIL K9729/Turkey	4	13	4
ASIL K1938/Indonesia	3	13	4
Texas-2/USA	4	19	5
BA1031/South Africa	4	25	5
BA1016/South Africa	4	31	5
ASIL K4241/Italy	2	36	5
ASIL K1963/Canada	4	36	7
ASIL K1671/Norway	3	44	7
ASIL K4849/Mozambique	2	44	5
ASIL K0776/Canada	4	50	5
BA1002/Vellum 1B	2	55	7
BA1007/USA	4	55	5
ASIL K5093/Croatia	3	55	5
ASIL K5285/Canada	4	75	5
BA0016/Canada	3	100	NA[4]
ASIL K3519/Tanzania	4	31	4
ASIL K2087/USA	4	50	5
ASIL K7282/Germany	3	44	5

1. VNTR= Variable Number Tandem Repeat 2. Sixteen animals per group 3. TTD=Average Time to Death 4. NA= Not applicable

Safety Considerations

Even if the vaccine were not effective against all anthrax strains, and not against large inoculums of anthrax spores, one might still wish to use it for its residual efficacy if it were perfectly safe. The Department of Defense suggests that, in fact, this is the case. They report only 39 adverse reactions in 550,000 inoculations given. The following table reports these reactions as of February 1999.

Adverse Reactions

Anthrax Vaccine Adverse Event Reporting System (VAERS)
Week Ending 12 Feb 99

Service	VAERS Reactions	Classification			
		Local Reaction			Systemic Reaction
		Mild	Moderate	Severe	
USA	[illegible]	0	0	[illegible]	0
USN	[illegible]	0	0	[illegible]	0
USAF	[illegible]	0	0	[illegible]	1
USMC	[illegible]	0	0	[illegible]	0

Cumulative Data

Service	VAERS Reactions	Classification			
		Local Reaction			Systemic Reaction
		Mild	Moderate	Severe	
USA	27	7	6	[illegible]	5
USN	5	0	0	[illegible]	3
USAF	12	2	2	[illegible]	7
USMC	[illegible]	0	0	[illegible]	[illegible]

Mild
- Duration 24 - 48 Hours
- Local Redness and Hardness 1 to 2 Centimeters

Moderate
- Local Redness and Hardness 5 Centimeters
- Subcutaneous Nodule at Injection Site

[illegible]
- Swelling At Injection Site and Entire Forearm

[illegible]
- Malaise
- Chills and Fever
- Anaphylaxis

VAERS
- Loss of Duty > 24 Hours
- Hospitalization

39 Adverse Reactions of 550,248 Vaccinations Given = .007%

ANTHRAX VACCINE IMMUNIZATION PROGRAM AVIP

However, a variety of other data sources suggest that the rate of adverse reactions used for public consumption grossly underestimates the true rate. A USAMRIID publication reports a rate of systemic reactions of 0.7-1.3%. It also acknowledges the lack of definition of constituents and quantities of material in the vaccine and the significant variation from lot to lot, and the content of PA, as well as all the other components of the vaccine. It further admits that the only published human trial [redacted] a different vaccine and had insufficient data to show efficacy against inhalation anthrax.

USAMRIID

PROBLEMS WITH CURRENT MDPH VACCINE

Prolonged immunization schedule

Reactogenicity:

- Systemic reactions: 0.7-1.3%
- Significant local reactions: 2.4-3.9% (5.7%)

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 insuffcent data to show efficacy against inhalation anthrax

Made from spore-forming strain requiring dedicated production facility

In fact, three unpublished D.O.D. studies shed some light on the adverse reaction rate for the vaccine:

1. Tripler Army Medical Center (ongoing)
2. Bioport IND Study
3. Fort Bragg Study (Anthrax and Botulinum vaccines used).

1. Tripler Army Medical Center Ongoing Anthrax Vaccine Side Effects Study

- 7.9% of 595 vaccinees reported systemic symptoms after the first inoculation.
- 5.4% stated they could not perform their normal duties due to symptoms.
- 4.2% sought medical care.
- 2.5% lost duty time.
- 2.2% both sought medical care and lost duty time after the first anthrax vaccination.

After the initial three injections, only 3 VAERS reports were filed. The first was on a 35-year-old physician who developed muscle pain, muscle tremors and weakness, and was treated with prednisone. The second was a 38-year-old physician who developed a large local reaction lasting about ten days. The third was a 32-year-old patient with pulmonary sarcoidosis who experienced chest pain, shortness of breath, arthralgias, myalgias, fever and chills for 3 or 4 days beginning thirty minutes after his first injection.

The author of the initial report on the Tripler study said, "If reported side effects are solely attributable to the anthrax vaccine, one could argue that the vaccine is highly reactogenic." He also said, "This survey corroborates the relatively high incidence of minor side effects with subcutaneous administration of anthrax vaccine previously observed in this (smaller) cohort study at U.S. AMRIID."

2. Investigational New Drug Application for Anthrax Vaccine Adsorbed, September 15, 1998
Submitted by Dr. Robert C. Myers, D.V.M., Director, BioPort, to Dr. Carolyn Hardegree, Director, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research, FDA

- Blood was collected from volunteers at least monthly for the first year and at 13 months, 18 months, 21 months and 24 months.
- However, information on adverse reactions was only collected for the first 30 days.
- It was an ideal schedule to inquire about possible long-term side effects, but these data were never collected.

Appendix H Adverse Events Data

Table H1. Systemic Adverse Events by Route of Administration of AVA after Dose 1 (a)

Reaction	0-2-4 SQ N = 28	0 SQ 25	0 IM 25	0-2 SQ 25	0-2 IM 25	0-4 SQ 23	0-4 IM 22
Headache	2 (7)	4 (16)	5 (20)	4 (16)	1 (4)	3 (13)	5(23)
Malaise	0	2 (8)	5 (20)	3 (12)	0	3 (13)	0
Anorexia	0	0	4 (16)	1 (4)	0	1 (4)	2 (9)
Respiratory	1 (4)	1 (4)	2 (8)	2 (8)	1(4)	0	0
Nausea or							
Vomiti	0	2 (8)	1(4)	0	0	1 (4)	3 (14)
ng	0	2 (8)	2 (8)	1 (4)	0	1 (4)	1 (4)
Myalgia							
Generalized	0	2 (8)	0	1 (4)	0	0	0
pruritis	1 (4)	0	0	1 (4)	0	0	0
Fever							

(a) Data are reported as number of volunteers in group with systemic reaction (percent).

The Annual Report (BB-IND 6847 Amendment No. 005) was prepared using preliminary data which were not subjected to quality control review. Additionally, different grouping and scoring criteria were used to sort reactions for the Annual Report and this report. The data presented here were extracted from the statistical database which had undergone a thorough review by the database manager and the statistician.

Table H5. Local Adverse Events After Dose 1 by Route

Reaction N=	0-2-4 SQ 28	0 SQ 25	0 IM 25	0-2 SQ 25	0-2 IM 25	2-4 SQ 23	0-4 IM 22
Tenderness	20(71)	19(76)	14(56)	17(68)	14(56)	18(78)	10(46)
Erythmema	12(43)	8(32)	2(8)	10 (40)	1(4)	15(65)	1(5)
Induration	6(21)	1(4)	0	2(8)	0	8(35)	1(5)
Edema	0	1(4)	0	0	0	2(8)	0
Local pruritis	2(7)	5(20)	0	1(4)	2(8)	4(17)	1(5)
Warmth	3(11)	5(20)	0	4(16)	2(8)	4(17)	0
Arm motion limitation	0	4(16)	3(12)	1(4)	2(8)	4(17)	2(9)
SQ nodule	10(36)	10(40)	0	10(40)	0	14(61)	0
Axillary nodule	0	1(4)	0	0	0	0	0
Necrosis	0	0	0	0	0	0	0
Abscess	0	0	0	0	0	0	0

(a) Data are reported as number of volunteers in group with local reaction (percent).

3. Final Report to the U.S. FDA: Fort Bragg

Protocol: Serologic Response to Anthrax and Botulinum Vaccines
Protocol #FY92-5, M109, Log #A-5747
Principal investigator Lt. Col. Philip R. Pittman, M.D., MPH
United States Army Medical Research Institute of Infectious Diseases
Fort Dietrich, Maryland
Total Number in the Study: 486
Adverse Reaction Profile

Subjective Local Reactions During the First Seven Days of Study in the Right "Anthrax Vaccine" Arm:

- Induration (firmness) 22.3%
- Erythema (redness) 25.2%
- Swelling 19.8%

"Evaluation of safety records show that one or more systemic symptoms occurred in 44% of recipients of vaccines within the first seven days after the booster doses."

Adverse Reaction Profile

Systemic Systems (occurring at any time over the entire 30-day study):

- All/any systemic symptom 44%
- Headache 16.5%
- Illness Feeling 16%
- Joint Aches 12.6%
- Muscle Aches 30%
- Fever ≥ 100.5°Fahrenheit 2.8%

Systemic Symptoms Occurring >30 days following Anthrax or Botulinum Administration

- All/Any Symptoms - 3.2%

The third Fort Bragg study looked at persons immunized with anthrax vaccine alone, botulism toxoid vaccine alone, or in the majority of cases, the combination. Therefore, the reaction rates reflect dual vaccination. However, in each of these studies, the rate of systemic reactions is at least 7% and possibly as high as 40%. These rates do not square with the package insert which suggests a 0.2% rate of systemic reactions, or the material presented by D.O.D., which suggests a rate of 0.007%.

Surely it is clear from these data that the actual reaction rate being experienced by servicemembers inoculated today is grossly underreported. One must ask why, and one must also inquire about the ethical implications of this underreporting. Accurate reporting is essential for the public health. Underreporting on this scale demands oversight on health matters outside D.O.D.

Manufacturing Problems

There has been a significant controversy about manufacturing problems: inability to meet the standards of good manufacturing practices at Michigan Biologic Products Institute, now Bio-Port. The FDA inspection report lists a plethora of violations, yet the Army Surgeon General states repeatedly that the problems only had to do with recordkeeping. Who is telling the truth?

"Although MBPI has had some production problems, mostly due to an aging facility, the FDA has inspected and approved every lot of anthrax vaccine produced there since it was licensed in 1970. The FDA adheres to rigorous standards and would have certainly closed the facility and ordered the destruction of any products that they deemed unsafe."

Ronald R. Blanck, Lt. General, U.S. Army Surgeon General
Letter to the Editor, Belleville News-Democrat
29 May 1998

"... Eleven lots of anthrax vaccine were voluntarily quarantined by MBPI as a result of your telephone conversation with the FDA on or about February 27, 1998. During that conversation, the FDA raised concerns about inspectional issues related to potency testing, sterility testing, and the presence of particulates in a number of lots of anthrax vaccine.

... Please verify in writing that these eleven lots are, and will remain, in quarantine until further notification from the agency."

Kathryn C. Zoon, Ph.D., Director, Center for Biologics Evaluation and Research
Letter to Robert Myers, Director, Michigan Biologic Products Institute
April 28, 1998

The following document, 'Anthrax Vaccine Stockpile Overview,' tells an entirely different story. Of 31 lots subjected to supplemental testing, only six passed. And one of these was found to be unusable after it was shipped to Southwest Asia.

ANTHRAX VACCINE STOCKPILE OVERVIEW
REPORT DATE: July 15 1998

Number of Lots	Doses Originally in Inventory	Doses Remaining in Inventory[1]	Supplemental Testing Status	Mitretek Release Status	Comments
6	1,260,000	778,000	Completed	Acceptable	482,000 doses from these lots already shipped to DoD as of report date all available doses are labeled and packaged[2]
8	1,479,000	1,464,000	Only potency testing required	N/A	• Quarantined by MBPI pending resolution to various issues raised by FDA in February '98 inspection[4] • Potency testing to be completed by October 1998 (estimated)
2	414,500	414,500	Only potency testing required	N/A	• Quarantined by MBPI pending resolution to various issues raised by FDA in February '98 inspection • Requires satisfactory resolution to OOS[3] supplemental phenerol testing observation
15	2,913,000	2,837,000	Completed; Pending resolution to test issues	N/A	• 7 lots Quarantined by MBPI pending resolution to various issues raised by FDA in February '98 inspection • 8 lots Quarantined pending resolution of OOS supplemental testing observations
6	1,243,000	1,243,000	Not included in Supplemental Test Program[5]	N/A	Quarantined by MBPI pending FDA approval of BLA supplement (estimated resolution 10/31/98)
37	7,309,000	6,737,000			

[1] Doses remaining = doses originally in inventory - doses shipped
[2] Includes FAV019 (~ 215,000 doses); deemed unusable after temperature excursion during shipment.
[4] Resolution of FDA inspection issues projected by early October 1998.
[3] OOS = Out-of-specification.
[5] Lots manufactured at MBPI after Supplemental Test Plan was drafted.

OPTIONAL FORM 99 (7-90)
FAX TRANSMITTAL
LTC Randolph

The following document, from D.O.D.'s anthrax vaccine website, confirms the fact that only six lots have passed.

DefenseLINK

U.S. DEPARTMENT OF DEFENSE

Home Site Map Search

NEWS MULTIMEDIA PUBLICATIONS QUESTIONS?

SUPPLEMENTAL TESTING OF ANTHRAX VACCINE

"In December 1997, Secretary Cohen announced plans that would lead to the systematic vaccination of all U.S. military personnel against the biological warfare agent, anthrax. He further stated that the vaccinations would start after several conditions were met. One of those conditions was to conduct supplemental testing, consistent with the Food and Drug Administration's standards, to assure the sterility, safety, potency and purity of the vaccine

The Joint Program Office for Biological Defense contracted Mitretek Systems, Inc. to oversee and report on this supplemental testing to be performed by the manufacturer. Supplemental testing of the anthrax vaccine stockpile began in January 1998, and is scheduled lot by lot until all are completed at end of calendar year 1998. All lots of vaccine distributed in support of the DoD's Anthrax Vaccine Immunization Program (AVIP) since approval of the Accelerated AVIP in March 1998 have passed supplemental testing.

The supplemental testing results to date are:

Lot FAV017 Successfully completed on 12 Mar 98

Lot FAV019 Successfully completed on 2 Mar 98

Lot FAV020 Successfully completed on 2 Mar 98

Lot FAV030 Successfully completed on 13 Mar 98

Lot FAV034 Successfully completed on 27 Mar 98

Lot FAV036 Successfully completed on 3 Apr 98

Updated: 21 Sep 1998

Contact Us

Security and Privacy Notice

D.O.D. seems to have been well aware of problems at the plant and developed contingency plans following the March 1997 warning letter from FDA to the manufacturer:

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Anthrax Vaccine Producer / FDA Interaction

11 Mar 97 FDA letter to Michigan Biologic Products Institute (MBPI)

- Series of Inspections with significant deviations in related biologic product lines
- Systemic issues in QA/QC & Good Manufacturing Practices (GMP)
- Must achieve compliance to prevent license revocation

Immediate action needed:

- MBPI commitment to correct w/i 10 days
- MBPI comprehensive corrective action plans with milestones & resources w/i 30 days

Impact (Worst Case):

- Potential loss of FDA license for Anthrax Vaccine
- Derailment of BOT TOX IND contingency licensing initiative

UNCLASSIFIED

UNCLASSIFIED

Possible DoD Supportive Actions - MBPI

Immediate

- Proactive partnership with MBPI, State of Michigan and primary commercial customers
- Assessment Team (assistance in regulatory affairs, QA/QC, technical/training)
- Engage FDA (CBER) as requested

Near-Term

- COR staff on-site TDY (facilitate corrective action plan)
- Negotiate contract for facility modernization/expansion
- Transition management to JVAP PMO*

Long-Term

- Transition contract management to DPSC following FDA licensure of new production capability

*Program Management Office for Joint Vaccine Acquisition Program

UNCLASSIFIED

Is There Evidence for Long-term Vaccine Safety?

D.O.D. says the vaccine has been safely and routinely administered to veterinarians, laboratory workers, and livestock handlers since 1970.

1. The veterinarians and livestock handlers cannot be found, and do not appear to exist.

2. Four hundred to 500 laboratory workers and special operations troops per year have received this vaccine. They have not been screened for adverse effects.

3. Kathryn Zoon, head of the FDA's Center for Biologics Evaluation and Research, pointed out in a May 1998 letter that data on long-term side effects for this vaccine have never been submitted to the FDA.

The largest group of people to have received the vaccine prior to 1998 are the Desert Storm veterans, both deployed and non-deployed. There are many with chronic illness in both groups, but the relationship between vaccination and subsequent illness has never been studied in the United States.

Have Fort Detrick workers suffered adverse effects from repeated vaccinations? Anthrax vaccine has been administered to hundreds of workers for over 30 years.The answer is not clear.

Three studies have been published looking for the effects of multiple vaccinations in workers at Fort Detrick: in 1958, 1965, and 1974. None have been published since.

These studies point out that intensive immunization of experimental animals has been shown to produce delayed adverse consequences, such as amyloidosis, arteritis, multiple myeloma, and other hypersensitivity reactions.

The studies have repeatedly demonstrated abnormalities in the blood of the multiply-immunized when compared with controls. There are increased lymphocytes in the blood, and differences between the workers and controls in liver and kidney function, serum iron level, and sedimentation rates. The final report had this to say:

"Chronic stimulation of the immunoglobulin-producing system in man is thought to be associated with amyloidosis, plasma cell dyscrasias, and autoimmune diseases. . . Despite cautious extrapolation from animal findings to man, evaluation of these potentially adverse effects remains speculative, because few intensively immunized human populations have been available for study."

The authors concluded, "Nevertheless, the presence of two persons with neoplastic disease of lymphoid origin in the total immunized population by 1970, of approximately 1500 individuals at Fort Detrick, suggests that continued surveillance of the entire group of repeatedly immunized persons is warranted."

White, C. S. et al. "Repeated Immunization: Possible Adverse Effects" Annals of Internal Medicine. 1974.

What evidence exists regarding Gulf War Illness and anthrax vaccination?

To date, only one study has been published which looks at this question. It examined British Gulf War vets:

"Vaccination against biological warfare and multiple routine vaccinations were associated with this CDC multi-symptom syndrome in the Gulf War cohort."

Catherine Unwin, et al. "Health of U.K. Servicemen who served in Persian Gulf War." The Lancet; Volume 353, January 16, 1999.

"Vaccination against plague and anthrax before deployment to the Gulf correlated highly with illnesss. The investigators speculate that these vaccines – more so than the routine ones give to service personnel – had unanticipated effects."

Stephen E. Straus, NIAID, NIH. "Commentary on the Unwin Study". The Lancet. January 16, 1999.

Central to the issue of whether vaccination contributed to or caused Gulf War illnesses is the question of missing immunization records. At the last hearing, Army Surgeon General Blanck reported that anthrax vaccinations had been entered into servicemembers' personal medical records, although they had not been entered in an automated,

centralized format. His assertion runs contrary to the reports of hundreds of veterans who have obtained copies of their vaccination records and find no mention of anthrax in them, even when they were told by medical personnel that anthrax vaccine was being administered.

Where Are the Gulf War Vaccination Records?

From Joint Staff Action Processing Form, Action #J-4A 01206-91 Subject: Freedom Of Information Act request:

"Following Operation Desert Storm, the BW defensive program for D.O.D. has remained properly classified at the SECRET level. The only exception has been the documentation of immunizations into the individual's medical record in order to ensure availability of such information for purposes of epidemiological tracking. All original records and documents used in identifying units and personnel immunized during ODS are still considered classified information.

There are numerous memoranda and decision papers regarding the biological defense program, which while classified, are not responsive to the FOIA request.

Conclusion: Disclosure of the information requested in the detail requested would not be in the D.O.D.'s best interest and could be expected to cause serious damage in the future."

This references ASD (HA) memorandum, "Recording of vaccinations received in Operation Desert Storm in the medical immunization record (SF601)," 22 July1991

The document cited above suggests that there are central vaccination records that have been classified, which may still exist, and which are likely to help prove whether vaccinations in fact led to Gulf War illness. Those records must be found, declassified and shared with ill veterans and the medical personnel who are attempting to care for them.

Treatment studies for Persian Gulf Illnesses currently do not address vaccine injury. Perhaps Congress will see fit to remedy this omission.

Gulf War "Expert Panels"

A series of "expert panels" have been convened to explore the relationship between Gulf War illness and various exposures. Remarkably, none of these panels reviewed actual data regarding the relationship between vaccines and Gulf Illness. Each panel performed a superficial overview of the issue, citing the fact that there were "no known" long-term adverse effects of anthrax vaccination. They neglected to mention that no studies existed, and therefore, there was no data one way or the other.

Is anthrax vaccine a contributor to Gulf War illnesses? Comments by four expert panels

The remarks below were prepared for an interview between DOD spokespeople, and reporters for the program "60Min". I have inserted the comments in italics to clarify the conclusions of these four panels. The question of whether Gulf War illnesses may be related to anthrax vaccination has certainly not been laid to rest, despite the deliberations of four respected panels, because none of them actually reviewed any data. Nor did they investigate the ways in which anthrax vaccine may be significantly different from the civilian vaccines with which the panelists were more familiar.

Four different panels: The Institute of Medicine, The Presidential Advisory Committee, The Department of Veterans Affairs, and the National Institutes of Health have investigated the cause of Persian Gulf Illness (PGI) and concluded that the anthrax vaccine does not explain the long-term, chronic effects associated with PGI.

None of these four panels actually studied the incidence of PGI in vaccinated versus non-vaccinated Gulf War troops. NO data has been published in the open literature on this issue in the United States. The one published study to look at British veterans' vaccination status at the time of the Gulf War, and its correlation with subsequent development of PGI, was published in the Lancet January 16, 1999. (British troops received UB-made anthrax vaccine, as well as anthrax vaccine produced in England.) This study, whose first author was Catherine Unwin, showed a statistically significant association between vaccination (for anthrax as well as multiple vaccinations) and PGI. The data collected for the VA on PGW veterans should allow this type of comparison as well, but has not been published.

The Presidential Advisory Committee (PAC) on Gulf War Illnesses: Final Report, December 1996: p. 114, states: "The committee concludes it is unlikely that health effects reported by Gulf War veterans today are the result of exposure to the Botulinum toxoid or anthrax vaccines, used alone or in combination.

Again, the committee concluded this on the basis of what is known about vaccines in general, and without reviewing actual incidence data. What did the PAC Special Report, which followed the Final Report, say about DoD's vaccination policy?

"As determined by FDA, DoD's use of TBE vaccine during Operations Joint Endeavor/Joint Guard has violated federal regulations pertaining to investigational products on several accounts, including: record keeping failures; failure to monitor fully the study's progress; failure to ensure the protocol was followed so safety and efficacy can be assessed; promotion of safety and efficacy for the investigational product; and failure to obtain Institutional Review Board approval of informed consent documents. FDA also expressed uncertainty about whether there had been a violation of Army record keeping and documentation requirements, which mandate that service members' permanent records accurately reflect TBE immunizations. "

Health Consequences of Service During the Persian Gulf War: Recommendations for Research and Information Systems, Institute of Medicine (IOM), 1996: P. 85, 2nd paragraph: concerning adverse interactions due to multiple exposures. "All of these possible drug interactions (and others not mentioned) cause acute and short-term problems. The committee knows of no evidence of any chronic effect."

The Persian Gulf Experience and Health, NIH Technology Assessment Workshop Panel. JAMA, August 3, 1994-Vol 272; No. 5, p.391-395: P. 394, vaccines: general discussion including botulinum and anthrax vaccines."No long-term adverse effects have been documented."

A Working Plan for Research on Persian Gulf Veterans' Illnesses. Department of Veterans Affairs, November 1996: P. 26, 4.1.6 vaccines: "Both vaccines (anthrax and botulinum toxoid) have been used for many years without adverse effects. All three (IOM, PAC, and the Defense Science Board) review panels stated that no long-term adverse effects have been documented or would be expected. Further study of the potential adverse effects of

vaccines in this population is not recommended by any of the three panels, nor is it endorsed in this plan."

The three quotes from three panels above are examples of an interesting phenomenon. If you never look for something, you are sure never to find it. These three panels noted that there was a lack of evidence of long term adverse effects. But no study of long term adverse effects was ever published; nor were such effects ever collected and submitted to FDA, according to Kathryn Zoon (Zoon, KC. Letter from the Director of the FDA Center for Biologics Evaluation and Research to Patrick Eddington . FDA via FOIA. April 28, 1996).

DOD was the owner of the equipment used to produce the vaccine, the employer of virtually all vaccine recipients, and the employer of health care workers administering and monitoring vaccinations. No meaningful postmarketing surveillance appears to have ever been performed, with the exception of the standard passive VAERS reporting system. Even after reports of severe illness in PGulf War veterans, the relationship between vaccination and illness has never been subjected to statistical analysis in the United States. Yet there do exist immunization records for thousands of veterans, and surveys using veteran recall of vaccine status could also be done. So yes, there is no evidence of long-term adverse effects, but the 1974 study of multiply vaccinated persons at Fort Detrick did not exclude the real possibility of such effects, and also acknowledged that they do occur in animal models.

Where do the GWI expert panels get their information?

Every reference cited by the PAC is to a DOD briefer (Philip Russell being a former Commander at Fort Detrick; the others are current employees). No peer reviewed literature is cited. Side effects of the vaccine are minimized. The issue of multiple vaccines given together is trivialized, with no review of the existing literature on the topic. The committee claims its conclusions are "based on available evidence" but cites none.

Presidential Advisory Committee on Gulf War Illnesses: Final Report

Anthrax and Botulinum Toxoid Vaccines

Anthrax vaccine. In 1970, FDA licensed anthrax vaccine to protect civilian workers against possible infection by anthrax bacteria. Since 1967 and before the Gulf War, more than 20,000 inoculations had been routinely administered to at-risk populations, including laboratory personnel who work with the bacteria that causes anthrax, persons in industries that work with animal hides and wool (which can be a source of anthrax infection), and veterinarians who come in contact with anthrax-infected animals.

Although active long-term safety surveillance is not generally part of the FDA vaccine licensing process, the FDA encourages U.S. health care providers and the law requires manufacturers to report serious adverse reactions for all licensed vaccines.305 FDA has not received data that raise concerns about the safety of the anthrax vaccine.

Historical data for short-term health effects of the anthrax vaccine indicate up to six percent of recipients experience mild discomfort, including tenderness, redness, swelling or itching at the inoculation site for up to 72 hours. Fewer n one percent experience a more severe local reaction that potentially limits the use of the arm for one to two days. systemic reactions, e.g., fever, malaise, are uncommon (about 0.1 percent).102,103

According to DOD, medical monitoring and surveillance conducted during the Gulf War found the expected short-term side effects of anthrax vaccines occurring at approximately the historical rates.53 A single hospitalization for a vaccination site infection was reported. DOD points out that precise information about all possible short-term side effects is unknown, however, because of difficulties in collecting such data during and after the Gulf War.

53. Eitzen, E., U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, unpublished report to Presidential Advisory Committee on Gulf War Veterans' Illnesses, October 1995.

102. Johnson-Winegar, A., Director, Medical, Chemical, and Biological Defense Research, U.S. Army Medical Research Development Command, testimony before the Presidential Advisory Committee on Gulf War Veterans' Illnesses, May 1996.

103. Johnson-Winegar, A., Director, Medical, Chemical, and Biological Defense Research, U.S. Army Medical Research Development Command, Fort Detrick, briefing for Presidential Advisory Committee on Gulf War Veterans' Illnesses staff, December 1995.

Health effects of multiple vaccines. The human immune system has evolved the capability to deal with thousands of foreign substances, to sort them out, and to regulate immune response. Humans live among a vast population of hostile microorganisms, and vaccinations-even multiple, contemporaneous vaccinations-are a small part of total immune stimulation. Individual vaccines can cause adverse effects, but several studies of the effects of giving multiple vaccinations at one time have found no adverse effects associated with the practice. Research on this issue continues, but based on available evidence, the Committee believes it is unlikely that multiple vaccines are responsible for illnesses

reported today by Gulf War veterans.202,219,268

hat do we conclude about the risks of vaccines to Gulf War veterans? The Committee concludes it is ..ilikely that health effects reported by Gulf War veterans today are the result of exposures to the BT or anthrax vaccines, used alone or in combination.

202. Pittman, P.R., "Anthrax and Botulinum Vaccines: Antibody Prevalence and Immune Response to a Booster Dose in Military Personnel Initially Vaccinated During Desert Shield/Desert Storm: Preliminary Report," in review for submission to U.S Food and Drug Administration to supplement BB-IND3723, March 1995.

219. Russell, P.K., Department of International Health, Johns Hopkins University, testimony before the Presidential Advisory Committee on Gulf War Veterans' Illnesses, April 1996.

268. U.S. Army, Medical Research Institute of Infectious Diseases, Protocol: (Retrospective) Assessment of the Health of Workers Formerly Employed at Fort Detrick, MD, P.R. Pittman, Principal Investigator, September 1996.

I recently discovered the existence of an interesting D.O.D. study, initiated in September 1998. Seventh-day Adventists, who had participated in "Project Whitecoat" in the 1950's through the 1970's -- they had been volunteer guinea pigs for the biological warfare program at Fort Detrick -- had received anthrax vaccination as well as other vaccinations during their tenure at Fort Detrick. Now, 25 years after the program ended, Detrick researcher Col. Philip Pittman, a principal investigator in other anthrax vaccine studies, has approached these Adventists to learn more about possible long-term effects of their stay at Fort Detrick earlier. What was the Department of Defense looking for? It appears they are seeking evidence of a Gulf War-type illness in these volunteers. The symptoms they are inquiring about are as follows:

FROM 410 362 8481 04-28-99 09:19AM TO 12022252382,,99 #192 P.5/28

Seventh Day Adventist Follow-Up Study,
conducted by Lt. Col. Phillip R. Pittman

The data will be used "in developing a body of knowledge about whether there are any long-term effects of these immunizations." (Carea Van Linden, USAMRIID Public Affairs, 10/2/98)

24 Below is a list of common symptoms. They are associated with wide range of conditions. Please carefully review each symptom an answer with the one answer that best applies to you.

Difficulty sleeping
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Fatigue
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Joint aches and pains
- ^ Never a problem
- Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Headaches
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Unexplained Rashes
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Muscle aches
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- Regular, but not serious, problem
- Constant or serious problem
- o Major or disabling problem

Fevers
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Tremors or uncontrollable shaking
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Depression
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Memory loss
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Abdominal pain
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Feeling sick or 'not right'
- o Never a problem
- o Minor or infrequent problem
- o Occasionally a problem
- o Regular, but not serious, problem
- o Constant or serious problem
- o Major or disabling problem

Is A New Epidemic Emerging?

Most important to the discussion we're having today is the question of whether servicemembers currently being vaccinated are developing chronic, adverse effects from the anthrax vaccination. Because we do not have long-term data from prior to the current immunizations, it is essential that servicemembers be studied now to see whether there are one or more common disease syndromes emerging in servicemembers who report illness. I have had an unusual role to play in trying to discern whether this is the case. As a publicly-known expert on the anthrax vaccinations, I have been contacted by 50-100 servicemembers who report a variety of symptoms. I have not had the opportunity to examine these people, but many have filled in detailed questionnaires for me regarding their symptoms, and some have sent copies of their medical records. Fortunately, you will be hearing from some of them today.

I am sorry to report that the illness symptoms described to me are remarkably similar, and also mimic the symptoms reported by numerous ill Gulf War veterans. This illness resembles Chronic Fatigue Syndrome, with fatigue, sleep disturbance and cognitive deficits. There is a significant component of headache, muscle pain and joint pain, along with respiratory and abdominal complaints. In addition, many servicemembers report neurologic symptoms including sensory neuropathies and widespread autonomic dysfunction. Many report sensory hypersensitivity, and some chemical sensitivity. Their symptoms often worsen after the six month (4th) booster vaccination.

- The predominant initial symptoms are:
  - Abdominal cramping
  - Diarrhea (sometimes bloody)
  - Fever
  - Chills
  - Headaches
  - Malaise
  - Respiratory distress

- Later, persisting symptoms have included:
  - Chronic fatigue
  - Dizziness
  - Joint and muscle pain
  - Headaches
  - Memory loss/cognitive disturbances
  - Sleep disorders
  - Peripheral sensory neuropathies
  - Intermittent abdominal pain
  - Intermittent diarrhea
  - Chest pains
  - Recurring rashes

- Blackouts or seizures

- The majority of complaints of illness have been associated with vaccination using lots 020 and 030. Each lot contains approximately 200,000 doses.

- Anthrax vaccine is composed of an uncharacterized mix of bacterial products. Concentrations of these materials vary significantly from lot to lot. Because the constituents of this vaccine have never been defined, it is impossible to establish purity. It is also unknown whether any vaccine components cause adverse effects.

- Because many ill servicemembers remain on active duty and are trying to stay in the military, their names and medical records cannot be provided. They are attempting, unsuccessfully, to receive appropriate medical care within the military. This is difficult when the existence of a post-vaccination syndrome is being denied by D.O.D.

- Both the features of their illness, and the official response to it, echo the plight of ill Gulf War veterans, who remain without a defined illness, and without meaningful approaches to treatment.

Legal Issues

Unfortunately, the discussions we are having today have significant legal implications. Servicemembers who have refused the vaccine have faced a variety of punishments, including court martial. Some of those who have become ill subsequent to the Gulf War, or to the recent rounds of vaccinations, feel they may have been given unapproved vaccines which are not licensed by the FDA, and which D.O.D. had no legal right to use. They are interested in seeking redress, if they can demonstrate such vaccines were administered to them.

The following article suggests that in fact, one or more unapproved anthrax vaccines has been given to servicemembers.

"Military Immunizations: Past, Present and Future Prospects," written by a former Fort Detrick Commander, states that unlicensed anthrax vaccine has been used.

"LIMITED USE VACCINES AND PRODUCTS

Limited use vaccines and products are defined as those ***unlicensed*** **experimental vaccines**, toxoids, and immunoglobulins that have been developed against specific military threats associated with high morbidity. These products would be used in specific contingency situations. Some of the limited use vaccines could be considered to be experimental deployment vaccines, since they are directed against serious region-specific endemic diseases. Limited use vaccines include Venezuelan equine encephalitis, Eastern equine encephalitis, Western equine encephalitis, Rift Valley fever, tularemia, Q fever

and ***anthrax***. Botulinum toxoid (types A through E) is also included in the category of limited use products."

Ernest T. Takefuji, M.D., MPH, and Philip K. Russell, M.D., from Military Immunizations: Past, Present And Future Prospects, Infectious Disease Clinics of North America, March 1990, Page 156.

A number of servicemembers are now awaiting court martial for their refusal to submit to anthrax vaccination. Is the order to vaccinate a lawful order? Given all the questions that have been raised today, one wonders whether D.O.D. has the right to order a vaccine of questionable efficacy and dubious safety to be administered, willy-nilly, to 2.4 million service members.

Secretary of Defense William Cohen established four pre-conditions before he would approve the anthrax vaccination program.

Were Secretary Cohen's four pre-conditions for approval of the anthrax vaccination program actually met?

If not, was the order to vaccinate a lawful order?

1. Secretary Cohen asked for an **independent expert** to review and approve the program.

   - Gerard Burrow, M.D., is a maternal-fetal thyroid expert at Yale University. Anthrax vaccine is not approved for use in pregnancy, nor in children under 18. He therefore has no experience with the vaccine, and has never published any papers on anthrax, infectious disease, or biological warfare.

   - How was he chosen to review this program? Is his independence as illusory as his expertise?

2. Secretary Cohen asked for supplemental testing, consistent with Food and Drug Administration standards, to assure sterility, safety, potency and purity of the vaccine.

- Sterility – three of the eleven quarantined lots in April 1998 failed due to sterility testing. The February 1998 inspection also noted that several sublots which had failed sterility testing were used in the production of lots.
- Safety -- Safety can only be judged by long-term follow up of people who have received the vaccine. Until now, such follow up has never been accomplished.
- Potency -- Of the eleven lots quarantined by FDA on April 28, 1998, seven failed potency testing. Some of these had previously passed potency tests. Because MBPI retested lots until they achieved a pass on potency testing, this is no surprise.
- Purity – "The vaccine is composed of an undefined crude culture supranatant absorbed to aluminum hydroxide. There has been no quantification of the protective antigen content of the vaccine or of any of the other constituents, so the degree of purity is unknown."

  Dr. Arthur Friedlander, MC Colonel and head of Bacteriology at Fort Detrick's USAMRIID [Brachman PS and Friedlander AM: Anthrax. In Plotkin SA and Mortimer EA (eds): Vaccines, ed 2. Philadelphia, WB Saunders, 1994, pp. 729-739.]

In summary, there is no good evidence for vaccine safety, effica cy or necessity. D.O.D. may have illegally used unapproved vaccines on servicemembers in the past, and has not demonstrated that the order to vaccinate is a lawful order. Persian Gulf illness appears to be related, at least in part, to anthrax vaccination. D.O.D. had obfuscated the causal role of vaccines by classifying immunization records and controlling the deliberations of expert panels. Current servicemembers are now falling ill from the same disease.

What will it take to call a halt to the current round of vaccinations?

Equally important, what will it take to investigate these illnesses and develop treatment protocols that are serious about getting answers and providing care?

The smoke and mirrors have to go!

I would like to conclude by thanking the Committee again for allowing me to present this testimony. I would be happy to supply supporting documents and any other information that may shed light on the considerable questions which remain unresolved regarding the anthrax vaccine.

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EMPLOYMENT

12/97 - present	Emergency Physician Parkview Hospital Brunswick, Maine
9/97 - 11/97	Private Practice, Internal Medicine Women to Women 3 Marina Road Yarmouth, Maine
3/95 - 8/97 and 7/86 - 7/93	Emergency Physician Wing Memorial Hospital Palmer, Massachusetts
1/94 - 3/95	Emergency Physician Franklin Medical Center Greenfield, Massachusetts
7/93 - 1/94	Internist Kaiser Permanente Amherst, Massachusetts
7/85 - 7/86	Emergency Physician Emergency Doctors Group Springfield and Turners Falls, Massachusetts
7/80 - 6/82	Medical Consultant Disability Determination Services Jackson, Mississippi
2/75 - 8/76	Laboratory Technician II Department of Immunology John Curtin School of Medical Research Canberra, Australia

EDUCATION and TRAINING

1986	Diplomate in Internal Medicine
1985	Completed Internal Medicine Residency University of Mississippi Medical Center Jackson, Mississippi
1980	M.D., University of Mississippi Medical School Jackson, Mississippi
1974	B.S., Biology, Massachusetts Institute of Technology Cambridge, Massachusetts G.P.A. 3.9
1969	National Merit Scholar

TEACHING

1989 - 1993	Instructor, Department of Internal Medicine University of Massachusetts Medical School
1985 - present	Frequent EMT course lectures ACLS presentations

ADDITIONAL SKILLS

- Computer literate
- Excellent at search, review and synthesis of the medical literature
- Excellent writing ability
- Excellent rapport with patients and colleagues
- Broad public speaking experience, to physicians, medical students, and a variety of public organizations. Extensive interview experience
- Easy development of proficiency in new areas

OTHER PROJECTS

- Member, Federation of American Scientists Working Group on Biological Weapons Verification. Coauthored a report which describes the most comprehensive methodology for the investigation of allegations of biological

weapons use ever published. This report was presented to the Biological Weapons Convention Review Conference in 1996.

- Consultant, Cuban Ministry of Health, 1993. I identified and analyzed possible etiologies of an unprecedented epidemic of 50,000 cases of optic and peripheral neuropathy. As a result I was invited to Cuba to meet with top Cuban researchers, where I assisted in the planning of further evaluation and treatment regimens.

- Investigator: I spent three years studying the world's largest recorded anthrax epidemic, which took place in Zimbabwe from 1979-1980. I developed methods to distinguish a natural outbreak from an episode of biological warfare, and published a detailed analysis of the epidemic in 1992. In 1998, the Minister of Health of Zimbabwe acknowledged in a BBC documentary that anthrax was in fact used for biological warfare in his country, and confirmed a number of the conclusions in my report.

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ANTHRAX VACCINE

Model of a Response to the Biologic Warfare Threat

Meryl Nass, MD

Anthrax in nature is a usually fatal zoonotic disease that was a scourge of livestock until vaccines were developed in the 1880s. Animals acquire the disease from consuming contaminated soil in which preexisting anthrax spores are likely to have germinated, then sporulated under appropriate soil and weather conditions, increasing their concentration in soil to infectious levels.[66,79] Human disease results from exposure to contaminated animal products. Cutaneous disease is most common. The mortality is neglible if treated, and has been 15% due to septic complications when untreated. Gastrointestinal and meningeal cases are rarely seen. Inhalation anthrax (woolsorters' disease) results from inhaling spores, most often in poorly ventilated areas. It is about 90% fatal. Antibiotics and standard interventions begun after symptoms develop rarely prevent a fatal outcome. The human infectious dose is unknown, but is estimated to be between 100,000 and 100,000,000 spores.[66,79] In animals the infectious dose is highly strain dependent, and this is likely to be true in humans as well. The high infectious dose probably accounts for the rarity of human cases.

ANIMAL VACCINES

Pasteur, Toussaint, and Greenfield developed the first animal anthrax vaccines about 1880.[27,49] Sterne developed an attenuated live animal vaccine in 1935 that is still used, and derivatives of this strain

From the Departments of Internal Medicine and Emergency Medicine, Parkview Hospital, Brunswick, Maine

account for almost all vaccines used in the world today.[87] The most significant problem with the Sterne vaccine is that it retains some virulence. Goats, llamas, and occasionally other animals may die following vaccination.[32, 40, 41, 43, 85, 88] This vaccine, along with improvements in animal husbandry and industrial hygiene, has made anthrax an almost negligible problem in the developed world. There are rare animal outbreaks in the United States, and less than one human case reported per year.[87]

The Sterne vaccine strain lacks the plasmid pX02, which codes for the d-glutamic acid polypeptide capsule. The capsule inhibits phagocytosis and opsonization. The Sterne strain does retain the toxin plasmid pX01, which codes for the three toxin proteins: (1) protective antigen (PA); (2) lethal factor (LF), a zinc metallopeotease that inhibits mitogen-activated protein (MAP) kinase-kinase[19]; and (3) edema factor (EF), a calmodulin-dependent adenylate cyclase that generates cyclic adenosine monophosphate in the cytoplasm of eukaryotic cells.[32, 89] PA is an 82-kD protein that binds to receptors present on most mammalian cells. It is then cleaved by a cell surface protease to a 63-kD fragment, exposing a site that binds competitively to either EF or LF. The PA-LF or PA-EF complex then enters cells.[90, 91]

HUMAN VACCINES

Japan developed anthrax as a biologic weapon in the 1930s,[92] and the United States and Great Britain followed in the 1940s.[3, 6, 29] Little is known about the actual use of anthrax in biologic warfare (BW), although it is reported to have been used by Japan against China in World War II,[93] against livestock belonging to blacks during the Rhodesian civil war in 1978,[94] and by Germany against pack animals in World War I.[95]

Human vaccines were developed in the Soviet Union by 1940,[96] and in the United States and Great Britain in the 1950s.[97] The current US vaccine was formulated in the 1960s and licensed in 1970, 2 years before efficacy data were required for licensing.[3, 98] Russia and China use live attenuated strains for their human vaccines. The Chinese and Russian vaccines may be given by aerosol, scarification, or subcutaneous injection.[99, 81] The Russian vaccine was manufactured at the George Eliava Institute of Bacteriophage, Microbiology and Virology in Tbilisi, Georgia, until 1991 (Nina Chanishvili, PhD, personal communication, June 1998). Efficacy of the live Russian vaccine is reported to be greater than that of the killed US or British vaccines.[31, 50, 98, 100]

The US and British vaccines are filtrates from two different anthrax strains, each lacking the capsule plasmid. They are composed chiefly of PA. The British vaccine consists of alum-precipitated toxin proteins and has larger amounts of EF and LF than the US vaccine.[88] The US vaccine uses aluminum hydroxide (alhydrogel) to adsorb PA, and to serve as an adjuvant that is believed to stimulate humoral but not cell-mediated immunity.[98] According to Hambleton and Turnbull ".[S]uch vaccines can

produce some protective activity in experimental animals and may be effective in humans."[98]

The US vaccine is termed *MDPH-PA* (produced until February 1998 by the Michigan Department of Public Health, at the Michigan Biologic Products Institute [MBPI]), under contract to the Department of Defense [DOD]) or *MDPH-AVA* (anthrax vaccine adsorbed). The facility was sold in September 1998 and has been renamed BioPort.

The vaccine consists of a culture filtrate from the toxigenic, nonencapsulated strain of *Bacillus anthracis* V770-NP1-R.[24] It was administered to only several thousand people until 1990. One textbook states that there have been no controlled clinical trials in humans of the efficacy of the currently licensed US vaccine[7] and no published studies of its safety exist.

Three problems with this vaccine have stimulated interest in an improved human anthrax vaccine:[97, 31, 33, 38–43, 98]: (1) the immunization schedule involves six initial doses over 18 months followed by yearly boosters; (2) immunity is not protective against all natural anthrax strains in guinea pigs; and (3) there is a high incidence of local reactions (30% according to the package insert). The vaccine is an undefined mix of bacterial products.[7, 32, 47] Furthermore, the potency of both the UK and MDPH-PA vaccines is found to vary significantly between lots.[37, 48, 49]

Therefore, attempts have been ongoing since the early 1980s to develop an improved human vaccine. It is proposed that better vaccines should generate cell-mediated as well as humoral immunity, inhibit spore germination, and possibly other factors, and be well-defined chemically. Although virulence factors other than the toxin proteins and capsule have been identified, their roles are only beginning to be defined.[50] These include a type 1 DNA topoisomerase coded for by pX01,[51] and chromosomally encoded factors including extracellular proteases.[52, 53, 54] Vaccine development has been hampered by limited understanding of anthrax pathogenicity and lack of knowledge of epitopes that contribute to the improved immunity conferred by live vaccines.[40, 45, 48, 55, 56]

In the United States, two approaches toward an improved vaccine have been taken.[32] First, a chemically pure PA vaccine has been sought.[40, 42, 98] One candidate has been derived from a recombinant anthrax strain that lacks the capsule, LF and EF, achieving 98% purity and retaining PA's biologic activity.[21] Whether it stimulates adequate immunity is not yet known. In the second approach, a live vaccine that is safe, produces PA but also contains other immunogenic epitopes, and presents the antigens more effectively than a chemical vaccine is being sought.[42] Although a variety of live vaccine candidates have been tested, none yet has been found to be ideal.[17, 20, 40, 41, 98]

The only human field trial of an anthrax vaccine in the West was conducted by Brachman et al[8] in goat hair mills in New England in the late 1950s. During the 4-year study period there were 26 cases of anthrax, of which 21 were cutaneous and 5 were due to inhalation. One case of cutaneous anthrax occurred in a recipient of the complete injection series, and two in recipients of the partial vaccine series. The five inhalation cases were too few to draw any conclusion about vaccine efficacy with regard to inhaled organisms."

Table 1. GUINEA PIG SURVIVAL FOLLOWING PARENTERAL ANTHRAX SPORE CHALLENGE

Author (year)	Vaccine	No. Doses	Anthrax Strain	Survival (%)	
				Vaccinated	Control
Little and Knudsen,[26] 1986	MDPH	3	Vollum 1B	100	13
	MDPH	3	Ames	0	17
	Sterne	3	Ames	100	17
Ivins and Welkos,[27] 1988	MDPH	3	Vollum 1B	67	0
	Sterne	3	Vollum 1B	67	0
Turnbull et al.[28] 1988	MDPH	3	Ames/New Hampshire/penicillin resistant	17	0
	UK human	3	Ames/New Hampshire/penicillin resistant	33	0
	Sterne	3	Ames/New Hampshire/penicillin resistant	55	0
	Russian human	3	Ames/New Hampshire/penicillin resistant	72	0
Ivins et al.[29] 1990	MDPH	3	Ames	75	0
	Sterne	2	Ames	88	0
Ivins et al.[30] 1992	MDPH	3	Ames	100	0
Ivins et al.[31] 1994	MDPH	2	Vollum 1B	89	0
	MDPH	2	Ames	83	0

Since then, the vaccine formulation has been changed, and the current MDPH-PA vaccine contains an estimated four to six times more PA than the earlier vaccine.[9] The in vitro assessment of vaccine-induced immunity in humans is limited, however, because no reliable chemical correlates of immunity have been identified.[9] Although PA appears to be a primary and necessary component of all anthrax vaccines, the serum levels of anti-PA antibodies (by enzyme-linked immunosorbent assay) are not predictive of immunity in animals, when compared with the results of an anthrax spore challenge.[26,27,28,29,30,31] The reason for this is obscure. Thus, vaccine efficacy and potency cannot be assessed reliably without resorting to anthrax challenge studies, so one is left with the conundrum of how these results translate to humans.[9,32]

The Russians use an anthrax skin test (similar to the purified protein derivative) to detect immunity.[33] The test reliably identifies recent or remote anthrax infection, and even after many years 73% of those with prior infections remain positive. Following immunization, however, skin test sensitivity wanes rapidly with only 34% positive at 1 year. Whether immunity fades as rapidly is unclear.[33]

VACCINE EFFICACY

Both the US and British vaccines have been extensively tested for efficacy in animal challenge studies. Table 1 provides data from six studies of anthrax vaccines, showing survival rates following parenteral anthrax challenge of vaccinated guinea pigs. Table 2 does the same for studies in mice. Table 3 reviews the data from aerosol challenge studies in guinea pigs. Although there are large variations in design of the different studies, in the infectious doses used, and in the results, it is obvious that protection conferred by the MDPH vaccine to vaccine-sensitive Vollum anthrax strains is modest in guinea pigs, but that protection is unsatisfactory for other vaccine-resistant anthrax strains as well as for all anthrax strains in mice. Protection is only slightly better with the UK human vaccine.[31] According to Jones et al. "[Further work on aerosol infection conducted at CAMR (Porton Down) in 1991 (unpublished data) confirmed that the current UK vaccine affords poor protection to guinea pigs challenged with an aerosol of spores of the Ames strain."

Different animal species vary greatly in their resistance to infection by anthrax, as well as in their sensitivity to intravenous challenge with lethal toxin, composed of LF plus PA.[34] Because it is not known how closely the responses of experimental animals parallel the human response, it is also not known how the animal studies of vaccine efficacy can be extrapolated to humans.[34]

As noted previously, a long history of research using guinea pigs and mice suggests that the US and UK vaccines confer moderate protection against the types of exposures being faced in agriculture and industry, but mar[illegible]ular less protection against strains selected for virulence or vaccine [illegible]ance. Two recent reports from Fort Detrick of monkeys

Table 2. MOUSE SURVIVAL FOLLOWING PARENTERAL ANTHRAX SPORE CHALLENGE

Author (year)	Vaccine	No. Doses	Mouse Strain	Anthrax Strain	Survival (%)	
					Vaccinated	Control
Welkos et al.[m] 1988	MDPH	3	A/J	Vollum 1B	0	0
	MDPH	3	CBA/J	Vollum 1B	10	0
Welkos et al.[m] 1990	MDPH	3	CBA/J	Ames	10	0
	Sterne	3	CBA/J	Ames	50	0
Ivins et al.[m] 1990	MDPH	3	CBA/J	Ames	3	0
	Sterne*	3	CBA/J	Ames	56	0
Ivins et al.[m] 1992	MDPH	2	CBA/J male	Ames	0	0
	MDPH	2	CBA/J female	Ames	10	0
	MDPH	2	A/J	Ames	0	0

*Eleven of 32 mice died following the first Sterne immunization.

Table 3. GUINEA PIG SURVIVAL FOLLOWING AEROSOL ANTHRAX SPORE CHALLENGE

Author (year)	Vaccine	No. Doses	Anthrax Strain	Survival (%)	
				Vaccinated	Control
Ivins et al.[m] 1985	MDPH	3	Vollum 1B	71	0
	Sterne	4	Vollum 1B	100	0
Ivins and Welkos,[m] 1988	MDPH	3	Vollum 1B	67	0
	Sterne	3	Vollum 1B	87	0
Brooter and Hibbs,[p] 1990	UK human	3	Vollum	100	0
	UK human	3	New Hampshire	0	0
	UK human	3	Ames	33	0
	Sterne	1	Vollum	100	0
	Sterne	1	New Hampshire	100	0
	Sterne	1	Ames	67	0
Ivins et al.[m] 1995	MDPH	2	Ames	23	0
Jones et al.[r] 1996	UK human	3	Ames	49	18
	UK human	3	New Hampshire	88	36

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immunized with MDPH-PA and exposed to up to 900 times the LD50 of aerosolized Ames spores, however, gave quite different results.[34, 66] Nearly every immunized monkey survived, and all the controls died. The findings were presented to the International Workshop on Anthrax in 1995, but they have not been published elsewhere.[41, 66] In earlier monkey studies done by the same group, anthrax vaccine administered to monkeys on days 1 and 15 after an aerosol challenge led to survival no better than unvaccinated controls.[34]

EXPOSURE ISSUES SPECIFIC TO BIOLOGICAL WARFARE (BW)

The ways vaccines will be required to function to mitigate the effects of a BW attack may be different in some ways than their use against natural pathogens. BW exposures could be characterized by the following:

1. Exposure will probably be via aerosol, although subsequently there may be an increased risk of exposure from soil.[50]
2. Especially virulent strains are likely to be used.[73] There may be a mixture of strains, as suggested by the work of Jackson et al,[40] who strain-typed specimens from the Sverdlovsk outbreak.
3. More than one type of disease organism may be used simultaneously or in tandem. For example, a pathogen that attacks mucous membranes may be used to enable easier penetration of the host by a second pathogen. This reduces the infectious dose, increasing the attack rate.
4. Strains are likely to be selected for antibiotic resistance and vaccine resistance, or genetically engineered to maximize these properties and perhaps add unusual virulence factors.[48, 73]
5. Recombinant anthrax strains may not require PA to introduce LF and EF into cells, as suggested by work done by Pomerantsev, et al.[9, 73]
6. Very high concentrations of microorganisms are likely to be faced, which may overcome vaccine protection.[34, 66]
7. Exposure may be detectable early, in advance of symptomatic illness, using sensors and intelligence information.
8. Novel syndromes may occur.
9. Herd immunity has allowed existing vaccines to keep infectious diseases out of immunized populations, although immunity within a population is significantly less than 100%. The advantage conferred by herd immunity will not be experienced in a BW setting; therefore, successful vaccines will need to approach 100% efficacy.

Consequently, for prophylaxis of BW, an anthrax vaccine should be effective against aerosol exposure, high doses, the most virulent strains, and have extremely high efficacy. Ideally, it should inhibit spore germination, to [illegible]ress the disease at an earlier stage than the current vaccine,[67] as well as neutralize other virulence factors. If it is solely directed against PA, it would probably provide no protection against a recombinant anthrax strain lacking PA. Postexposure therapies would also be highly desirable.

ADJUVANT STUDIES

Experiments beginning in the 1980s showed that the addition of certain adjuvants, either killed or attenuated bacteria, or novel adjuvant formulations, greatly improved the efficacy in terms of survival rates of the US and British anthrax vaccines in animal studies.[34, 42, 43, 67, 68, 69, 94] Adjuvant use led to more rapid development of immunity than the standard vaccines, so fewer doses were needed.[69]

Tables 4 and 5 show the effects of boosting the British and US vaccines with these adjuvants. To summarize the results, guinea pigs fared much better with the novel adjuvants than without them. Mice could not be adequately protected by MDPH-PA alone; CBA/J mice benefited somewhat from adjuvants, whereas A/J and Balb/c [17] did not.[41, 43, 68]

BOOSTING VACCINE EFFECTS IN HUMANS

Just prior to the Gulf War, amid fears of BW use, and with limited available supplies of anthrax vaccine, the British immunized their troops against various infectious diseases including anthrax, and included a killed *Bordetella pertussis* vaccine preparation as an adjuvant for the anthrax vaccine.[14, 57, 61]

The basis for this appears to have been research carried out on animals by Turnbull et al who wrote: "the human chemical vaccines as constituted have limited protective activities, lower than that induced by live spore vaccines available for use in the USSR . . . however, nonspecific killed microbial additives, such as Freund's Complete Adjuvant, *Bordetella pertussis* (as in the human vaccine) or *Corynebacterium ovis* can enhance the protective action of PA in the chemical vaccines to levels equivalent to or exceeding those of the live spore vaccines."[69]

Butler[14] felt that use of the pertussis vaccine in this way was highly experimental, relying on preliminary results from Ministry of Defense-sponsored research at the Centre for Applied Microbiology Research at Porton Down, but was done to get troops out to the Gulf quickly. Questions have since arisen regarding possible adverse effects from this anthrax-pertussis combination in humans. It was noted in the animal trials that a group of guinea pigs that received three doses of a PA preparation plus *B. pertussis* and one dose of Freund's complete adjuvant, showed signs of aging (hair loss, anorexia, and wasting in a proportion of the animals).[69] The researchers therefore challenged the animals with anthrax spores 4 months earlier than originally planned.

Might these vaccines contribute to immune system disease?

Table 4. IMPROVED SURVIVAL IN GUINEA PIGS WITH ADDITION OF NOVEL ADJUVANTS

Author (year)	Vaccine	No. Doses	Adjuvant(s)	Anthrax Strain	% Survived Vaccinated	% Survived Control
Turnbull et al[29] 1988	MDPH	3	None	Ames	40	0
	MDPH	3	Killed *Corynebacterium ovis*, or Freund's complete adjuvant	Ames	100	0
	UK human	3	None	Ames	45	0
	UK human	3	*Corynebacterium ovis*, or Freund's complete adjuvant or *Bacillus cereus* live	Ames	100	0
Turnbull et al[30] 1990*	PA*	3	None	Vollum	83	0
	PA	3	None	Ames/New Hampshire	8	0
	PA	3	*Bordetella pertussis*	Vollum	100	0
	PA	3	*B. pertussis*	Ames	58	0
Ivins et al[31] 1992*	MDPH (7300 Ames spores im)	2	None	Ames	73	0
	PA*	2	Detox	Ames	83	0
	PA	2	Triple mix	Ames	100	0
	PA (4300 Ames spores im)	1	Alhydrogel	Ames	76	0
	PA	1	Detox	Ames	100	0
	PA	1	Triple mix	Ames	100	0
	PA (200,000 Ames spores im)	1	Alhydrogel	Ames	25	0
	MDPH	1	None	Ames	38	0
	PA	1	Detox	Ames	82	0
		1	Triple mix	Ames	95	0
et al.[32] 1995†	MDPH	2	None	Ames	23	0
	PA†	2	MPL & SLT	Ames	50	0
Jones et al[33] 1996	UK human	3	None	Ames	36	10
	UK human	3	Triple mix	Ames	93	10
	UK human	3	None	Vollum	80	10
	UK human	3	Triple mix	Vollum	100	10
	UK human	3	None	New Hampshire	89	36
	UK human	3	Triple mix	New Hampshire	90	36

Adjuvant descriptions are contained in text.
MDPH is formulated with alhydrogel (aluminum hydroxide)
UK human vaccine is formulated with alum
*PA is produced and purified as described by Leppla 5,6; Methods Enzymol 165:103, 1988
†PA is produced and purified as described in reference 39
MPL = monophosphoryl lipid A; SLT = squalene-lecithin-tween 80.

Table 5. IMPROVED SURVIVAL IN MICE WITH ADDITION OF NOVEL ADJUVANTS

Author (year)	Vaccine	No. Doses	Adjuvant(s)	Anthrax Strain	Experimental Animal	% Survived Vaccinated	% Survived Control
Welkos et al[illegible] 1990	MDPH	3	None	Ames	CBA/J	10	0
	PA	3	Alhydrogel	Ames	CBA/J	20	0
	PA	3	Triple mix	Ames	CBA/J	89	0
Ivins et al[illegible] 1992*	MDPH	2	None	Ames	CBA/J male	0	0
	PA	2	Detox	Ames	CBA/J male	8	0
	PA	2	Triple mix	Ames	CBA/J male	25	0
	PA	2	Threonyl-MDP	Ames	CBA/J male	25	0
	MDPH	2	None	Ames	CBA/J female	10	0
	PA	2	Triple mix	Ames	CBA/J female	60	0
	PA	2	Threonyl-MDP	Ames	CBA/J female	80	0
	MDPH	2	None	Ames	A/J	0	0
	PA	2	Detox	Ames	A/J	0	0
	PA	2	Triple mix	Ames	A/J	36	0
	PA	2	Threonyl-MDP	Ames	A/J	0	0

*PA is purified and produced as described by Leppla SH: Methods Enzymol 165:103, 1988

and Zumla[illegible] have proposed that Gulf War illnesses may be caused by a shift in cytokine balance from Th1 to Th2. This can be induced by use of multiple vaccinations, particularly pertussis and possibly by exposure to carbamate and organophosphate insecticides as well, which inhibit Th1 function.[illegible] The British Ministry of Defense is now sponsoring a trial on the effects of the combination of anthrax and other treatments given to troops.[illegible]

In the United States, the most effective adjuvant formulations used with PA in animals were Detox, Triple mix (also known as Tri-Mix) and monophosphoryl lipid A (MPL) (all produced by Ribi Immunochem Research Hamilton, Montana). MPL was mixed with a squalene-polysorbate-80 emulsion.[illegible] Tables 4 and 5 show a comparison of efficacy with and without these adjuvants. Detox contains the cell wall skeleton of either *Micrococcus luteus* or boris, which includes muramyl dipeptide (MDP), and MPL (in a 10:1 ratio) in a base of 2% squalene. Triple mix contains the same ingredients with the addition of trehalose dimycolate, all in equal proportions, also in a 2% squalene base. These materials are immunogenic, but they are not harmless. Significant side effects, including uveitis, and adjuvant arthritis, have been described.[illegible] In one experiment where guinea pigs were given PA plus threonyl-MDP in an emulsion vehicle, five died unexpectedly 1 to 5 days postvaccination.[illegible]

Only aluminum-based adjuvants are licensed for human use in the United States, and military spokespersons have denied that unlicensed adjuvants or anthrax vaccines were given to US soldiers at the time of the Gulf War.[illegible] Asa and Garry, however, describe having found antiquitene antibodies in the blood of hundreds of patients reporting symptoms of Gulf War illness, and in rare controls (Robert Garry, PhD, personal communication, April 1996). This observation has reopened the issue of whether the US military, like the British Ministry of Defense, may have adjuvanted its anthrax vaccine in a novel way. In this case presumably using squalene-containing adjuvants.[illegible] Although efficacy may be improved by adding such adjuvants to a human anthrax vaccine, safety questions must be resolved before any large scale use in humans is attempted.[illegible]

OTHER APPROACHES TO ANTHRAX PROPHYLAXIS: POSTEXPOSURE THERAPIES

In contrast to the limited efficacy of vaccines, antimicrobial treatment begun either shortly before or shortly after exposure to anthrax (though prior to development of clinical illness) has led to significant long-term survival.[illegible] It promises to be very useful therapy, as long as the anthrax challenge strain is not antibiotic resistant. Doxycycline and ciprofloxacin have been the best performers of the drugs tested.[illegible] A [illegible]-month course of postexposure vaccination plus antibiotics may be more [illegible]cious than antibiotics alone. The Russians have created an antimi-

crobial-resistant vaccine strain for which they can use postexposure, live spore vaccination, and antibiotic therapy simultaneously.[64, 84]

One problem found with use of postexposure therapy is that a significant number of residual spores can be seen in the lungs of experimental animals after 3 or more weeks of antibiotic therapy, and may germinate following cessation of antimicrobial therapy, leading to death.[36, 66, 67, 68] It has been reported that the Russian live vaccine inhibits spore germination, whereas the chemical vaccines do not.[69] Whether administering a live vaccine after anthrax exposure, simultaneously with antibiotics, improves survival remains to be seen.

The use of antisera in the treatment of anthrax goes back to the preantibiotic era. Multiple case reports as well as experimental studies have documented some benefit of this approach, particularly because other treatments had little impact on systemic anthrax infections.[36, 70, 71, 72, 73, 74, 75, 76] In China, the use of a polyclonal antiserum, in addition to antibiotics (obtained after equine hyperimmunization with a mix of avirulent strains) is standard therapy for anthrax infection.[38] The development of monoclonal or polyclonal antianthrax antibodies and antisera for clinical use, however, [redacted]

ANTHRAX VACCINE MANUFACTURE IN THE UNITED STATES

The sole US supplier of human anthrax vaccine is now Bioport—formerly MBPI and MDPH. Persistent quality control problems have plagued these vaccine manufacturers, as noted by a series of Food and Drug Administration (FDA) inspection reports over the past 5 years.[77] In 1997, the FDA threatened to revoke MBPI's license, citing an inadequate response to previous concerns raised by the FDA.[78] The FDA report of the most recent February 1998 inspection contains 11 pages of quality control failures in anthrax vaccine manufacture, including grossly inadequate standardization and testing, placing lots that failed testing into use, and use of vaccine from lots in which contaminants were found in some vials, without further testing of the remaining lot.[79]

In December 1997, the US DOD announced a program to vaccinate all 2.4 million US active duty and reserve servicemembers with MDPH-PA as prophylaxis against a BW attack, and vaccinations began in March 1998. Canada and Great Britain also began vaccinating some troops. Suggestions for using anthrax vaccine in civilians have been made as well, although at the present time the current anthrax vaccine is not stockpiled for civilian use.[80]

The first shipment of anthrax vaccines to the Gulf was recalled because it had apparently frozen during shipment. The anthrax vaccine lot then used for troop immunization by DOD beginning in March 1998 was FAV 020. This lot had been identified in the February 1998 FDA inspection r[illegible] as having expired, been retested, and returned to use.[79]

The report noted that the lot was mislabeled, so that it appeared to remain within the original expiration period.

Although lots received potency testing in order to return them to use following expiration, no testing was done for the presence of degradents, and no testing for stability was done prior to 1997.[80] One issue that does not appear to have been considered is that of adjuvant stability. Newman and Powell[81] state that adjuvants, such as alum, are prone to physical denaturation and any degradation that alters the protein-binding capacity can decrease the adjuvant activity. The reverse situation, where protein cannot undergo normal desorption in vivo, can also be a problem in aged alum formulations. Alhydrogel has a recommended 2-year shelf-life[82] but some lots of vaccine have been stored for at least 6 years.[83]

The MBPI anthrax line was shut down in February 1998 for refurbishing at DOD expense. The DOD intends to utilize its stockpile of 7 million doses (a number of which were cited for problems in the FDA report) while the plant is being improved. The sale of the MBPI by the state of Michigan to BioPort Corp, a firm directed by former chairman of the Joint Chiefs of Staff Admiral Crowe, was announced in July 1998.[84]

WHEN DOD DRIVES THE VACCINATION PROCESS

Ethical concerns arise when a medical treatment is used primarily or exclusively by the DOD. In the case of the anthrax vaccine, several issues have emerged:

1. Annas[2] states that military regulations hold that, although a serviceperson must accept standard medical treatment or face court-martial, soldiers have no obligation to accept interventions that are not generally recognized by the medical profession as standard procedures. Because anthrax vaccination is not a standard civilian treatment, there may be no legal justification for forcing servicemembers to be vaccinated. Despite this, the current anthrax vaccination program is mandatory, and reprisals have been used against service personnel who have refused vaccination.[4, 85]
2. After reviewing the history of the troubled MBPI, it might be suspected that FDA oversight of the manufacturing process was influenced by DOD concerns, because numerous infractions of federal regulations were allowed to persist.[86, 87]
3. Military recordkeeping has not complied with civilian guidelines. The records of anthrax vaccinations administered at the time of the Gulf War apparently cannot be found, and the injections were not entered into the personal medical records of servicemembers.[15, 16, 71]
4. Postmarketing surveillance must be performed to detect adverse events associated with vaccination and to monito

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safety of practices such as simultaneous vaccination.[67] Postmarketing surveillance did not take place after the first large-scale use of MDPH-PA vaccine, at the time of the Gulf War, and evaluation of long-term safety of the anthrax vaccine administered to Gulf troops has not yet taken place. The safety profile of the vaccine therefore remains unknown, and questions persist regarding its role in the development of Gulf War illnesses.[68, 69]

According to the head of the FDA's Center for Biologics Evaluation and Research, data for clinical studies conducted on the long-term health effects of taking the anthrax vaccine have not been submitted to the FDA.[69] Yet, the DOD's independent reviewer of the anthrax vaccination program reported, in answer to a question about the need for medical surveillance of vaccinees, that "anthrax vaccine is an FDA-licensed vaccine and no followup is required."[72]

EXPANSION OF MILITARY VACCINATIONS

The DOD has proposed a large vaccine initiative, termed the Joint Vaccine Acquisition Program, for which initial funding of $321 million was approved in November 1997.[73, 74, 75] The goals of the project are to develop about 17 vaccines directed at BW threat agents, take them through the FDA licensing process, and arrange for manufacturing and administration to military personnel. The vaccinations against anthrax may be considered the prologue to this program.

As the Joint Vaccine Acquisition Program moves forward, the DOD is to fund and control all steps in the vaccine process, from initial research and development to manufacturing and administering the vaccines. If history is a guide, assessment of efficacy and safety, stringent manufacturing controls, and normal FDA oversight may be compromised. If the vaccines are licensed, as proposed, no informed consent need be obtained and vaccinations will probably be mandatory.

The DOD is assuming greater authority over the medical interventions given to troops at the same time that it has failed to follow agreed upon procedures for the use of experimental drugs and vaccines. This was noted both during the Gulf War and later in Bosnia. According to the October 1997 Presidential Advisory Committee on Gulf War Veterans Illnesses Special Report, "As determined by FDA, DOD's use of tick-borne encephalitis vaccine during Operations Joint Endeavor/Joint Guard has violated federal regulations pertaining to investigational products on several accounts, including: recordkeeping failures; failure to monitor fully the study's progress; failure to ensure the protocol was followed so safety and efficacy can be assessed; promotion of safety and efficacy for the investigational product; and failure to obtain Institutional Review Board approval of informed consent documents. FDA also expressed uncertainty about whether there had been a violation of Army recordkeeping and documentation requirements, which mandate that

servicemembers' permanent records accurately reflect TBE immunizations."[77]

Should DOD be given carte blanche over the use of vaccines and therapeutics, when DOD will control all facets of production of those same materials, and the normal checks and balances of our proprietary system may be missing or unenforced? The ethics and legal implications of this situation have yet to be examined publicly.

ARE VACCINES A GOOD STRATEGY TO COUNTER THE BW THREAT?

Vaccination may be a good idea in the short-term, particularly if national intelligence indicates that potential perpetrators are limited to microorganisms for which effective vaccines are available. Naturally occurring strains of anthrax, however, routinely overwhelm MDPH-PA vaccination in mice and guinea pigs. Whether this will carry over to humans has not been established. The ability of new adjuvants or new immunogens to solve this problem safely is uncertain.

In the longer term, vaccines appear to be less likely successfully to defend against BW threats. Given advances in biotechnology, and allegations that recombinant strains of anthrax and other microorganisms with both greater virulence than the native strains, and with added resistance to vaccines and antibiotics already exist,[78] it is unlikely that the present generation of vaccines will be protective.

Furthermore, it can take years to develop, test, license, manufacture, administer, and induce immunity using vaccines. Once one has created or obtained novel organisms, however, it takes only days or weeks to produce weaponizable quantities. Because of the necessity to perform human testing of vaccines and therapeutics, and make longitudinal observations prior to large-scale use,[8, 19] the development of medical countermeasures will necessarily lag far behind the creation of new bioweapons. The fact that we have no better vaccine to protect troops against anthrax 7 years after the end of the Gulf War puts this sharply into focus.

Development of biologic weapons has historically involved multiple microorganisms or toxins.[8, 79] If our troops are vaccinated against anthrax, an enemy may simply choose to use a different microorganism or toxin for which no vaccine is available. Although there is probably a role for vaccines, they should not be expected to provide a robust BW defense.

CONCLUSIONS: THOUGHTS ON THE MEDICAL RESPONSE TO BW

Therapeutic Strategies

The present human anthrax vaccine probably provides only limited protection for troops facing a BW attack by anthrax. Postexposure prophylaxis are likely to improve the outcome for victims following exposure.

strain used is not antibiotic resistant. Monoclonal antibodies and antisera may well have a role in the treatment of anthrax; additional research should be done in this area. Defense planners should consider developing a library of monoclonal or polyclonal antibodies and vaccines to virulence factors of existing microorganisms. This will produce therapies that may be effective for novel organisms, when the recombinant organisms make use of known virulence factors.

Problems with Military Vaccines

If the DOD controls all steps in the vaccine development and production process, and is the employer of both physicians administering vaccines and servicemembers receiving vaccines, some or all of the following may result:

1. Ethical conflicts of interest for those engaged in the process
2. Insufficient testing of products or combinations
3. Inadequate quality control of production
4. Enforced administration of medical treatments or procedures that are not standard practice for civilians
5. Inadequate record keeping
6. Lack of proper surveillance for side effects following use.

There will be loss of the checks and balances implicit in the civilian medical system. Effective oversight of DOD's health-related activities, such as vaccination, is therefore imperative.

Physical Protection

Protection for troops is challenging in a bioweapons attack; for civilians, it may be impossible. Medical interventions that protect troops will be accompanied by other measures, such as ready availability of barrier masks and suits, and use of air samplers and biodetectors. Although detectors are still rudimentary, they hold the promise of early biogent detection in the future. These measures are not routinely achievable for the civilian population. Yet, is a perpetrator more likely to use bioweapons on vaccinated troops, or on unprotected civilians?

Primary Protection

BW is now, and will continue to be, difficult to deal with medically. There may well be no effective medical response to weapons that already exist, as well as to those that may be created. Therefore, the utmost efforts at primary prevention are demanded. Creation of and adherence to an international biologic weapons treaty regime that contains the most rigorous verification measures possible, including surprise inspections and stiff penalties for possession or use of biologic weapons, is needed. Improvements in global infectious disease surveillance and communication, [illegible] outbreaks should be made.

Although measures of this kind may not be completely effective at preventing biowarfare incidents, it is generally agreed that a strong BW treaty would still have significant positive effects. The possibility of being inspected without warning would deter many bioweapons programs. UN inspections in Iraq have clearly established the usefulness of such strategies at uncovering BW programs.

Before a multibillion dollar commitment is made to use vaccines as the primary strategy for mitigation of BW, a careful evaluation of their benefits and costs should be made. Strategies for prevention of BW should be moved to their rightful place at the forefront of the biologic weapons debate.

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Addendum to the testimony of Meryl Nass, MD

Committee on Government Reform
Subcommittee on National Security, Veterans Affairs and International Relations
Hearing on Anthrax Vaccine Safety, April 29, 1999

As a general principle, is vaccination a good defense against biological warfare?

What if a vaccine was 100% effective against all natural strains of anthrax, which nobody claims? An enemy would simply choose another biological agent: one that occurs naturally or one created using genetic engineering.

The Defense Advanced Research Projects Agency (DARPA) identified 65 naturally-occurring biological and toxin warfare agents directed against humans: there exist vaccines for less than ten of these.

"It takes 18 months to develop a weapons-grade (biological) agent, and ten more years to develop a good vaccine against it."

William Patrick, former head of the Biowarfare Program, Fort Detrick. New York Times, November 3, 1998.

"The plethora of real and constructible microbial pathogens, and the numerous ways in which exposure to them can occur, makes development of agent and route-specific defenses both foolish and futile."

Jay Jacobson, M.D., "Biologic Warfare Testing," Hearing: Committee on Armed Services, House of Representatives, May 3, 1988

"One cannot overstate our inability to deal with novel agents . . . [To] unprepared public health authorities who know nothing of the weapons' origins, its structure, its pathogenic mechanism and transmission, the task of producing a vaccine or drug and doing it very rapidly is almost impossible . . . Today the number of potential agents has multiplied to the point where it is no longer possible to plan or respond with defenses. There is no public health or medical strategy."

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Despite the fact that vaccines are unlikely to provide a robust defense against known biological agents and are even less likely to provide a defense against novel, genetically engineered agents, Congress appropriated $322 million in 1997 for the Joint Vaccine Acquisition Program. Its goals are to develop new vaccines for more than ten known biowarfare pathogens and administer the vaccines to all US servicemembers.

The anthrax vaccine immunization program can be regarded as the introduction to this much larger, and less well-known, program. FDA has stated publicly that it will expedite licensing for these biowarfare vaccines.

Are we already embarked on a misadventure that will dwarf the anthrax vaccine program in cost, futility, and medical repercussions?

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F-483 100M 10/90 Rev. 10/87

ANTHRAX VACCINE ADSORBED

DESCRIPTION

Anthrax Vaccine Adsorbed is a sterile product made from filtrates of microaerophilic cultures of an avirulent, nonencapsulated strain of *Bacillus anthracis* which elaborates the protective antigen during the growth period. The cultures are grown in a synthetic liquid medium and the final product is prepared from the sterile filtered culture fluid. The potency of this product is confirmed according to the U.S. Food and Drug regulations (21 CFR 620.23): Additional Standards for Anthrax Vaccine Adsorbed. The final product contains no more than 2.4 mg aluminum hydroxide (equivalent to 0.83 mg aluminum) per 0.5 cc dose. Formaldehyde, in a final concentration not to exceed 0.02%, and benzethonium chloride, 0.0025%, are added as preservatives.

CLINICAL PHARMACOLOGY

Anthrax Vaccine Adsorbed is used in man to promote increased resistance to *Bacillus anthracis* by active immunization (1,2).

INDICATIONS AND USAGE

Immunization with Anthrax Vaccine Adsorbed is recommended for individuals who may come in contact with animal products such as hides, hair, or bones which come from anthrax endemic areas and may be contaminated with *Bacillus anthracis* spores; and for individuals engaged in diagnostic or investigational activities which may bring them into contact with *B. anthracis* spores (1-5). It is also recommended for high risk persons such as veterinarians and others handling potentially infected animals. Since the risk of exposure to anthrax infection in the general population is slight, routine immunization is not recommended.

If a person has not previously been immunized against anthrax, injection of this product following exposure to anthrax bacilli will not protect against infection.

CONTRAINDICATIONS

A history of a severe reaction to a previous dose of anthrax vaccine is a contraindication to immunization with this vaccine.

WARNINGS

1. Any acute respiratory disease or other active infection is generally considered to be adequate reason for deferring an injection.
2. Persons receiving cortico-steroid therapy or other agents which would tend to depress the immune response may not be adequately immunized with the dosage schedule recommended. If the therapy is short termed, immunization should be delayed. If the therapy is long termed, an extra dose of vaccine should be given a month or more after therapy is discontinued.

PRECAUTIONS

1. *General:* Epinephrine solution, 1:1000, should always be available for immediate use in case an anaphylactic reaction should occur, even though such reactions are rare.
2. *Carcinogenesis, Mutagenesis, Impairment of Fertility:* Studies have not been performed to ascertain whether Anthrax Vaccine Adsorbed has carcinogenic action, or any effect on fertility.
3. *Pregnancy:* PREGNANCY CATEGORY C. ANTHRAX VACCINE ADSORBED
   Animal reproduction studies have not been conducted with Anthrax Vaccine Adsorbed. It is also not known whether Anthrax Vaccine Adsorbed can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Anthrax Vaccine Adsorbed should be given to a pregnant woman only if clearly needed.
4. *Pediatric Use:* This antigen should be administered only to healthy men and women from 18 to 65 years of age because investigations to date have been conducted exclusively in that population.

ADVERSE REACTIONS

Local Reactions: Mild local reactions occur in approximately thirty per cent of recipients and consist of a small ring of erythema, 1-2 cm in diameter, plus slight local tenderness(1). This reaction usually occurs within 24 hours and begins to subside by 48 hours. Occasionally, the erythema increases to 3 to 5 cm in diameter. Local reactions tend to increase in severity by the 5th injection and then may decrease in severity with subsequent doses.

Moderate local reactions which occur in 4 per cent of recipients of a second injection are defined by an inflammatory reaction greater than 5 cm diameter.

These may be pruritic. Subcutaneous nodules may occur at the injection site and persist for several weeks in a few persons. A moderate local reaction can occur if the vaccine is given to anyone with a past history of anthrax infection.

More severe local reactions are less frequent and consist of extensive edema of the forearm in addition to the local inflammatory reaction.

All local reactions have been reversible.

Systemic Reactions: Systemic reactions which occur in fewer than 0.2 per cent of recipients have been characterized by malaise and lassitude. Chills and fever have been reported in only a few cases. In such instances, immunization should be discontinued.

DOSAGE AND ADMINISTRATION

Dosage

Primary immunization consists of three subcutaneous injections, 0.5 mL each, given 2 weeks apart followed by three additional subcutaneous injections, 0.5 mL each, given at 6, 12 and 18 months(1).

If immunity is to be maintained, subsequent booster injections of 0.5 mL of anthrax vaccine at one year intervals are recommended.

Administration

1. Use a separate sterile needle and syringe for each patient to avoid transmission of viral hepatitis and other infectious agents.
2. Shake the bottle thoroughly to ensure that the suspension is homogeneous during withdrawal. The rubber stopper should be treated with an appropriate disinfectant and allowed to dry before inserting the needle.
3. This preparation must be given subcutaneously after cleansing the overlying skin with an antiseptic.
4. Follow the usual precautions to avoid intravenous injection.
5. After withdrawing the needle, the injection site may be massaged briefly and gently to promote dispersal of the vaccine.
6. The same site should not be used for more than one injection of this vaccine.
7. Do not syringe-mix with any other product.
8. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED

Anthrax Vaccine Adsorbed is supplied in 5 mL vials containing 10 doses each.

STORAGE

THIS PRODUCT SHOULD BE STORED AT 2 TO 8 °C (35.6 to 46.4 °F). Do not freeze. Do not use after the expiration date given on the package.

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These recommendations are prepared by the Michigan Department of Public Health only for the guidance of the physician. They do not replace the experience and judgment of the physician, who should be familiar with the recent pertinent medical literature before administering any biologic product.

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Auth.: Act 368, 1978

Mr. SHAYS. Thank you, Dr. Nass. That is very comprehensive and helpful. Thank you.

Now our next three witnesses are civilians who have taken the anthrax vaccine. Is that correct?

Ms. GROLL. Correct, sir.

Mr. SHAYS. And we will start with you, Ms. Martin-Allaire.

Ms. MARTIN-ALLAIRE. I would like to thank Congress for expressing an interest to the anthrax vaccination immunization program and allowing me the opportunity to speak about my experiences of adverse reactions to the anthrax vaccination and problems seeking medical care I have incurred as a civilian.

My name is Randi Martin and I am a civil service technician at the 110th Fighter Wing Air National Guard Base, located in Battle Creek, MI. I received my first anthrax injection on September 18, 1998, for a volunteer overseas deployment, which was scheduled to deploy on November 11th, 1998. The second injection was administered on October 2nd, and a third on October 16th.

According to my shot record, all injections were from lot FAV030. During this timeframe our base was preparing for an operational readiness inspection, which was scheduled for October 17th to the 23rd, 1998. I felt tired, sluggish, and slow during this timeframe, but associated it to the numerous hours of overtime and stress that comes with any inspection with the military.

On March 14th, 1999, I received my fourth injection. The lot number I received is yet to be determined. The next couple of days after my injection I felt sluggish, tired, and a little disorientated. However, I considered that to be normal with past experiences of inoculations. On March 17th, I realized this was no longer normal. I was so tired I could not get out of bed. My days for the next week consisted of numerous hours of sleeping. I was awakened only to eat.

The following 2 weeks, I attempted going to work a couple of times, but lasted only for a couple of hours each day and then had to leave. The reasons were I was too tired, my head felt like it was going to explode, my abdominal cramping had me doubled-over, or I was just too disorientated.

I began to notice that my memory seemed to be getting worse as I could not remember passwords to programs that I use everyday at my work.

On March 31st I went to the emergency room with the complaints of abdominal cramping, my body was running hot and cold in temperature, a severe headache, shortness of breath, and feeling nauseated. I told the doctor I thought it was a reaction to the anthrax vaccination. The doctor inquired why I was not at a military hospital as they did not know anything about the anthrax vaccination.

I informed him of our situation at our base, where there is no full-time medical physician available. In his willingness to help, he looked through the immunization pamphlets but could find nothing on the anthrax vaccination. This is the second time on the civilian side I have run into this. The doctor called the CDC only to get the answering machine. He left a message, told me to go home and he would call me back when he had an answer.

I left the emergency room with no answers, but at least had a prescription for Motrin. While waiting for a call from the hospital, I was having a conversation with my father. I could not complete sentences without having to stop and gasp for air. I was so winded I literally felt as though I was going to pass out. The hospital called me in about an hour with the number the CDC gave them to give to me.

I called the number but did not catch where I called. I was talking to a woman by the name of Kathy who seemed very nice and wanted to know what my symptoms were. When I started stating them, she interrupted me to say that some of the reactions had not previously been reported as adverse reactions from the vaccine, so she was not going to report some of my symptoms as being any type of adverse reaction.

Her response was I must have caught a virus because symptoms associated with the vaccine last 2 to 3 days and not 2 weeks. I told Kathy of my situation, that doctors were not aware of the anthrax vaccination and did not know what to do for me. Kathy's response was, they haven't heard of the anthrax vaccine? You must live in a small town. Don't they watch TV?

I asked where I called, and she told me the Department of Defense. It then became clear to me how the DOD can state there are few adverse reactions associated with the vaccine. How can you begin a trend of adverse reactions when the DOD states they will not report them?

On April 2nd, our vice wing commander, Colonel Seidel, called a meeting with individuals from the group who received the fourth injection. It was discussed during this meeting that actions were taking place to get us down to Wright Patterson Air Force Base, located in Ohio, the closest military hospital. There seemed to be a lot of legality issues, considering we were civilians and this was a military issue.

Colonel Seidel stated that the soonest we were able to get to Wright Patterson to see a military allergist was April 23rd. However, he was trying to get us in sooner as he found this date to be completely unacceptable.

On April 7th, the first group of four left Battle Creek Air National Guard Base at 7:45 a.m. to Wright Patterson to see the military allergist. During my examination, the allergist examined my ears, eyes, nose, and throat, felt my abdomen, checked my reflexes, and examined my VAERS report. I received a chest x ray at my request. I was told I was fine. During this time, the allergist was aware of my symptoms. The allergist stated in my medical record that I had a local reaction and to followup with my civilian doctor. Subsequently, two civilian physicians that I have seen so far know nothing about this vaccination. We returned to our base at 11:30 p.m. still with many questions and no answers.

April 14th in the morning I was feeling very ill. I had abdominal cramping, a headache, and was feeling extremely nauseous. I went in at 8 a.m. to inform my boss that I was leaving ill. The response was that I needed to watch my sick leave as I was in the hole. My sick leave available balance seemed to be the only concern, even though she was previously made aware of the problems I was experiencing from the vaccination.

My position at work requires you to be multi-task orientated. Since coming back to work, I am unable to accomplish this. I can now only do one task at a time, as it takes every bit of concentration to focus on just the task at hand. One month after the injection, I am still having continuous headaches, which medication no longer has any effect on. I am still having abdominal cramping; I am still feeling nauseous; I am experiencing memory problems; and I am continuously tired. I cannot walk up a flight of stairs without becoming winded. My joints are achy when they are bent for longer than a couple of minutes. I have extreme lower back pains, and just recently have developed back spasms. I have gained nearly 20 pounds in 1½ months. I have absolutely zero tolerance for anybody or for anything. I do a lot of typing at my job. Normally I can type 75 words per minute. Now if I type more than 5 minutes, I find myself needing to stop as all of my fingers seem to tighten. I am only 25 years old and this should not be happening. I was off work for nearly a month with the only explanation being I have caught some kind of a mysterious virus that no one can explain or yet detect.

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. A VAERS form was never shown to us or offered. We found our own VAERS form on the internet, filled it out ourselves, and sent it forward. I never even knew a VAERS form existed, and I have been in the military for 8 years. I have recently learned that our base clinic was never aware of a VAERS form due to the fact that it is not a military form. The lack of knowledge for a mandated program that has been displayed by the "key personnel" has been completely appalling.

The medical treatment that was given down at Wright Patterson to myself was nothing short of get her in and get her out. The Department of Defense's response of not reporting some of my reactions I find very troubling. Due to the fact that I was cutoff from the DOD, I never even finished stating all of my symptoms.

I have found the situation I am in puzzling, that consideration on what to do if a technician or Guardsman becomes sick was never taken. This seems like an important step missing considering it is now mandatory for military personnel, active duty or civilian.

There seems to be no answers to my questions on why I am feeling the way that I am feeling. The only responses are the vaccine is safe, has been routinely used for 30 years, and will protect me in bio-warfare. My concerns from this vaccination are legitimate concerns. If reactions get worse after each injection, with what I have experienced on the fourth injection, what am I going to have to look forward to on the fifth injection? The sixth? The annual boosters? Why are my symptoms being categorized as local, which consists only of swelling from the elbow to the shoulder and a sore arm when there are clearly more reactions involved? How many other soldier's reactions are being classified lower than what they really are? There are too many unanswered questions associated with this program. And there are too many vague responses.

I am neither a medical physician nor a scientist; however, I feel I am the most qualified to know what is going on with my own body. I know what my health is now as opposed to where it was before I started taking the anthrax injections. There is a massive difference, and there is something wrong.

Thank you.

[The prepared statement of Ms. Martin-Allaire follows:]

Congressional Hearings

Anthrax Vaccination Immunization Program

House Government Reform and Oversight Committee

Chairman Shays Presiding

29 April 1999

Written Statement by:

Randi J. Martin-Allaire

I would like to thank Congress for expressing an interest to the Anthrax Vaccination Immunization Program (AVIP), and allowing me the opportunity to speak about my experiences of adverse reactions to the Anthrax vaccination, and problems seeking medical care I have incurred as a civilian. My name is Randi Martin, and I am a civil service technician at the 110th Fighter Wing Air National Guard Base located in Battle Creek, MI. I received my first Anthrax injection on September 18, 1998 for a volunteer overseas deployment which was scheduled to deploy on November 11, 1998. The second injection was administered on October 2nd, and the third on October 16th. According to my shot record, all injections were from lot FAV030.

During this time frame, our base was preparing for an Operational Readiness Inspection, which was scheduled for October 17-23, 1998. I felt tired, sluggish and slow during this time frame, but, associated it to the numerous hours of overtime, and stress that comes with any inspection with the military. On October 18th, two days after the 3rd injection, during one of our condition "blacks" (full MOPP gear), I was under the mask for about ten minutes. I started to feel light headed and dizzy as I was sitting on a stool, and dropped to my knees. One of my supervisors, MSGT Tom Starkweather, took off my mask so I could get air. One of the inspectors saw the situation, and took me outside for fresh air. He wanted me to stay outside for ten minutes. I didn't know what was the matter, as I have never had to take off my mask during any exercises because I couldn't breathe, or for any other reason. I felt like I was just being a wimp, so joining the rest of the group in the exercise was my first and foremost concern. I joined the group earlier than advised, and just kept telling myself to "suck it up, and drive on". I feel this was a very important point to make, considering that I have never had a problem with any MOPP exercises, and this particular problem actually made me have to take off my gas mask.

On March 14th, 1999, I received my fourth injection. The lot number I received is yet to be determined. My official shot record states that I received lot FAV0306. (See attachment A) When I questioned our clinic and my commander, Maj Dvorak, I was informed that there was an administrative error, and that I actually received lot FAV036. The next couple of days after my injection, I felt sluggish, tired and a little disorientated, however considered that to be normal.

On March 17th, I realized this was no longer normal. I was so tired I could not get out of bed. My days for the next week consisted of numerous hours of sleeping. I was awakened only to eat. The following two weeks, I attempted going to work a couple of times, but lasted only for a couple of hours each day, and then had to leave. The reasons were I was too tired, my head felt like it was going to explode, my abdominal cramping had me doubled over, or I was just too disorientated. I began to notice that my memory seemed to be getting worse, as I could not remember passwords to programs that I use everyday at my work.

On March 31st, I went to the emergency room with the complaints of abdominal cramping; my body was running hot and cold in temperature, a severe headache, shortness of breath and feeling nauseated. I told the doctor I felt it was a reaction to the Anthrax vaccination. The doctor inquired why I was not at a military hospital, as they did not know anything about the anthrax vaccination. I informed him of our situation at our base which is that we have no full time medical physician available. In his willingness to help, he looked through their immunization pamphlets, but could find nothing on the anthrax vaccination. This is the second time on the

civilian side I have run into this situation. He called counterparts, and they did not know anything about the immunization. He called Poison Control Center who did not know what to do, however gave him the number to the CDC. He then called CDC only to get the answering machine. He left a message, and told me to go home and he would call me when he had an answer. I left the emergency room with no answers, but had a prescription for Motrin. While waiting for a call from the hospital at home, I was having a conversation with my father. I could not complete sentences without having to stop and gasp for air. I was so winded, I literally felt as though I was going to pass out. The hospital called me in about an hour with a number the CDC told them to give to me. I called the number but did not catch where I called. I was talking to a woman by the name of Kathy who seemed very nice, and wanted to know what my symptoms were. When I started stating them, she interrupted me to say that some of the reactions had not previously been reported as adverse reactions from the vaccine, so she was not going to report some of my symptoms as being any type of adverse reaction. Her response was I must have caught a virus, because symptoms associated with the Anthrax vaccine lasts 2-3 days, not 2 weeks. I told Kathy of my situation that doctors were not aware of the Anthrax vaccination, and did not know what to do for me. Kathy's response was, "They haven't heard of the Anthrax Vaccine? You must live in a small town? Don't they watch T.V.?" I asked where I called, and she told me the Department of Defense. It then became clear to me how the Department of Defense can claim there are few adverse reactions associated with the vaccine. How can you begin a trend of adverse reactions, when the Department of Defense states they will not report them? I received a call from TSGT Dave Churchill on March 31st. Our vice wing commander, Col. Seidel, just heard word of our situation. He wanted a report on what happened from the time of injection up to now, (March 31st), of events that took place with our chain of command and medical facility. (See attachment B)

On April 2nd, Col. Seidel called a meeting with the individuals from the group who received the fourth injection. I was off sick that day, but came in for the meeting. It was discussed during this meeting that actions were taking place to get us down to Wright Patterson Air Force Base, located in Ohio, the closest military hospital. There seemed to be a lot of legality issues considering we were civilians and this was a military issue. Col. Seidel stated that the soonest we were able to get to Wright Patterson to see a military allergist, was April 23rd. However, he was trying to get us in sooner, as he found this date to be unacceptable.

On April 7th, the first group of four left Battle Creek Air National Guard Base at 7:45 a.m. to Wright Patterson to see the military allergist. We were to take either sick or annual leave and be placed on a military non-pay status for our trip. During my examination, the allergist examined my ears, eyes, nose and throat, felt my abdomen, checked my reflexes and examined my VAERS report. I received a chest X-ray at my request. I was told I was fine. During this time, the allergist was made aware of my symptoms. (See attachment B) As the allergist from Wright Patterson was looking through my medical record, he noticed I was in a car accident in 1994, had a concussion and experienced a headache as a result. His interpretation of my continuous headaches was associated back from four years ago. When I was twelve, I stood up to fast, and experienced a dizzy spell, which per his interpretation, explains why thirteen years later I am having balance problems. The allergist stated in my medical record that I had a local reaction, and

to follow up with my civilian doctor. Subsequently, two civilian physicians that I have seen so far know nothing about the vaccination.

We returned to our base as 11:30 p.m., still with many questions and no answers. I came into work the following day at 9:00 a.m. for a couple of hours and then had to leave early, still sick.

April 14th in the morning, I was feeling very ill. I had abdominal cramping, a headache and was feeling extremely nauseous. I went in at 8:00 a.m. to inform Maj Dvorak, that I was leaving ill. Her response was that I needed to watch my sick leave as I was in the hole. My sick leave available balance seemed to be the only concern, even though I previously made her aware of problems I was experiencing from the vaccination. (See attachment C) I finished the week of work with help from motrin, ibuprofen and vivarin.

My position at work requires you to be multitasked orientated. Since coming back to work, I am unable to accomplish this. I can now only do one task at a time, as it takes every bit of concentration to focus on just the task at hand. One month after the injection, I am still having continuous headaches which medication no longer has any effect on. I am still having abdominal cramping. I am still feeling nauseous. I am experiencing memory problems. I am continuously tired. I cannot walk up a flight of stairs without becoming winded. My joints are achy when they're bent for longer than a couple of minutes. I have extreme lower back pains, and just recently developed back spasms. I do a lot of typing at my job. Normally, I can type 75 words per minute. If I type more than five minutes, I find myself needing to stop, as all my of my fingers seem to tighten. I am only 25, and this should not be happening.

I was off work for nearly a month with the only explanation being I have caught a mysterious virus that no one can explain, or yet detect. There previously had been no follow up by our clinic with any of the personnel receiving this anthrax injection during the first three injections. After the complaints started after the fourth injection, most individuals were given an appointment to see our medical liaison. Our base does not have a full time physician, so, we had to wait until drill weekend which was scheduled April 10-11 to see them. I however, never received an appointment for this nature. 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. A VAERS form was never shown to us or offered. I found my own VAERS form on the Internet and filled it out myself and sent it forward. I never even knew a VAERS form existed, and I've been in the military eight years. I've recently learned that our base was never aware of a VAERS form due to the fact that it is not a military form.

The lack of knowledge and concern for a mandated program that has been displayed by the "key personnel" has been completely appalling. (See attachment D) The medical treatment that was given down at Wright Patterson to myself was nothing short of get her in, and get her out. The Department of Defense's response of not reporting some of my reactions I find very troubling. Due to the fact that Kathy at the Department of Defense interrupted me, I never even finished stating all of my symptoms.

I have found the situation I am in puzzling that consideration on what to do if a Technician or Guardsman becomes sick was never taken. This seems like an important step missing considering it is now mandatory for military personnel, active duty or civilian.

There seems to be no answers to my questions on why I am feeling the way I am feeling. The only responses are the vaccine is safe, it has been routinely used for thirty years, and will protect me in bio warfare. My concerns from this vaccination are legitimate concerns.

1. How come there have been no studies to find out if this vaccination causes cancer, has any long-term health effects, or causes infertility? Shouldn't thirty years be a long enough time to answer these questions?
2. If reactions get worse after each injection, with what I've experienced on the 4th injection, what am I going to experience on the fifth injection? The sixth? Annual boosters?
3. Why are my symptoms being categorized as local, which consists only of swelling from the elbow to the shoulder, and a sore arm, when there is clearly more reactions involved? How many other soldier's reactions are being classified lower than what they really are?

There are too many unanswered questions associated with this program, and there are too many vague responses.

The research I have done in this past month makes me wish I had done so beforehand. I am neither a medical physician, nor a scientist; however, I feel I am the most qualified to know what my body is experiencing. I know what my health is now as opposed to where it was before I started taking the Anthrax injections. There is a mass difference, and there is something wrong. The bottom line is that the way I am feeling now is at the hands of the Anthrax Vaccine Immunization Program.

Mr. SHAYS. Thank you very much. That is a very powerful statement. And I am sorry for what you have encountered. At least information should be available to you.

Ms. Groll.

Ms. GROLL. Mr. Chairman and members of the committee, I sincerely thank you for your interest in the anthrax vaccine immunization program and for allowing me to testify today on the effects and obstacles I have faced since starting this vaccine program. Please note that any opinions I express are my own and in no way reflect the opinions of the Michigan Air National Guard or those of my superior officers.

I am currently a technical sergeant in a civil service GS–9 management and systems analysis, assigned to the 110th Logistics Squadron, Battle Creek, MI. I received my first of the anthrax series on September 18th in preparation for a possible voluntary deployment to Qatar. The deployment was voluntary, and the vaccine was a prerequisite to the deployment. I acted on blind faith in the Department of Defense, my superiors, and trusted in the individuals I felt qualified to administer the vaccine.

Following the first two shots of the series, I noticed I was extremely fatigued and nauseous; however, during the same period of time I was working numerous hours in preparation for an upcoming operational readiness inspection. I attributed the symptoms to the extra hours and stress, not to the vaccine.

On October 16th, I receive No. 3 of the inoculation series. Coincidentally, this inoculation coincided with the beginning of the ORI. The third inoculation not only enhanced the same symptoms, but I also noticed I was becoming increasingly short-tempered, emotional, nauseous, experienced loss of appetite, and achy joints. Once again I attributed this to the stress and the long hours of our inspection.

For the following month, my health continued to become progressively worse, until finally I sought medical attention on November 12. I was then placed on antibiotics and antidepressants for chronic fatigue.

On March 14, I was notified that our clinic was waiting for our group to report to the clinic for our fourth anthrax vaccination. Upon our arrival at the clinic, the medical personnel were quite agitated and appeared unorganized. For the first time, I felt apprehensive about receiving this or any other vaccine. We questioned the medical staff as to why we were receiving our shot early. We were told that it was OK as long as we received it within a 24-hour window.

We were given our inoculation and sent to the holding area. While waiting to be released, I noticed that my shot record indicated the date of inoculations as March 16th. This was March 14th. I compared my records with the other individuals present and theirs also reflected the 16th.

Sergeant Martin questioned Major Jermeay on why the date read the 16th. He appeared upset, collected our shot records, and disappeared. When he returned with our shot records, the dates had been changed to reflect the date of inoculation as March 15th. It is still the 14th.

We once again questioned him on this, and we were told the date was within the 24-hour period recommended by DOD so that it was OK. My shot records also indicate that I have received all four lots from lot FAV030, which would indicate that my final inoculation to be from an expired vaccine.

Mr. SHAYS. Excuse me a minute.

[Pause in testimony while chairman confers.]

Ms. GROLL. That evening I started to feel ill: chills, fever, and nausea. My symptoms increased over the next few days to include headache, dizziness, diarrhea, and abdominal pain. On Wednesday, March 17, as non-commissioned officer in charge of the base honor guard, I was rendering services—honors at a memorial service for a former member of the U.S. Air Force. During the memorial service, I developed tremors and dizziness. I went home immediately following the services. The next few days were again spent in bed.

By Friday, March 19, my symptoms had increased to include shortness of breath. Once again I sought medical attention. During the medical evaluation, I stated that I had received my fourth anthrax inoculation on Sunday, March 14th. My physician immediately ordered blood work, urinalysis and referred me to an infectious disease and pulmonary specialist. Upon consultation with him, he in turn referred me to neurologist for my tremors and advised me that I was having an adverse reaction to the vaccine and that I needed to inform my supervisors so they could complete the necessary paperwork. He also advised me not to have any further vaccinations.

Later that day I informed my supervisor, the first link in my chain of command, what I had been told by my doctor. He in turn passed it up the chain. The following day, March 24th, I received a phone call at home from my supervisor stating the information had been passed along to the chief of supply, the Group commander, and also to the senior medical technician. He further requested that I call senior master sergeant Keller as he indicated that she was confused as to why the clinic would need to complete forms, the VAERS forms.

He further stated that I should not have to use my civilian leave for this illness since it was related to the military and that the clinic, in his opinion, should be completing a line-of-duty investigation.

He also informed me that he had discussed the situation with Lieutenant Colonel Allen and that he would have our squadron commander, Major Karen Dvorak, research the issue once she returned from Texas on March 30th.

I feel it is important to recognize at this time that we as a group were placed on annual training order for each of our inoculations with the exception of the fourth inoculation, which we were in unit training assembly status. We were told originally that we needed to be on military status to receive the vaccine. This is in case we had an adverse reaction——

Mr. SHAYS. Let me say that you are trying to accommodate us by reading fairly quickly, and so I realize that you—you can slow down just a spec, but it is very interesting testimony.

Ms. GROLL. Thank you, sir.

We were told that we needed to be in military status to receive the anthrax vaccine. In case we had an adverse reaction to the inoculation, the military would be responsible for our medical care.

On April 7, I was scheduled for a 1 o'clock appointment with Colonel Dr. Garramone from Wright Pat Air Force Base. Dr. Garramone questioned me thoroughly concerning my symptoms and performed what I thought to be a thorough examination, including a pulmonary exam. I feel it is important to note that out of the 11 individuals that were examined by the medical personnel at Wright Patterson Air Force Base, I was the only one Colonel Garramone examined.

Colonel Garramone recommended that I be examined by a neurologist and personally escorted me to the neurology clinic. However, they were unable to see me until the next day at 8 a.m. Colonel Garramone then telephoned Battle Creek at 2 p.m. and talked with Lieutenant Colonel Barker, support group commander, requesting that I be allowed to remain until the following day to be examined by the neurologist and to have further blood and urinalysis work completed.

By 4:45 p.m., the others had completed their examinations and their laboratory work. However, we were still waiting for a decision from Battle Creek on if we could stay for further testing the following morning. It was inevitable that—obvious, that supervision could not make that decision.

Between 4:45 and 5:15, Colonel Garramone made the decision that he was going to send us home. He prescribed a pain medication and completed an Air Force form, form 422, a physical profile, indicating that I had a possible neurological reaction to the anthrax vaccine and to also rule out fibromyalgia.

He talked further with Colonel Seidel and informed him, since he was sending us home, that I needed to be followed up with a military neurologist. We arrived home in Battle Creek at 11:30 that night very exhausted. It was very apparent that very little preparation had gone into preparing us for this trip.

The remaining few weeks since my fourth inoculation had consisted of several more doctor visits, all civilian, and numerous diagnostic tests being performed. As of this writing, I have worked 19 hours since March 17th, 1999, and have used close to 400 hours of my civilian leave overall due to what I feel is due to the anthrax vaccination.

I am still suffering chronic fatigue, shortness of breath, memory loss, weight loss, mood swings, abdominal pain, occasional nausea, and diarrhea, and tremors in my right arm.

Today, I have not been notified of if or when I will be scheduled up for the followup with a military neurologist that was recommended on April 7th by Colonel Garramone at Wright Pat.

I am not, and would never profess to be, a qualified medical professional; however, I do feel as though I am in touch with my own body and I know that something is wrong. I have taken my career seriously, devoting 14 years of my life playing a role in the defense of our great Nation. Throughout my tenure with the 110th Fighter Wing, I have always been amongst the first to volunteer to support the mission, always challenged myself to go above and beyond what is required of my position.

Unceasingly devoting numerous hours to the base honor guard and to other community service events. However, the events of the past few weeks have tarnished my faith in my unit and in the Department of Defense. I feel as though I have been misinformed and betrayed by the same country I seek to defend.

It is my impression through my own research that the anthrax vaccination immunization program belongs to and the success lies with the line commanders, yet, whenever a question has been addressed to our commander, they have repeatedly gone unanswered. Furthermore, I find it extremely disheartening that the only superior officer within my unit who has shown any concern for us whatsoever has been Colonel Roger Seidel. The response, lack of knowledge, and inaccurate recordkeeping from the medical squadron has been deplorable.

I consider trust, integrity, and accountability to be a vital link between all leadership and employees. Is it possible that leadership is not taking an active role in these three values? Is it possible that this is why service men and women are choosing to defy a lawful order and not to be inoculated with the anthrax vaccine?

I personally was very hesitant to testify in this hearing today for fear of reprisal. It is only through the encouragement of my family and friends that I was convinced that I need to come forward with my experiences. The reality is that numerous individuals are becoming ill following the anthrax vaccine. Numerous individuals are afraid to come forward for fear of reprisal, loss of income, inability to support their families.

It is for my fellow members of the services that I testify before you today. I pray that others will also have the strength now to come forward.

I again thank you for the honor and privilege of testifying before you today. I ask that the subcommittee seriously considers as a minimum, a moratorium on the anthrax vaccination program until all questions concerning safety and health of our service men and women are answered.

Thank you.

[The prepared statement of Ms. Groll follows:]

Congressional Hearings

Anthrax Vaccination Immunization Program

House Government Reform and

Oversight Committee

Chairman Shays Presiding

29 April 1999

Written Statement by:

Roberta K. Groll

Mr. Chairman and members of the committee, I sincerely thank you for your interest in the Anthrax Vaccine Immunization Program and for allowing me to testify to you today on the effects and obstacles I have faced since I have started the vaccine program. Please note that any opinions I express are my own and in no way reflect the opinions of the Michigan Air National Guard or those of my superior officers.

I am currently a Technical Sergeant and a civil service GS-9, Management and Systems Analysis assigned to the 110th Logistics Squadron, Battle Creek, Michigan. I received my first of the anthrax series on the 18th of September in preparation for a possible deployment to Qatar. The deployment was voluntary and the vaccine was a prerequisite to the deployment. To my knowledge, the 110th Fighter Wing has yet to be notified of the implementation date for mass inoculations. Prior to volunteering for the deployment I had no knowledge of the anthrax vaccine pro or con. I acted on blind faith in the Department of Defense, my superiors and trusted in the individuals I felt were qualified to administer the vaccine. I considered this vaccine as safe as all other vaccines that I have received in the line of duty. Following the first two shots of the series I noticed that I was extremely fatigued and nauseous. However, during the same period of time I was working numerous hours of over time in preparation of an upcoming operation readiness inspection. I attributed these symptoms to the extra hours and stress, not to the vaccine. On October 16, 1998, I received number 3 of the inoculation series. Coincidentally this inoculation coincided with the start of our ORI-operational readiness inspection. The third inoculation not only enhanced the same symptoms but I also noticed that I was becoming increasingly short tempered, emotional, nauseous, experienced loss of appetite, and achy joints. Once again, I attributed this to the stress and long hours of our inspection. For the following month, my health continued to become progressively worse until I finally sought medical attention on November 12, 1998. During my first visit I was placed on antibiotics for bronchitis and had blood drawn for possible thyroid problems. During my follow up visit the following week, my test had returned negative to thyroid problems. At this time my physician and I discussed other possibilities including the possibility of Chronic Fatigue Syndrome. Being that I was also a smoker with a chronic cough we (my physician and I) decided upon a treatment of Wellbutrin. She felt it would serve two causes: one assists me to quit smoking, two it is an antidepressant used to treat Chronic Fatigue. During the following two weeks my symptoms appeared to decrease however I developed an allergic reaction to the antidepressant Wellbutrin and was placed on Prozac. The following month my nausea, and cough subsided however I was still fatigued, experiencing achy joints and moodiness.

On March 14, 1999 at approximately 3:15 p.m., I was notified by our acting commander that the clinic was waiting for our group to report to the clinic for our 4th anthrax vaccine. Upon our arrival at the clinic the medical personnel were quite agitated and appeared unorganized. For the first time I felt apprehensive about receiving this or any other vaccine. We questioned the medical staff as to why we were receiving our shot early. We were told that it was ok as long as we received it within a 24-hour window.

One of the individuals in front of me, the nurse actually had the needle up to his arm when MAJ Jermeay yelled "don't inject him" he's not due until Friday. We were then all put into a "holding pattern" while MAJ Jermeay instructed the medical staff not to inject anyone else until he personally approved the injection. The others and myself were then given our inoculations and sent to the holding area. While waiting to be released I noticed that my shot record indicated the date of inoculation as 16 March 99, as opposed to 14 March 99. I compared my records with the other individuals present and there's also reflected the 16th. SSG Martin questioned MAJ Jermeay on why the date read the 16th. He appeared upset collected our shot records and disappeared. When he returned with our shot records, the dates had been changed to reflect the date of inoculation as the 15th of March. We once again questioned him on this and were told that the date was within the 24-hour window so that it was ok. That evening I started to feel ill, chills, fever, and nausea.

My workweek consists of 4 ten-hour days with Monday being the off day. I stayed home all day and could hardly get out of bed to take my son to school. Tuesday, March 16, 1999, I went to work and barely made it through the day. My symptoms had increased to include headache, dizziness, diarrhea, and slight abdominal pain.

On Wednesday, March 17, 1999 as Non Commissioned Officer In charge of the Base Honor Guard, I rendered honors at a memorial service for a former member of the Michigan Air National Guard and United States Air Force. During the service I developed tremors and dizziness. I went home immediately following the service. The next few days were spent in bed. By Friday, March 19, 1999 my symptoms had increased to a severe tremor in my right arm and shortness of breath I finally sought medical attention. During the medical evaluation I stated that I had received my 4th anthrax inoculation on Sunday, March 14, 1999. My physician ordered blood work, urinalysis and referred me to an infectious disease and pulmonary specialist. Upon my consultation with him on March 23, 1999, he in turn referred me to a neurologist for the tremor. He further advised me that I was having an adverse reaction to the vaccine, and that I needed to inform my superiors so that they could complete the necessary paperwork. He also

advised me not to receive any further shots. Later that day I informed my supervisor (the first link in my chain of command) of what I had been told by the doctor. He in turn passed it up the chain of command. The following day March 24, 1999, I received a phone call at home from my supervisor stating that the information had been passed along to the Chief of Supply, the Group Commander, LTC Thomas Allen and also to the Senior Medical Technician, SMS Kate Keller. He further requested that I call SMS Keller, as he indicated that she was confused to why the clinic needed to complete the VAERS form. He also informed me that they needed to have Randi Martin and myself sign a release letter authorizing our doctors to send the clinic their findings on our illnesses. We also discussed the issue of leave during this conversation. He further stated that I should not have to use my leave for this illness since it was related to the military and that the clinic in his opinion should be completing an LOD- line of duty.

SMS Watkins also informed me at this time that he had discussed the situation with LTC Allen and that he would have our Squadron Commander, MAJ Karen Dvorak research the issue once she returned from Texas on March 30th. I feel it's important to recognize at this time that we as a group were placed on Annual training orders for each inoculation with the exception of the 4th shot which we were in UTA- Unit Training Assembly status. We were told originally that we needed to be in military status to receive the anthrax vaccine. In case we had an adverse reaction to the inoculation the military would be responsible for our medical care. March 25, 1999 I called SMS Keller to inquire what type of documentation if any she may need. I was informed that she needed me to sign a medical release form. I inquired if this was for the LOD and she replied yes and that we would be scheduled to see one of our military physicians the next drill weekend. She also appeared to be unaware of the VAERS form when questioned.

March 30, 1999, I went to work for the first time since March 17th, 1999. We met with our squadron commander at 2:00 p.m. We gave her all our information to include medical questionnaires, copies of Immunizations records indicating the date change and also that we had been given an expired vaccine. She questioned us as to why the medical squadron hadn't initiated a line of duty investigation yet.

March 31, 1999, I was notified by SSG Randi Martin and TSG Dave Churchill that MAJ Dvorak had a meeting with everyone to conclude her findings. They were as follows:

1. The immunization clinic had made an administrative error in our immunization records that we had not received FAV 030, but had actually received FAV 036. We were all instructed to turn in our records so that the clinic could correct this error.

2. We were to all complete the VAERS form and turn into SMS Keller for placement in our medical records.

3. Get any lab results from our civilian physicians and turn those into SMS Keller.

4. Sign a medical release form; give this in turn to SMS Keller.

It was relayed to me that it was made apparent by MAJ Dvorak that concern for our health or providing us any assistance was no longer the issue. I found this to not only be disturbing but totally unacceptable. TSG Churchill and myself scheduled a 5:00 p.m. meeting with COL Roger Siedel, Vice Wing Commander. During the meeting with COL Siedel he was very concerned and distraught over the events that had transpired following Drill weekend. The impression was that he was unaware of many of our concerns. He assured us that our concerns were his top priority and would investigate what was happening.

On Friday, April 2, 1999, COL Siedel called a meeting with the individuals that had received their 4th inoculation. Several of us were still off work but attended anyway. The meeting consisted of COL Siedel, Vice Wing Commander, MAJ Dvorak, Logistics Squadron Commander, MAJ Donna Kowalski, 110 FW/Comptroller, SMS Keller, MSG Mary Moross, Medical squadron, and CPT Alice Neidergall, 110FW/JAG. During the meeting COL Siedel expressed his main concern was our health. He had put the above team together to determine the legality issues regarding technician versus military status, financial issues, etc. He continued to state that SMS Keller was working the issue of having us be seen by a military allergist at Wright Patterson Air Force Base. The first possible date they had open was April 23, 1999; they were nevertheless working all angles to have us examined earlier. He further stated that at this time they unfortunately would have to send us in an active duty non pay status. Monday April 5, 1999 I received a call at home from MAJ Dvorak. She stated that the clinic was able to secure 4 appointments on Wednesday, April 7, 1999 with the allergist from WPAFB for TSG Dave Churchill, SSG Randi Martin, SMS Harold Stewart and myself. She further informed me that MSG John Zink would be driving us down in a military vehicle. I asked her several questions regarding what status we were going to be traveling in, also would we be spending the night, who were we going to be seeing etc. She was short with me stating that I would find out these answers when I arrived at the base in the morning and to be there at 7:30 a.m. Upon arrival at the base the following morning, we were all instructed to sign out our shot records from SMS Keller. I asked SMS Keller what was to transpire throughout the day. She provided me with an appointment letter and stated that MSG Zink would provide the answers to any questions we might have on the way to Wright Patterson. We departed Battle Creek at 7:45 a.m. and arrived at Wright Patterson AFB, at 12:45 p.m. I was scheduled for a 1:00 p.m. appointment with Dr. (COL) Garramone. Dr Garramone questioned me thoroughly concerning my symptoms and performed what I thought to be a thorough examination, including a pulmonary exam. I feel it's important to note that out of the 11 individuals that were examined by medical personnel at Wright Patterson AFB, was the only one COL Garramone examined. COL Garramone recommended that I be examined by a neurologist and personally escorted me to the Neurology clinic. However, due to their heavy schedule that day, they were unable to see me until the next day at 8:00 a.m. COL Garramone then phoned Battle Creek at 2:00 p.m. and talked with LTC James Barker, Support Group Commander, requesting that I be allowed to remain until the following day to be examined by the neurologist and to have further blood and urinalysis work completed. By 4:00 p.m. we had still not received an answer from Battle Creek on if we were to return to the base or stay etc. By 4:45 p.m. the others had all completed their examinations and laboratory work however we were all waiting for a decision from Battle Creek on if we were to return home. The intention of the 110 Fighter Wing was for the other individuals to return home after placing me in a hotel. Furthermore, the only information provided was that MSG Zink was to place me in a hotel. There were no answers as to what I would use for transportation, availability of meals etc. At this point due to the severity of my illness and pure frustration of my superiors incapacity to make a decision I started to cry. Between 4:45 p.m. and 5:15 p.m. COL Garramone made the decision that he was going to send me home. He prescribed a pain medication and completed an AF Form 422, physical profile indicating a possible neurologic reaction to anthrax vaccine and to also rule out fibromyalgia. He talked further with COL Seidel and informed him of his decision to send us all home and instructed him that I needed to be followed up with a neurologist possibly an IMA doctor that attends drills at the 110 Fighter Wing Clinic. We departed Wright Patterson AFB, OH at 5:30 p.m. and arrived in Battle Creek at 11:30 p.m. very exhausted. It was apparent that very little preparation had gone into this trip. The following two days I remained at home recovering. On Friday April 9, 1999, I received a call from my supervisor. He stated that even though I was on a physician's

excuse that I needed to attend drill on Saturday April 9, 1999 because I was due a periodic physical, and once it was complete I would be able to return home. Reported to the base clinic at 8:00 a.m. April 9, 1999 for my physical. The military physicians performed a complete physical, recorded all of my recent symptoms and then released me at approximately 10:00 a.m. Later that evening my husband took me to the emergency room due to severe abdominal and back pain, dizziness and headaches. After 7 hours and numerous tests I was returned home with more tests and follow-ups scheduled. Once again received another diagnosis to my mystery illness. It is my experience that there is a general lack of knowledge at our installation and with several civilian physicians in our area concerning the anthrax vaccine.

The remaining few weeks consisted of more doctor visits and numerous diagnostic tests being performed. As of this writing I have worked 9 hours since March 17, 1999 and have used close to 400 hours of leave overall due to illness since October 1998. I am still suffering from chronic fatigue, shortness of breath, memory loss, weight loss, mood swings, abdominal pain, and occasional nausea and diarrhea. To date I have not been notified if or when I will be scheduled for a follow-up with a military neurologist that was recommended on April 7, 1999 by COL Garramone. On April 22, 1999 we received a letter concerning Line of Duty paperwork instructing us to complete ASAP. I find it totally appalling and unacceptable that over a month has past since our symptoms were first reported and this paperwork has just been started. I am not and would never profess to be a qualified medical individual however; I do feel as though I am in touch with my body and when something is not right. Since I have been receiving the anthrax vaccinations my system is rebelling against something and I have become seriously ill.

I've taken my career seriously devoting 14 years of my life playing a role in the defense of our great nation. Throughout my tenure with the 110th Fighter Wing I have always been amongst of the first to volunteer in support of the mission, always challenging myself to go above and beyond what is required of my position. Unceasingly devoting numerous hours to the Base Honor Guard and to other community service events. However, the events of the past few weeks have tarnished faith in my unit, and the Department of Defense. I feel as though I have been misinformed and betrayed by the same country I seek to defend. It is my impression through my own research that the Anthrax Vaccination Immunization Program belongs to and the success lies with the Line Commanders. Yet, whenever a question has been addressed to our Commander, they have repeatedly gone unanswered. Furthermore, I find it extremely disheartening that the only superior officer within our unit that has shown concern has been COL Roger Siedel. The response, lack of knowledge, and inaccurate record keeping from the Medical Squadron has been a disgrace. I consider trust, integrity, and accountability to be a vital link between all leadership and employees. Is it possible that leadership is not taking an active role in these three values? Is it possible that this is why servicemen and women are choosing to defy a lawful order and not to be inoculated with the anthrax vaccine? I was personally very hesitant to testify in this hearing for fear of reprisal. It was only through the encouragement of family and friends that I was convinced that I needed to come forward with my experiences. The reality is that numerous individuals are becoming ill following the anthrax vaccine, numerous individuals are afraid to come forward for fear of reprisal, loss of income and the ability to support their families. It is for my fellow servicemen and women that I testify before you today. I pray that others will also have the strength to come forward.

I again thank you for the honor and privilege of testifying before you today. I ask the Subcommittee seriously considers at the minimum a moratorium on the Anthrax Vaccination Immunization Program until all questions concerning the safety and health of our servicemen and women are answered.

[Home]

Mr. SHAYS. Thank you, Ms. Groll.

Let me just comment on both the testimonies we have heard. We could make an assumption that you are typical of many others that are suffering, or we could make an assumption that you are the exception to the rule. But in either case, you are, once you agree to take on the mission, required by your Government to take these vaccines.

Ms. GROLL. Correct.

Mr. SHAYS. This is really a message that we will convey to the DOD, you need to be assured that every need that you have is addressed and that if, in fact, like the statistics say, there will be some who will suffer. A vast majority won't, if the statistics are right. And you tend to be the very few under their view that are suffering. You shouldn't go under this kind of experience. You should be—your every concern should be addressed.

And I apologize that it hasn't been as a member of the Government.

Ms. MARTIN-ALLAIRE. May I add something?

Mr. SHAYS. You may add something and then we will get to Mr. Churchill. Yes. Why don't you put the microphone right next to you.

Ms. MARTIN-ALLAIRE. I just wanted to add, being as how you were talking about numbers, that there were 12 at our base that got this injection, starting back on September 18th, and out of the 12, there were 9 of them that had very bad, adverse reactions.

Mr. SHAYS. That is very helpful to know. Thank you.

Mr. Churchill.

Mr. CHURCHILL. Mr. Chairman and subcommittee members, thank you for allowing me to testify today. I am here today under my first amendment right, and this testimony does not reflect anything against the U.S. Air Force and the Michigan Air National Guard.

I work for the Michigan Air National Guard as a civil service technician. I am a technical sergeant for the Air National Guard and also I have served on active duty my first 3 years of service. I have served in the U.S. Air Force in some capacity for the past 17 years this December.

I have volunteered for numerous trips, including Southern Watch both in 1994 and 1996, and I volunteered for this trip that we were talking about to Qatar last November. As a prerequisite for this Qatar trip, 10 other civil service technicians along with two traditional Guardsmen were required to receive several anthrax vaccinations before we were allowed to go, the same vaccinations which brings me here today to testify about.

I would now like to testify before you about the medical complications that I have experienced, complications that I believe are directly attributed to the anthrax vaccination that I received. Mr. Chairman and subcommittee members, we have no full-time medical doctors at our unit. This being the case, we had to turn to the civilian medical community.

A little background on me. I have studied karate for quite a few years and I am an avid speed walker and do numerous activities to stay in shape. However, I have noticed since I received my fourth injection on March 14 that, when I went to my karate class,

I have no stamina. I just thought I was out of shape. I spent the next 2 days after I did my class, which is a 2-hour karate class, trying to recuperate.

Anything as far as sitting for a period of time, then standing, my legs ache, my joints in my hips, knees, and ankles crack and snap. I have a pain in my lower back, which comes and goes, I have found blisters inside my mouth. The last one I wasn't sure what it was. So I pinched it with my fingers and filled my hand with blood.

I have little red bumps all over my body, mostly concentrating on my torso. My skin will turn red and hot at any time, but then I will get chills. My hands and feet sweat excessively, and I have a tightness in my chest that comes and goes. My hands have little bumps under the skin, and the skin around my fingers is peeling off, including the palms of my hands. I have been having sinus troubles with a lot of drainage in the morning, sometimes with a blood-like mixture. And I have and continue to experience memory loss, irritability, and shortness of attention span and abdominal cramping.

I am not tolerable of the cold weather. My hands and fingers hurt extremely when they are cold. I have also found that my skin sunburns now under very little exposure.

On about March 27th, I received a medical questionnaire from Dr. Meryl Nass and it raised concerns. I was told from Dr. Nass about the vaccination adverse events recording system forms on the Internet. She suggested that I fill it out immediately and fax it to the CDC. I then scheduled myself for an appointment to find out if these things I was feeling could have anything to do with the fourth injection.

On March 29th, I went to my physician for an answer to my symptoms. The doctor's words were, it is not anthrax, you would be incapacitated and on the floor. We know nothing about this vaccine. The military gave you the shot, the military needs to find out what is wrong with you.

March 31st we had a meeting with our squadron commander, Major Dvorak. We were told that it was impossible for a line-of-duty orders without a physician's recommendation. And concerns of the lot number and the dates were addressed as administrative errors. The shot records would be collected, and the right information would be annotated on the shot records. Along with the shot records, the other major concern was that those individuals that were being treated by civilian doctors would have to sign a medical-release form for the clinic so that they could obtain the information that the civilian doctors had accumulated.

With no concern of personal health being taken, I was stunned at what I was being told. I decided to become proactive, and started calling as many people as I could to see who would be interested in helping us. I could not believe this many people were sick with no concern being displayed to the well-being, other than fixing administrative errors.

At 3 o'clock on that same day, I sent an email to Senator Carl Levin's office and House Representative Nick Smith with concerns of individual health and care for our unit. At 5 o'clock, Tech Sergeant Groll and I met with Colonel Seidel, the vice commander,

and discussed the following issues: No. 1 was the people and their health; No. 2 was the clinic; and No. 3 was the commander's concern.

On April 6th, I was informed that Martin, Groll, Stewart, and myself would be going to Wright Patterson Air Force Base on the 7th to see an allergist. We were to make sure that we turned in a copy of the VAERS form to the clinic before we left so that they could input the information into the military immunization tracking system. When we arrived at—when we arrived, we checked into the allergy department.

The doctor looked over my VAERS and took down my symptoms. He then checked me out pretty thoroughly and asked me if I had been near any animals in Qatar. He then told me he was going to order my blood drawn, a urinalysis, and a chest x ray. I was told after review of my blood, urinalysis, and chest x rays that I was OK.

On April 13th, Tech Sergeant LaMore and Staff Sergeant Frank went to Wright Patterson also. The doctor told Tech Sergeant LaMore and stated in his medical record that he was having a systemic reaction. The doctor recommended after the next injection, if the same symptoms occur, to cease the rest of the series. Tech Sergeant LaMore has been the only person diagnosed with the systemic reaction although he had the same symptoms as the rest of the individuals involved.

Some individuals, in fact, had worse reactions.

We are told people at high levels of the Guard that they are working on issues such as us using our civilian and technician sick and annual leave, our insurance payments, to include some high-cost prescriptions that my insurance does not pay for. There are a number of us that are getting our blood taken to have it sent for testing for squalene.

I hope these symptoms can be diagnosed and treated. These symptoms because I do not know if they are short-term, long-term, or treatable. Will they affect any of my future children? Or will they affect any of my family members?

In talking to Lori Greenleaf and Meryl Nass and others that have much more time and sources in this, they tell me there is a cure for the way that I feel. I cannot believe that I have received more information from people that have no interest in me other than the concern for another human being. This is appalling to me, considering my 17-year commitment to the U.S. Air Force and the Air National Guard.

I have taken more sick leave from work in the past 4 months than I have over the last 3 years. This statement is very true for just about all of the individuals involved in this situation. I ask that you please keep pursuing the truth into this vaccination. The information is there. There are just too many questions that nobody can answer at this time.

I again thank you, Mr. Chairman, subcommittee members. I will accept any questions at the end of this testimony.

[The prepared statement of Mr. Churchill follows:]

Congressional Hearings

Anthrax Vaccination Immunization Program

House Government Reform and

Oversight Committee

Chairman Shays Presiding

29 April 1999

Written Statement by:

David J.Churchill

Mr. Chairman and Sub-committee members thank you for allowing me to testify today. I am here today under my first amendment right and this testimony does not reflect anything against the United States Air Force or the Michigan Air National Guard. I work for the Michigan Air National Guard as a Civil Service Technician (CST), I am a Technical Sergeant for the Air National Guard and have also served on Active duty my first three years of service. I have served in the United States Air Force in some capacity for seventeen years this December. I have volunteered for numerous trips. I went to support Southern Watch both in 1994 and 1996 and I was selected for a trip to Qatar last November to perform maintenance on vehicles that had been left there from Desert Storm and Desert Shield operations. As a prerequisite for this Qatar trip, several other CST and I (including my backup, TSG Groll) were required to receive several Anthrax vaccinations. The same vaccination which brings me here today, to testify about. I held no reservations about these injections as I have received many other injections during the span of my career. I would now like to testify before you about the medical complications that I have experienced. Complications that I believe are directly attributed to the anthrax vaccination that I received. My testimony will also include experiences reported to me by individuals in my unit who have experience in seeking both a determination of the cause of our illness and treatment for that illness. Mr. Chairman and Sub-committee members, we have no full time medical doctors at our unit. This being the case, we have had to turn the civilian medical community.

14 March 1999

After receiving my fourth injection on March 14th I noticed the following symptoms. I study karate, am an avid speed walker, and do numerous other activities to stay in shape. However, I have noticed since I've began these injections, I can no longer do karate, as I have no stamina. I went to class three weeks ago, and just thought I was out of shape. I spent the next two days trying to recuperate from a 2-hour karate class. When sitting for a period of time, then standing, my legs ache, my joints in my hips, knees and ankles crack and snap. Sometimes the ones in my feet hurt so badly when they crack, it nearly brings me to the ground. I've got a pain in my lower back, which comes and goes. I've found blisters inside my mouth. The last one, I wasn't sure what it was, so I pinched it with my fingers, and it filled my hand with blood. I have little red bumps all over my body, mostly concentrating on my torso. My skin will turn red and hot at any time, but then I will get chills. My hands and feet sweat excessively, and I have a tightness in my chest that comes and goes. My hands have little bumps just under the skin. The skin around my fingers is peeling off. I have been having sinus trouble with a lot of drainage in the mornings, sometimes with blood like mixture. I have and continue to experience memory loss, irritability, and shortness of attention span and abdominal cramping. I am not tolerable of the cold weather. My hands and fingers hurt extremely when they are cold. I have also found that my skin sun burns now under very little exposure.

17 March At a memorial service with the Honor Guard for a fallen service member, watching TSG Groll start shaking so badly during the service, I really didn't know if she was going to make it. We had attributed it to not eating properly or some kind of flu.

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27 March

We have received a medical questionnaire from Dr. Meryl Nass and it raised concerns. I was told from Dr. Nass about the Vaccination Adverse Events Reaction System (VAERS) forms on the Internet. She suggested that I fill it out immediately and fax in to the Center of Disease Control (CDC). Those of us with medical questions talked about the questionnaire from Dr. Nass. We then found that there were like symptoms of rashes, headaches, body aches, flu like symptoms, sweating excessively, uncontrollable shakes, and blood in the urine. I then scheduled myself for an appointment to find out if these things I was feeling could have anything to do with the fourth injection.

29 MarchI went to my physician for an answer to my symptoms. In my description of the things that were happening to me I made reference to most of these things had started after taking the Anthrax Vaccination series. The doctor asked why I was getting Anthrax shots and I told them it was mandatory for the part of the world that I had just returned from. The doctor's words were "It's not Anthrax, you'd be incapacitated, and on the floor. We know nothing about this vaccine, the military gave you the shot, the military needs to find out what's wrong with you".

30 March

Had a meeting with Maj. Dvorak, our Logistics Squadron Commander, to take down information to research possibilities of a Line of Duty (LOD) order, medical attention and gathering facts for individuals having reactions to the vaccination.

31 March

Had another meeting with Maj. Dvorak. We were told that it would be impossible for LOD's without physician's recommendation, and that the concerns of the lot numbers and dates were addressed as administrative errors. The shot records would be collected, and that the "right information" would be annotated on the shot records. Along with the shot records a major concern was that those individuals that were being treated by civilian doctors would have to sign medical release forms for the clinic. With no concern of personal health being taken. Following the chain of command, SSG Martin and myself addressed our concerns with Lt. Col. Allen, or Logistics Group commander. He mentioned that some of the information he had no knowledge of, and would address these issues with Col. Heaton. Later that afternoon, I called Col. Allen, and was told that all issues were being addressed, and that Maj. Dvorak had told him everything was being handled as far as the shot records to be corrected of the "administrative errors". Col. Allen further stated that Maj. Dvorak would be handling all concerns of this situation, as she had all the information, and to keep in contact with her. I was stunned at what I was being told. I decided to become proactive and started calling as many people as I could to see who would be interested in helping us. I could not believe this many people were sick with no concern being displayed to their well being, other than fixing administrative errors.

3:00 p.m.

Sent email to Sen. Carl Levin and House rep Nick Smith with concerns of individual health and care.

4:00 p.m.

Called Col. Seidel, our vice wing commander, to set up meeting with intentions to file a Medical Inspector General complaint on lack of medical treatment for the personnel on base.

5:00 p.m.

TSG Groll and I met with Col. Seidel discussed the following issues, #1. People (health) #2. Clinic #3. Commanders

6:00-8:00 p.m.

Phoned most all the individuals with the outcome of the meeting with Col. Seidel to see if they were interested in medical treatment if or when it becomes available.

1 April

Sent names to Col. Seidel of those interested in medical treatment. Two people had reservations or hesitation because of reprisal or retaliation. I was told that Col. Heaton, our wing commander, was notified and that he recommended that all individuals that had received the forth injection would be scheduled to see the doctors at Wright Patterson Air Force Base. An information team was built to research all sources on the probability of these individuals getting to Wright Patterson.

2 April

Meeting with Col. Seidel, Maj. Kowalski, the financial comptroller, Maj. Dvorak, Cpt. Neidergall, the base JAG, SMS Keller, the Senior Health Technician and TSG Moross, public health technician. We were told that all angles being worked. The only way for us to receive treatment would be in a non-pay military status. All this is on tape.

4:30 p.m.

Phoned Col. Seidel back with concern that there was no more that "we" or "I" could do to help this situation. Col. Seidel then told me about a Col. Garrimone who had called and left a message to return his call, Col. Seidel was not sure who he was. Col. Seidel was going to call him and see if he had new information.

5:05 p.m.

Col. Seidel phoned back stating that Col. Garrimone was the head Allergist at Wright Patterson. The concern was that we get there ASAP not the 23rd. They had talked about Neurology work, blood tests and more. Possibly getting the entire group in on the 13th April. More to follow, I then exchanged phone numbers with Col. Seidel in case we needed to reach anyone, to include TSG Groll and SSG Martin.

6 April

Information had changed now four individuals Martin, Groll, Stewart, and myself would be going to Wright Patterson Air Force

Base on the 7th to see the allergist. We were going to be driven to Wright Patterson Air Force Base, so that we didn't have to drive over the eight-hour day permitted to travel. Orders would be made out for the 7th and 8th. I was told by Maj. Dvorak that in order to receive the per diem for the trip to make sure it took at least the 12 hours on that day, and that we would be coming home the same day. Travel would

be in military clothing on a non-pay status. To make sure that we turned in a copy of the VAERS form to the clinic before we left so they could input it in the MIT'S system. Talked to Maj. Dvorak about the pay status and she was very short with me and said that we were told that we would be in a non-pay status. I mentioned to her that I had spoke to the civilian pay technician and there were some differences in what we were being told.

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7 April

I turned over my VAERS form to the medical technician before leaving for Wright Patterson Air Force Base also signed out our medical records. We then packed into a military van for the five-hour drive to Wright Patterson Air Force Base. When we arrived we checked into the Allergy department. TSG Groll and SMS Stewart's appointment were first at 1:00 p.m. SSG Martin's appointment was for 2:00 p.m., and mine was for 3:00 p.m. SMS Stewart then came out and they called SSG Martin in. SMS Stewart told me while I waiting to go in that his checkup was nothing. They had ordered no blood tests, did not perform a urinalysis, and no x-rays. He also stated the allergist had shown very little concern. SSG Martin and TSG Groll had came out, and they were taking TSG Groll to the neurology clinic to do tests on her. I was then called in. The doctor looked over my VAERS and took down my symptoms. He then checked me out pretty thoroughly, and asked me if I had been near any animals in Qatar. He then told me he was going to order my blood drawn, a urinalysis, and a chest x-ray. When I completed all my test requirements, I came back to find TSG Groll crying in the chair, she stated that she was in severe pain. I asked SSG Martin what was going on, and she told me that it seemed that the neurological work could not be done on TSG Groll until the next morning. They also wanted blood work and urinalysis done as well. They had been in contact with the base since 2:00 p.m., but during this time frame, our wing and vice wing commander were out flying, and the person left in charge could not make a decision on whether we could stay the night, or come home. Funding seemed to play a big part in this inability to make a decision. In talking to TSG Groll and the medical personnel at Battle Creek, they wanted us to take her downtown to a hotel because base billeting was not available. Other than making an appointment, our base clinic never made any plans for anything longer than a one-day trip. We had no transportation for TSG Groll and were not going to leave her stranded for two days until the next group of people came down. I then went to discuss this with Col. Garrimone who said he was not happy with our unit, because they had taken almost four hours, and still had made no decision. I then informed Col. Garrimone of the later trips that we had on Friday and the following Tuesday. I then asked if it was possible that she be allowed to make an appointment on one of those days and return back down to complete these other medical appointments. Col. Garrimone got on the phone with Col. Seidel and stated Robin was coming home with us, and that the base needed to make further arrangements to have more tests completed. Col. Garrimone put TSG Groll on a physical profile citing possible neurological reactions to the anthrax vaccination. We left Wright Patterson at about 5:30 p.m., TSG Groll was feeling very relieved that she was coming home, and was not going to be left alone. We arrived back at Battle Creek at 11:15-11:30 p.m., all physically and emotionally drained, due to the long and unsatisfactory trip.

8 April

Went in to work around 9:00 a.m., scheduled a meeting with Col. Seidel to discuss dis-pleasures with the trip, the different treatments as far as TSG Groll and mine being more thorough than the other two. SSG Martin joined me during this meeting. I told him I was hoping that it had nothing to do with the fact that TSG Groll and I had filed the I.G. complaint. Col. Seidel told me he would look into the issues of my complaint. However, assured me the difference in treatment had nothing to do with the complaint. That evening, still physically exhausted, I fell asleep around 6:00 p.m., and awoke the next morning at 6:00 a.m., with a bacterial infection in both eyes. I was told by my personnel physician to stay home from work for at least 24 hours.

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9 April

TSG Groll and I talked on the phone. I was telling her that I was "sick again". She said the base had called and ordered her to be there on Saturday, the next scheduled UTA, which was the following day, even though she had a doctor's excuse from her civilian

doctor excusing her from work/UTA.

11 April

When I came into drill, I received a phone call from TSG Groll. She sounded exhausted. She informed me that her husband had to rush her into the emergency room the night before. They had spent over seven hours trying to find the cause for her abdominal cramping which was doubling her over. The doctor's had scheduled her for numerous tests for the rest of the following week.

13 April

Spoke with one of the twelve individuals in our group, their civilian doctor's have been doing numerous tests. Seems that this person was experiencing chest pains, and shortness of breath. The doctors have determined that they have pularcy. This may just be coincidental. That same day, TSG LaMore and SSG Frank went to Wright Patterson. SSG Frank told me that the doctors didn't do any blood work or any other lab work on either one of them. The doctor just reassured them that the Anthrax vaccine was okay, and they have the documentation to prove it. The doctor told TSG LaMore and stated in his medical record, that he was having a systematic reaction. The doctor recommended after the next injection if the same symptoms occur, to cease the rest of the series. TSG LaMore has been the only person diagnosed with a systematic reaction, though he had the same symptoms as the rest of the individuals. Some individuals in fact had worse.

16 April

Phoned the Calhoun County Health Department to see if they were interested in looking into our situation. Talked to a communicable disease nurse by the name of Sue Stieldenner. She took down the information, and stated she had no knowledge of the Anthrax vaccines. I asked whom I should contact at the state level, and she referred me to Dr. Bill Hall at the State Health Department. I phoned his office, his secretary informed me he was not in. She asked what it was regarding, and I told her. She referred me to Bio-Port, and she transferred me to them directly. A person from Bio-Port answered, and I informed her of my situation, and who I was. She said that I should speak to the director, Bill Nummy, and that she would transfer me. After a couple of minutes she came back on the line, and said that he referred me to the quality office at Bio-Port. I was to speak to a Cindy Kramer. After telling Cindy what my situation was, she said that I needed to speak to the director, Bill Nummy. I informed her he sent me to her. She said she would have to get some forms and call me back. A couple of hours later, she called. She asked if I had filed a VAERS form, what my symptoms were, and she would note them.

I cannot speak for the other 11 individuals, but the lack of compassion and care on this issue has been appalling. There are a number of people involved on this issue, but it appears that no one can make a decision. We are told people at high levels of the Guard are working on issues such as using our sick and annual leave, our insurance payments to include some high cost prescriptions that my insurance does not pay for. Having to travel to Wright Patterson in a non-pay status, made to go to Wright Patterson and back in one day, which subsequently was an 18-hour day. There are a number of us that are getting our blood taken to have it sent for testing for Squalene. I hope these symptoms can be diagnosed and treated. These symptoms scare me because I don't know if they are short term, long term or treatable. Will they effect any of my future children, or will they effect any of my family members?

In talking to Lori Greenleaf and others that have much more time and sources in this, they tell me there is a cure for the way that I feel. I can not believe that I have received more information from people that have no interest in me other than concern for another human being. This is appalling to me considering my seventeen-year commitment to the United States Air Force or to the Air National Guard. I have been made to feel that I am just a number that they have that works for them which contributes to their statistics.

I have taken more sick leave from work in the past four months than I have over the last three years (this statement is very true for just about all the individual involved in this situation). I ask that you please keep pursuing the truth into this vaccination. The information is there. There are just to many questions, which no body can answer at this time. I again thank you Mr. Chairman and subcommittee members. I will accept any questions at the end of the rest of the testimonies.

Supporting documentation given with testimony 1. Notarized copy of shot records. 2. Copies of orders to administer shots. 3. Letter of appointment to Wright Patterson to see allergy department. 4. Copy of medical record from my visit to Wright Patterson. 5. Letter from MSG John Zink driver who took us to Wright Patterson. 6. Letter from clinic on notice of forth shot, explaining the

situation of no doctor on staff creates.

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Mr. SHAYS. Thank you, Mr. Churchill. I hope that you are finding that you are getting a better response now than you were getting. Are you finding that?

Ms. GROLL. No, sir.

Mr. SHAYS. OK. We will address that.

Mr. Shepard. Excuse me, nice to have you here, sir.

Mr. SHEPARD. Good afternoon, Mr. Chairman. Thank you for your indulgence. I am going to be as short as possible, but I really think the message I have is really important and needs to be heard in its entirety.

Mr. SHAYS. Well, that is why you are here.

Mr. SHEPARD. My name is Sergeant Michael Shepard. My family and I are residents of Potter County. That is in the 5th Congressional District in rural north-central Pennsylvania. Congressman John Peterson represents us. I am currently finishing a 4-year enlistment as a military intelligence analyst in the U.S. Army. I am proud of my service and deeply respect the military and the great freedom it defends everyday.

I am here to speak for what I believe is a silent majority in the armed forces on the anthrax vaccine immunization program. At this point, I want to make it clear for the record that my opinions on this issue are not tied in any way to the possibility of me being deployed. I am not on deployment orders, have not been in the past year, and do not intend to be deployed in the near future. However, I am prepared to deploy at a moment's notice.

Furthermore, my service record is impeccable at this time. I have never been accused of misconduct, given non-judicial punishment, or even given a negative counseling statement. My record demonstrates achievement far and beyond my peers in such a short period. These statements are to totally disarm the suggestions that have been made or will be made in the future regarding my motivation or my fellow soldiers' motivation who oppose the AVIP.

My testimony today expresses my convictions and is not intended to reflect or represent the Army's policies or views. My comments regarding safety and efficacy today are meant to communicate the situation that faces the average enlisted soldier. My credibility does not lie in what I know about science, but what I know about soldiers.

We have heard opposing views regarding the safety of this vaccine on several fronts. The first, no long-term studies available. The second, the nature of the FDA approval. The third, serious questions regarding the production facility. Fourth, the current reactions of the service members. And fifth, circumstantial evidence linking vaccinations, possibly anthrax, to Gulf war illnesses.

In addition, the efficacy of the vaccine has been debated in regards to it being developed for cutaneous anthrax exposure.

The exacerbating element of the AVIP is the shrinking credibility of the DOD. Since your last hearing, the Army has changed its AVIP brochure to retract its claim that veterinarians routinely use this vaccine. In addition, the publication of the investigation in Vanity Fair on the anthrax vaccine's possible tie to Gulf war illnesses has further damaged the DOD's credibility, even if you dismiss half of the article as sensationalism.

Finally, the military's heavy-handed tactics for producing a "successful" program have been brought to light by the reversal of the decision—or it is in limbo now—regarding PFC Lundbom's, you recall from your last hearings, discharge. It was announced here in your committee hearing and then changed when he returned to his unit.

Any service person that has completed basic training recognizes that the DOD's claims to this committee and the congressional staff, which it is vociferously lobbying, that this vaccine is, "as important as carrying a rifle or gas mask" or is a vital piece of "body armor," as you heard in the first hearing, are quizzical at best. In fact, aren't these claims troubling when you consider that these senior leaders are expecting us to believe that the crude technology of the 1950's and 1960's is the body armor, my body armor of the next millennium?

Is this the best we can do as the most modernized military in the world? Why aren't we researching and developing the best protective gear that combines a more effective protective mask with protective clothing that allows for more flexibility to accomplish the mission?

If we are this concerned with an imminent attack, we need to make it the highest priority to obtain the best protective equipment and tightly control the national stock so that we are always ready to go to war.

In light of these real concerns, I believe the information available to soldiers and the lack of candor exhibited by DOD officials when pointedly questioned on the information leaves the enlisted soldier two options. The soldier can blindly trust the DOD and accept the shots at his own risk, or refuse the shots and accept the current contextualization of this act as disobeying an order.

If this were all an academic discussion, then it would certainly be intriguing at this point. However, even as we speak, men and women in uniform are facing very serious and difficult choices that have long-term consequences just like this vaccine.

You see, this issue is about class too. Most members of an all-volunteer force are from the middle and lower classes of society. This service is generally comprised of citizens from urban and rural America, rural districts just like my own. These people are barely paying their bills with their paychecks.

Place yourself in the boots of a 23-year-old PFC who is a single mother struggling to get by on her salary and additional assistance. She has followed the AVIP issue until it is her turn. She is faced with these very serious, legitimate, and real questions regarding the effects on her health on the one hand and loss of her livelihood, educational benefits, and loss of an honorable characterization of her loyal service to the U.S. Army on the other.

What does the specialist who is getting married this summer do? He needs leave in June and he needs the GI bill to provide for his wife and family. What about the soldier who has three kids and 10 years in service, like most enlisted soldiers, barely making ends meet and cannot even imagine a fine, let alone the loss of rank. These personnel may initially refuse, but after continual threats and consideration of their future, will yield to the harassment and submit their bodies because of a dollar bill.

In my personal experience, I am aware several initial AVIP refusers who were threatened with military punishments and then complied with the program. Every soldier I speak to has reacted substantially to these shots, with several suffering diarrhea, abdominal cramps, malaise, flu-like symptoms, including fever, headache, and, in some cases, vomiting.

In addition, local swelling has lasted longer than any shot they have ever taken. It is a big deal.

Some soldiers' arms have stayed swollen for over 2 weeks. I asked these soldiers about using the VAERS forms. They did not know it existed and were not issued one when vaccinated. Nor were these soldiers briefed on how to report the actions or the importance of reporting these reactions for the very success of this program.

In essence, you are not getting the truth: "Passive monitoring," is being generous.

At my level, my observations on the impact of this program as you asked me as a first-line supervisor include the following. First, soldiers overwhelmingly distrust the DOD on this issue because of the available information. Second, soldiers put their career, livelihood, and educational benefits before their legitimate concerns for their health.

Third, soldier morale and trust in our leadership is suffering due to the obvious steamrollering over legitimate concerns and questions. They will continue to do so if this program is allowed to continue unabated, and if future vaccination programs follow this particular model, this will affect retention in both direct and indirect ways.

Fourth, soldiers are confused with the sudden paranoia about NBC attacks in the public and private sector. The defense establishment has known about weaponized anthrax and other elements since at least 1990 if not long before. The threat has always been real, but taking action for action sake does not help the situation. It seem more like a Band-Aid than strategy. Those of us at the lowest echelons in the intelligence community have taken time to pause because we are confused. The nation of Israel, arguably the greatest enemy of our current adversaries in the Gulf region, is not scrambling like the United States to inoculate their civilians and soldiers. They have protective equipment ready for use if necessary.

And the fifth is 200,000-plus compliant service persons are not an endorsement of the AVIP. The silent majority does not want to take these shots based on the legitimate concerns that were present before this committee investigation began and still have not been answered by this probe.

Soldiers are not disputing that they are in the armed forces and must respect the orders of superiors. Trust and respect work both ways. In times of peace, the military must train as they fight in order to be confident that in the day of battle each soldier will understand their duty and will execute without question upon order.

However, let us make sure we keep the AVIP in context. You were told in your first hearing that soldiers, "cannot choose which order to follow." Very true. But how do you expect soldiers to trust the orders of their superiors on the day of battle when, during peace, they poorly plan and execute programs like this one.

To add injury to insult, they attempt to convince the American people and us that this 1950's technology is my, "body armor," and is important as my gas mask for attacks of biological-chemical cocktails.

Soldiers are not fooled and I hope you will not be either.

This issue will affect me personally in the near future. I do not want to risk my personal health for this program that is extremely suspect, at best, in light of the current information available. There are legitimate concerns as we have outlined them.

I have contacted both Senators and my Congressman, John Peterson, regarding the issue. I am not aware of any written policy regarding service personnel with less than 18 months. When I am forced to choose whether to take the shots in June, I will have only 10 months left in the Army. Even if I suspend critical analysis of the situation and blindly trust the DOD and take the shots, I will have no recourse if it causes my family or I future problems—health problems. This is because of the legal precedent of the early 1950's commonly referred to at the Feres doctrine.

The doctrine has held that the Government is not liable for the effects of military service. The lawsuits stemming from birth defects in children of Gulf war veterans have been dismissed based on the Feres doctrine in the past 2 years.

The most I could hope for if I take the shots and suffer future health problems is treatment from the Department of Veterans Affairs, if my income is low enough. Therefore, in light of the current information, I do not feel compelled to comply with the AVIP.

The consequences of not complying, if I do not comply, will likely be demotion, fines, and threats of a prejudicial discharge. I do not want to face these consequences; however, I will do so if I am forced to. I will do it not only for me but also for my fellow service members and citizen soldiers in my congressional district that are without a voice.

The majority of service personnel in my unit and, if surveyed, the entire military do not want to take the vaccine. The majority of a volunteer force is from the lower portions of our society in terms of affluence. This means that the majority of service personnel cannot take the financial hardship of fines. In addition, a discharge that is not honorable will take away the soldier's GI bill, which is why many young Americans of modest means join the military service, a promise of access to education to build a brighter tomorrow for themselves and their families.

In my opinion, with so many questions outstanding at this time, it is wrong, even immoral, to force service personnel into choosing between these alternatives. It is time for Members of Congress, especially Members representing districts like mine, to step forward, take a principled stand, and ask that this program be halted, made voluntary, or, at minimum, suspended until the deliberative bodies of the U.S. House and Senate complete their reviews of the AVIP and report their findings.

Thank you, Mr. Chairman.

[The prepared statement of Mr. Shepard follows:]

Statement of Sergeant Michael B. Shepard

Before the Subcommittee on National Security,

Veterans Affairs, and International Relations

Of the Committee on Government Reform

Of the House of Representatives

April 29, 1999

My family and I are residents of Potter County that is in the 5th Congressional District in rural northcentral Pennsylvania. Congressman John Peterson represents us. I am currently finishing a four year enlistment as a military intelligence analyst in the U.S. Army. I am proud of my service and deeply respect the military and the great freedom it defends everyday. At this time, I serve as the training non-commissioned officer(NCO) and the assistant Nuclear, Biological, Chemical Warfare Non-commissioned officer in my unit. I am here to speak for, what I believe, is the silent majority in the armed forces on the Anthrax Vaccine Immunization Program(AVIP).

At this point, I want to make it clear for the record that my opinions on this issue are not tied in any way to the possibility of me being deployed. I am not on deployment orders, have not been in the past year, and do not intend to be deployed in the near future. However, I am prepared to deploy at a moment's notice. Furthermore, my service record is impeccable. I have never been accused of misconduct, given non-judicial punishment or even given a negative counseling statement. My record demonstrates achievement far and beyond my peers in such a short period. I was promoted with two waivers and affirmed my superiors' confidence by graduating from the Army's leadership school as the honor graduate. This year I was chosen to assist my commander in managing our unit training which is a slot usually filled by a soldier at least one grade higher than mine. These statements are to totally disarm the suggestions that have been made or will be made in the future regarding my motivation or my fellow soldiers' motivation who oppose the AVIP. We work everyday to defend our freedom and are willing to enter harm's way at any time for our country. My testimony today expresses my convictions and is not intended to reflect or represent the Army's policies or views.

My comments regarding safety and efficacy today are meant to communicate the situation that faces the average enlisted soldier. My credibility does not lie in what I know about science but in what I know about soldiers. We have heard opposing views regarding the safety of this vaccine on several fronts:

1. No long-term studies available on the effects of this substance over a long period of time other than the anecdotal, non-scientific, non-peer reviewed examples that there are no ill health effects in military lab workers

2. FDA approval is based on pre-1970 study that apparently would not meet a FDA standard today.

3. Serious questions regarding the production facility.

4. Current reactions of service members.

5. Circumstantial evidence linking vaccinations, possibly anthrax, to Gulf War Illnesses.

In addition, the efficacy of this vaccine has been debated.

1. The vaccine was developed for cutaneous anthrax exposure and studies on inhalation anthrax are limited at best.

2. Senate reports indicate efficacy of vaccine is unknown based on the limited testing.

The exacerbating element of the AVIP is the shrinking credibility of the DOD. Since your last hearing, the Army has changed its AVIP brochure to retract its claim that veterinarians routinely use this vaccine. The claim that most friendly vets that take care of our domestic pets take this vaccine comforted many service personnel until is was debunked. In addition, the publication of the

investigation in Vanity Fair on the anthrax vaccine's possible tie to Gulf War Illnesses has further damaged the DOD's credibility even if you dismiss half of the article as sensationalism. Finally, the military's heavy-handed tactics for producing a "successful" program have been brought to light by the reversal of the decision regarding PFC Lundbom's discharge that was announced before this very committee and then changed when he returned to his unit.

Any service person that has completed basic training recognizes that the DOD's claims to this committee and the Congressional staff, which it is vociferously lobbying, that this vaccine is "as important as carrying a rifle or gas mask" or is a vital piece of "body armor" are quizzical, at best. In fact, aren't these claims troubling when you consider that these senior leaders are expecting us to believe that the crude technology of the 1950's and 1960's is the body armor of the next millennium? One soldier who was in the Gulf region last year and began his anthrax vaccinations while serving in the Gulf had this story. Upon returning from the deployment he turned in his NBC protective equipment. The NBC NCO chuckled and told him it was a good thing they did not get hit because this soldier's equipment was outdated by military standards and would have been little use to him. Is this the best we can do as the most modernized military in the world? Why aren't we researching and developing the best protective gear that combines a more effective protective mask with protective clothing that allows for more flexibility to accomplish the mission? If we are this concerned with an imminent attack, we need to make it the highest priority to obtain the best protective equipment and tightly control the national stock so that we are always ready to go to war.

In light of these real concerns, I believe the information available to soldiers and the lack of candor exhibited by DOD officials, when pointedly questioned on the information, leaves the enlisted soldier two options. The soldier can blindly trust the DOD and accept the shots at his own risk or refuse the shots and accept the current contextualization of this act as disobeying an order.

If this were all an academic discussion then it would certainly be intriguing at this point. However, even as we speak, men and women in uniform are facing very serious and difficult choices that have long-term consequences just like this vaccine. You see this issue is about class, too. Most members of an all volunteer force are from the middle and lower classes of society. The service is generally comprised of citizens from urban and rural America. Rural districts just like my own. These people are barely paying their bills with their paychecks.

Place yourself in the boots of a 23 year-old PFC who is a single mother struggling to get by on her salary and additional assistance. She has followed the AVIP issue until it is her turn. She is faced with these very serious, legitimate, and real questions regarding the effects on her health on the one hand and the loss of her livelihood, educational benefits, and loss of an honorable characterization of her loyal service to the U.S. Army on the other. What does the specialist who is getting married this summer do? He needs leave in June and needs the G.I. Bill to provide for his wife and future family. He absolutely does not want to risk his health in this program especially since he will leave the military in 10 months anyway. What are his choices? What about the soldier who has three kids and has 10 years in the service and is like most enlisted soldiers: barely making ends meet and cannot even imagine a fine let alone loss of rank.? These personnel may initially refuse but after continual threats and consideration of their future will yield to the harassment and submit their bodies because of a dollar bill. In my personal experience I am aware of several initial AVIP refusers who were threatened with the military punishments and then complied with the program. Every soldier I speak to has reacted substantially to the shots with several suffering diarrhea, abdominal cramps, malaise, flu-like symptoms including fever, headache, and in some cases vomiting. In addition, local swelling has lasted longer than any shot they have ever taken. Some soldiers' arms have stayed swollen for over two weeks. I asked these soldiers about using the VAERS form. They did not know it existed and were not issued one when vaccinated. Nor were the soldiers briefed on how to report reactions or the importance of reporting these reactions for the success of this program.

At my level, my observations on the impact of this program as a first-line supervisor include the following:

1. Soldiers overwhelmingly distrust the DOD on this issue because of the available information.

2. Soldiers put their career, livelihood, and educational benefits before their legitimate concerns for their health.

3. Soldier morale and trust in our leadership is suffering due to the obvious steamrollering over legitimate concerns and questions. It will continue to do so if this program is allowed to continue unabated and future vaccination programs follow this model. This will affect retention in both direct and indirect ways.

4. Soldiers are confused with the sudden paranoia about NBC attacks in the public and private sector. The defense establishment has known about weaponized anthrax and other elements since at least 1990 if not long before. The threat has always been real but taking action for action's sake does not help the situation. It seems more like a Band-Aid than strategy. Those of us at the lowest echelons in the intelligence community have taken time to pause because we are confused. The nation of Israel, arguably the greatest enemy of our current adversaries in the Gulf region, is not scrambling like the U.S. to inoculate its civilians and soldiers. They have protective equipment ready for use if necessary.

5. 200,000 plus compliant service persons are not endorsements of the AVIP. The silent majority does not want to take these shots based on the legitimate concerns that were present before this committee investigation began and still have not been answered by this probe.

Soldiers are not disputing that they are in the armed forces and must respect the orders of superiors. Trust and respect work both ways. In times of peace, the military must train as they fight in order to be confident that on the day of battle each soldier will understand their duty and will execute it without question upon order. However, let us make sure that we keep the AVIP in context. You were told in your first hearing that soldiers "cannot choose which orders to follow." True. But how do you expect soldiers to trust the orders of their superiors on the day of battle when, during peace, they poorly plan and execute programs like this one? And to add injury to insult, they attempt to convince the American people and us that this 1950's technology is my "body armor" and as important as my gas mask for attacks of biological-chemical cocktails? Soldiers are not fooled and I hope you will not be either.

This issue will affect me personally in the near future. My unit will be lined up on June 7th, 21st, and July 6th and forced to take the first three vaccinations. I do not want to risk my personal health for this program that is extremely suspect, at best, in light of the current information available. There are legitimate concerns, as outlined in Mr. Shays' statement that opened the initial proceedings on this issue, about the long-term safety of the vaccine, the manufacturing processes, and the DOD's past record on medical matters. In addition to these concerns, I am concerned about the recent findings in the GAO report to Congressman Metcalf and the Vanity Fair investigation. I have contacted both of my U.S. Senators and my Congressman John Peterson regarding this issue.

This vaccine is administered in six shots over 18 months. I am not aware of any written policy regarding personnel with less than 18 months in service. When I am forced to choose whether to take the shots in June I will have only 10 months left in the Army. Even if I suspend critical analysis of the situation and blindly trust the DOD and take the shots, I will have no recourse if it does cause my family or I future health problems. This is because of the legal precedent of the early 1950's commonly referred to as the Feres doctrine. The doctrine has held that the government is not liable for the effects of military service. Lawsuits stemming from birth defects in children of Gulf War veterans have been dismissed based on the Feres doctrine in the past two years. The most I could hope for if I take the shots and suffer future health problems is treatment from the Department of Veteran's Affairs if my income is low enough. Therefore, in light of the current information I feel compelled to not comply with the AVIP.

The consequences of not complying, if I do not comply, will likely be demotion, fines, and threats of a prejudicial discharge. I do not want to face these consequences. However, I will do it if I am forced to do so. I will do it not only for me but also for my fellow service members and the citizen soldiers in my Congressional District that are without a voice. The majority of service personnel in my unit and, if surveyed, the entire military, do not want to take this vaccine. The majority of a volunteer force is from the lower portions of our society in terms of affluence. This means that the majority of service personnel cannot take the financial hardship of fines. In addition, a discharge that is not honorable will take away that soldier's GI Bill which is why many young Americans of modest means join the military service: the promise of access to education to build a brighter tomorrow for themselves and their families. In my opinion, with so many questions outstanding at this time, it is wrong, even immoral, to force service personnel into choosing between these alternatives. It is time for a Members of Congress, especially Members representing Districts like mine, to step forward, take a principled stand, and ask that this program be halted, made voluntary, or at minimum, suspended until the deliberative bodies of the U.S. House and Senate complete their reviews of the AVIP and report their findings.

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Mr. SHAYS. Thank you, Mr. Shepard.

Mr. Shepard—I am going to refer to him as Mr. Shepard. You are in uniform but you are testifying as a private citizen? Is that correct?

Mr. SHEPARD. I am testifying—I can testify as a member of the Service with the invite that you gave me. I checked with legal counsel. And testifying as an enlisted person as well as a private citizen——

Mr. SHAYS. You are in uniform and you are a sergeant. Correct?

Mr. SHEPARD. Yes, sir.

Mr. SHAYS. OK. Let me just say to you that I would not want you to in any way infer from these hearings that it would be our recommendation that you not comply based on your orders. This would be clearly a personal decision, and I would respect your personal decision. But I just want to make sure that you wouldn't feel false cover by coming to this committee and then taking that stand and inferring—because I have concerns about it being mandatory and voluntary, and maybe concerns that go deeper than that, that I not mislead you.

Mr. SHEPARD. I appreciate that, Mr. Chairman. I recognize it is a personal choice and all the personal consequences that may follow will fall upon my head.

Mr. SHAYS. Well, your statement was very articulate and extremely well thought out and impressive, as were all the testimony.

I am just going to say it again, and that is, we are trying to determine whether this is the right policy for the military. We are trying to determine whether we can feel comfortable that the anthrax vaccine is safe. We are trying to determine whether or not—how we want to weigh in on this.

The one thing I feel pretty convinced about is, given what I know, that it should be voluntary and that you shouldn't be, Mr. Shepard, placed in the situation you feel placed in.

And the other thing I know is that we don't even have to get into a debate on the issues that we heard from Ms. Martin-Allaire and Ms. Groll and Mr. Churchill about the fact that you have taken the vaccine and you do know your bodies, you know how you felt before, and you know how you felt afterwards. And you shouldn't be left in this vacuum, trying to fend for yourself. Your employer, your government should be by your side, helping you in every way, and you shouldn't even have even a speck of feeling somewhat deserted and betrayed.

And if nothing else, I certainly would want to weigh in on that side of it. I am going to just ask any of you—your testimonies are pretty comprehensive, they are fairly consistent. In the case of Ms. Allaire, Ms. Groll, and Mr. Churchill, you are also making a statement besides the fact that you do not feel well. And you describe symptoms that are quite similar. You are making the statement that others you work with are encountering the same problem.

Out of how many? If you would, Ms. Martin-Allaire. Why don't you move that microphone over a little bit further.

Dr. Nass, you kind of got us into this whole issue, but I am just going to focus on those that have been on the firing line right here as——

Ms. MARTIN-ALLAIRE. In our group this past time, around in September, there was 12 of us that started receiving the shots.

Mr. SHAYS. And how many are not—are feeling the effects?

Ms. MARTIN-ALLAIRE. There was nine.

Mr. SHAYS. Nine out of 12.

Ms. GROLL. Sir?

Mr. SHAYS. Yes.

Ms. GROLL. I think it is important to note too that we are the first, we are the, say, guinea pigs. But they have called us the guinea pigs, too. We are the first ones at our base to receive the shots. We are the first group of individuals to receive them.

Mr. SHAYS. It kind of makes you wonder too though if you don't have a batch that is not up to the level it should be. Well, we will be pursuing that as it relates to the 12 of you.

Mr. Churchill, you are not part of the same——

Mr. CHURCHILL. Yes, sir.

Mr. SHAYS. So you are three of the nine? OK.

Mr. CHURCHILL. Also, I would like to make mention that on Tuesday, before we came down here, I had called our clinic because I wanted to get a copy of my VAERS form that I sent to the CDC. And there is a lot of debate about these VAERS forms that they are taking their numbers from.

When I called our senior health technician at our clinic, I had referred to if I had my copies still in my medical records before I went to Wright Patterson, and she said yes. And I had questioned if I could get a copy of that form from her, and she said sure. Well, I in turn had mentioned what had happened to the other forms that were filled out for all the other individuals that were sent to Wright Patterson, being all 12 of us, and she said she still had them and the only ones that were probably sent out she didn't know what to do with them still, other than she had inputted the information into the military immunization tracking service. But she never forwarded them to anybody else.

So they are still sitting in our unit since they were filled out the second week in March.

Ms. GROLL. The only VAERS forms that the CDC has received have been from the three of us, and that is because we independently either faxed them or I personally mailed mine. And I have a confirmation. I included that as part of my written testimony from VAERS that they received my vaccine. The rest of the individuals that counted on the clinic to forward them on, it has never happened.

Mr. SHAYS. Tell me what you think the significance is of the misdating, that it was just carelessness or intentional?

Ms. GROLL. What was the question?

Mr. SHAYS. The misdating of the shots.

Ms. GROLL. I personally feel it was intentional. As I stated in my statement, sir, that it is their impression, and it is also out on I believe it is the DOD Web site, there's a 24-hour window. By giving us the shot on Sunday, and this an impression, sir, and an opinion of my own——

Mr. SHAYS. I understand. That is what I am asking for.

Ms. GROLL. By giving it to us on Sunday, we were on annual, in UTA status. So we were in a military status. To get it in the mid-

dle of the week, when we were supposed to receive it, they would have had to once again put us on orders and also to bring in a physician. And they didn't want to have to do this. That is why the decision was made at—we didn't even receive our shots until almost——

Mr. SHAYS. I am sorry. I don't understand the significance of why they would have to have a physician—I mean what is——

Ms. GROLL. They would have to bring someone in because we do not have any full-time nurses or physicians at the base.

Mr. SHAYS. But how does the misdating exempt them from that?

Ms. GROLL. Because they gave it to us 2 days early while we were in a military status.

Mr. SHAYS. Oh, I see. So the implication was that it was done while you were——

Mr. CHURCHILL. We were on drill status on the weekend.

Ms. GROLL. Right. They needed to give it to us in a military status, otherwise it would have cost them significant amount of money. As when we were sent to Wright Patterson, we were also sent to Wright Patterson and we had to take annual leave from our civilian side. As a GS employee, we had to take annual leave, and they sent us to Wright Patterson in a non-paid duty status.

Mr. SHAYS. That is interesting.

Ms. GROLL. We sit before you very broken.

Mr. SHAYS. What is that?

Ms. GROLL. We sit before you very broken and frustrated.

Mr. SHAYS. Yes. I know.

Ms. MARTIN-ALLAIRE. Sir, can I add something to that too?

Mr. SHAYS. Sure.

Ms. MARTIN-ALLAIRE. On the dates of the shot records, I have since during all of this time, contacted the Pentagon and asked them what the requirements were on if you could be given the shots early. And if you can, you know, whatever. And the response that I got back from the Pentagon was that you can't even get the shot 24 hours early.

Mr. SHAYS. See, the problem for us in Government, you know, on this side, is that we are told, that this is what the need is, this is how we do it, and it sounds a lot more efficient than the real-life story of how you encounter it. And it sounds a little more, when you have those who are involved in implementing it, they—you get the sense that it has a little bit more feeling and compassion to it than the kind of experiences that each of you have put on our congressional record.

Mr. Shepard, tell me what—summarize what is motivating you to be so out-front here?

Mr. SHEPARD. I had—Mr. Chairman, I had no intentions of being out front. My conversation with your staff indicated that my strategy was to keep my concerns close to my vest until I had to make this very personal decision. I was collecting information in regards to this issue. I wanted to find out what this committee was doing so I could give the pertinent information to my elected representatives.

So in that process, my concerns, as indicated here, were communicated with your staff and thus they obviously conferred with you and issued an invite to me.

I had a decision to make at that point, whether to stay private or to go public.

Mr. SHAYS. No. I realize that we asked you to be here. So——

Mr. SHEPARD. Right. Well——

Mr. SHAYS. I want the record to state that. You came at our request.

Mr. SHEPARD. The reason being, the reason I am speaking is because I have, quite frankly, I have a limited ability to withstand the financial punitive measures, and if I decide to make that decision, I will have the ability to weather that type of storm. Ninety-nine point nine percent of the people that I am speaking—that I work with cannot—that is the first thing, that they can't even deal with these legitimate concerns that are here because of the dollar bill that they need to pay their next paycheck with.

Mr. SHAYS. You know, your reference to paying the next paycheck, our committee oversees the defense and intelligence community and State Department for waste, fraud, and abuse. We don't pass laws. We investigate, make recommendations, and then work very hard to have the committees of jurisdiction make changes to the statute or the appropriators fund the money.

But one of the things that we are looking at is the working conditions of our military. Why we don't have the recruitment success that we have had? Why are we not having people re-enlist?

And one of the things that has been a real eye-opener for me is the pay scale that so many of our men and women have to abide by and live by. So it is very poignant for you to——

Mr. SHEPARD. You will get the type of compliance that you have been—that has been reported to you if you deal with what everybody understands, including the DOD, and obviously Congress deals with it, money.

And obviously, at the lower rungs of society, at the lower levels of affluence as I have indicated, that in an all-volunteer force you are going to get socio-economically, you can contextualize not wanting this shot and then refusal as disobeying an order. That speaks volumes because the other side has nothing to speak.

Mr. SHAYS. Well, I have been very impressed with the men and women that I have seen in our service, at all levels of command. But it really gives you cause with your kind of testimony.

Dr. Nass, what is your reaction to what you have heard? Let me just say to all of you, I am going to kind of close this up because I think your statements speak volumes and now it will be our job to personally follow, in particular, the four of you as you sort this out. And we will try to do our best to help and also, given that you are 9 out of 12, it sort of gives us a pocket to look at. It will tell us a lot.

I want you to make sure, if I don't say this to you later, that you feel very willing to be back in touch with our committee, and, if you are not satisfied, and I know you will be, but if you are not, with what the committee is doing, to call my office personally. And let me know that personally.

Dr. Nass.

Dr. NASS. I am not quite sure what question you are asking.

Mr. SHAYS. Well, I am asking you a very general one. You gave a testimony in the beginning. Were you surprised by what you heard? Do you think this is typical? Do you have any——

Dr. NASS. Yes.

Mr. SHAYS. OK. So I am just asking for a general but not long answer to the question.

Dr. NASS. Based on purely anecdotal evidence, which is all that exists, reports of probably from 50 to 100 people, some who filled out questionnaires and some who only wrote me a little bit about their symptoms, I believe that the syndrome that these three people have described is fairly typical, although they may be more severe than most.

From what I know, there are two lots in particular, each lot being approximately 200,000 doses, that have caused the majority of symptoms and that those people who report to me also—when they are ill and they survey other people who receive vaccine at the same time that they did, they find that a large number of those people also seem to be having chronic symptoms——

Mr. SHAYS. Yes. Let me interrupt a second to say: Are you told the lot numbers when you are given the shot?

Ms. GROLL. It is indicated in our shot records, sir. And I believe—I know I did, I submitted copies of my shot record. And they are all FAV030 is what it is recorded.

Mr. SHAYS. OK. We will trace that. I am sorry.

Dr. NASS. So, anyway, what I hear is that 020 and 030 are the major problems. But we know that only six or eight lots passed testing. We don't know how many of those lots have actually been used. So there may only be four lots that have been used and whatever.

It may be that, you know, when the generals say they haven't had any adverse effects, I believe them. And I hear from some people on board ship that hardly anyone has had an adverse effect, and then on another ship everybody has had an adverse effect. So I think what we need is active surveillance, which has not yet taken place.

I don't know what the numbers will be in the end. You know, it is hard to even say how many people are suffering severe symptoms from Gulf war illness, although over one-seventh of those who went to the Gulf have reported problems.

It is impossible to say at this point how widespread this is going to be, but I—I mean I have a list from one base where 38 names were given to me of people who are ill.

So——

Mr. SHAYS. Well, that is a helpful way to kind of wrap this up. And I would like to acknowledge and thank Dr. Myers for staying and listening to this testimony. I frankly think that is a fine thing for you to have done.

And with that, we will, unless there is any other comment. And I would welcome any other comment. We will call this hearing adjourned.

[Whereupon, at 2:17 p.m., the subcommittee was adjourned.]

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