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STATE DEPARTMENT

Serious Problems in the Anthrax Vaccine Immunization Program

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The Honorable Jesse A. Helms
Chairman, Committee on Foreign Relations
United States Senate

The Honorable Benjamin A. Gilman
Chairman, Committee on International Relations
House of Representatives

The Honorable Walter B. Jones
House of Representatives

In the spring of 1998, the Department of State stockpiled anthrax vaccine and antibiotics at a number of its diplomatic posts located within SCUD ballistic missile range of Iraq. According to the State Department, these supplies were stockpiled with the intent to administer post-exposure immunization and antibiotic treatment following any possible anthrax attack by Iraq. The State Department purchased and received 8,000 doses of anthrax vaccine from the Department of Defense in May 1998, which it distributed to eight U.S. diplomatic posts.

One year later, in May 1999, the State Department announced that it was instituting a voluntary, worldwide Anthrax Vaccine Immunization Program for eligible U.S. government employees, their families, and other personnel serving abroad. First, a pilot project was started in October 1999 at a U.S. mission in the Persian Gulf area.[1] Using the experience from the pilot project, the program was to be gradually expanded to posts that State believed could be the target of an Iraqi biological attack; then to posts in 40 countries that State has identified as at critical, high, or medium risks to terrorist attack; and finally, to all posts worldwide. According to the Food and Drug Administration, full pre-exposure protection from anthrax requires a series of six anthrax vaccine immunizations given over an 18-month period, followed by an annual booster. Due to the insufficient supply of anthrax vaccine approved by the Food and Drug Administration, the State Department announced in September 2000 that its plans to

[1] According to the State Department, the locations of U.S. missions where the anthrax vaccine was stockpiled and where the pilot program was conducted are sensitive and cannot be identified in this report.

expand the program beyond the pilot site were suspended until more vaccine is available.

You asked us to review the State Department efforts to administer anthrax vaccine at U.S diplomatic missions overseas through the contingency stockpiling of vaccine at U.S. diplomatic missions for post-exposure administration and the voluntary Anthrax Vaccine Immunization program. Specifically, you requested that we (1) discuss the rationale for the State Department's decision to establish a voluntary anthrax vaccine immunization policy and (2) examine how well the stockpiling of vaccine at diplomatic posts and the voluntary anthrax immunization program have been implemented to date.

Results in Brief

The State Department established a voluntary anthrax vaccine immunization policy for its employees and their dependents based on its interpretation of an intelligence assessment that U.S. diplomatic and consular establishments abroad are threatened by potential biological and chemical attack. According to intelligence analysts involved in the assessment, however, the assessment was an extremely limited and general assessment that did not evaluate the relative risks of chemical and biological attack on U.S. missions overseas, identify the chemical and biological agents likely to be used, or assess the ability of states or terrorist groups to disperse chemical or biological agents and cause casualties. Diplomatic Security officials in the State Department and Central Intelligence Agency analysts agree that they have no clear evidence that U.S. missions or interests overseas are threatened by foreign state or terrorist attacks using biological or chemical agents at this time. According to these officials, terrorist attacks involving the use of conventional bombs are considered the greatest threat to U.S. overseas missions. The State Department has suspended expanding its anthrax vaccine immunization program beyond the pilot site because of the unavailability of vaccine and it plans to reassess the need for the program after obtaining a more complete threat assessment.

The State Department's prepositioning of anthrax vaccine at diplomatic posts in 1998 and the voluntary anthrax vaccine immunization program conducted at the pilot site to date have been poorly implemented. When a SCUD attack did not occur, 80 percent of an initial shipment of 8,000 doses of anthrax vaccine the State Department prepositioned at eight U.S. missions overseas expired and had to be destroyed. State Department attempts to minimize such waste by redistributing the unused vaccine to

the Department of Defense to be used elsewhere failed because it could not provide assurances that the vaccine was properly stored and refrigerated. Moreover, because the State Department could not provide assurances that the vaccine was properly stored, the quality of the remaining 20 percent (2,000 doses) that was used was uncertain. In addition, vaccine requirements for the voluntary program were not accurately estimated based on a comprehensive analysis of potential users at all posts beyond the pilot site. As of July 2000, none of the recipients at the pilot site received the full series of immunizations on schedule because procedures were not implemented that would allow all recipients to complete the full regimen of anthrax vaccinations on schedule. Finally, surveillance procedures used in the pilot program to monitor reactions to the vaccine may be underreporting the incidence of adverse reactions to the vaccine because recipients were not actively monitored to determine if they had adverse reactions.

This report contains recommendations for the State Department to take several measures to better define the need for a voluntary anthrax immunization program and to improve the implementation of future immunization efforts if the Department resumes the expansion of its anthrax vaccine immunization program to other U.S. missions overseas. The State Department provided written comments on a draft of this report and concurred with all the report recommendations, stating that they can help improve the voluntary program when sufficient vaccine becomes available to implement it. However, the State Department expressed concern about statements made in the report that it believed reflected a misunderstanding of the prepositioning effort and the voluntary immunization program, which could mislead readers. We revised the report to more clearly differentiate the prepositioning of anthrax vaccine at U.S. missions overseas from the voluntary program.

Background

State's Office of Medical Services administers and manages the State Department voluntary anthrax vaccine immunizations program. The program's implementation plan calls for the anthrax vaccine to be phased in on a voluntary basis to all direct hire U.S. government employees,[2] their family members between the ages of 18 and 65, and Foreign Service National employees[3] worldwide. State Department employees typically serve a 2-year tour of duty at U.S. missions overseas before transferring to new assignments. In addition, State planned to explore the possibility of providing the vaccine on a voluntary basis to individuals and family members under the age of 18 or over 65 years of age and pregnant women. The anthrax vaccine is to be administered following the Food and Drug Administration's (FDA) guidelines requiring a six-shot series given over 18 months followed by an annual booster.[4]

State purchases the anthrax vaccine from the Department of Defense (DOD), which currently procures the vaccine for DOD and State anthrax vaccine immunization programs solely from one private manufacturer, BioPort Corporation.[5] In 1998, BioPort shut down its production facility for renovation and to address numerous manufacturing problems identified by FDA during its inspections. As of this date, the manufacturer has not satisfactorily responded to FDA's concerns. Consequently, the facility has not received approval from FDA to release additional lots of vaccine. On July 11, 2000, DOD announced that it was temporarily scaling back its anthrax vaccine immunization program because of the inadequate supply of FDA-approved anthrax vaccine. As a result, the State Department will

[2] Direct hire U.S government employees includes all Civil Service, Foreign Service, and U.S military personnel from all U.S. government agencies, bureaus, and departments. U.S. military personnel, however, receive anthrax vaccine immunizations under the mandatory DOD anthrax vaccine immunization program.

[3] Foreign Service National employees are primarily host country citizens hired by U.S. government agencies at U.S. missions overseas.

[4] The regimen for this vaccine is an initial series of three vaccinations at 2-week intervals, followed by three additional vaccinations at 6, 12, and 18 months with annual boosters thereafter.

[5] We have testified on various issues surrounding DOD's anthrax vaccine immunization program. *Medical Readiness: Safety and Efficacy of the Anthrax Vaccine* (GAO/T-NSIAD-99-148, Apr. 29, 1999); *Medical Readiness: Issues Concerning the Anthrax Vaccine* (GAO/T-NSIAD-99-226, July 21, 1999); *Anthrax Vaccine: Safety and Efficacy Issues* (GAO/T-NSIAD-00-48, Oct. 12, 1999); and *Medical Readiness: Safety and Efficacy of the Anthrax Vaccine* (GAO/T-NSIAD-99-148, Apr. 29, 1999).

not receive any new supplies of the vaccine for its needs until the manufacturer receives FDA approval to release additional lots of the vaccine.

Anthrax Immunization Policy Based on Uncertain Threats

In the spring of 1998, the State Department deployed anthrax vaccine and antibiotics as a precautionary measure to a number of U.S. missions within Iraqi SCUD ballistic missile range against possible biological weapon attack. These supplies were stockpiled with the intent to administer post-exposure immunization and antibiotic treatment following an anthrax attack.[6] According to the Director of Environmental and Preventative Medicine at State's Office of Medical Services, the stockpiling of anthrax vaccine at U.S. missions within Iraqi SCUD range was based on an intelligence assessment that Iraq had SCUD missiles capable of carrying anthrax and would use them in an attack against U.S. missions. The Director could not, however, identify the specific threat assessment or the agency that did the assessment.[7]

Following the August 1998 bombings of the Nairobi and Dar Es Salaam embassies, security concerns were heightened, and, according to the State Department's Medical Director, the view that posts outside of SCUD range were also at high risk led to the development of more extensive measures to protect U.S. missions overseas from chemical and biological attack. In January 1999, the Under Secretary of State for Political Affairs requested the National Intelligence Council[8] to conduct an assessment of chemical and biological threats to U.S. interests overseas[9] and to complete the assessment in 48 hours. In a February 1999 Decision Memorandum to the Under Secretary of State for Management, the Office of Medical Services recommended that a worldwide anthrax immunization policy be adopted

[6] The administration of antibiotics and anthrax vaccine, if administered within 48 hours of exposure can be life saving.

[7] Intelligence agencies continuously assess the foreign and domestic threats to the United States from foreign states and terrorists. The U.S. foreign intelligence community, which includes the Central Intelligence Agency, the Defense Intelligence Agency, and others, monitors the foreign-origin threats to the United States.

[8] The National Intelligence Council is an organization composed of 12 National Intelligence Officers who report directly to the Director of Central Intelligence.

[9] U.S. interests overseas are defined as including embassies, military and civilian facilities, international transportation, and businesses.

on a voluntary basis. It based its recommendation primarily on conclusions presented in the National Intelligence Council assessment that (1) U.S. missions overseas were at increased risk of a chemical and biological attack and (2) terrorist groups can procure and utilize biological weapons. The State Department formally adopted a voluntary, worldwide anthrax immunization policy in May 1999.

However, according to several intelligence analysts involved in conducting the assessment, because they were only given 48 hours to complete the assessment, it should be considered extremely limited in how it is used as a basis for State's anthrax vaccination program. The assessment was more general in nature and was not a comprehensive vulnerability study of U.S interests abroad. The assessment did not evaluate the relative risks of chemical and biological attacks on each potential target overseas. It did not identify specific biological or chemical agents that foreign states or terrorist groups would employ, whether states or terrorist groups actually have them in their possession, or have the capability to use and weaponize any agents to effectively disseminate them and cause casualties. While the threat assessment predicted the chance of a chemical and biological attack against U.S. interests in the next decade, the intelligence analysts said this was based on their best judgment from a reading of all the available reporting rather than on a sound methodology. The intelligence analysts also, however, stated that with regard to terrorist groups, intelligence community assessments conclude that conventional weapons continue to be of highest concern.[10]

[10] In our past reporting, we have noted that the Central Intelligence Agency has found that interest among non-state actors, including terrorists, in biological and chemical materials is real and growing, but that terrorists are less likely to use chemical and biological weapons than conventional explosives. See *Combating Terrorism: Need for Comprehensive Threat and Risk Assessments of Chemical and Biological Attacks* (GAO/NSIAD-99-163, Sept. 7, 2000).

Similarly, the Coordinator of Chemical and Biological Countermeasures at State's Bureau of Diplomatic Security told us that the intelligence community has no clear evidence supporting the notion that states such as Iraq would use biological weapons such as anthrax against U.S. missions overseas or that U.S. posts outside of SCUD range are also at risk of biological and chemical attack. In addition, these officials agree that intelligence community assessments offer no clear evidence that terrorist groups currently have the capability to develop and deploy anthrax.[11] According to these officials, the more likely threat from terrorist groups is the use of conventional bombs against U.S. missions.

Problems in Administering Anthrax Vaccine at U.S. Missions Overseas

The State Department's efforts to stockpile anthrax vaccine at diplomatic missions for post-exposure treatment against a possible anthrax attack by Iraq and establish a voluntary anthrax immunization program for its employees and their dependents at U.S. missions overseas have been poorly implemented. In prepositioning the vaccine at eight U.S. missions overseas and at the State Department's Office of Medical Services in 1998 and implementing a pilot program at one location starting in October 1999, the Office of Medical Services did not (1) document whether the vaccines stockpiled at U.S. missions overseas were kept at proper temperatures to ensure that unused vaccine could be redistributed to DOD for potential use elsewhere, (2) accurately estimate future vaccine requirements for U.S. missions overseas based on a comprehensive analysis, (3) develop procedures allowing for recipients assigned to high-threat missions to receive complete and timely anthrax vaccine immunizations, and (4) actively monitor adverse reactions to the vaccine.

[11] Our past testimony also points out that public statements regarding intelligence community assessments of the chemical and biological threat to U.S. interests do not contain important caveats or qualifications that must be recognized regarding limitations to terrorist capabilities to weaponize and disseminate chemical and biological weapons. See *Combating Terrorism: Linking Threats to Strategies and Resources* (GAO/T-NSIAD-00-218, July 26, 2000).

Anthrax Vaccine Stockpiled at Overseas Posts and the State Department Was Not Used and Needed to Be Destroyed

The State Department could not redistribute unused anthrax vaccine stockpiled at overseas posts in 1998, and 80 percent of the vaccine had to be destroyed upon its expiration date. State made its request for the initial supply of anthrax vaccine from DOD in April 1998 and requested that DOD provide 12,000 doses of the vaccine and other chemical defense materials for the protection of personnel assigned to U.S. missions in the Persian Gulf region. Because of anthrax vaccine supply shortages within the military, DOD was only able to initially provide 8,000 doses, with the remaining 4,000 doses to be provided at a later date.[12] In May 1998, 780 vials (equivalent to 7,800 doses, with each vial containing 10 doses) of the anthrax vaccine were received by State and shipped to eight U.S. missions in the Persian Gulf region to be prepositioned as a contingency measure against Iraqi SCUD attacks. An additional 20 vials, or 200 doses, were provided to the State Department's Office of Medical Services. The shipment of 800 vials consisted of two lots, with one lot of 61 vials having an expiration date of February 6, 1999, and the other lot of 739 vials expiring on February 23, 1999.

According to the State Department, when Iraqi SCUD attacks did not occur as anticipated and therefore the stockpiled anthrax vaccine was not needed, it tried to redistribute the unused vaccine to DOD before its expiration. However, DOD refused to accept the vaccine when State could not provide assurances of the vaccine's "cold chain of custody"—that is, whether it was properly refrigerated at required temperatures at State medical clinics. Anthrax vaccine has a 1-year shelf life and the vaccine must be stored at 35.6 to 46.4 degrees Fahrenheit[13] and constantly monitored for proper temperature, expiration dates and replacement. None of the U.S. missions where the anthrax vaccine was prepositioned had refrigeration units with automatic temperature monitoring alarms that could ensure the cold chain of custody for the anthrax vaccine was maintained. DOD requires that all refrigeration systems have temperature-indicating devices to maintain and monitor proper storage temperatures for anthrax vaccine. If temperatures are manually monitored, DOD requires that readings must be annotated every 12 hours and a record

[12] The State Department paid DOD $144,620 for 12,000 doses of anthrax vaccine, antidote treatment kits, and injection units.

[13] Storage requirements call for the vaccine to be stored at 2 to 8 degrees Celsius (35.6 to 46.4 degrees Fahrenheit) and the vaccine cannot be frozen or used after the expiration date on the package.

of these readings must be maintained at the location of the refrigeration system.

The Project Manager for the State Department anthrax vaccination program stated that existing refrigeration units at U.S. missions were used to maintain vaccines at proper temperatures. According to State, the vaccine was properly stored with other refrigerated vaccines at required temperatures in accordance with State Department and FDA guidelines on storage and administration of vaccines. The refrigerators also had thermometers that were checked by the nurses, but the health units kept no written records of their temperature monitoring of the anthrax vaccine because they were not required to do so. However, DOD officials told us that with no assurances of the viability of the vaccine, they could not accept the vaccine for use elsewhere. Consequently, 642 of the 800 vials—or over 80 percent of the vaccine—had to be destroyed on their expiration date, including the 20 vials distributed to State's Medical Services Office in Washington, D.C. According to Office of Medical Services data, eight vials were used at two U.S. missions.

State stated that FDA guidelines on the storage and administration of anthrax vaccine only require it to store the product at the required temperatures, but do not require it to maintain records of refrigerator temperatures. Recording refrigerated temperatures of vaccine is only required for DOD users of the vaccine. In addition, State stated that even if temperature records were kept, DOD would not be able to use the additional vaccine because DOD was trying to manage the use of its own vaccine to minimize waste in its own program. The Director of the Anthrax Vaccine Immunization Program at the U.S. Army Surgeon General, however, told us that the main reason for not accepting State's unused vaccine was the lack of proof of the vaccine's cold chain and DOD would have accepted the vaccine and used it quickly if the vaccine's cold chain was verified.

Exchanges of Vaccine Stored at Pilot Site Could Be of Questionable Quality

Despite DOD's refusal to accept the vaccine because of the lack of assurances that it met the cold chain of custody, State Department medical personnel at the U.S. mission where the pilot program was conducted made a series of anthrax vaccine exchanges with a nearby U.S. military installation. However, without assurances that the vaccine was properly stored at the pilot site, it is possible the vaccine rotated may have been substandard. In January 1999, State medical personnel at the mission arranged to rotate the total number of vials of anthrax vaccine at the

mission (150 vials) with the military installation before the vaccine expired in February 1999. The Head Nurse at the pilot site's medical unit said that these vials were used to immunize U.S. military service members at the installation. Officials at the installation, in exchange, provided the mission with 150 vials of anthrax vaccine with an expiration date of February 23, 2000. The U.S. mission used 30 of these vials to administer immunizations to State Department employees and their dependents during the pilot program but the remaining 120 vials were returned to the military installation in exchange for 30 additional vials of vaccine with a later expiration date of September 2001. These vials are being used to continue pilot program immunizations as well as for contingencies at the mission.

According to a State Department Medical Services' official, medical personnel at the pilot mission were able to meet the cold chain of custody criteria by manually monitoring the vaccine's refrigerated temperatures rather than storing the vaccine in refrigerators with automatic temperature monitoring alarms. However, the official said that medical personnel at the mission did not maintain any records of their manual monitoring because they were not required to do so. A DOD official from the Office of Counterproliferation Policy involved in reviewing State Department anthrax vaccine requirements told us that, because DOD did not receive assurances that the vaccine was stored and refrigerated at the proper temperatures, the vaccine rotated to the military unit might have been of questionable quality. We did not determine whether soldiers receiving the vaccine from the vials had any ill effects from the vaccine.

State's Medical Services office had plans to purchase new refrigeration units for delivery to 40 high-threat U.S. posts, including the pilot post at a cost of $160,000 to enable their medical units to maintain the cold chain of custody for future supplies of the vaccine. Medical Service officials say, however, that their purchase is being reconsidered because vaccine shortages have delayed the need for the refrigeration units, and they want to explore less expensive alternatives.

Future Vaccine Program Requirements Were Overestimated

State's request for additional anthrax vaccine for expansion of the program was based on inadequate data and analysis. In December 1999, State's Office of Medical Services submitted a request to DOD for 8,360 doses of additional anthrax vaccine for expansion of the anthrax vaccination program to State Department personnel in countries designated as high-threat areas during fiscal year 2000. The request was based on an estimate that 50 percent of U.S. government direct hires and their

dependents age 18 and over and 30 percent of the Foreign Service Nationals at each of the missions would participate in the program. Office of Medical Services officials acknowledged, however, that these assumptions were not based on a comprehensive survey of employees at the posts beyond the pilot site, but on their best guesses.

As shown in table 1, based on these assumptions, 50 percent (54 of 109) of direct hires and their eligible dependents and 30 percent (78 out of 261) of Foreign Service Nationals at the pilot post were expected to volunteer for the anthrax vaccine immunizations. Altogether, 36 percent of all eligible personnel at the post were expected to participate. As shown in table 1, however, from the inception of the pilot project in October 1999 through July 5, 2000, a total of 15 percent of all U.S. personnel, dependents and Foreign Service National employees at the post actually volunteered for immunizations.[14] While 45 percent of all eligible U.S. direct hires and their dependents at the mission volunteered for the immunizations, only 3 percent of all Foreign Service Nationals employed at the mission accepted the shots. Actual participation of U.S. direct hires and their dependents at the pilot site (45 percent) was therefore close to the State Department projection of 50 percent, while actual participation of foreign service national employees (3 percent) was significantly less than the projected 30 percent.

[14] Seven U.S. military personnel assigned to the U.S. mission also received anthrax vaccine immunizations. However, they are excluded from the number of U.S. personnel who actually volunteered for immunizations because they are required to get immunizations under the mandatory DOD program.

Table 1: Expected and Actual Participation Rates in the Pilot Program

Personnel category	Total number of eligible personnel[a]	State Department projected participation rate (percent)	Actual participation rate[b] (percent)
U.S. direct hire employees and dependents	109	55 (50)	49 (45)
Foreign Service National Employees	261	78 (30)	7 (3)
Total	**370**	**133 (36)**	**56 (15)**

[a]On board as of November 18, 1999.

[b]As of July 5, 2000, and excluding U.S. military personnel

Source: Department of State Office of Medical Services.

Procedures Were Not Implemented to Provide Complete and Timely Immunization of All Recipients at High-Threat Missions

None of the U.S. direct hires, their dependents, and Foreign Service National employees who volunteered for anthrax vaccinations at the pilot site received the full six-dose regimen of the vaccine as of July 2000, and several recipients could not complete the shot regimen after their transfer from the mission. One difficulty the State Department faced in implementing a voluntary worldwide anthrax program was administering the required series of six vaccinations, which takes 18 months to complete to a workforce that typically transfers after serving a 24-month tour of duty at an overseas mission. The State Medical Services Office adopted a phased anthrax vaccination program, beginning with personnel assigned to high-threat U.S. missions and phasing in other missions worldwide, believing it was the best way to immunize a mobile State Department population and to supply U.S. missions with limited supplies of the vaccine. However, State's Medical Office did not establish procedures to start offering anthrax vaccine immunizations to employees and their dependents before their arrival at pilot site. As a result, several recipients at the pilot site could not complete the full regimen of anthrax vaccine immunizations on schedule after they transferred from the mission to other locations because of the short supply of anthrax vaccine.

As of July 5, 2000, none of the recipients at the pilot site received the full six-shot series. The first series of anthrax vaccine immunizations in the pilot program started in October 1999. Of the 56 U.S. direct hires, dependents, and Foreign Service Nationals who participated in the

program, 3 voluntarily dropped out and the remaining 53 participants have received varying doses of the vaccine. As shown in table 2, 31 of the 53 recipients of the anthrax vaccine have received the first three doses in the six-shot series and 22 have received four to five doses.

Table 2: Number of Anthrax Vaccinations Received by Recipients in the Pilot Program (as of July 5, 2000)

Employee category	First 3 doses	4-5 doses
U.S. direct hires	15	14
Dependents and other	9	8
Foreign service nationals	7	0
Total	**31**[a]	**22**

[a]Three additional U.S. direct hire recipients voluntarily discontinued from the program after receiving the first two shots.

Source: Office of Medical Services, Department of State.

Because State did not implement procedures to ensure that participants at the pilot site complete the immunization regimen on schedule, 20 participants who have transferred from the mission will not be able to complete the full regimen of shots. A State medical official said that, because of the short supply of vaccine, anthrax inoculations would be discontinued for personnel moving to nonthreat posts, but continue for those moving to other high-threat posts. State personnel transferring to nonthreat U.S. posts would have to stop the shot regimen and restart the regimen again when they transfer back to high-threat posts. According to FDA, however, no studies have been conducted to determine the impact on the vaccine's effectiveness and immunity from anthrax if six-shot regimen is interrupted.

In the past, FDA officials have emphasized the need for the DOD anthrax vaccine immunization program to strictly follow the FDA-approved regimen of six doses administered over 18 months and an annual booster shot afterward, without deviations. In a September 29, 1999, memorandum to DOD, the Director of FDA's Center for Biologics Evaluation and Research states that “this schedule is the only regimen shown to be effective in protecting humans against anthrax and is the only schedule approved by FDA.” The Director also states that “we are unaware of any data demonstrating that any deviation from the approved intervals of doses found in the approved labeling will provide protection from anthrax

infection." In a testimony before the Senate Armed Services Committee on July 12, 2000, the same FDA Director again cautioned that an interruption in the vaccine schedule would not be consistent with FDA-approved label directions for administering the six-shot series. However, the Director added that because of the shortage of FDA-approved vaccine and the views of an advisory committee on immunization practices regarding interruptions in the administration of vaccines,[15] FDA "would not object" to a resumption of shots after an interruption.

Reporting Procedures May Be Understating Adverse Reactions to the Anthrax Vaccine

State adopted a surveillance system that may have led to underreporting of adverse reactions to anthrax vaccine. Adverse events include injection-site reactions (such as redness and swelling) and systemic events (such as hypersensitivity, fever, and muscle aches). State adopted DOD procedures in which adverse events after vaccination are to be submitted to the Vaccine Adverse Event Reporting System (VAERS) using the VAERS form. VAERS is a passive surveillance system used to alert FDA and the Center for Disease Control and Prevention of adverse events that may be associated with licensed vaccines. VAERS is considered a passive surveillance system since information is voluntarily reported to VAERS by health care providers, patients, or families, who are encouraged to report any adverse events after a person receives the vaccine. Individual vaccinations are documented in the individual health record and State's Medical Immunization Tracking System.

According to State Office of Medical Services' data, out of the 53 anthrax vaccine recipients in the pilot program, nine reported adverse reactions and eight of them were female—about 30 percent of all female recipients. They reported symptoms such as "hard nodules," "lumps," or "knots" on the site of injection, prolonged soreness of the arm, and for three recipients, the knot or nodule was described as lasting 4 to 6 weeks. State records also show that three additional female recipients also had reactions, but chose not to report them as adverse reactions through the VAERs reporting

[15] In a September 1998 memorandum on DOD policy on deviation from anthrax vaccine immunization schedule, the Assistant Secretary of Defense for Health Affairs cited the Advisory Committee on Immunization Practices, U.S. Public Health Service, as stating in 1994 that it did not generally recommend reinstitution of the entire series of a vaccine because of an interruption in the schedule. For the anthrax vaccine, this approach was supported by unpublished data in humans showing a robust antibody response to the anthrax vaccine 1 to 2 years after a partially completed primary series. However, DOD policy continues to adhere to the published immunization schedule.

system. The nurse at the pilot mission's medical clinic said that there have been a wide range of reactions to the vaccine among the participants, but only adverse reactions known to be associated with anthrax vaccine, as indicated in FDA instructions accompanying the vaccine, were documented. She said that because the burden is on the recipients to report adverse reactions in a passive reporting system, she did not encounter any unusually delayed reactions, but believed she could have obtained more information on reactions using procedures to actively monitor recipients.

In our previous testimony on the DOD anthrax immunization program, we reported on the relative merits and weaknesses of the VAERS passive surveillance system in determining adverse reactions.[16] VAERS has several advantages. It is a relatively affordable way to supplement data on short-term adverse events that are collected using active means during clinical trials before a vaccine is licensed. Most important, however, VAERS serves as a signal for the detection of previously unreported adverse events and/or unexpected increases in reported events. Both the general public and doctors can report adverse events to the system, and the data is open to public scrutiny.

However, we reported that VAERS also has several disadvantages. Studies show that adverse events are often substantially underreported in a passive surveillance system. One study cited that "only about 1 percent of serious events" attributable to drug reactions are reported to FDA.[17] Reporting of adverse events appears to depend on several factors, such as the clinical seriousness of the event, the length of time between the shots and the event, and health care workers' awareness of and obligation to report particular adverse events. Also, outcomes with delayed onset after vaccination or outcomes not generally recognized to be associated with vaccination are often underreported. According to the National Vaccine Information Center, there is no mechanism within VAERS for a 1-, 3-, or 10-year follow-up to evaluate vaccine reactions that have a long latency period. According to the Centers for Disease Control, the limitations of

[16] *Medical Readiness: Issues Concerning the Anthrax Vaccine* (GAO/T-NSIAD-99-226, July 21, 1999).

[17] D.A. Kessler, "Introducing MED Watch: A New Approach to Reporting Medication and Devise Adverse Effects and Product Problems," *Journal of the American Medical Association*, vol. 269 (1993), pp. 2765-2768, and H.D. Scott, et al., "Rhode Island Physicians' Recognition and Reporting of Adverse Drug Reactions," *Rhode Island Medical Journal,* vol. 70 (1987), pp. 311-316.

VAERS data suggest it is not a valid source for assessing the rate of adverse events. In an active surveillance system, which is generally more costly to administer, health care workers monitor people that have been vaccinated to find out if they have had adverse reactions.

Conclusions

The State Department established the worldwide voluntary anthrax immunization program based on a general assessment of chemical and biological threats to U.S. interests overseas. This assessment did not evaluate the relative risk of chemical and biological attacks on each potential target, identify the chemical and biological agents likely to be used, or assess the ability of states or terrorist groups to disperse the agents and cause mass casualties. As a result, the extent to which U.S. overseas missions are vulnerable to chemical and biological attacks is uncertain. Therefore, the basis for State's worldwide anthrax vaccine immunization program is questionable.

Notwithstanding the issues surrounding the need for a worldwide immunization program, State Department efforts to immunize its employees and their dependents were poorly implemented. Most of the vaccine prepositioned at U.S. missions overseas and at the State Department in 1998 were not used or redistributed for use elsewhere and the vaccine had to be destroyed upon its expiration date. The State Department also did not have a sound basis to estimate the level of future vaccine requirements for participants in the voluntary immunization program. In addition, none of the anthrax vaccine recipients in the pilot program received the full series of anthrax vaccinations because State did not implement procedures that would have enabled participants to begin the required regimen of immunizations before their arrival at high-threat missions and to complete the regimen on schedule. According to FDA, failure to complete the full six-shot regimen on schedule will leave these recipients without full protection from anthrax. Finally, adverse reactions to the anthrax vaccine from the pilot program could have been underreported because passive, rather than active procedures, were used to monitor reactions. In previous testimony on the use of passive surveillance procedures to track adverse reactions in DOD's anthrax vaccine immunization program, we reported several weaknesses in using passive surveillance systems and studies showing that adverse events are underreported.

Because the anthrax vaccine is in short supply, the State Department has suspended expansion of its vaccination program to other U.S. missions

overseas. If the vaccine becomes available in the future and the State Department resumes the vaccination program, these issues must be addressed to minimize the potential waste of the vaccine and maximize the potential for full immunization of participating employees.

Recommendations for Executive Action

To better define and evaluate the need for the voluntary anthrax immunization program and improve the implementation of any future immunization efforts, we recommend that the Secretary of State take the following steps before resuming the vaccine program in U.S. missions overseas:

- To determine whether a voluntary anthrax vaccine immunization program is the most effective approach to protecting U.S. personnel at U.S. missions overseas, obtain from the intelligence community a more complete assessment of the threat and probability of a chemical and biological attack on U.S. diplomatic and consular missions. This assessment should address the (1) relative risks of a chemical or biological attack for each mission, (2) types of chemical and biological agents likely to be used, and (3) ability of states or terrorist groups to disperse these agents and cause casualties. In addition, the Secretary should reassess the need to continue the pilot program until a complete threat assessment is conducted.
- To improve the implementation of any future immunization efforts, (1) require that appropriate vaccine storage and redistribution mechanisms are in place before anthrax vaccine is shipped overseas; (2) develop estimates of anthrax vaccine requirements based on actual experience at the pilot location and a site survey of U.S. employees, their dependents and foreign service nationals at the next locations to receive the vaccine; (3) develop procedures that provide for each participating employee assigned to high-risk posts to complete the full six-shot regimen of anthrax vaccine on schedule and also seek additional scientific evidence in consultation with FDA and DOD to determine the impact of deviations from the approved dosage schedule on immunity; and (4) take steps to determine whether active surveillance procedures would be more appropriate to track adverse reactions of future recipients in the program.

Agency Comments

The State Department provided written comments on a draft of this report. They are reprinted in appendix II. The State Department concurred with all

the report recommendations, stating that they can help improve the voluntary program when sufficient vaccine becomes available to implement it. However, State expressed concern about statements made in the report that it believed were presented out of context. State commented that we confused two initiatives: (1) the initial 1998 prepositioning of anthrax vaccine at certain high threat posts within SCUD ballistic missile range of Iraq and (2) the voluntary anthrax vaccine immunization program. We agree that the report was not as clear as it could have been in describing the two initiatives and we have made additional changes in the report to make a clearer distinction between the efforts. In addition, State provided technical comments that were included in the report where appropriate.

With respect to our finding that State established its voluntary anthrax vaccine immunization policy based on a threat assessment that was limited and general, State acknowledged that it did not know the relative risks of a biological attack at U.S. missions overseas, but it said that the decision to stockpile anthrax vaccine in 1998 and begin a program in 1999 was based on a perceived threat of biological attack. However, State does not challenge our conclusion that a decision to start and devote resources to an anthrax immunization program should be based on a complete threat assessment using valid and objective threat data and fully evaluating the risks of biological and chemical attacks on U.S. missions overseas. State agreed with our recommendation to request a more complete threat assessment from the intelligence community and to re-evaluate the need for a voluntary immunization program.

Regarding the destruction of anthrax vaccine stockpiled at selected U.S. missions and the State Department, State commented that the vaccine had to be destroyed because it expired and not because it was improperly maintained. State also stated that even if temperature records were kept, DOD could not utilize State's unused vaccine because DOD did not need additional vaccine and was trying to manage the use of its own to minimize waste from its own program. We agree that the vaccine was destroyed because it expired and revised our report to make that point more explicit. However, we believe the central point is that DOD would not accept the vaccine for redistribution to be used elsewhere before expiration because State could not provide assurances that the vaccine was properly refrigerated at required temperatures. Consequently, most of the 8,000 doses of anthrax vaccine stockpiled at U.S. missions had to be destroyed upon their expiration. Further, DOD officials told us that they would have accepted the vaccine and could have quickly used it elsewhere if the vaccine's cold chain was verified.

With respect to maintaining the cold chain of custody of anthrax vaccine stockpiled at several U.S. missions overseas, State claimed that the vaccine was properly refrigerated at required temperatures at U.S. missions and that it was not required to document temperature monitoring. While we agree that State was not required to document temperature monitoring, it would have been prudent to maintain the cold chain standards at all times to ensure that anthrax vaccine stocks could be redistributed to DOD prior to their expiration date in order to minimize vaccine wastage. Redistribution through the DOD supply system requires written validation that the vaccine was monitored for proper storage temperature. State acknowledged that recording refrigerator temperatures is a prudent practice and based on our recommendation it is a requirement it will implement in the future.

In response to our finding that future vaccine requirements were not accurately estimated based on a specific analysis, State indicated that its estimates were based on health care providers polling Americans and Foreign Service National employees at the missions to determine their participation. State claimed that it estimated acceptance rates of 50 percent for U.S. government employees and dependents and 30 percent for Foreign Service National employees from a range of responses received from several posts. However, State Medical officials directly told us that these estimates were not based on a comprehensive survey of personnel at missions beyond the pilot site, but on their best guesses. In addition, as State acknowledges, it did not revise these estimates at the pilot site to account for changes in circumstances such as changes in personnel and their acceptance of the vaccine and Foreign Service National employee concerns. We believe that State must have a sound basis for estimating vaccine requirements that reflects actual experience, varying circumstances at posts, and a comprehensive survey of U.S. employees, their dependents and foreign service nationals at missions designated to receive the vaccine. Based on our recommendation, State now plans to adjust the estimates based on what is actually needed at each mission.

Regarding our statement that none of the recipients in the pilot program has received the full schedule of anthrax vaccine shots, State commented that because the pilot program started in October 1999, no one in the program could be fully vaccinated with the series of six shots that takes 18 months to complete. Our report recognized the difficulty that the State Department faces in trying to administer the required six-shot series of anthrax vaccine, taking 18 months to complete to a workforce that typically transfers to new locations after a 24-month tour of duty at an

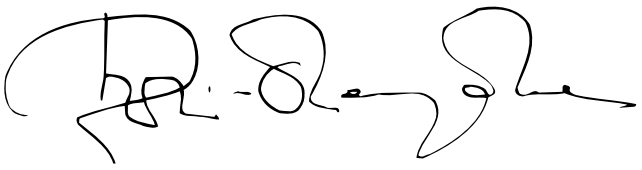
overseas mission. Knowing that, however, State did not implement procedures to ensure that employees in the pilot program who volunteered for immunizations would have the opportunity to receive the complete six shots on schedule without interruption before transferring to other locations. The most complete and accurate data State provided to us on anthrax vaccine recipients at the pilot site was as of July 2000 and showed that no one received the full series of shots, including 20 participants who transferred from the mission to other locations. In concurring with our recommendation, State said that when sufficient vaccine becomes available to implement the program, it would take additional steps to allow recipients who move to different posts to continue the vaccine series consistent with the FDA-approved vaccine dosage schedule.

In response to our statement that procedures used in the pilot program to monitor reaction to the vaccine may be underreporting the incidence of adverse reactions, State commented that medical staff at the pilot post took several measures to ensure that potentially adverse events were recorded, including the "Statement of Information and Affirmation" that is distributed to each recipient. As our report indicates, State adopted passive monitoring procedures used under the VAERS passive surveillance system and that the use of these procedures has been demonstrated to substantially underreport adverse events. The health care practitioner at the pilot site health unit told us that the use of active monitoring procedures would have yielded more information on adverse reactions. State previously provided us with information on its proposal to work with the Center for Disease Control and Prevention to develop a patient survey card to record reactions to anthrax vaccine. This "health report card" was not used in the pilot program; therefore, we did not include it when we assessed efforts to monitor adverse reactions. State did not provide us with details of its proposal or how it will be implemented so that we could assess it. However, State concurred with our recommendation to implement an active surveillance system when sufficient vaccine becomes available to implement the program.

As agreed with your offices, unless you publicly announce the contents earlier, we plan no further distribution of this report until 30 days after its issue date. At that time, we will send copies of this report to Senator Joseph Biden, Jr., Ranking Minority Member, Senate Committee on Foreign Relations; Senator Fred Thompson, Chairman, and Senator Joseph Lieberman, Ranking Minority Member, Senate Committee on Governmental Affairs; Senator Ted Stevens, Chairman, and Senator Robert Byrd, Ranking

Minority Member, Senate Committee on Appropriations; Representative Sam Gejdenson, Ranking Minority Member, House Committee on International Relations; Representative Dan Burton, Chairman, and Representative Henry Waxman, Ranking Minority Member, House Committee on Government Reform; and Representative Bill Young, Chairman, and Representative David Obey, Ranking Minority Member, House Committee on Appropriations . We will also send copies to the Honorable Madeline Albright, Secretary of State and the Honorable William S. Cohen, Secretary of Defense. Copies will also be made available to others on request.

If you have any questions regarding this report, please contact me or Sushil K. Sharma at (202) 512-3992. Jason Fong, Robert Repasky, and Susan Woodward also made key contributions to this report.



Kwai-Cheung Chan
Director, Applied Research and Methods

Scope and Methodology

To determine the basis for the Department of State policy to immunize its employees with anthrax vaccine, we interviewed officials and obtained documents from the Office of Medical Services and the Office of Chemical Biological Countermeasures Program, Bureau of Diplomatic Security at the Department of State. We also interviewed intelligence analysts at the Central Intelligence Agency and reviewed a classified National Intelligence Council assessment on chemical and biological threats to U.S. interests overseas and a classified intelligence community assessment on the foreign biological and chemical weapons threat to the United States. In addition, we reviewed the First Annual Report of the Advisory Panel to Assess Domestic Response Capabilities for Terrorism Involving Weapons of Mass Destruction.

To examine how well the State Department's voluntary anthrax vaccine immunization program was implemented, we interviewed officials and obtained documents from the Office of Medical Services at the Department of State; State Department medical personnel at a U.S. mission in the Persian Gulf region where anthrax vaccinations were carried out; the U.S. Army Surgeon General; the Office of Counterproliferation Policy, Requirements, and Plans under the Assistant Secretary of Defense for Strategy and Threat Reduction at the Department of Defense; and the Food and Drug Administration. We also analyzed assumptions used by the State Department Office of Medical Services to estimate anthrax vaccine requirements for U.S. missions overseas; data on anthrax vaccine supplied to overseas posts; and medical and demographic information on U.S. government employees, dependents and foreign service national employees who received anthrax vaccine immunizations at a U.S. mission in the Persian Gulf region from October 1999 to July 2000.

We conducted our review from December 1999 through November 2000 in accordance with generally accepted government auditing standards.

Comments From the Department of State

United States Department of State

Chief Financial Officer

Washington, D.C. 20520-7427

NOV 8

Dear Ms. Westin:

We appreciate the opportunity to review your draft report, "STATE DEPARTMENT: Serious Problems In The Anthrax Vaccine Immunization Program," GAO/01-21, GAO Job Codes 713058.

The enclosed comments (including attached statement of information and affirmation form) are submitted with this letter as an appendix to the final report. Technical corrections were provided directly to your staff.

If you have any questions concerning this response, please contact Mr. Michael Wertz, Office of Medical Services, Bureau of Human Resources, at (202) 663-1486.

Sincerely,

Bert T. Edwards

Enclosure:

As stated.

cc:
GAO/IAT – Mr. Kwai Chan
State/M/DGHR/MED – Dr. Dumont

Ms. Susan S. Westin,
Managing Director,
International Affairs and Trade,
U.S. General Accounting Office.

Department of State Comments on the GAO Draft Report
"STATE DEPARTMENT: Serious Problems In The Anthrax Vaccine Immunization Program," GAO/01-21, GAO Job Code 713058

Introduction

We are surprised by the title of the GAO Report "Serious Problems in the Anthrax Vaccine Immunization Program" and by multiple statements in the report which we believe reflect misunderstanding on the part of the investigators. We are concerned that some of these statements could potentially mislead readers. While factually correct, some statements are presented out of context. In reviewing this report, we believe the GAO has confused two initiatives: 1) the initial prepositioning in 1998 of anthrax vaccine and antibiotic at posts located within SCUD range of Iraq; and 2) the voluntary anthrax immunization program which we understood the GAO to be investigating. The latter began operating as a pilot program in October 1999. We assume that this review by the GAO "conducted in accordance with generally accepted government auditing standards" is meant to be an objective, unbiased report. Therefore, to clarify this report about the Department of State's voluntary anthrax immunization program, we offer the following facts.

A. Background

In 1998, the Department of State (DOS) made a decision to keep a stockpile of anthrax immunizations and antibiotics at certain high threat posts as a contingency measure to treat casualties in case of a potential anthrax attack. The vaccines were to be used only in case of an anthrax attack. Luckily, the vaccines in the stockpile contingency initiative never had to be used. The vaccines, which had a shelf life of one year, expired in Feb 1999 and were subsequently destroyed.

In May of 1999, a separate decision was made to offer a voluntary anthrax vaccine to State's Foreign Service employees and their families. This voluntary immunization program was to begin as a pilot program at certain high threat posts and then expand. However, in 1999 new vaccine was not readily available, and Department of State was (and continues to be) unable to get vaccine. One post, which had been part of the vaccine stockpile initiative, was able to trade vaccine with a local Department of Defense (DOD) establishment before it expired. This single embassy health unit had vaccine, and a pilot program for voluntary immunization was begun at this post in October 1999. This one embassy's pilot program in operation for less than one year is the basis for the GAO's report "State Department - Serious Problems in the Anthrax Vaccine Immunization Program."

B. Threat Assessment - A perceived threat existed. Department of State felt obliged to offer its employees a way to decrease that threat.

While we admit that we do not know the relative risk of a biological attack in every country where Foreign Service officers are posted, a perceived threat existed. In 1998 and 1999, decisions were being made concerning stockpiling anthrax vaccine and beginning a

voluntary anthrax immunization program. At that time, testimony before the House and Senate Select Committees on Intelligence and open source newspaper articles contained information that the intelligence community was growing increasingly concerned about the proliferation of chemical and biological weapons of mass destruction. There was information that Iraq has production facilities for anthrax spores, and UNSCOM inspectors found munitions loaded with anthrax spores.[1] Our Embassies in Dar es Salaam and Nairobi had been bombed and our employees felt they were and are targets for terrorism and other attacks. In 1998, the U.S. mission at the pilot site had several evacuations of non-essential personnel. Some of the decisions about evacuating children and elders from post were related to a risk that included biological weapons. Our employees and their families felt threatened.

In certain posts, a large percentage of the officers under the Chief of Mission were military personnel who were required to have the anthrax vaccine. These officers were colleagues working side by side with State Department officers in the same buildings, offices, and housing. State Department Officers had no legal access to the vaccine if they wanted it.

For these reasons, Department of State took positive action to offer voluntary protection against the threat through the use of an existing FDA licensed vaccine. We reasoned that if a threat exists and there is a way to prevent that threat, our employees must be given the opportunity to have the prevention. Anthrax is a fatal disease. Vaccine administered before exposure can prevent the disease and save lives.

Nonetheless, as in all health care offered by the Department of State, individuals are free to decide for themselves whether or not to take a vaccination. Each person who decides to receive the vaccine is given an information sheet with possible risks and benefits of the vaccine. (See attachment)[2] The Department of State has clearly stated in its message cable announcing the voluntary program that:

> "While the Department has no information to indicate that there is a likelihood of use of anthrax as a weapon in the immediate future, it does recognize that bioterrorism has become a potential health risk to U.S. Government employees and their families serving abroad."[3]

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[1] Senate Hearing 105-587, *Current and Projected National Security Threats to the United States,* Jan. 28, 1998; *Special Policy Forum Report, Iraq's Biological Warfare Program: Past, Present and Future Challenges,* POLICYWATCH, The Washington Institute for Near East Policy, Feb. 6, 1998; *Hidden Iraqi Scuds Threaten Israel, Gulf countries,* The Washington Times, Feb. 11, 1998; Excerpts from testimony of John Lauder, Special Assistant to the Director of Central Intelligence for Nonproliferation, House Permanent Select Committee on Intelligence, March 3, 1999

[2] *U.S. Department of State Voluntary Anthrax Immunization Program Information Statement and Affirmation,* as provided to the GAO as Tab J of our initial response, dated February 28, 2000

[3] Cable dated 142138Z MAY 99, UNCLAS STATE 090129, SENSITIVE, NOFORN, Subject: The Department's Anthrax Immunization Program, provided to the GAO as Tab D of our initial response, dated February 28, 2000

By offering the vaccine on a voluntary basis, the Department of State has been able to increase the level of personal confidence in those employees and family members who perceive themselves as being at risk.

C. Contingency stockpiling of vaccine was a separate initiative undertaken before the voluntary immunization program. Most of the 8,000 doses of vaccine obtained for the contingency stockpile were destroyed because they expired.

In 1998, the Department of State recognized that the threat of anthrax attack existed and that lifesaving measures were available to counter the threat. The Department of State opted to preposition enough vaccine and antibiotics to provide post exposure treatment and immunization in the event of an anthrax attack. This was purely a contingency measure - to be used only in case of an anthrax biological attack. No vaccinations were to be administered unless an attack occurred. As noted in the GAO report, anthrax vaccine manufactured at that time had a shelf life of only one year. We are thankful that no attack occurred and we did not have to use the vaccine. The majority of the 8,000 doses of vaccine maintained in stockpile at Department of State posts reached their scheduled expiration date before they could be used. These vaccines served their intended purpose, which was to be prepared for an emergency. We would have been prepared to treat potential anthrax casualties at those posts where the vaccine was stockpiled. *The vaccine had to be destroyed because it expired, not because it was not properly maintained.*

When no attack occurred, the Department of State tried to redistribute the unused vaccine before it was due to expire. The Department of State Medical Staff met with DOD Anthrax Vaccine Immunization Program (AVIP) staff on November 25, 1998 to discuss issues surrounding the stockpiled vaccine. The DOD officials in attendance stated that they could not use the vaccine in question for two reasons. First, as reported by the GAO, the Department of State had no records to demonstrate proof of the cold chain.[4] Second, DoD would face greater challenge to have used the quantity in question before its scheduled expiration date even if temperature records had been kept. DoD was already aggressively managing immediate use of quantities of vaccine with the same lot number and expiration date to minimize any waste in their own program.

D. Additional Points of Clarification on the Implementation of the Voluntary Immunization Program

The voluntary immunization program has only been minimally implemented due to a lack of available anthrax vaccine. Nonetheless, the Department of State has offered vaccine to every person at the pilot post who is eligible based on the FDA's licensure. Lack of available anthrax vaccine has prevented the Department of State from fully implementing the program to more than just the pilot post as originally scheduled.

1. *Anthrax vaccine was properly stored. Since the inception of the voluntary program in October 99, there has been no loss of vaccine at the pilot program site due to the improper storage or mechanical failure of refrigeration equipment.*

[4] These records are required for vaccine maintained in storage by DOD facilities

The anthrax vaccine was stored properly. Health unit personnel ensured that, like all vaccines requiring routine refrigeration, the anthrax vaccines were stored at 2 to 8 degrees C (35.6 to 46.4 degrees F) in the main compartment of a standard size refrigerator. The anthrax vaccine was stored with other refrigerated vaccines. The refrigerator had a thermometer that was checked by the nurses. There were no power outages, accidental unpluggings, or any other reason to think that proper temperatures were not maintained. The health unit kept no written proof of temperature monitoring, but was not required to do so. The requirement to use recording thermometers and alarms is one imposed by the U.S. Army Medical Materiel Agency (USAMMA) as policy for DOD users of the vaccine.

Regarding storage of the vaccine, the memorandum of understanding (MOU)[5] with DOD required only that the Department of State: "Comply with all applicable Food and Drug Administration guidelines and restrictions on the storage and administration of the anthrax vaccine as specified in the products package insert." The package insert[6] simply states: "THIS PRODUCT SHOULD BE STORED AT 2 TO 8 degrees C (35.6 to 46.4 degrees F). Do not freeze. Do not use after the expiration date given on the package." There is no requirement to maintain records of refrigerator temperatures. In fact, the only records that the Department of State was obligated to keep under the provisions of the MOU were those relating to "...administration of the vaccine..." not storage of the vaccine.

Both Department of State[7] and the Centers for Disease Control and Prevention (CDC)[8] have published guidance to users of all vaccines, which indicate proper procedures for storage and handling. Yet neither *requires* that written records be maintained to verify that healthcare providers in fact perform temperature checks on a regular basis. No regulatory requirement exists for electronic recording devices, except those published by USAMMA as DOD policy for maintaining their anthrax vaccine.

All of the above notwithstanding, recording refrigerator temperatures is a good practice and this is an improvement we will try to implement in the future.

2. Estimated Vaccine Requirements Were Based On Surveys Of Posts.

To estimate the number of doses required to vaccinate the American and foreign service national employee populations at the pilot program, the health care provider there talked to both American and FSN leadership about the vaccine. The health care provider actually polled FSNs and Americans to see who would like to receive the vaccine. Between the time the poll was taken and the vaccinations started, post leadership changed and the threat level dropped. Apparently, there were changes in personnel and some of

[5] Memorandum of Understanding Between the Department of Defense and Department of State for the Provision of Anthrax Vaccine and Medical Chemical Defense Materials, 1 April 1998, provided to GAO as Tab F of our initial response, dated February 28, 2000
[6] Provided to GAO as Tab B of our follow-up response, dated July 5, 2000
[7] 1997 Immunization Guidelines, State Department Medical Program, p. 25
[8] Epidemiology and Prevention of Vaccine-Preventable Diseases, 6th Ed., Jan 2000, App. D

new personnel did not want to receive the vaccine. The health care provider believes that this fact, as well as FSN concerns about not being able to vaccinate their wives and families, affected the local guard service's desire for vaccination.

Similar estimates from several other high threat posts expected to be part of the initial program were also sent to the Office of Medical Service's from health care providers. Because of the range of responses received, the Office of Medical Services estimated acceptance rates of 50 percent for U.S. Government employees and dependents, and 30 percent for Foreign Service National and foreign contractor employees. They used these percentages as planning factors to seek authority to procure the vaccine. The Department of State intends to adjust the estimates. However, the perceived threat and level of acceptance of the program by the U.S. Government and FSN personnel vary widely from post to post. The demand for vaccine also seems to vary over time based on local circumstances. The Office of Medical Services plans to order for shipment only what is needed, based upon detailed request from the health unit. We plan to send enough for first three doses per person, then refine future orders based on lessons learned.

3. Immunization tracking and follow-up is extensive.

The anthrax immunization program is new. No one in the voluntary anthrax immunization program has yet to complete the full series of vaccinations because this pilot program has existed less than the 18 months needed to fulfill a full schedule of vaccine.

The GAO report states that no one in the Department of State voluntary immunization program has received a full schedule of the vaccine yet. As the GAO report correctly states, a full series for the anthrax vaccine takes 18 months. The GAO did their investigation until August 2000. The voluntary immunization program started in October 1999. Hence, only 11 months had passed -not enough time for *anyone* in the new voluntary immunization program to be fully vaccinated, regardless of whether the immunizations had been administered at post, in the United States, or elsewhere before the recipients arrived at the pilot post.

A rigorous program is in place to help keep patients on schedule for their anthrax immunizations. A member of the health unit staff telephones each recipient and tells the recipient on what date the next dose is due. It is then up to the individual to return voluntarily to the health unit to receive the next dose in the series. Since this program is voluntary, as are all immunizations provided by the Department of State, the recipients are free to decide for themselves whether or not to start the program and whether or not to continue.

In addition to phone reminders made by health unit staff to recipients due for a vaccine, a record of each immunization given is sent to the Office of Medical Services in Washington, DC for entry into the Medical Immunization Tracking System (MITS) database. The MITS generates reports identifying which recipients are overdue for their next dose, and which recipients are due within the next 45 days. The data in the MITS is

reviewed with the staff of the health unit periodically to ensure that all information is up to date.

Department of State has proven its ability to administer vaccine maintenance doses to personnel who change locations. To date, the Department of State has coordinated the administration of anthrax vaccine to DOD personnel under Chief of Mission Authority at over 50 posts worldwide. These personnel had started the series based on their assignment or travel to the designated high threat areas, then moved to other posts. However, because vaccine is currently not available, Department of State employees who began immunizations under the pilot program are unable to continue the series when they transfer to other posts.

4. Reporting Of Adverse Effects Is Thorough

The medical staff involved in delivering the voluntary immunization program at the pilot post takes several measures to ensure that potentially adverse events are recorded. Each voluntary recipient of the anthrax vaccine is given a four-page document entitled "Statement of Information and Affirmation" that was prepared in consultation with CDC.[9] The first three pages of this statement include information about anthrax disease, the vaccine, contraindications and warnings, possible side effects from the vaccine, instructions for reporting adverse effects believed to be linked to the vaccine, and description of the program as voluntary. These pages are to be kept by the recipient for future reference. The fourth and final page of the statement, entitled "Anthrax Vaccine Administration Affirmation," is an informed consent form signed by each recipient and kept on file in the health unit. Therefore, the Department of State has taken steps to educate each recipient, to include recognition and reporting of potential vaccine side effects, and to gain informed consent before administration of the vaccine.

Additionally, the healthcare practitioner in charge of the health unit at the pilot site issued instructions to medical staff members to interview each recipient on subsequent visits to the health unit to determine what, if any, side effects the recipients experienced. The medical staff members then record the recipients' statements in the "Additional Comments" line of the Vaccine Immunization Record form, and if warranted, submits a Vaccine Adverse Event Report.

Also, pending the availability of vaccine to implement the program, the Department of State has partnered with CDC to develop an active monitoring study, entitled "DOS/CDC Adverse Events Surveillance for Anthrax Vaccination in State Department Personnel." The Department of State provided a copy of this study proposal to the GAO.[10] As part of this study, each recipient of the anthrax vaccine will be given a "health report card" at the time of immunization. The recipient is to fill out the report card and record any symptoms experienced on days 1, 2, 3, 4, 5, 6, 7, and 13 following the immunization.

[9] The Department of State provided a copy of this statement to the GAO as Tab J of our initial response, dated February 28, 2000, and a copy is attached.
[10] Provided to GAO as Tab I of our initial response, dated February 28, 2000.

The recipient will then fold the card and place it in the mail for delivery to CDC for compilation in the study.

E. Conclusion/Recommendations

We trust that these comments containing facts represented in their true context will assist the readers of this report in making objective evaluations concerning the Department of State's voluntary anthrax vaccine immunization program.

We welcome the recommendations made by the GAO which can help us to improve our voluntary program when sufficient vaccine becomes available to implement it.

Regarding specific recommendations:

1. We will request from the intelligence community a more complete assessment of the threat and probability of use of chemical and biological agents against our missions. Based on the results of this assessment, we will re-evaluate our need to implement the voluntary immunization program.

2. We are considering the purchase of temperature monitoring devices to improve existing vaccine storage in our health units. These devices will facilitate the documentation of the vaccine cold chain, thus allowing us to comply with the DoD requirements for redistribution of vaccine. We have purchased four refrigeration units, which are specifically designed to maintain vaccine during shipping. These units, currently on hand in the Office of Medical Services, are available for worldwide use as needed for redistribution of vaccine in the future.

3. When sufficient vaccine becomes available to implement the program, we will have our health units conduct surveys of the employees and family members at our posts to determine more accurately what the voluntary vaccine acceptance rates will be at that time. We will base our requests for vaccine on these figures and adjust accordingly as the program progresses.

4. When sufficient vaccine becomes available to implement the program, we will supplement our existing immunization tracking and reminder systems to allow us to follow recipients who move to different posts in order to offer continuation of the vaccine series.

5. We will continue to work closely with the Food and Drug Administration and the Department of Defense to learn of new scientific evidence regarding the current vaccine or any new vaccines that may be developed in the future. In the mean time, we will continue to follow the FDA-approved vaccine dosage schedule and CDC's general rules of vaccine administration regarding deviation from the approved schedule.

6. When sufficient vaccine becomes available to implement the program, we will implement the active surveillance system that we have developed in cooperation with CDC, entitled "DOS/CDC Adverse Events Surveillance for Anthrax Vaccination in State Department Personnel."

Our staff is available to provide additional information as necessary.

U.S. DEPARTMENT OF STATE

VOLUNTARY ANTHRAX IMMUNIZATION PROGRAM INFORMATION STATEMENT AND AFFIRMATION

IMPORTANT INFORMATION ABOUT ANTHRAX VACCINE

Please read this carefully!

What is Anthrax?

Anthrax is a bacterial infection resulting from infection with the bacteria Bacillus anthracis (*B. anthracis*). The bacteria are present in the soil of many parts of the world, and occasionally the bacteria infect livestock and wild animals. In naturally occurring anthrax, these infected animals and products from these animals are the source of infection for humans. In the normal ecology of anthrax, human infection with *B. anthracis* occurs following direct contact with infected animals, or animal products such as wool, meat or hides. This direct contact with the bacteria leads to a skin ulcer that is slow in healing and accompanied by swelling. This cutaneous form of anthrax is the predominant, naturally occurring form of the disease in humans. However, naturally occurring anthrax can also result from inhaling the bacteria or from swallowing them.

B. anthracis has been developed for biological warfare. In this setting, people can be infected by inhaling (breathing) the bacteria. This inhalation could lead to a form of the disease called inhalational anthrax. Inhalational anthrax may initially mimic the symptoms of a cold but is usually followed in a few days by fever, respiratory distress, shock, and death. If inhalational anthrax is not treated immediately after exposure or as soon as symptoms begin, the death rate in non-immunized healthy individuals is estimated at 80 to 90%. Anthrax vaccine may provide protection against this form of anthrax (discussed below).

While the Department has no specific information to indicate that there is the likelihood of use of anthrax as a weapon in the immediate future, it does recognize that bioterrorism has become a potential health risk to U.S. Government employees and their families serving abroad. The Office of Medical Services of the Department of State considers the pre-exposure administration of vaccines to be the most effective means to protect against infectious health risks, including inhalational anthrax. Consequently, the Department of State has decided to institute a voluntary, worldwide anthrax immunization program for eligible employees and family members because of the potential benefits of the vaccine.

The Anthrax Vaccine

Anthrax vaccine is licensed by the Food and Drug Administration for protection against anthrax. The vaccine does not contain any dead or living anthrax bacteria and is not infectious. Licensed since 1970, this vaccine was originally used for persons who came into contact with animal products such as hides or hair from animals in areas where anthrax is endemic and for persons engaged in laboratory work with *B. anthracis*. Scientific data on the effectiveness of the anthrax vaccine in protecting against disease following inhalational infection is very limited, because it is a very rare exposure and disease. Animal testing demonstrates that the vaccine does protect against otherwise lethal doses of inhaled anthrax.

Dosage

The vaccine is given in 0.5 ml doses by injection under the skin. Immunization consists of six injections. The second and third doses are given 2 and 4 weeks after the first dose. Three additional injections are given 6, 12, and 18 months after the first dose. To maintain immunity, booster doses should be given every year after the initial series.

Contraindications and Warnings

An individual who has a history of a severe reaction to a previous dose of anthrax vaccine should not have any more doses of vaccine. In addition, the safety and efficacy of the vaccine has not been determined for persons who are under age 18 or over 65 or pregnant. For this reason, the anthrax vaccine is not offered to these individuals at this time.

If you have a mild illness at the time vaccination is scheduled, you can still take the vaccine. However, if you are moderately or severely ill, you should wait to get the vaccine. You should advise the doctor or health practitioner administering the vaccine if you are ill.

Possible Side Effects From the Vaccine

Side effects, also known as adverse reactions, following vaccination can be classified as local (at the site of the injection) or systemic (involving the rest of the body).

Local reactions are classified into three categories: mild, moderate, and severe. A mild reaction is defined as redness, swelling, and induration (firm swelling on the surface of the skin) of less than 30 mm (1.2 inches). For the anthrax vaccine, mild reactions are expected to occur following 20 to 30 % of all vaccinations. A moderate reaction is induration of 30 to 120 mm (1.2 to 4.8 inches). Moderate reactions are expected to occur for up to 3 % of all vaccinations. A severe local reaction is defined as induration greater than 120 mm. (4.8 inches) accompanied by marked limitation of arm motion or tenderness of the lymph nodes in your armpit. Severe local reactions are expected in up to 1 % of all vaccinations. Local reactions usually appear within 24 hours after vaccination and begin to subside within 48 hours after an injection. Some recipients of the anthrax vaccine have also developed firm, painless nodules under the skin at the injection site. Though no definite data exists on the time of resolution of these nodules, the nodules usually disappear in a few weeks to several months.

Mild systemic reactions, consisting of any combination of fever, chills, body aches, nausea, or diarrhea, are uncommon. These systemic symptoms resolve with rest and over-the-counter pain medication. Rare severe systemic events reported in association with the vaccine include high fever, allergic reaction, rashes, joint aches, persistent fatigue, numbness and tingling sensations, breathing difficulties, and a severe neurologic [Guillain-Barre] syndrome. Although these severe events have been reported following the vaccine, they have not been proven to be caused by the vaccine.

If you become sick following anthrax vaccination, or if you experience a moderate or severe local reaction following vaccination, please report this information to your Health Unit and consult with your health care provider. Severe local reactions and severe systemic reactions are reasons for stopping the vaccination series.

ANY ADVERSE REACTIONS SHOULD BE EVALUATED BY A HEALTH CARE PROFESSIONAL PRIOR TO ANY ADDITIONAL IMMUNIZATIONS FOR THAT INDIVIDUAL.

Monitoring for New Side Effects of the Vaccine

As larger populations receive a vaccine or drug, new information may become available regarding side effects. Sometimes as more people receive the vaccine, isolated cases of illness occur in association with the vaccine that may not or may not be caused by the vaccine. It is through large population surveillance and reporting of possible vaccine reactions that trends for any previously unrecognized or rare vaccine reactions are identified. There are monitoring and reporting programs for anthrax vaccine in the military and through the Food and Drug Administration and Centers for Disease Control and Prevention's Vaccine Adverse Event Reporting System (VAERS): 1-800-822-7967.

Please report any reactions that you believe are linked to the vaccine to your Health Unit and permit or request the Health Unit to report any suspected adverse reactions through the VAERS. You may also directly report these events to VAERS yourself.

Immunization is Voluntary

As with all immunizations made available through the Department of State Medical Program, your decision to receive anthrax immunizations is completely voluntary, and will not affect the benefits to which you are entitled under the Department of State Medical Program. Should you have questions regarding this advisory, please contact your local health care provider or the State Department's Office of Medical Services at:

M/DGP/MED/EHPM
U.S. Department of State
209D SA-1
2401 E Street, N.W.
Washington, D.C. 20522-0102

Please Keep These First Three Pages
for Your Records and
Sign the Vaccine Administration Affirmation
on Page Four.
Please Return the Signed Page to the Health Care
Provider Who Administers the Vaccine to You.

ANTHRAX VACCINE ADMINISTRATION AFFIRMATION

Your doctor or health practitioner may want to keep this information in your medical file.

I have read or have had explained to me the information about anthrax and anthrax vaccine on pages 1 through 3 of this form. I believe I understand the benefits and risks of anthrax vaccine and ask that it be given to me. I am between the ages of 18 and 65, am not pregnant, and am not experiencing delayed onset of menses at this time.

Signature of person receiving vaccine:_____ **Date:**_____

Information about the person receiving the vaccine. (Please print.)

Last Name_____ **First Name**_____ **Middle Name**_____

Birthdate _____ **(mm/dd/yy) Age** _____

Employee I.D. Number or Social Security Number _____

Street_____ **City**_____**State** _____

Zip or Postal Code _____ **Country** _____

Clinic/Health Unit Information. (Please Print.)

Clinic Name _____

Street _____**City** _____**State**_____

Postal Code _____ **Country** _____**Vaccination Date**_____

PRIVACY ACT NOTICE:
The information requested on this form is requested under the authority of section 904 of the Foreign Service Act of 1980, 22 U.S.C. 4084, to assist the Office of Medical Services to track the anthrax vaccine immunizations you have received as well as to assure that you have read the Department of State Voluntary Immunization Program Information Statement and Affirmation containing information about anthrax and anthrax vaccine. Where the employee identification number is your Social Security Number, collection of this information is authorized by Executive Order 9397. Furnishing the Social Security Number as well as other data is voluntary, but failure to do so may delay or make it impossible to determine the timing and number of anthrax vaccine immunizations you have received and thus result in a decision not to offer you an anthrax vaccine immunization. The information furnished will be kept in your medical record file and may also be kept in an anthrax vaccine immunization tracking system to be developed by the Office of Medical Services. Medical records are normally used by medical and administrative personnel of the Office of Medical Services. Such records may be disclosed under the conditions specified in 5 U.S.C. 552a(b), or in accordance with the routine uses permitted for Department of State records systems subject to 5 U.S.C. 552a (see 41 Fed. Reg. 41330, 41342 (Sept. 21, 1976), or to third parties with the permission of the individual to whom the record pertains.

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