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SIX YEARS AFTER ANTHRAX: ARE WE BETTER PREPARED TO RESPOND TO BIOTERRORISM?

HEARING

BEFORE THE

COMMITTEE ON HOMELAND SECURITY AND GOVERNMENTAL AFFAIRS UNITED STATES SENATE

ONE HUNDRED TENTH CONGRESS

FIRST SESSION

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SIX YEARS AFTER ANTHRAX: ARE WE BETTER PREPARED TO RESPOND TO BIOTERRORISM?

TUESDAY, OCTOBER 23, 2007

U.S. SENATE,
COMMITTEE ON HOMELAND SECURITY
AND GOVERNMENTAL AFFAIRS,
Washington, DC.

The Committee met, pursuant to notice, at 10:01 a.m., in Room SD–342, Dirksen Senate Office Building, Hon. Joseph I. Lieberman, Chairman of the Committee, presiding.

Present: Senators Lieberman, Akaka, and Collins.

OPENING STATEMENT OF CHAIRMAN LIEBERMAN

Chairman LIEBERMAN. Good morning and welcome to our hearing today where we will assess whether the Federal Government has developed the tools that we need in the post-September 11, 2001, world to respond to bioterrorist attacks on the United States and also to the effects of pandemic events.

Six years ago—just one week after the September 11 attacks traumatized America—we were shaken again by a string of anthrax attacks that, over the course of 2 months, killed five people, sickened 22, and drove more than 10,000 others to take powerful antibiotics as a precautionary measure. Postal Service workers were hit the hardest as the attack came in letters through the mail, but I will say, it also hit close to home. In Wallingford, Connecticut, a wonderful woman, Ottilie Lundgren, was one of those who died because she opened a letter containing the deadly substance.

I know that we all certainly here in the Capitol remember those days because a mailroom employee of then-Majority Leader Tom Daschle opened a letter containing the deadly white powder. The Hart Building was evacuated, closed for months while environmental HAZMAT teams scoured the building.

Regrettably, whoever was responsible for the anthrax attacks, has remained unknown and, therefore, unfortunately, unpunished. But we do know that a catastrophe can strike Americans in their homes or places of work or places of assembly as a result of bioterrorism or naturally occurring diseases such as pandemic flu. And, therefore, we must be ready.

So 6 years after those anthrax attacks, are we better prepared to respond to bioterrorism than we were then? My answer, unfortunately, is yes, but not much, and certainly not enough. And I base that on the testimony and the GAO report that we will hear today.

We have a lot to do in the area of medical readiness. Last week, the Administration finally produced its National Strategy for Public Health and Medical Preparedness. It covers the range of emergency responses that would be required after various types of biological attacks. As I read it, I became increasingly concerned that right now we are far from capable of achieving many of those requirements as stated in the National Strategy. For instance, we are still not able to monitor biological incidents and their effects on people in real time. We cannot reliably field sufficient medical surge capacity to respond to either a bioterrorism attack or a naturally occurring pandemic. We cannot dispense drugs to entire populations or track the spread of disease through a community. These are essential requirements of national health security post-September 11, 2001, and they are today, unfortunately, unmet. So we will ask why we have not met those requirements and how together we can do so as soon as possible.

Today's hearing will also consider how well the government is protecting its citizens from biological threats through medical countermeasures and technologies, and here I specifically mean a 21st Century anthrax vaccine, a system of biological sensors in cities throughout the Nation, and better standards for anthrax field tests to speed response and reduce false alarms.

In these areas, the status of our government's activities I think has been mixed. On the up side—and there is an up side here—the Strategic National Stockpile has been enlarged with additional doses of an anthrax vaccine, new antidotes to counter the toxins it produces, antibiotics for over 40 million people, and countermeasures to other diseases such as smallpox and botulism toxins that can be spread by a terrorist attack.

As a result, the ability to treat victims of biological attacks with medical countermeasures has genuinely improved since 2001. Our research is also getting better as a result of centers that have been established specifically to study bioterrorism agents, their compositions, capabilities, and provenance.

On the down side, however, the Department of Health and Human Services' efforts to develop a second-generation anthrax vaccine have, in a word, failed. This is a very disappointing breakdown that has put us back at square one after 4 years of work, a lot of it apparently misguided, to improve on the 30-year-old technology that we now have in the stockpile.

Today, this Committee is releasing a report by the Government Accountability Office,[1] the first of a series in related topics that reviews HSS' missteps, describes the Department's failure to minimize waste of the stockpiled vaccine, and provides recommendations for how to avoid similar mistakes in the future.

I must say that I am particularly concerned about this problem because the Department of Health and Human Services is preparing to seek bids on a new contract for an anthrax vaccine without, according to GAO, having conducted a thorough postmortem of its errors with regard to the awarding of the first contract.

[1] GAO Report to Congressional Requesters, "Project Bioshield—Actions Needed to Avoid Repeating Past Problems with Procuring New Anthrax Vaccine and Managing the Stockpile of Licensed Vaccine," GAO–08–88, October 2007, appears in the Appendix on page 116.

The brief history of this vaccine began after Congress passed the BioShield legislation in 2004 to establish a method for the Federal Government to buy medical countermeasures to biological agents. The first contract was awarded later that year to a small company called VaxGen. They were to develop a next-generation vaccine to replace the current one, which, though safe, is often painful, requires six injections to be effective, and has had problems maintaining required purity.

Multiple problems arose, as we know, in the VaxGen contract, and they have been well documented in previous congressional hearings so we need not go over them here. The contract was eventually canceled, and, needless to say, the second-generation vaccine was never produced.

Today in its report, GAO points out that HHS has not yet fully examined its BioShield failure, much less adopted measures to avoid a repeat of it. So I will ask our HHS witness this morning how the Department expects to avoid similar failure the next time around.

Beyond countermeasures, we are also going to look at detection technologies under development and those already being implemented. And there is some encouraging news here, too, including the Department of Homeland Security's BioWatch system, a network of sensors placed in over 30 cities to test the air for anthrax and other biological agents. How successful has that program been and should it be expanded further? I am going to ask the Department of Homeland Security also for an explanation of why it has not yet adopted standards it and other stakeholders created for anthrax field tests so that new technologies will be as effective as possible.

To say the obvious, we are very fortunate that during the last 6 years we have not experienced another attack from biological agents or any other form of weapon of mass destruction. And so far we have, fortunately, also managed to avoid the major pandemics that seem to sweep the globe naturally every few decades. But that obviously does not mean that we will be so lucky in the future.

The Departments of Homeland Security and Health and Human Services, working in coordination with State and local governments and the private sector, have very awesome responsibilities here to protect the public from deadly biological attacks, awesome in the sense of the scope of the responsibility and what has to be done to meet it. This Committee wants to work with both Departments to get it right because the consequences of failing to do so would obviously be catastrophic.

I look forward to the testimony of our witnesses today. I thank you for being here, and now I am pleased to call on Senator Collins.

OPENING STATEMENT OF SENATOR COLLINS

Senator COLLINS. Thank you, Mr. Chairman.

Six years ago, anthrax-laced letters resulted in the deaths of five people, widespread concern about the safety of postal workers and the U.S. mail, the treatment of thousands of people with powerful antibiotics, and the evacuation of the Hart Senate Office Building.

Today's hearing concerns two matters of great importance for this Committee and for all Americans: Our preparedness for bioter-

rorism and efficiency in government operations. Unfortunately, the report that Senator Lieberman and I requested from the GAO makes clear that the Federal attempt to procure an improved anthrax vaccine has yielded not a new vaccine but instead a textbook example of prodigious waste.

As the GAO also discovered, taxpayers stand to lose $128 million in 2008 as the stocks of the current vaccine expire. The Department of Health and Human Services currently has no system to transfer them for use by the Department of Defense, the only large-scale user of anthrax vaccine, before the stocks expire.

In 1996, former Army Chief of Staff Gordon Sullivan wrote a wise book on a systematic approach to management in settings of uncertainty and change. Its title alone offers a kernel of wisdom: "Hope Is Not a Method."

The story of the now canceled $877 million procurement contract between HHS and VaxGen demonstrates the danger of relying on hope for progress. The Department hoped that a small company could not only develop an effective vaccine, but also could obtain approval for it and manufacture 75 million doses all on an unrealistically fast track.

VaxGen officials hoped that they could meet the terms and deadlines of a contract that lacked specific requirements and was critically vulnerable to future decisions by the Food and Drug Administration.

VaxGen also hoped that its small staff, lack of expertise in vaccine formulation, and limited access to additional capital would not impede the required rapid progress to contract fulfillment.

Not one of these hopes survived the collision with reality.

The reality is that HHS' contracting practices for Project BioShield have displayed many of the same problems that this Committee has observed in procurements in other departments and agencies related, for example, to Hurricane Katrina and to reconstruction work in Iraq and Afghanistan—flaws that we hope to correct through contracting reform legislation.

HHS was responding to a crisis in the wake of the September 11, 2001, terrorist attacks and the anthrax mailings. No one knew how soon or in what number follow-on attacks might appear. But the risks, uncertainties, and vulnerabilities revealed by the anthrax attacks made a methodical approach to vaccine procurement more, not less, important.

A methodical rather than a hopeful approach to Project BioShield contracts might have included a more realistic evaluation of the suitability of using a small vendor with limited experience, a vendor that had been de-listed from the NASDAQ securities market 3 months before the November 2004 contract signing.

A methodical approach would have included a fact-driven assessment of vaccine development prospects and production capabilities—an assessment that GAO's interviews with industry experts suggest would have been bleak indeed.

And perhaps most important, a methodical approach would have identified and specified contract requirements up front.

I have no doubt that many lessons could be drawn from this very troubling story. But as the GAO notes, HHS has yet to conduct a formal lessons-learned study.

We will spend additional time today discussing two other disturbing issues outside the immediate ambit of the VaxGen contracts—the lack of a process to move the stocks of current anthrax vaccine to the military before they expire, and the reported willingness of HHS to deploy the vaccine even if it has expired.

I look forward to hearing the testimony of our witnesses today on the procurement and the other challenges we must address to ensure that our Strategic National Stockpile fulfills its purpose of maintaining readily available stocks of vital medical supplies for victims of major disasters. I am particularly interested in hearing Admiral Cohen's thoughts on how the findings from the GAO report can be applied to the important work he is leading at DHS.

The only good news in the GAO report was the obvious observation that we have suffered no new anthrax attacks since 2001. If we had, our hearing could have unfolded in the wake of another tragedy. We must apply the lessons learned from the failures documented by the GAO to improve our preparations for a possible terrorist attack using biological weapons before it is too late.

Chairman LIEBERMAN. Thanks, Senator Collins, for that excellent opening statement.

We appreciate the four witnesses before us who can help us answer the questions we have. We will begin with Jay Cohen, Under Secretary of the Department of Homeland Security for the Science and Technology Directorate, Retired Admiral of the U.S. Navy. Good to see you. This is actually your first appearance before the Committee since assuming this role. We welcome you. I think you know that the Science and Technology Directorate is one of the totally new entities created at the Department of Homeland Security effectively by this Committee. So just to make you feel younger, we take a paternalistic interest in what you are doing. Admiral Cohen?

TESTIMONY OF HON. JAY M. COHEN,[1] UNDER SECRETARY FOR SCIENCE AND TECHNOLOGY, U.S. DEPARTMENT OF HOMELAND SECURITY

Mr. COHEN. Well, good morning, Chairman Lieberman, Senator Collins, and distinguished Members of the Committee. I am honored to appear before you on this solemn occasion of the sixth anniversary of the anthrax attacks against our Nation to report on the progress made by the Department of Homeland Security's Science and Technology (S&T) Directorate. Those events of 6 years ago served as a wake-up call that an adversary could produce or obtain biological agents to use against this country.

Thank you for entering my formal written statement into the record. I will quickly summarize it here. But before I do, I wanted to thank the Congress, this Committee, and your very professional staff for the strong bipartisan leadership and support you have given me and the dedicated, hard-working men and women of the Department of Homeland Security Science and Technology Directorate as they work to make the Nation safer. Thomas Jefferson said, "The price of freedom is eternal vigilance." And vigilant we must be.

[1] The prepared statement of Mr. Cohen appears in the Appendix on page 29.

I am humbled to appear alongside such distinguished panel members. The Congress and the American people want to know, 6 years after anthrax, are we better prepared to respond to bioterrorism? And I will tell you the answer is yes, and I would like to give you a few examples.[1]

Prior to the anthrax attack, the Nation lacked a comprehensive understanding of the risks posed by acts of bioterrorism. We did not have a dedicated research and development capability for addressing those risks, civilian attack warning systems to know if we had been attacked, dedicated forensic analysis capabilities and adequate capacity to rapidly characterize samples from the attack to help others in trying to identify who might have perpetrated the attacks, plans and tools for cleaning up after such an attack, and focus on the additional significant threats posed by bioterrorism.

In the intervening 6 years, DHS S&T, in collaboration with its interagency partners, represented here and in the audience, conducted formal risk assessments of 28 biological agents. This analysis is guiding the prioritization of the Nation's biodefense efforts and has resulted in nine additional material threat determinations, a list of key agents to be detected by warning systems, and identification of key vulnerability and research gaps.

We established a National Biodefense Analysis and Countermeasures Center to provide a dedicated capability for conducting both unclassified and classified biodefense research; developed and operated the Nation's first bioattack warning system, which has already been referred to here, known as the BioWatch system. This system, first fielded in 2003—and I am very pleased that Dr. John Vitko, who is my Director of the Chemical and Biological Division, is largely responsible for that development and deployment. It was fielded in 2003 and is operating in more than 30 cities, as has already been stated, and has conducted some 4 million tests to date without a single false positive.

We have conducted development of the next-generation fully autonomous detection systems to significantly increase the BioWatch capabilities, and I know your interest in that, and those systems are now entering field tests; developed standards and processes for biodetection tools to be used by first responders; in partnership with HHS, DOD, Department of Justice, the Postal Service developed a coordinated national biomonitoring architecture; established a National Bioforensic Analysis Center, and we are conducting operational bioforensic analysis today in partnership with the FBI.

This provides the Nation with its first dedicated contamination-free biocontainment laboratory space for forensic analysis and the necessary analytic tools and chain of custody control for conducting that analysis. We have worked with the EPA, HHS, and State and local authorities to develop protocols and tools for cleaning up complex transportation hubs following a biological attack, and we are working closely with the U.S. Department of Agriculture to better characterize the existing veterinary countermeasures for agro-defense and to develop next-generation countermeasures.

In the future, I am pleased to tell you that we will extend the formal risk assessments to include all of chemical, biological, radio-

[1] The slides submitted by Mr. Cohen appear in the Appendix on page 38.

logical, and nuclear threats. We will complete construction and occupy the new National Biodefense and Analysis Countermeasures Center (NBACC) facility at Fort Detrick, Maryland, and that should occur at this time next year. And working with our colleagues on the National Interagency Biodefense Campus at Fort Detrick, we will provide the Nation with the understanding it needs to identify and prioritize threats and the tools it needs to defend them.

We will develop the understanding and tools to defend against enhanced and advanced biological threats. We will complete testing of the next-generation BioWatch systems and work with the DHS Office of Health Affairs—and thank you for establishing that customer for me, critically important—to transition BioWatch III into operation. We will develop an expanded range of detection systems and tools for use in facility protection, protection of the food supply, and first responders. We will partner with the EPA, HHS, and State and local governments to develop the framework, plans, and tools for restoring entire city neighborhoods in the event of a biological attack. We will partner with the U.S. Department of Agriculture to develop next-generation veterinary countermeasures. And, finally, we will design, construct, and operate the National Bio- and Agro-defense Facility (NBAF), to provide the Nation with state-of-the-art biocontainment laboratory space to accelerate the development of veterinary countermeasures against foreign animal and zoonotic diseases. And you know we look to have that down-select at this time next year.

And so before I conclude, I am pleased to be joined here today, as I said, by Dr. John Vitko, and also Jamie Johnson, who is my Director of the Office of National Labs in the S&T Directorate, who will help this shade tree engineer with your more technical questions.

Additionally, my DOD partners have brought examples of devices that we have developed together for our first responders. You see a new chem/bio suit that our firemen can use.

So, in summary, DHS S&T has taken the wake-up call of the 2001 anthrax events very seriously. Much has been accomplished. However, because of the evolving nature of the threat, much also remains to be done. We look forward to continuing to support the Nation in responding to this challenge. I welcome your oversight, and I welcome your questions. Thank you so much.

Chairman LIEBERMAN. Thanks, Admiral. Do you want to take a minute to describe the chem/bio outfit?

Mr. COHEN. Yes, sir. In today's world, where we ask our heroes, our first responders—the enabling legislation that you so eloquently put in place, I am reminded that it is 183 pages of which 17 pages are DHS S&T. I just completed 6 years as Chief of Naval Research, and the legislation in Title X for the Office of Naval Research, 1946, is half a page. It says there will be an Office of Naval Research, it will be led by an admiral, you will do good S&T, and you will report to the Secretary of the Navy.

Here, 60 years later, we have 17 pages, and it shows you the impact of word processing on the legislative process. But it is very well thought out.

Chairman LIEBERMAN. You and your predecessors made a lot out of that half-page. [Laughter.]

Mr. COHEN. And we continue to, I can assure you. But everyone is well represented. It is very well thought out, and, of course, the support I got from your Committee and from all of the Congress the first 3 weeks I was on board a year ago, in August, in getting the new organization in place and the new investment portfolio was because I xeroxed those 17 pages, I highlighted them, and we organized to fulfill your vision, which I think was very thoughtful.

But today, and I think you are very wise in this, I am not to recreate National Institutes of Health, National Science Foundation, DOD or DOE labs. But you have given me the authorities to leverage them and take my precious dollars and add on top.

So we deal with the Technology Support Working Group (TSWG), which is a very strong, very proactive, and very innovative Department of Defense group, and working together with them, what you see here is an ensemble for our firemen where, when they go into a hazardous situation—and, as you have indicated, Chairman, they may not know initially that there are biological or chemical hazards. It provides the additional protection because we know they do not only have to worry about smoke and worry about the heat and the fire, but we know that when they come out we can monitor them, and they will not have been exposed internally to chemical and biological threats. And we do that through filters, the self-contained breathing apparatus, even the gloves—and there are two different variations because I am a big believer, as is TSWG, in competition of ideas. The gloves have magnetic seals, so when you put the glove on, even at the glove area you do not get the leakage. And so these are, in fact, in operation today.

We have an iris scanner. Now, this is really expensive. It is about $15,000 a copy. But it will give us detection against your face of biological and chemical threats. If we were to deploy these in the hundreds, it would be $10,000 to $15,000 a copy, but you can imagine—and this is a wonderful thing about America, our innovation, the Bayh-Dole Act that you provided. In thousands, we would drive the price down, and this would be an export for American technology.

Chairman LIEBERMAN. What would you do with that? Just take a minute.

Mr. COHEN. You would just put it—I am the first responder.

Chairman LIEBERMAN. Yes, you want to make sure that the first responder has not been compromised.

Mr. COHEN. Or a victim.

Chairman LIEBERMAN. Or a victim, right.

Mr. COHEN. It does not matter. It is the human subject. We put it there, we press the button, and it will give us a readout for the various biological and chemical contamination and give us a high confidence level.

Chairman LIEBERMAN. That is great.

Mr. COHEN. This is in the final stage of testing.

And, finally—and you are very kind to give me this extra time, Chairman—this little device, I thought it was a chocolate wafer. I was really pleased that my staff had provided that for me. I am a chocoholic. But it is actually this disposable mask. You can carry

this in your back pocket. And, again, this provides the near-term—not against smoke, but against biological and chemical hazards so that you can evacuate the area of contamination.

This is just a small example. We filled up the Cannon Caucus Room last spring, DHS and TSWG, showing the kind of progress that we have made in all these areas. Thank you so much.

Chairman LIEBERMAN. Thanks, Admiral. I am glad you did that. Look, part of why Senator Collins and I wanted to put the S&T Directorate in DHS was because we in our service on the Armed Services Committee had seen the power of putting Federal money into research when there is, in that case, national security, and now here, homeland security. And, of course, there is tremendous spillover into commercial applications as well. So it has been very encouraging to see the combination of American innovation or American entrepreneurship come together to try to meet the needs that we have now. You are going to give that first responder the rest of the morning off?

Mr. COHEN. Yes, sir. We will give him gangway liberty. [Laughter.]

Chairman LIEBERMAN. OK.

Dr. Parker, welcome. Thank you for being here. Principal Deputy Assistant Secretary, Office of the Assistant Secretary for Preparedness and Response at the U.S. Department Health and Human Services. We welcome your testimony. Obviously, GAO had some tough things to say about HHS, so this is your opportunity to respond.

TESTIMONY OF GERALD W. PARKER, D.V.M., PH.D., M.S.,[1] PRINCIPAL DEPUTY ASSISTANT SECRETARY, OFFICE OF THE ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. PARKER. Thank you and good morning. Chairman Lieberman, Ranking Member Collins, and distinguished Members of the Committee, I am honored to be here today to discuss the development and acquisition of medical countermeasures to address the threat of bioterrorism.

I would like to make it clear that medical countermeasures development and acquisition is only one component of our overall preparedness efforts that range from research, development, and acquisition of medical countermeasures to response delivery platforms that support State and local authorities in dealing with the medical aspects of major disasters.

Today I will focus on three themes related to how HHS has made significant progress in our medical preparedness activities.

First, we have made significant progress; we have made significant acquisitions for the stockpile against the most serious threats facing the Nation.

Second, as a result of the lessons learned from previous acquisition successes and setbacks, and with the help of Congress, we have changed the way we do business at HHS.

[1] The prepared statement of Mr. Parker appears in the Appendix on page 42.

Third, we have taken an all-hazards approach to public health preparedness. The gains we make against each threat will help us across the spectrum of public health emergencies and disasters.

HHS has already achieved a significant level of preparedness against a number of threats using all authorities available to us. For example, we have a stockpile of antibiotics that provides a substantial level of preparedness for bacterial threat agents, including anthrax, plague, and tularemia. This includes enough antibiotics for the first-line defense against anthrax to provide a 60-day post-exposure prophylaxis for over 40 million people. We also have enough smallpox vaccine for every American. That includes a new vaccine, ACAM–2000, developed by Acambis, that was just licensed by the FDA this year. Project BioShield, enacted in 2004, authorized the $5.6 billion Special Reserve Fund for the procurement of security medical countermeasures.

During the first 3 years of implementation, Project BioShield awarded procurement contracts for the current and next-generation anthrax vaccines, anthrax antitoxins, a next-generation smallpox vaccine, botulism antitoxins, and two medical countermeasures for radiological threats. Additionally, we have made great progress in improving our Nation's ability to respond to an influenza pandemic.

Since December 2005, HHS has awarded over $3 billion to support the first stage of our pandemic preparedness activities, including expanding and diversifying domestic influenza vaccine production and surge capacity, increasing H5N1 vaccine and antiviral stockpiles, and supporting advanced development of cell culture and antigen-sparing influenza vaccines, antivirals, and diagnostics.

While we have achieved successes, we have also learned lessons. The discovery and development of new medical countermeasures is complex and an inherently risky endeavor. The termination of the contract to procure an rPA anthrax vaccine exemplifies the multifactorial challenges encountered in implementation of Project BioShield. We have observed several lessons in implementing Project BioShield:

First, contract terms dictated by the BioShield statute were challenging, particularly for less experienced companies.

Second, it is critical that developers establish effective relationships with the FDA to gain a clear understanding of the regulatory requirements with respect to their product for the stockpile.

And, third, or finally, absence of a robust advanced development program placed too much risk on BioShield projects.

In response to these lessons, in July 2006, HHS established the Public Health Emergency Medical Countermeasures Enterprise to coordinate the range of work being done to develop and procure countermeasures against terrorist and naturally occurring threats and to define priority requirements and make more efficient decisions.

We have established the Biomedical Advanced Research and Development Authority (BARDA), as called for in the Pandemic and All-Hazards Preparedness Act. And we are working to improve and accelerate medical countermeasures advanced research and development using these new authorities. We also are building on the successes of the pandemic influenza program to support an ad-

vanced development portfolio of new products and technologies across the threat spectrum.

We have requested $189 million for advanced development for fiscal year 2008 to increase the maturity of potential Project BioShield products, bridging the Valley of Death gap between NIH and other research and development programs in Project BioShield procurements.

I cannot overstate the importance of advanced development, and the fiscal year 2008 request for advanced development funding is critical to BARDA implementation and effective utilization of the Special Reserve Fund for Project BioShield. We are using new BARDA authorities, such as advanced and milestone payments, in the new BioShield contract for the next-generation smallpox vaccine and have recently awarded a number of advanced development contracts. These include advanced development contracts for anthrax antitoxins, rPA anthrax vaccine, a smallpox antiviral, novel antibiotic formulations, and radiological/nuclear medical countermeasures.

We are facilitating stakeholder discussions with the FDA to establish a better understanding of the regulatory requirements for countermeasures. We will continue to insist on and verify demonstrated understanding of those requirements by manufacturers.

Last spring, we released the enterprise strategy and implementation plans which identified the top priority medical countermeasures development and acquisition thrust and requirements. These plans were informed by significant stakeholder input. The strategy and implementation plan reaffirms and further identifies our commitments to the development and acquisition of anthrax vaccines, anthrax antitoxins, and therapeutics for radiological and nuclear threats. It also identifies the need for the continued development and acquisition of broad spectrum antibiotics, antivirals, and diagnostics against the high-priority threats identified by the Department of Homeland Security.

The National Biodefense Science Board was established last May to provide expert advice and guidance to the HHS on all matters related to preparedness and response to public health emergencies resulting from current or future threats, whether naturally occurring, accidental, or deliberate. These and other efforts signal our commitment to greater transparency, predictability, and partnership with our stakeholders. We will build on past successes, lessons learned, and new authorities to continue to improve implementation of all BARDA programs, including Project BioShield.

This concludes my testimony, and I would be happy to answer any questions. Thank you.

Chairman LIEBERMAN. Thanks, Dr. Parker. We look forward to the questions.

Our next witness is Keith Rhodes, who is the Chief Technologist of the Government Accountability Office and Director of the Center for Technology and Engineering. In this capacity, Mr. Rhodes provides assistance throughout the Legislative Branch, throughout Congress, on issues requiring significant technical expertise.

Mr. Rhodes, we welcome your testimony. As I mentioned in my opening statement, one of the things that I found most troubling in your testimony was the conclusion that the folks at HHS had

not done a thorough postmortem of the failed VaxGen contract, which was particularly troubling since they are in the process of going to a second try at it. Dr. Parker has just used the phrase "lessons learned" and mentioned some things, and I welcome your response as to whether that is adequate to meet the concerns that you expressed in your report.

TESTIMONY OF KEITH A. RHODES,[1] CHIEF TECHNOLOGIST, CENTER FOR TECHNOLOGY AND ENGINEERING, APPLIED RESEARCH AND METHODS, GOVERNMENT ACCOUNTABILITY OFFICE

Mr. RHODES. Thank you, Mr. Chairman. I will try and address that as quickly as I can.

Chairman Lieberman and Senator Collins and Members of the Committee, thank you for asking us here to discuss our findings on Project BioShield's first major procurement contract for the new rPA anthrax vaccine and the potential for waste in the Strategic National Stockpile. My statement is based on our report,[2] which we are releasing today, and will focus on the following two issues that you asked us to address: One, factors that contributed to the failure of ASPR's first Project BioShield procurement effort with VaxGen for an rPA anthrax vaccine; and, two, potential for waste in the licensed anthrax vaccine BioThrax in the Strategic National Stockpile.

In November 2004, ASPR awarded VaxGen a procurement contract for $877.5 million. Two years later, in December 2006, ASPR terminated VaxGen's contract for failure to meet a critical contractual milestone. We identified three major factors that contributed to the failure of this effort:

First, ASPR awarded the first BioShield procurement contract to VaxGen when its product was at a very early stage of development, when many critical manufacturing issues such as stability and scale-up production had not been addressed. Similarly, the requirement to deliver 25 million doses of rPA anthrax vaccine within 2 years was not based on objective data. This requirement, according to industry experts, would have been unrealistic even for a large pharmaceutical firm, given that the product was at such an early stage of development.

Second, VaxGen took unrealistic risks in accepting the contract terms. According to VaxGen officials, they understood that their chances of success were limited. Nonetheless, they accepted the contract terms in spite of the aggressive delivery timeline, their lack of in-house technical expertise and stability in vaccine formulation, and their limited options for securing additional funding should the need arise for additional testing to meet regulatory requirements.

Third, important FDA requirements regarding the type of data and testing required for the rPA anthrax vaccine to be eligible for use in an emergency were not known to FDA, NIAID, ASPR, and VaxGen at the outset of the procurement contract. The requirements for use of the new anthrax vaccine were defined later when

[1] The prepared statement of Mr. Rhodes appears in the Appendix on page 54.
[2] The report by GAO appears in the Appendix on page 116.

FDA introduced new general guidance on emergency use authorization and specifically in January 2006, after VaxGen asked FDA for clarification. In addition, ASPR's anticipated use of the rPA anthrax vaccine was not articulated to all parties clearly enough and evolved over time.

Finally, according to VaxGen, the purchase of BioThrax for the stockpile as a stopgap measure for post-exposure situations increased the requirements for using the VaxGen rPA vaccine.

All of these factors created confusion over the acceptance criteria for VaxGen's product and significantly diminished VaxGen's ability to meet contract timelines.

According to industry experts, the lack of clear requirements is a cause of concern to companies asked to partner with the government since they invest significant resources in just trying to meet government needs. These companies are now questioning whether the government can clearly define its requirements for future procurement contracts.

With regard to potential for waste in the stockpile, we identified two issues:

First, ASPR lacks an effective strategy to minimize waste. Vaccine valued at more than $12 million has already expired and is no longer usable. Without an effective management strategy in the future, over $100 million per year could be lost over the life of the licensed anthrax vaccine currently in the stockpile. ASPR could minimize such potential waste by developing a single inventory system for BioThrax in conjunction with the Department of Defense, with rotation based on a first-in, first-out principle.

Second, ASPR plans to use expired vaccine in violation of FDA's current rules. According to CDC, ASPR told CDC not to dispose of the three lots of BioThrax vaccine in 2006 and 2007. ASPR officials told us that the agency's decision was based on the possible need to use the lots of vaccines in an emergency. However, FDA rules prohibit the use of expired vaccine. Thus, ASPR's planned use of expired vaccine would violate FDA's current rules and could undermine public confidence because ASPR would be unable to guarantee the potency of the vaccine.

Mr. Chairman, in our May 2006 testimony, we concluded that ASPR's procurement strategy for rPA anthrax vaccine had been very aggressive. We stated that, "It is important to understand the unique issues at stake in this early phase of implementation for the biodefense strategy. The rest of the biotechnology sector will be watching to see whether the industry and the U.S. Government can make this partnership work."

And so, Mr. Chairman, Senator Collins, as you have said, 6 years after the anthrax attacks of 2001, the government does not have a new, improved anthrax vaccine for protecting the public. The failure of this procurement effort has raised large questions regarding our country's ability to build a partnership between pharmaceutical and biotechnology firms and the government to develop both new vaccines and a robust and sustainable biodefense industrial base. This goes beyond just this individual vaccine procurement and could have an impact on how the biotechnology industry responds to government overtures in the future for tools to counter the many biothreat agents still to be addressed.

Finally, given that the amount of money appropriated to procure medical countermeasures for the stockpile is limited, it is imperative that ASPR develop effective strategies to minimize waste. This point is the basis for maintaining public confidence. Since vaccines are perishable commodities that should not be used after their expiration dates, it is prudent for ASPR to destroy the expired lots to ensure the public that they will not be given an expired vaccine in case of an emergency. In addition, ASPR should find users for the stockpiled products before they expire to minimize waste.

Regarding your question on lessons learned, we have seen no formal lessons learned. We have seen no documentation. If Dr. Parker's statements are credible, that is fine, but we have not seen a formal document explaining what I just explained to you and what we have stated in our report and in the testimony.

Mr. Chairman, Senator Collins, this concludes my summary. I will be happy to answer any question you or other Members of the Committee may have.

Chairman LIEBERMAN. Thanks, Mr. Rhodes.

Dr. Parker, during the question-and-answer period, we will give you a chance to respond.

Our final witness on the panel, returning by popular demand, Dr. Tara O'Toole is the CEO and Director of the Center for Biosecurity at the University of Pittsburgh Medical Center and a professor of medicine at the University of Pittsburgh. The center conducts policy analyses and works to prevent the development and use of biological weapons, among other challenges it takes on.

It is very good to see you, and I look forward to your testimony now.

TESTIMONY OF TARA O'TOOLE, M.D., M.P.H.,[1] DIRECTOR AND CHIEF EXECUTIVE OFFICER, CENTER FOR BIOSECURITY, UNIVERSITY OF PITTSBURGH MEDICAL CENTER

Dr. O'TOOLE. Thank you, Mr. Chairman, Senator Collins, and Members of the Committee. Thanks for the opportunity to be here today and thank you for this Committee's continuing dedication to homeland security and biodefense issues.

I would like to start by thanking the Federal employees who have worked so hard on these vital programs, including Admiral Cohen and his team and Dr. Parker and his colleagues. I have been amongst the sternest critics of both of these programs, and at this point, after studying biodefense issues since 1998, I think my colleagues and I have concluded that the scale of the challenges we face in constructing an adequate biodefense exceeds all our expectations as of 2001. The challenges are technical, they are organizational, and they are political.

I will also say that I think that our narrow gauge and focus of some of these programs and the absence of what I would call a biodefense strategy has led us to miss some opportunities that we might take advantage of in our efforts to create a biodefense.

What we are going to have to build is systems, not just technologies and vaccines, but systems for getting and deploying and using technologies and countermeasures, and those take a long

[1] The prepared statement of Dr. O'Toole appears in the Appendix on page 71.

time to build and, frankly, a lot more money than we have invested in biodefense so far. But I would like to start by reviewing why we are having this hearing and why we are worried about this problem.

The Defense Science Board said in 2000, 6 months before the anthrax attacks, that there are no technical barriers to terrorist groups or individuals building and disseminating a devastating biological attack. That is even more true today. In 2005, the National Intelligence Council Report said that of all the terrorist attacks and challenges facing U.S. security, they were most worried about a biological attack, which they thought was more likely than a nuclear attack. Those are the only two types of assaults that could really destabilize the United States of America.

Chairman LIEBERMAN. We are more worried—excuse me for interrupting—because of the relative ease with which a devastating amount of bioterrorist agents can be brought into the country.

Dr. O'TOOLE. I think it was the ease of carrying out a biological attack, because these organisms live naturally in the world and are available in hundreds of gene banks across the world, and also because these are replicating organisms. So if you can mount one attack, you can make enough anthrax, for example, if you are patient, to do two or ten attacks. So everyone is going to feel vulnerable after the first attack. The whole country is going to want anthrax vaccine. That is why sitting here today with enough anthrax vaccine to cover only about 3 million people is so worrisome and, I suspect, part of the reason behind HHS' reluctance to get rid of expired vaccine. It might not be perfect, it might not be what you would use on a good day, but it might be a lot better than nothing in the breach.

So we need to take, I believe, a much more strategic look both at these two programs that we are discussing today—and they are both vital programs—as well as at our overall biosecurity strategy.

I think there is a lot of complacency and misinformation abroad in the leadership of the country about the biothreat and biodefense. I think people think the threat is much more remote and much less potentially destabilizing than is the case, and I think they believe we are more prepared than is the case because we have done a lot. We have worked hard and spent about $40 billion since 2001 on civilian biodefense.

But the problem is that drugs and vaccines are a lot harder and trickier to make and a lot more expensive than sensors or engineering products. I do not think that when we embarked on the BioShield program in 2004, the complexity of this endeavor was fully realized either by the Congress or by HHS.

The fact is that the $5.6 billion in BioShield is a fraction of what we are going to need, and part of the delay on HHS' part is trying to figure out how do we get countermeasures for all the possible CBRN threats within that sum of money. We are not asking, "What do we need to defend the country against bioattacks?" We are, in effect, asking, "What countermeasures can we get for this amount of money?" We are basically shopping at Costco. This is part of the reason why big pharmaceutical companies do not want to get into the game. It is also why we are dependent upon small, daring biotech companies who have never made anything before,

and making a new drug or a vaccine is a lot more art than science. That is just where we are. We are in the midst of a revolution in bioscience. There are lots of very tempting possibilities coming down the pike in terms of new drugs and new vaccines. But at the current pace, it is going to take us about 10 years to get there.

So the whole problem of trying to get what we need for a fairly paltry sum of money when you compare it to other national security expenditures is one of the big problems with countermeasures.

There have also been real process problems, as HHS staffed up and figured out how to do what it was trying to do. Some of these process problems are very well documented in the GAO report. I think some of these problems have been improved upon. The BARDA legislation that the Congress passed last year attempts to fix a lot of these process problems, but Congress has not appropriated any money for BARDA yet. And that is sending, I think totally unintentionally but very loudly, a message to the biotech and pharmaceutical companies who are in this game that Congress does not really take biodefense seriously. I know that is not the truth as far as this Committee is concerned, but that is how it is being read. I would be happy to talk more about that, but I think one of the vital tasks before this Congress is to appropriate some money for BARDA.

Finally, I think the BioWatch program has made tremendous progress over the years. I think it is good technology. It is not clear to me that it is the right technology given our choices. It may be that we could make more strategic purchases, particularly in obtaining situational awareness, the information we need once an event is underway, through other investments. My recommendation is that DHS or an interagency process steps back and takes a strategic look at what we are doing across the board in biosurveillance and sets out clear goals for what we want to be able to do in 5 years and 10 years. Thank you.

Chairman LIEBERMAN. Thanks, Dr. O'Toole. As usual, very good testimony.

Let me go back briefly to the discussion between Mr. Rhodes and Dr. Parker. Dr. Parker, obviously there is a lot of concern here on Capitol Hill and generally about the VaxGen experience because we ultimately have spent hundreds of millions of taxpayer dollars with nothing to show. Mr. Rhodes in his report is upset that HHS did not do a very thorough postmortem at all, or lessons learned. Today you cited some lessons learned in your testimony. Mr. Rhodes said he is not satisfied with that. He would like to see, particularly as you go on and try to do this, something more formal about what you put in place to avoid repeating the mistakes. So tell us what you are doing and what you are going to do to make sure that the next millions of dollars get something for that.

Mr. PARKER. Thank you, Senator, and actually, if I may, I may also pick up on a couple themes that Dr. O'Toole picked up, because I think that is important.

Chairman LIEBERMAN. Yes.

Mr. PARKER. There are some themes that she mentioned as well, in addition to Keith's comments.

Chairman LIEBERMAN. So just respond to Mr. Rhodes first, and then you can——

Mr. PARKER. Yes, I will, but a little bit about my history. I joined the Department just a little over 2 years ago—actually just before Hurricane Katrina, and so I was completely engrossed for about 3 months in Hurricanes Katrina, Rita, and Wilma. And when I began to then take a look at Project BioShield and the progress and the potential setbacks that were already kind of looming there, it became obvious that there needed to be some corrections and fixes.

I think Dr. O'Toole properly described it as a young program, setting up a new organization. So we actually looked at some of these things, and we kind of categorized these issues as internal, interagency, and external with our stakeholders. And, yes, internal within the Department, within our office, did we have a large enough staff to effectively manage this, particularly when the experience was that we did not have large pharmaceutical companies, that we were dependent upon the up-and-coming, energetic biotechnology industry. We needed a larger staff because this was going to require greater government oversight and hand-holding, so to speak, to be successful in this endeavor.

So, we had to go and get the budget resources and the direct management of budget line items so we could build the staff of qualified professionals, and we are doing that.

Chairman LIEBERMAN. So you feel that is one lesson learned that you are beginning to make better.

Mr. PARKER. Yes, sir. We are building a highly qualified acquisition and scientific staff so we can provide much better oversight of all of our BARDA programs, not only Project BioShield but pandemic influenza and the advanced development program authorities that we just got in the Pandemic and All-Hazards Preparedness Act.

Interagency: If you are not really familiar with the BioShield—most people do not understand the details of the BioShield statute and the legislation, and the fact that contracts—there are really fixed-cost procurement contracts, and you can build some of the R&D into that development cycle. But there is so much uncertainty in R&D that the earlier you let a contract for a procurement under Project BioShield, the higher the risk. And so that was a recognized need that we needed to bring products further into the pipeline, developmental, and mature them before we would bring them into Project BioShield. But also associated with that interagency is it is a very complex, also, approval process to make any acquisition decision. We need two Cabinet Secretaries and the President—now it has been delegated down to the OMB Director—to make a decision on individual procurements.

Chairman LIEBERMAN. So the decisionmaking process has been better streamlined now.

Mr. PARKER. The decision has been better streamlined, and then the other part was transparency in working with industry.

Chairman LIEBERMAN. Let me interrupt you there because I have only got about a minute and 45 seconds. Let me suggest first that you and the Department present your responses of lessons learned in writing to GAO so they can respond to it, also for the benefit of the Committee. But I wanted to give you a little bit of time on another topic because I noticed you were shaking your head when

there was reference to the vaccines that may be distributed that have expired. So why were you shaking your head?

Mr. PARKER. First, we totally agree with the GAO report that those expired products need to be destroyed, and we would do so. HHS never had an intention to use expired vaccine in an emergency use, so those products will be discarded. But it is also important to note—I think it has come up—but medical products, medical countermeasures, particularly biologics, they have a discrete shelf life.

Chairman LIEBERMAN. Sure.

Mr. PARKER. And so we are always going to be in a position that as they expire, they need to be discarded.

Now, in regard to can we do a better job working with the Department of Defense to look at inventory management, sure, and we had begun, before the GAO began looking at this, talking to DOD about this. We have some particular challenges involved that include contracting, legal, and liability and so forth, but we are redoubling our efforts with the Department of Defense to see how we can better overcome some of those challenges so that we can minimize—we will never completely eliminate it, but perhaps minimize some that has to get discarded.

Chairman LIEBERMAN. OK. My time is just about up. I do want to say very briefly that Dr. O'Toole made a good point, and part of the problem that led HHS to enter into this enormous contract with really an untested start-up company, VaxGen, was because you could not get the big pharmaceutical companies interested in it. And part of the problem here is still us, Congress, in the sense—it is not that it is an easy problem, but we have to find a way literally to entice the big pharmaceutical companies to get into this because there is not an obvious typical market incentive to do it. And we have tried various ways to try to create that incentive for the public good. They all run into some interest group that does not like the incentive. But, meantime, the Nation remains vulnerable to a bioterrorist attack, and the strongest part of our country to present an answer—a vaccine, a treatment—is essentially not on the playing field, and we have got to find a way to get them out there.

My time is up. Senator Collins.

Senator COLLINS. Thank you, Mr. Chairman.

Dr. O'Toole, you made a very interesting comment when you said that we need to be building systems that can deliver the countermeasures or the technologies, and then you went on to make a very interesting comment about the BioWatch project. This is the project that deploys sensors in some 30 cities. I have always thought that it was an excellent idea, an early-warning system. But I think you are causing us to take a second look at how we are deploying our resources.

If there is a biological agent that is detected by Project BioWatch, how prepared do you think State and local first responders and emergency managers are to respond? In other words, we may have a great technology in place to detect a biological agent's release. But if we do not have the system in place to respond to that detection, are we any further ahead?

Dr. O'TOOLE. Yes, well, that is the question, Senator, and I cannot directly answer your query as to how the public health officials who are charged with triggering response would react. But I can tell you that at a meeting called by the White House last spring, which included about 60 public health officials and emergency response experts, there was quite a widespread articulation of skepticism about BioWatch. And I have heard in other hearings of users being very critical of the resources BioWatch takes, of the lack of coordination in some places—not all—between those who operate the BioWatch system and those who are charged with public health. I am sure those kinds of problems are fixable, but they do need attention because this complaint litany has been going on for years now.

My concern is that we cannot afford to put sensors in every nook and cranny of every city or every town in the country, so the first question is: Will the BioWatch sensors detect a release? The second question is basically the hinge point upon which BioWatch, at least its efficacy, depends. The whole idea of BioWatch is that early warning gets you an earlier and hence a better response. But it is not clear that public health is going to be willing to pull the trigger to respond—to move the stockpile, to tell everybody we have had an anthrax attack, etc.—until they have clinical evidence of an attack, meaning someone who is sick with symptoms or a lot of people who are sick with symptoms similar to a bioterror agent, or clinical diagnostic tests—cultures, PCRs, saying, yes, this person is infected with anthrax. That has been the case so far.

Now, in practice, if they do get a BioWatch alert, public health starts actively querying emergency rooms and so forth for people who are sick and fit the description of this disease. Would we be better off—if it is a zero sum game—investing some money in rapid point-of-service diagnostic tests so that a doctor could tell you immediately or within an hour that you have anthrax or you do not? Would we be better off making electronic links between hospital emergency rooms and public health, which more or less do not exist in most places today? Are we spending too much of our attention on detecting a bioattack based on the unproven and untested assumption that early detection improves response? Or would we be better off investing in systems that are going to give us more situational awareness during an attack? Situational awareness is going to be critical to managing an attack effectively and to mitigating the consequences. We are spending almost nothing on situational awareness right now comparatively in terms of energy, talent, and money, and I think that would be a very important part of the strategy.

Senator COLLINS. Thank you. Admiral Cohen, I am going to ask you to comment on Dr. O'Toole's comments. I know that you are working on second-generation technology that is going to shorten the time involved in issuing an alert, and I have always thought the idea of sensors in key places in key cities was an excellent idea. But I think Dr. O'Toole also raises a very good point about what happens next.

What is your response? Are we prepared in terms of public health authorities, emergency managers, medical personnel, first

responders, to react quickly when you issue a report based on the BioWatch sensors?

Mr. COHEN. Well, Senator, first of all, I think your question is right on the mark, and I think Dr. O'Toole's comments are very articulate, very thoughtful, and get right to the heart of the issue.

Now, in my prepared statement, I told you that the existing BioWatch sensors have processed over 4 million samples, and we have had no false positives. But we have had close to two dozen positives in that same period of time. All of those positives that were determined to be valid, they were environmentally based. In the 14 months that I have been on board in this position, I have had an opportunity to see how different cities, different health organizations at the State, city, and local level, respond to the report of those valid positives. And I must tell you it varies significantly.

In some of our larger metropolitan areas, they go, as we say, to battle stations. They take it very seriously. They bring in secondary sensors. They do surveys. They check the pharmacies to ensure that the Tylenol shelves are not emptied. They check with the emergency rooms. They do all of the things that you and Dr. O'Toole indicated would be necessary as part of a system, a systems approach. In other areas, well, it is a time-late sample, and if something is going to develop, we will know about it anyway.

The Founding Fathers were very wise. Those powers not specifically given to the Federal Government are retained by the States and locals. So we wanted an inefficient and confrontational form of government, and the good news is that is what we have, and the bad news is that is what we have.

In defense, it was quite easy. We can tell medical doctors and we can tell the patients what to do, what vaccines you are going to take, when to report to sick bay. It is not that simple or straightforward in health care, certainly the distributed health care or public service health care that we have throughout.

So as we go forward, I do think Dr. O'Toole has one thing especially right. The more ubiquitous the sampling, the less expensive the sampling, the more responsive, meaning short time and accuracy, the sampling, whether it is at point of care or it is distributed throughout a city or it is on mobile trucks, or one of the things we are working on in my high-risk portfolio is what we call "Cell-All." There are 2.8 billion cell phones today. Now, a cell phone is no longer just a phone. It is a mini-computer that has computing power that exceeds what a super-computer had 10 years ago. It has voice, it has video, it can take pictures, it has GPS in it. So if we could have even a single sensor, whether it is radiological or biological, every one of us would have a sensor and would then report through 911 the location, the fact there was a radiological or a biological event occurring. We are not talking about a CO, carbon monoxide, monitor that has numbers. It is a 1 or a 0. Did it hit the trip point that was established by HHS, CDC, etc.? And then if we have multiple of these in a metro station or in a hospital, etc., we know an event is occurring.

Now, this is on the high end. This is the 9/11 Commission, not suffering from a lack of imagination, but I can tell you we are actively pursuing this. And coupled with BioWatch III, which will be more near term, wireless, more digital than BioWatch II, and be-

cause it will be cheaper, we will be able to put it, we hope, in four times as many cities. But we have got to go in the direction that Dr. O'Toole has said in the area of the response, in the linking of emergency rooms, etc., critically important, but I really do think that this is an HHS, CDC, and congressional area. We can give the tools. We cannot mandate their use.

Senator COLLINS. Thank you.

Chairman LIEBERMAN. Thanks, Senator Collins. Senator Akaka, good morning. Thanks for being here.

OPENING STATEMENT OF SENATOR AKAKA

Senator AKAKA. Thank you very much, Mr. Chairman. I want to congratulate you and the Ranking Member for having this hearing. It is fascinating for me to sit here and listen to all of this and to hear from our experts what they have been facing in dealing with the crisis.

I was interested, Secretary Cohen, in some of the new equipment that you have been holding up here, and I specifically wanted to ask you about the iris scanner that you have. I wonder how accurate it is. Can it detect specific chemical or biological agents?

Mr. COHEN. Well, Senator, aloha.

Senator AKAKA. Aloha.

Mr. COHEN. The short answer is yes, it does select specific agents, both chemical and biological. That is why we have an LED screen so that when you hold it up to the face and you press the button, it identifies to you which specific agent you might be looking at.

We are refining its accuracy, its false alarms, etc. This is cutting edge technology. It is in the final test phases. I am glad to come by and give you a demonstration, or your staff, or take for the record the specific sensitivities that it has. I was in your lovely State 2 weeks ago with Major General Bob Lee, your Adjutant General. Of course, Maine suffers from nor'easters, and Connecticut has the occasional influx where they lose all their beautiful elm trees about every 17 years—I remember that. But in Hawaii, you have not only the terrorist threats in the middle of the Pacific Basin, but you have a variety of natural threats, be it earthquakes or tsunamis, flooding, etc. And I am reminded of the loss of power on Oahu just months ago from the earthquake. And I am so pleased that we are able to work closely with your Adjutant General and all the Adjutants General in providing these kinds—initially in small numbers on an experimental basis so they can work with the first responders to make the people of Hawaii and the Nation safer.

Senator AKAKA. As these are developed, it is important that there is training down the line to the first responders so that it can be applied and used wherever it is necessary.

Secretary Cohen and Secretary Parker, going back to the earlier discussion on anthrax, why is anthrax vaccine the only near-term anthrax BioShield procurement priority? What other near-term or non-antibiotic therapies is HHS focusing on?

Mr. PARKER. Well, anthrax vaccine is not the only near-time priority, and anthrax vaccine is not the only component of our strategy to have therapeutics for anthrax. The first line of defense is

antibiotics; vaccine is important for post-exposure use in conjunction with antibiotics; but, also, anthrax antitoxins to treat symptomatic anthrax. And so it is important that we pursue that continuum and that complete tool chest for the medical countermeasures against anthrax.

But we also have other priorities, and they tier from the DHS threat assessment and the material threat determinations, but they include antitoxins and botulinum neurotoxins. They include the need to pursue medical countermeasures for the radiological and the nuclear threat. They also include the need to have medical countermeasures against smallpox. And as I mentioned in my opening remarks, we have a vaccine now for every American, and we are also under a Project BioShield contract pursuing a modified and a second-generation smallpox vaccine that could be particularly useful in certain populations, at-risk populations. But we also need an antiviral for smallpox, and we just continued and extended an advance development contract to continue the development of a smallpox antiviral. But with the list of threats that we do face, we need to be turning our attention—and we are—to looking at more broad spectrum, both antibiotics and broad spectrum antivirals.

One other category for which we actually have no medical countermeasures yet are the viral hemorrhagic fevers, but there has been a great deal of research and development in the discovery phase, and there is actually some reason for optimism that there may be some countermeasures for some of the viral hemorrhagic fevers that are maturing out of the tech base that could go into early development.

So there are a number of projects that we have underway, and, again, I must emphasize the need for advanced development to bring those out of the tech base and mature those in a way that will ultimately make them more suitable for a Project BioShield type procurement.

Senator AKAKA. Thank you very much, Mr. Chairman.

Chairman LIEBERMAN. Thanks, Senator Akaka.

I think we can do another round before a round of votes is called on the floor. I want to go back to the conversation about situational awareness. This Committee in our extensive investigation of Hurricane Katrina found that one of the great problems was that the responders did not have situational awareness. They could not talk to each other. They could not talk to their superiors. Here we are talking about something else, so I wanted just to ask you, Dr. O'Toole, give us a real brief definition of what you mean by situational awareness in a bioterrorist context or a pandemic context.

Dr. O'TOOLE. Well, imagine yourself mayor of a city that has been attacked with anthrax. You may have knowledge of half a dozen or a dozen people who are in the hospital sick, and what you know is there is more to come. What you are going to want to know is, for example, how many people are sick, how many people are at risk, where are the sick people. Are the hospitals caring for them about to collapse because they are being overwhelmed, both by people who are infected and people who fear they might be? Do they have the resources they need, whether they be drugs, equipment, ventilators, whatever? If not, where are those resources and how could I get them to where they are? And this situation of con-

fusion and of active management is not going to be over in a day or a week. It is going to go on for weeks and months.

In 1918, in Baltimore, the Public Health Department completely lost its credibility overnight during the pandemic flu epidemic by saying we are seeing fewer and fewer reports from doctors of new patients with flu. At that time, as now, doctors submitted little green cards saying "I have seen a case of flu" via the mail to the Health Department. And what was happening at the time was that the doctors were so busy taking care of the surge in patients that the little green cards were not getting filled out.

Chairman LIEBERMAN. Let me stop you there. That is an excellent introduction. I want to now turn to Admiral Cohen and Dr. Parker and ask them to respond because obviously it is almost 90 years after the Baltimore situation, so this is the question that we want to ask, which is that if a biological agent has been distributed in a population by terrorists or if a pandemic is beginning, what systems are in place for the authorities, locally and then nationally, to know quickly enough that this is happening? I mean, obviously, we have enormous electronic capacity, telecommunications capacity that did not exist in 1918. Still, I fear—as I mentioned when I read the National Strategy for Public Health and Medical Preparedness—that a lot of the requirements in the strategy I do not think we have yet.

Tell me where we are and what we are doing to try to close whatever gaps exist.

Mr. COHEN. Well, Chairman, I will start at a macro level, and in terms of the detail of the health care, I will leave that, of course, to Dr. Parker.

Chairman LIEBERMAN. Let me ask you, if you can from your position at DHS, to respond to that type of situation, not 1918 but to the mayor of a present-day city. Anthrax has been released in a city, a town, and it is beginning to turn up. Are we going to know about it quickly enough?

Mr. COHEN. Well, the short answer is if we are monitoring for it in BioWatch, we have a high probability of knowing about it. Of course, there are many other ways to detect the anthrax. There is a great sense of awareness and alertness today in the general population, whether you go on a plane or you open a letter, you do it carefully. You know there are many reports that we get of white powder. Some turn out to be false. We have had some naturally occurring anthrax, as you know, from untanned animal hides over the last several years.

Chairman LIEBERMAN. Right.

Mr. COHEN. It is a naturally occurring disease. But I have a higher confidence that in the near term, before we depleted the stocks of Tylenol, in major population areas we would know that there was a medical emergency occurring and that we would quickly know that it was anthrax.

Chairman LIEBERMAN. Would we know because of the monitors that you have set up or because there is a system where doctors will feed into some electronic process to let us know something is spreading rapidly?

Mr. COHEN. Well, for us it is the monitors, for us it is the number of sick people. You both are very familiar with our operations center, which has come an awfully long way.

Chairman LIEBERMAN. Right.

Mr. COHEN. You are aware that we do these exercises like TOPOFF. In fact, 2 weeks ago, we just did one in Phoenix. While it was a nuclear/radiological exercise, the dispersion models, etc., are very similar. We learned a lot about shelter in place, especially school children, the effect that the parents would worry about wanting to go out and get them. The doctor will talk much more about how you transmit these various diseases. Radiological is not biological. But there is a general awareness that, I think, works to our benefit. You then have to go into all of the other interoperability coordination issues and authorities that are necessary. And right now, last night we had with Secretary Chertoff a late-night phone call, all of the leadership, on how we are going to respond and help with the terrible tragedy that is occurring in California right now, with 250,000 people who have been displaced—Qualcomm Center, the convention center, working with the Red Cross, getting planes, cots, etc., there.

So while biological may be very threatening and unique and have medical aspects to it, these kinds of events tend to replicate in how they develop and how we respond.

Chairman LIEBERMAN. OK. Dr. Parker, I am over my time, but just take a moment and tell us whether there is an electronic system in place.

Mr. PARKER. Yes, if I can add to that, the CDC is developing an electronic system—they have several surveillance systems that are very effective and active and serve local and State public health communities. And one of the surveillance systems that they have been developing is called BioSense. And, in fact, we refocused it recently to make sure that it is focusing on some of the high-consequence bioterrorism pathogens. But it is designed to build that electronic bridge between the public health community and the medical community and to help speed the flow of information electronically.

Now, frankly, though, our vision really for the future to much better improve our situational awareness from a medical perspective is the electronic health record and to be able to use that in an improved way. But we are not there yet.

Chairman LIEBERMAN. We are not where we need to be there yet, are we? I would really challenge you to—I know a lot comes down to money, but to come back to us with a proposal for what we could do to facilitate that.

Mr. PARKER. I would be glad to.

Chairman LIEBERMAN. Because that will become the first line of defense.

Mr. PARKER. It is. And another thing with the Pandemic and All-Hazards Preparedness Act (PAHPA), recently, we have begun to also make sure that the Poison Control Centers are part of this because they are an important component in our real-time disease detection and monitoring.

But I also have to emphasize this is part of our all-hazards approach, and we have made a lot of accomplishments, I believe, in

our pandemic influenza preparedness activities and working with State and local communities on these very issues, and that will have implication for a bioterrorism event as well.

Chairman LIEBERMAN. OK. Senator Collins.

Senator COLLINS. Dr. Parker, I want to go back to the issue of the stockpiled anthrax vaccine. It seems so logical to me for you to have a joint effort with DOD whereby, as your vaccine is getting closer to the expiration date, you rotate it out to DOD to use, and then you buy new and repeat the process over and over again. And if that kind of system does not occur, we know from GAO's estimates that it is going to cost the taxpayers $128 million in 2008, and then each year another $100 million.

Now, you said you are working with the Defense Department on such a plan, but you alluded to certain obstacles. What are those obstacles? Are they legislative obstacles? Are they funding? What is the problem? It just seems like a common-sense solution to a problem that otherwise is going to cost the taxpayers hundreds of millions of dollars.

Mr. PARKER. Well, first, it does seem like a common-sense solution, and we are working to try to find that common-sense solution. But there are realities in the contracting issues because we use two different contracts, and we are working on that, too. That is another issue because we have worked very closely with the Department of Defense, particularly on all of our medical countermeasures, but even more specifically on Anthrax Vaccine Absorbed. But there are liability issues associated with each individual contract, and all that is associated with some legal issues. Both the Department and I, though, feel pretty optimistic that we can work through those issues. I have not identified that there is any need for legislative help on this, but we will be looking for that if it comes up. But so far, we will do everything we can to work through that and overcome it.

But let me just talk also about the expense. I am not quite sure I agree with the $100 million figure in 2008, but that is something we can talk offline and work on that. Fortunately, we have not had to use these medical countermeasures—hopefully we will never have to use these medical countermeasures. They are part of our preparedness activities. But as medical countermeasures expire, though, we will have to discard medical countermeasures.

I am not sure if I would want to couch the fact that we have to discard expired medical countermeasures in our stockpile because they passed their expiration and we cannot use them as wastage. That is part of our cost of being prepared. We know we are going to have to lose some of that. We will work and redouble our efforts with the Department of Defense to try to do everything we can to minimize what has to be discarded and make sure it can be appropriately utilized. But just knowing the requirements, what the Department of Defense does, and how our stockpile is going to grow, we can never eliminate it. We are always going to be in a position that some will have to be expired.

Senator COLLINS. Mr. Rhodes, do you see a potential for saving literally hundreds of millions of dollars over the next decade if we are able to come up with an integrated system whereby the BioShield vaccines are rotated to DOD to use?

Mr. RHODES. Yes, ma'am. I know Dr. Parker and I will probably always disagree on the exact number, and that is fine. But I think this also gets to the larger discussion that leads back to Dr. O'Toole's point about strategic vision. It is one thing to store vaccine in a vial. It is another to store it in bulk. It is one thing to rotate vials out of the Strategic National Stockpile and into DOD usage, the coordination between there. But it is also a function of how are we going to use it.

Dr. O'Toole is absolutely right. A series of vaccines that have gone a certain period of time beyond their expiration date may indeed be better than nothing. But that is the discussion that needs to take place at the strategic level based on scientific data so that we can maintain the public's confidence in our Nation's ability to respond.

Dr. Parker is absolutely right. Biologics expire. They get old. They die. They lose their efficacy. The point is to make certain that we have the strategy in place tied to the systems that Dr. O'Toole is describing where we can deliver the countermeasure and that we do have a pipeline for the countermeasure and we understand how the countermeasure is going to be used for emergency use. Is it directly in its most effective time of life? Can we rotate it to DOD? That is ultimately the message we are trying to deliver, is that broader view, whether it is looking at what is the next generation of anthrax vaccine going to be and how are we going to procure it, or how are we going to store what we already have.

Senator COLLINS. Mr. Rhodes, my time is almost expired. Let me just ask you one final question. We still need an improved anthrax vaccine, one that is easier to administer, less painful, etc. How prepared do you think HHS is at this point to award a new contract for the development of a new vaccine that does not have the same very unfortunate and expensive ending that the previous one had?

Mr. RHODES. I appreciate the Committee asking Dr. Parker to put together the lessons learned. Based on documentation that we have, I cannot give you the assurance here now that the next contract will be successful because I do not know that the lessons have been learned and incorporated directly into the process for acquiring the next version, letting the next contract.

While we were having discussions this summer, we were told that there was internal analysis about the lessons learned. We have not seen it. And at the same time, the contract was being let. So I have to go with what I have, and what I have does not counter the position—the track record that I have already seen.

Senator COLLINS. Thank you. Mr. Chairman, it looks like Dr. Parker wants to respond.

Chairman LIEBERMAN. Go ahead, Mr. Parker.

Mr. PARKER. I have just three major points as far as the lessons learned on individual contracts.

One, we have moved away from a performance-based contract, which was basically deliver the product, to one that has very detailed milestones and deliverables along the way to delivering the product. And so that way we ensure that there is complete understanding by all parties at the beginning of what are the specific milestones that must be met.

Two, we verify and ensure that there is early, often communication with the Food and Drug Administration; and as the science matures and the information matures, that the product continues to develop, it is critical that the manufacturer engage early and often with the FDA.

And then, finally, our ability now to have advanced development through the BARDA is just absolutely critical that we can take products further down the developmental pipeline and experience some of the setbacks that you are going to have and that you will have in R&D with the appropriate type of funding and advanced development and have those products so they are more mature before they do go into a Project BioShield procurement.

Senator COLLINS. Thank you, Mr. Chairman.

Chairman LIEBERMAN. Thank you very much, Senator Collins.

Dr. Parker, have you agreeded to respond in writing and present a kind of lessons learned plan to GAO?

Mr. PARKER. Yes, Senator.

Chairman LIEBERMAN. I appreciate that very much. The roll call has gone off, so Senator Collins and I have to go over to the Senate. We will have to close the hearing.

I do just want to draw attention to something Dr. O'Toole said in her testimony, and perhaps we will form a question to the panel on it. But it is that a concept of operations to counter another anthrax attack is lacking. And by coincidence, Senator Collins and I last week sent a letter to Secretary Chertoff in which we said that we know he is working on the National Response Framework, which is the groundwork for planning efforts, but there is no substitute for actual operational plans. In some of the materials we read here, I got the feeling that the vaccine might be able to be delivered to a general area, but then it was not clear how it would get to the people who really need it. And this is a critical factor to stress.

As you know, everyone talks about what keeps you up at night post-September 11, 2001. This keeps me and a lot of other people up at night for the reasons we have discussed. The ease of bringing biological agents into the country or actually preparing them here, and then the propensity they have to multiply and spread has devastating consequences.

So the Committee is going to stay on this. We are going to look over your shoulder at DHS and HHS. We do not consider ourselves to be antagonists, but we are representing the public that we all serve. We are also going to say to you, tell us what you are not getting that is standing in the way of you achieving what we need to achieve as soon as possible. And I am pleased to say that Mr. Rhodes and the Committee and GAO are going to be working together. We have agreed that the excellent report issued today is the first of a series that will be issued with regard to the bioterrorist threat to our country.

Admiral Cohen, do you want a last word?

Mr. COHEN. Yes, sir. I know you are facing a vote. I just want to make one clarification. On the retinal scanner, what we are looking at are the physiological effects on the human, which we then track back to various chemical and biological agents. And I wanted to correct that record. And you asked is there anything you could

do to help. I think your staff is aware that wisely you sunsetted many of the provisions of the initial Homeland Security Act, but one that is coming up on January 25, 2008, is the other transaction agreements. This is a critically important tool that we use, especially in the BioWatch and biodefense areas, and I would just with great respect ask that if there is any thing that its renewal could be attached to before it expires, we would greatly appreciate that and will not abuse it.

Thank you so much for your leadership.

Chairman LIEBERMAN. Time flies. That is quick. Thank you.

The record of the hearing will remain open for 15 days for any additional comments that the witnesses would like to submit or for us to ask you additional questions. This has been a very productive, direct hearing with, I think, the appropriate sense of urgency to it, and I thank you for all that you have all contributed.

Senator Collins, would you like to add anything?

Senator COLLINS. Thank you to our witnesses and to you, Mr. Chairman, for holding this very important hearing.

Chairman LIEBERMAN. Thank you. The hearing is adjourned.

[Whereupon, at 11:40 a.m., the Committee was adjourned.]

A P P E N D I X

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STATEMENT FOR THE RECORD

of

Mr. Jay M. Cohen.
Under Secretary for Science & Technology
Department of Homeland Security

Regarding a Hearing Entitled

"Six Years After the Anthrax Attack: Are We Better Prepared to Respond to Bioterrorism?"

Before the
U.S. Senate Committee on
Homeland Security and Government Affairs

October 23, 2007

INTRODUCTION

Good morning, Chairman Lieberman, Ranking Member Collins, and distinguished members of the Committee. I am honored to appear before you on this solemn occasion of the 6th anniversary of the anthrax attacks against our Nation to report on the progress being made by the Department of Homeland Security's (DHS) Science and Technology (S&T) Directorate. Those events of six years ago served as a wake up call that an adversary could produce or obtain biological agents to use against this country and when juxtaposed with the terrorist attacks on the World Trade Center and the avowed interest of terrorists to create mass casualties greatly raised the concerns about the possibility of potential high consequence acts of bio-terrorism. Recognizing that "biological weapons in the possession of hostile states or terrorists pose unique and grave threats to the safety and security of the United States and our allies", the President issued Homeland Security Presidential Directive 10 (HSPD-10), *Biodefense for the 21st Century.* HSPD-10 lays out a strategic blueprint for a comprehensive national biodefense built on four pillars: threat awareness, prevention and protection, surveillance and detection, and response and recovery. The activities of the DHS S&T are conducted in support of that integrated interagency strategy and its companion HSPD-9, *Defense of United States Agriculture and Food.*

Reflecting its roles in the National biodefense strategy, DHS S&T's activities emphasize threat awareness, surveillance and detection, response and recovery, and agro-defense, particularly against foreign animal diseases. Our progress in each of these areas is briefly summarized below and detailed more fully in the *DHS Strategic Plan in Support of the National Biodefense Strategy*, which was formally submitted to Congress this summer. These activities are performed in close collaboration with our interagency partners at the Department of Defense (DoD), Department of Health and Human Services (HHS), United States Department of Agriculture (USDA), Department of Justice (DOJ), Environmental Protection Agency (EPA), and the Department of State, whom we gratefully acknowledge.

THREAT AWARENESS

As required under HSPD-10, HSPD-18 (*Medical Countermeasures against Weapons of Mass Destruction)*, and the Project BioShield Act of 2004, DHS S&T has played the lead role in conducting assessments of the evolving biological threat "to guide prioritization of our on-going investments in biodefense-related research, development, planning and preparation" (HSPD-10). To date we have:

Established the National Biodefense Analysis and Countermeasures Center (NBACC). Prior to the events of 2001, the Nation lacked a dedicated capability for conducting both unclassified and classified biodefense research and development. The National Academy of Sciences report *Making the Nation Safer* recommended the creation of such a capability. To address this need, in 2003/4 DHS established at interim NBACC capability at Ft. Detrick and other contracted laboratories. In also began construction of a

dedicated NBACC facility on the National Interagency Biodefense Campus located on Ft. Detrick. The construction of the facility is well underway and on track for initial occupancy at the end of 2008 and initial operational capability in 2009.

Conducted the first, formal, quantitative, end-to-end risk assessments. HSPD-10 calls on DHS to provide "a continuous, formal process for conducting routine capabilities assessments to guide prioritization of our on-going investments in biodefense-related research, development, planning and preparedness." Furthermore, these risk assessments are to integrate "the findings of the intelligence and law enforcement communities with input from the scientific, medical and public health communities" (HSPD-18) The first BioTerrorism Risk Assessment (BTRA) was delivered in FY 2006 as required by HSPD-10 and addressed 28 agents of concern to human health. The BTRA provided the basis for the Secretary of Homeland Security's decision to issue nine additional Material Threat Determinations in support of Project BioShield and is being used by DHS and the EOP to prioritize other biodefense activities. A draft of the second BTRA has just been completed. The 2008 BTRA expands the list of agents from 28 agents to 40, including representative examples of potential future threats as well as key foreign animal agents and expands the consequence models to also consider economic impacts. This BTRA is on track for delivery to the Homeland Security Council (HSC) in January 2008. Due to the success of the 2006 BTRA, HPSD-18 calls on DHS to perform a similar integrated chemical, radiological, biological, and nuclear (iCBRN) risk assessment by June 1, 2008. This iCBRN risk assessment is also on track.

Issued 14 Material Threat Determinations (MTDs) in support of Project BioShield. The Project BioShield Act of 2004 charges the Secretary of DHS, in consultation with HHS, with determining which CBRN threats posed a significant enough risk to the national security to warrant the need for medical countermeasures. The S&T Directorate, in partnership with our interagency colleagues, have provided the supporting analysis. To date, MTDs have been issued for 14 agents: *Bacillus anthracis* (anthrax), Botulinum toxin, *Burkholderia mallei* (glanders), *Burkholderia pseudomallei* (meliodosis), Ebola virus, *Fransciscella tularensis* (tularemia), Junin virus, Marburg virus, multidrug resistant *Bacillus Anthracis,* nuclear agents, radiological agents, *Rickettsia prowazekii* (typhus), Variola virus (smallpox), and *Yersenia pestis* (plague). For each of these agents/threats we have provided HHS an associated Population Threat Analysis (PTA) which provides a plausible high consequence scenario along with estimates of the number of individuals exposed to 10, 100, 1000, 10,000 ... threat organisms. This is used by HHS to inform their requirements for medical countermeasures and the associated concepts of operations for delivering those medical countermeasures. It is anticipated that the on-going integrated CBRN Risk Assessment will result in the generation of additional MTDs.

Conducting Laboratory Experiments to address the key scientific gaps identified in the Risk Assessments. These gaps are uncertainties in scientific parameters that have a large impact on policy and operational decisions for protecting the nation against attack, e.g. the amount of an agent necessary to infect a given percentage of the exposed population or the time an agent will persist in the environment or in food supplies upon processing

and cooking. Current efforts seek to close the major gaps in our understanding of traditional agents by FY 2009 and to establish an approach to addressing future threats by FY 2010. Because of the very broad range of potential future threats, this approach is likely to be based on understanding and looking for the basic biological building blocks, often called pathways, that are needed for an organism to make a person sick – for example the pathways that allow it to infect a person, grow, and reproduce.

Undertaken Biodefense Net Assessments to take a broad look at the fundamental assumptions underlying the Nation's biodefense. These assessments are in fulfillment of the HSPD-10 requirement for "a periodic senior-level policy net assessment that evaluates progress in implementing this policy, identifies gaps or vulnerabilities in our biodefense policy posture, and makes recommendations for rebalancing and refining our investments among the pillars of our overall biodefense policy" (HSPD-10). The first *BNA* is due at the end of 2008 and is addressing eight to ten fundamental issues targeted to provide insight regarding the evolution of the Nation's biodefense strategy. Questions range from 'can deterrence play a greater role in biodefense' to 'where will we be if we stay on the current biodefense trajectory for the nest 5 years vs. where should we be'.

SURVEILLANCE AND DETECTION

Early detection and characterization of a biological attack is critical to permitting a timely response to mitigate the effects of that attack. HSPD-10 tasks DHS with the lead in coordinating such attack warning amongst our interagency partners. Major progress to date includes:

Deployment and operations of the BioWatch aerosol monitoring system and its subsequent transition to the DHS Office of Health Affairs (OHA). President Bush's State of the Union address on January 28, 2003 included the directive "(we) are deploying the Nation's first early warning network of sensors to detect biological attack." Following that declaration, it took just 34 days to implement the original BioWatch system, now referred to as Gen 1 (for 1st generation). Gen 1 BioWatch is currently operational in more than 30 cities across the United States. To date, some four million tests for anthrax have been conducted nationally, without a single false positive. Beginning in 2005, we began a two-to-four fold expansion of the number of BioWatch collectors in the top ten threat cities to (a) enable detection of smaller attacks; (b) provide indoor monitoring of selected critical facilities such as transportation hubs; and (c) provide each city with 10-12 collectors to deploy on an as needed basis to special events of their choosing (e.g. conventions, major sports events or celebrations). This expansion, known as Gen 2, will be complete and fully operational by mid FY2008. Given the operational status of Gen 1 and 2 BioWatch these systems were transferred to the DHS Office of Health Affairs (OHA) in 2007.

***Development of next generation (Gen 3) BioWatch* technology.** Current BioWatch operations are limited by the manual labor costs associated with picking up and transporting filter samples and then preparing them for analysis in offsite laboratories. These manual labor costs account for about 75 percent of the BioWatch operational cost

and hence limit the number of detectors that can be deployed and the frequency with which they can be picked up. Since 2004, we have been developing new technology that would allow the samples to be automatically collected and analyzed at the point of collection, with the results of the analysis wirelessly transmitted to the local public health laboratory. As a result, it will be possible to conduct multiple analyses per day (versus the current one per day) at per unit operational cost less than the Gen 1 and 2 systems. Two of the initial eight approaches pursued have successfully made it all the way through fieldable prototypes and are now to begin three months of rigorous independent testing at Edgewood Chemical and Biological Center.

Coordination of National Biomonitoring Activities. Currently, there are three major classes of on-going operational biomonitoring: environmental aerosols; suspicious materials; and mail. Within each of these classes, there are multiple Federal programs, each of which has been independently implemented. Because these programs were quickly deployed by multiple agencies to address their specific detection needs, improved inter-program and interagency coordination is needed to minimize confusion and increase confidence in results following detection of a biothreat agent.

To address this problem, we have led the development of an interagency Memorandum of Understanding (MOU) to coordinate all biomonitoring activities done by, or on behalf of, the signatory agencies. As an outgrowth of this MOU, we and our interagency partners have developed a National Biological Monitoring Architecture (NBMA) that identifies end state visions, transition strategies and multi-year milestones for accomplishing these goals in environmental, mailroom and suspicious material bio-monitoring. We are currently in the process of implementing this architecture including: (1) piloting a process to establish the equivalency of biodetection assays used by the signatories; (2) coordinating interim guidance and concepts of operations for Federal environmental, mailroom and suspicious material monitoring; and (3) establishing agreements to leverage technologies wherever applicable, such as the current and future BioWatch technologies.

Developing processes to make improved detection tools available to the first responder community. Currently, first responders are discouraged from directly testing suspicious materials, e.g. white powders, but instead are instructed to contact the Federal Bureau of Investigations (FBI) who will then take a sample and send it to a Center for Disease Control and Prevention (CDC) Laboratory Response Network (LRN) for testing. The reason for this is two-fold: (1) the performance of a number of commercial assays is not well characterized and historically have been prone to false alarms, and (2) such local testing can often use up much of the sample making it unavailable for subsequent FBI and CDC testing. In spite of these concerns, first responders have a strong desire to locally test suspicious materials and have often continued to do so. DHS S&T has taken three major steps to address these concerns:

Working with the Association of Official Analytical Chemists (AOAC International) we have developed and validated an independent process for testing certain classes of hand held assays for both laboratory and field use and have conducted the first round of these

tests. AOAC established a Task Force on *Bacillus anthracis* that included DHS, DOD, NIST, FDA, EPA, CDC, USDA, FBI and CIA as well as manufacturers of the assays and representatives from state and local emergency responder groups and the National Guard. In short order, this Task Force selected the spore types to be tested, selected US Army Dugway Proving Ground to provide the test materials and conduct the single lab validation of the assays, and chose 12 highly qualified federal and state labs to participate in a multilaboratory validation of the assays. The AOAC task force also established the acceptance criteria for the study and published the criteria in their Journal. Five assays were selected for testing; ultimately only one of the commercial assays met the criteria as judged by the Official Methods Committee of AOAC. This was, however, a successful study in that we achieved consensus on how such assay validations should be conducted, and the manufacturers now know where the bar is set for these assays.

Working with the international standards organization ASTM International, originally the American Society for Testing and Materials, we have developed a set of voluntary standards for local sampling of suspicious materials that preserves sufficient sample for subsequent LRN and FBI analyses. These standards recognize the importance of the official sample that is needed for public health and law enforcement, while still allowing the residual sample material to be used in a prescreening assay by the HAZMAT team. The National Institute of Standards and Technology (NIST) led the interagency team that included again CDC, FBI, DOD, DHS and EPA as well as the National Guard and representatives from state and local responders. Critical measurements to validate the standard were carried out at Dugway using civil defense teams and National Guard. This standard represented a big step forward in forging a consensus between local HAZMAT teams and the law enforcement and public health communities.

We are in the process of piloting a process to make ultra-high, ultra-specific assays, comparable to those used by Federal monitoring systems, available to commercial developers and through them to first responders. In the interim, DHS S&T and OHA are working with other federal agencies and at the state and local level to build on the consensus of the AOAC/ASTM standard to exercise their responses. The states of Georgia and Massachusetts provide two great examples. They are using these standards and the lessons learned from the standards development; they are developing exercises that engage all the players from the local HAZMAT team to the law enforcement and public health labs. At the end of the day, successful response to a biological event will hinge not just on technology, but on cooperation and mutual trust of the responders, incident managers, law enforcement officials, and public health laboratory personnel.

FORENSIC ANALYSIS TO SUPPORT ATTRIBUTION

Prior to the anthrax attacks of 2001, the United States did not have any dedicated facilities for analyzing the samples from biological crimes. The tens of thousands of samples that resulted from just this one relatively small event graphically emphasized the need for such a capability. To respond to this need, in 2003/4 DHS S&T, in partnership with the FBI, established the interim National Bioforensics Analysis Center (NBFAC) in

renovated leased space at the United States Army Medical Research Institute for Infectious Diseases (USAMRIID). This provided the Nation with its first secure, state-of-the art, contamination free, bio-containment space for the analysis of evidentiary material. The interim NBFAC also includes validated protocols for the biological, chemical, and physical characterization of suspect samples; rigorous "chain of custody" and quality control procedures to ensure the integrity of the sample and its analysis; and remote laboratories to provide specialized capabilities. In 2004, HSPD-10 designated NBFAC "as the lead Federal facility to conduct and facilitate the technical analysis and interpretation of materials following a biological attack in support of the appropriate lead Federal agency". The NBFAC has recently received initial accreditation by the American Association for Laboratory Accreditation (A2LA) to International Standards Organization (ISO) Standard 17025, similar accreditation to that used by FBI laboratories. Starting with a basic set of forensic protocols, its goal is to have a full set of validated and A2LA accredited assays – culture, genetic, and antibody – for the top 30 biothreat agents by FY 2009 and a comprehensive strain library against which to compare them.

RESPONSE AND RECOVERY

Biological agents have the potential to contaminate large portions of a city, covering multiple city blocks and the facilities therein. Based on our limited experience following the 2001 anthrax events, clean-up of even a few facilities can be extremely expensive and time-consuming. The objective of this program is to provide a more rapid and less expensive post-attack cleanup and restoration in such situations. This work is done in partnership with the EPA, who has overall lead in this area. The DHS emphasis is on developing a systems approach for the restoration of citywide areas and of critical facilities, such as major transportation hubs. Major progress to date includes:

Development of restoration protocols and tools for critical transportation hubs. Working with the San Francisco International Airport as the initial testbed and in partnership with EPA, CDC, FBI, state and local authorities, we developed improved sampling tools and EPA reviewed protocols for the restoration of airports following a biological attack. The output of these efforts were shared with local users through a series of regional airport workshops and are currently being applied to the restoration of subway (metro) and other transit systems.

Partnering with the DoD to develop protocols for the restoration of wide urban areas following a biological attack. In FY 2007, DHS S&T initiated the Interagency Biological Restoration Demonstration (IBRD) which focuses on cleaning up an entire neighborhood or district in a major U.S. city following an outdoor biological attack, using the city of Seattle WA and surrounding counties as the initial testbed. IBRD is co-sponsored by the S&T Directorate and the DoD Defense Threat Reduction Agency (DTRA) and involves multiple Federal (e.g. EPA, HHS), State and local stakeholders. Table-top exercises and field demonstrations will be conducted in FY 2008-2009 and will culminate in a set of protocols that are reviewed by the EPA and can be used by other

cities as a template in developing their own protocols for restoration following an outdoor attack.

Leading the interagency development of a validated sampling strategy. In response to the recommendations of the General Accounting Office in its 2005 report entitled *Anthrax Detection*, DHS is leading the interagency development of a coordinated, validated sampling strategy and methodology to determine the extent of contamination and remediation (after a contamination event) for public health determinations.

AGRO-DEFENSE

Recognizing, the large potential impacts of agro-terrorism, especially the potential for the intentional introduction of foreign animal diseases into the United States, the Homeland Security Act of 2002 transferred the operations of the Plum Island Animal Disease Center (PIADC) to DHS. HSPD-9 further designates DHS responsibilities in partnership with USDA and others, including the accelerated development of veterinary countermeasures, planning for state-of-the-art biocontainment facilities to support Research Development Test and Evaluation on foreign animal and zoonotic diseases and the establishment of university centers of excellence on agriculture and food defense. Major progress to date includes:

Operation and upgrading of PIADC. Since its transfer under the Homeland Security Act of 2002, DHS has been operating PIADC in close partnership with USDA. DHS is currently in the midst of upgrades to the security, infrastructure, and research capabilities of the facility.

Joint development of veterinary countermeasures with USDA. DHS and USDA have developed and are implementing a joint strategy for the research and development conducted on, and in support, of PIADC (*Report to Congress: A Joint DHS and USDA Strategy for Foreign Animal Disease Research and Diagnostic Programs,* August, 2004). This strategy emphasizes the development of vaccines, antivirals and high throughput diagnostics for preventing and mitigating outbreaks of foreign animal diseases. Each agency has distinct roles in this development strategy. The USDA's Agricultural Research Service (ARS) has the lead for the basic research portions of these activities, the DHS for the advanced development, and USDA Animal and Plant Health Inspection Service (APHIS) for transition into the field and into the National Veterinary Stockpile (NVS). Together, we have provided improved characterization of the current vaccines for Foot and Mouth Disease (FMD) and have successfully begun the development of next generation vaccines that allows for Differentiation of Infected from Vaccinated Animals (DIVA) – a key issue in resuming trade following an outbreak. The first DIVA vaccine is expected to transition to industry and into the NVS in 2009. In addition, we are now pursuing two candidate vaccines for Rift Valley Fever with the intent to bring one of them to licensure by FY2013.

Planning for the National Bio- and Agro-defense Facility (NBAF). PIADC is now more than 50 years old and is too small to meet the challenges of a greatly expanded

livestock industry with its global markets and with the new threat of agro-terrorism. Defending against FMD alone will require 10 to 14 vaccines to cover the major serotypes and sub-serotypes of FMD – yet the large animal holding space at PIADC will only support development of about one vaccine candidate per year. Further the Nation lacks the capacity for studying zoonotic diseases that affect both large animals and humans. Recognizing these needs, HSPD-9 has tasked the Secretaries of DHS and USDA to develop plans for state-of-the-art biocontainment space for foreign animal and zoonotic diseases and for the accelerated development of countermeasures to address them. To address these needs, DHS, in partnership with USDA, has begun the planning for, and the conceptual design of the National Bio and Agro-defense Facility (NBAF). Expressions of interest were solicited, proposals evaluated, and site visits conducted resulting in narrowing down the selection to five potential sites plus the current Plum Island site. These sites are currently being evaluated as part of the Environmental Impact Statement (EIS) process. Final selection is expected towards the end of 2008 with start of construction in 2010 and initial occupancy in 2013/14.

Established the National Center for Foreign Animal and Zoonotic Disease (FAZD). As per the direction of HSPD-9, we have also established "university-based centers of excellence in agriculture and food security". FAZD is a consortium of universities, led by Texas A&M University, focused on conducting some of the more basic R&D needed to address high consequence foreign animal and zoonotic diseases and to train the next generation of agro-defense researcher. FAZD is working closely with partners in academia, industry, and government to address potential threats to animal agriculture, including FMD, Rift Valley fever, avian influenza, and brucellosis.

Established the National Center for Food Protection and Defense (NCFPD). NCFPD is a consortium of universities, led by the University of Minnesota, charged with a mission to defend the safety of the food system through research and education, to establish best practices, develop new tools, and attract new researchers to manage and respond to food contamination events. The NCFPD addresses three major areas: real world modeling of food contamination events to guide response strategies; development of novel detection and decontamination systems to support that response; and establishment of innovative prevention, response and recovery strategies to minimize the consequences of any event.

CONCLUSION

In summary, DHS S&T has taken the 'wake-up call' of the 2001 anthrax events very seriously. As part of an integrated National biodefense strategy, we have made significant progress in characterizing and prioritizing the threats this Nation faces; in developing, fielding and operating detection systems to provide the earliest possible detection of an attack and initiation of mitigating measures; in developing frameworks and protocols for recovering from biological attacks; in providing the Nation with the needed bio-forensic capabilities to support attribution; and in partnering with the USDA to defend against foreign animal diseases. Much has been accomplished. However, because of the evolving nature of the threat, much also remains to be done. We look forward to continuing to support the Nation in responding to this challenge.

High Priority Technology Needs

May 2007

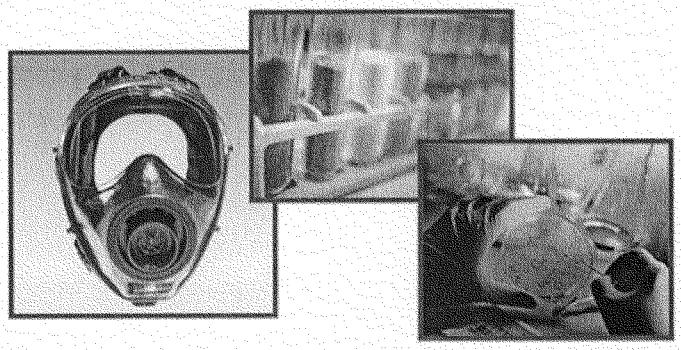
Homeland Security

Science and Technology

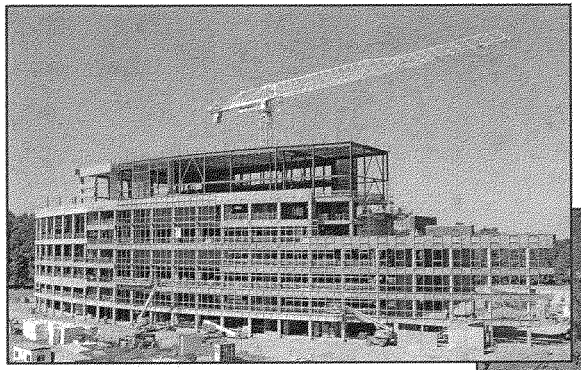
CHEM/BIO DEFENSE

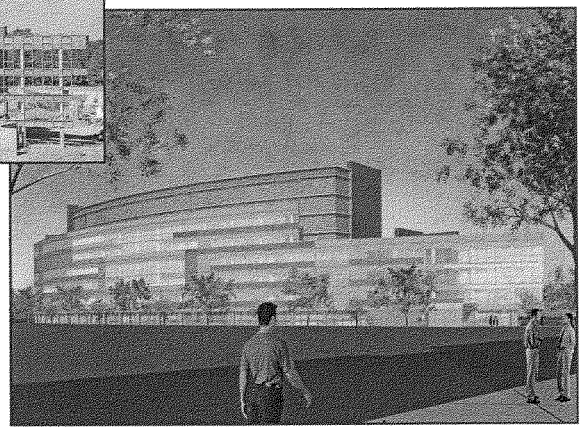
Chem/Bio Defense:
Representative Technology Needs

- Tools to detect and mitigate animal disease breakouts (Chem-Bio Division)
- Policy net assessments to provide fresh perspectives on fundamental elements of the national biodefense strategy (Chem-Bio Division)
- Improved tools for integrated CBRN Risk Assessment (Chem-Bio Division)
- Incident characterization capability for response & restoration (Chem-Bio Division)
- Improved ChemBio Forensic Analysis capability (Chem-Bio Division)
- National-scale detection architectures and strategies to address outdoor, indoor (e.g., highly trafficked transportation hubs) and critical infrastructure (Chem-Bio Division)
- Consequence assessments of attacks on chemical facilities and Chem Bio attacks on other critical infrastructure (Chem-Bio Division)
- Integrated CBRNE Sensor Reporting capability (Chem-Bio Division)
- Handheld rapid biological and chemical detection systems (Chem-Bio Division)
- Detection paradigms and systems for enhanced, emerging and novel biological threats (Chem-Bio Division)



National Biodefense and Analysis Countermeasures Center (NBACC)

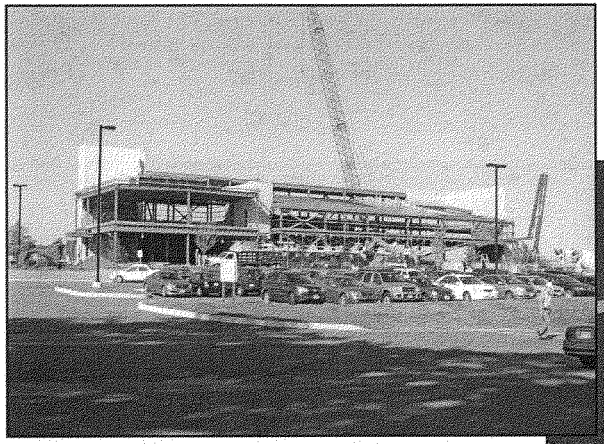


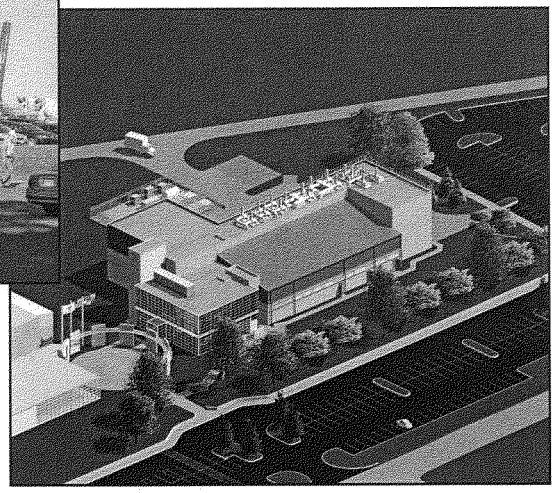


Homeland Security

Chemical Biological Radiological Sample Receipt Facility

DHS Chemical Security and Analysis Center (CSAC)





Homeland Security

Testimony
Committee on Homeland Security
and Governmental Affairs
United States Senate

HHS Progress in National Preparedness Efforts

Statement of

Gerald W. Parker, DVM, PhD, MS
Principal Deputy Assistant Secretary
Office of the Assistant Secretary
for Preparedness and Response
U.S. Department of Health and Human Services

For Release on Delivery
Expected at 10:00 a.m.
October 23, 2007

Chairman Lieberman, Ranking Member Collins, and distinguished Members of the Committee. I am honored to be here today to discuss the progress of Department of Health and Human Services (HHS) to enhance public health preparedness and to review our vision for moving forward.

Today I will focus on three themes related to how HHS has made progress in our bioterrorism preparedness: (1) we have made significant acquisitions for the stockpile against the most serious threats facing the nation; (2) as a result of the lessons learned from previous acquisitions, we have changed the way we do business at HHS; and (3) we have taken an all-hazards approach to public health preparedness – the gains we make against each threat will help us across the spectrum of public health emergencies and disasters. I will also discuss our progress in implementing the Pandemic and All-Hazards Preparedness Act (PAHPA), detail lessons learned from our acquisitions to date, and discuss some of our upcoming activities.

However, I would like to be clear that medical countermeasure development and acquisition is only one component of our overall preparedness efforts, that fits into an all-hazards preparedness approach. Our all- hazards preparedness involves a shared responsibility among our entire Department, our partners in the International community, the Federal interagency, state, local, tribal and territorial governments, the private sector, and, ultimately, individuals and families. We are supporting state and local authorities through the State and Local and Hospital Preparedness programs to establish stockpiles of critical medical equipment and supplies, as well as for developing plans for response, maintenance and distribution countermeasures, and sharing of resources. The Department has effectively accomplished the transfer of the National Disaster Medical System (NDMS), and has aligned activities in the department to more effectively coordinate the preparedness and response enterprise, which focuses on the continuum of preparedness from research and development of medical countermeasures to response delivery platforms that support State and local authorities in dealing with the medical impacts of major disasters.

In addition, we have hosted multiple Department-wide exercises with senior leadership to test how we will leverage the full scope of HHS resources and capabilities in response to threats to public health, in addition to encouraging and engaging in State sponsored exercises taking place in their regions.

Medical Countermeasure Acquisition and Oversight

Our progress in securing medical countermeasures for the Strategic National Stockpile begins with and depends on effective planning. The central framework for medical countermeasures initiatives in the Federal government is the HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE), established in July 2006. This coordinated interagency group is led by the Assistant Secretary for Preparedness and Response (ASPR), and includes the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), and the National Institutes of Health (NIH), and partners from the Department of Defense, Department of Homeland Security, and Department of Veteran Affairs. Through this Enterprise-wide effort, we are able to ensure that Federal activities with respect to needed medical countermeasures are effectively coordinated from research and development, to acquisition and ultimately deployment. This effort supports a range of programs that I will quickly summarize for acquiring medical countermeasures for manmade and naturally occurring public health threats.

Anthrax

Anthrax remains a top priority for the ongoing public health emergency preparedness efforts at HHS, and the Department is committed to developing and acquiring a robust, comprehensive portfolio of medical countermeasures against this threat.

Antibiotics represent the first line of defense to protect the nation following an anthrax attack. Today, we have over 40 million courses of antibiotics in the Strategic National Stockpile (SNS). Anthrax vaccines are also an essential element of our national

preparedness. It is possible that vaccines given as post-exposure prophylaxis in combination with antibiotics could provide longer-term protection, or allow for a reduction in the duration of the antibiotic regimen. HHS has awarded contracts for the acquisition of nearly 30 million doses of anthrax vaccine since 2005, including the recent contract award of 18.75 million doses of Anthrax Vaccine Adsorbed (AVA, BioThrax™). In addition, antitoxins are necessary to treat individuals with advanced stages of infection, and may contribute to a more successful therapeutic outcome. HHS has awarded contracts to two manufacturers to deliver antitoxins sufficient for treating 30,000 people. These vaccine and antitoxin contracts were awarded under the authorities of the Project BioShield Act of 2004. In addition, three BARDA contracts for the advanced development of other anthrax therapeutic candidates were recently awarded through a partnership with the National Institute of Allergies and Infectious Diseases (NIAID).

HHS remains committed to the development and acquisition of a second generation anthrax vaccine. While procuring and continuing to improve the currently available anthrax vaccine, HHS is using its new BARDA authorities to invest over $40 million in the continued development of an rPA anthrax vaccine. This investment builds on the rPA vaccine program that has been ongoing at the National Institute of Allergy and Infectious Diseases (NIAID) since 2002. BARDA is also finalizing a Request for Proposals (RFP) for an upcoming rPA vaccine acquisition. In addition, BARDA and NIAID released a Broad Agency Announcement in September 2007 for vaccine enhancement that will support important improvements in storage conditions and administration for vaccines against a wide array of biological threats.

Smallpox virus

In June 2007, BARDA awarded a contract for a next generation modified vaccinia Ankara (MVA) smallpox vaccine using performance-based milestone payments. The SNS currently contains sufficient smallpox vaccine for every American. HHS has also procured ACAM-2000, a live, single-dose smallpox vaccine developed by Acambis in

collaboration with CDC. This represents the first new biodefense vaccine to be approved by the FDA.

Botulinum toxin

In June 2006, HHS awarded a contract under Project BioShield to the Cangene Corporation for 200,000 doses of a botulinum antitoxin that targets all 7 serotypes of botulinum toxin. The $363 million contract will expand greatly our existing stockpiles in the SNS.

Radiological/Nuclear

We hold significant stockpiles of supplies to treat many of the complex array of medical problems following a potential radiological or nuclear attack, including antibiotics, anti-nausea drugs, and large quantities of supplies to treat burn and blast injuries. We have procured medical countermeasures to mitigate the effects of radiation exposure from either dirty bomb scenarios (Prussian blue and DTPA) or resulting from accidents or deliberate attacks involving nuclear power plants (potassium iodide (KI) in both pill and liquid form). HHS continues to pursue development and an initial acquisition of therapeutics to treat the effects of bone marrow suppression associated with the acute radiation syndrome (ARS) that might result from a nuclear blast. BARDA is also partnering with NIAID to fund advanced development of these medical countermeasures and for necessary testing facilities.

Pandemic Influenza

Since the emergency pandemic supplemental in December 2005, the scientists and public health experts at HHS have built an aggressive and broad-based medical countermeasures program for pandemic influenza. Congress has supported these efforts by allocating over $5.6B to the pandemic influenza preparedness efforts. This has allowed for a robust end-to-end approach that supports acquisition of existing products, research and development projects to produce next-generation countermeasures, and the retrofitting and construction of the facilities necessary to produce pandemic influenza vaccines. In particular, the pandemic influenza program is

focused on vaccines, antivirals, diagnostics, and non-pharmaceutical countermeasures. The President's FY08 Budget includes nearly $1.2 billion to further improve the Nation's preparedness, including $870 million for the development of vaccines and rapid diagnostics and the acquisition of additional antivirals.

With respect to vaccines, HHS has a number of efforts underway. These efforts supported the first U.S. licensure of an H5N1 vaccine in April 2007. By the end of 2007, HHS will have procured 26 million doses of pre-pandemic H5N1 vaccines. However, maintaining a domestic production capability for these priority countermeasures is also an essential component of the pandemic influenza preparedness strategy. Accordingly, in May 2007, we awarded two contracts for the retrofitting of existing domestic biological manufacturing facilities to produce egg-based influenza vaccines, and included warm base operations for up to five years. Finally, a strong advanced development program has led to the rapid maturation of next-generation vaccine production technologies, potentially supporting a shift from egg-based vaccine manufacturing to more flexible cell-based platforms. We anticipate a contract solicitation in 2008 to establish new domestic cell-based influenza vaccine manufacturing facilities that could produce at least 150 million doses of pandemic vaccine within six months.

Antivirals have become an increasingly important medical countermeasure for influenza. Today, the SNS contains 37.5 million treatment courses of antiviral drugs, and we will achieve our goal of 50 million treatment courses in 2008. HHS has also supported antiviral stockpiling at the state level. Through a federally subsidized program, states have purchased 15.1 million treatment courses of influenza antivirals to date and are expected to reach our goal of 31 million courses by July 2008.

The nature of severe influenza infections has also required us to focus on preparedness through non-pharmaceutical countermeasures, such as the essential role that ventilators play in the health care of critically ill patients. We are purchasing 2000 new

ventilators in 2007 for distribution during a pandemic, and there are opportunities for states to also invest in ventilator procurements. Developing ventilators that are more amenable to public health emergency use is a priority for advanced development. This presents a prime example of the integrative, all-hazards approach that the PHEMC Enterprise seeks. A more portable and easier to use ventilator could be an essential tool for responding to many different public health threats, when having a sufficient supply of ventilators could have an impact on the morbidity and mortality of exposure.

Pandemic and All-Hazards Preparedness Act Implementation

The Department has made significant progress in the implementation of PAHPA, which has resulted in tangible successes in the development and purchase of the necessary vaccines, drugs, therapies and diagnostic tools for public health emergencies.

Biomedical Advanced Research Authority

HHS has established the Biomedical Advanced Research and Development Authority (BARDA) to direct and coordinate the Department's countermeasure and product advanced research and development activities. In support of the mission and priorities of the HHS Public Health Emergency Medical Countermeasure Enterprise, (PHEMCE), BARDA establishes systems that encourage and facilitate the development and acquisition of medical countermeasures such as vaccines, therapeutics, and diagnostics, as well as innovative approaches to meet the threat of chemical, biological, radiological and nuclear (CBRN) agents and emerging infectious diseases, including pandemic influenza. BARDA provides an integrated, systematic approach to the development and purchase of the necessary vaccines, drugs, therapies and diagnostic tools for public health emergencies. It directs and coordinates the Department's countermeasure and product advanced research and development activities, including strategic planning for medical countermeasure research, development, and procurement.

Advanced Development

The Department has focused efforts on advanced development (AD) of promising medical countermeasure candidates for licensure. Advanced development support is necessary to move promising MCM candidate products from research through the rigorous advanced development pipeline to become eligible for procurement under the Project BioShield Special Reserve Fund (SRF). This activity is critical to bridge the gap from basic research and early development to procurement, to support multiple candidate products against multiple threats, to mitigate risk for Project BioShield acquisitions, and to successfully achieve the goals of BARDA.

BARDA and NIAID established a Memorandum of Understanding in FY2007 to jointly fund and manage the development of candidate medical countermeasures for CBRN agents. The first use of AD funds employed $99 million that was appropriated on May 25, 2007. In September 2007, the BARDA-NIAID partnership awarded contracts for the advanced development of anthrax antitoxins, anthrax rPA vaccine, smallpox antivirals, novel antibiotic formulations, and oral formulations of DTPA, a radiological/nuclear medical countermeasure.

Milestone Payment Authorities

Authorities for the award milestone payments in fulfillment of drug development goals provides two benefits: it allows the government to share drug development risks with manufacturers; and to closely monitor a company's progress from an earlier stage in drug development. PAHPA amended Section 319F-2 of the Public Health Service Act to allow milestone-based awards and payments for up to 50 percent of the total amount of a Project BioShield contract. In June 2007, BARDA awarded a contract employing these authorities for performance-based milestone payments for a next generation modified vaccinia Ankara (MVA) smallpox vaccine.

Stakeholder Outreach

HHS hosts regular meetings with representatives from relevant industries, academia, other Federal agencies, and international agencies. The 2007 PHEMCE Stakeholders Workshop, an annual event, was held July 31 through August 2, 2007. This Workshop encompassed BARDA, Project BioShield, and Pandemic Influenza, engaged with industry on the Department's present and future requirements, and solicited stakeholder feedback. The Workshop represents our intentions to maintain transparency and dialogue with our many partners in this effort. The first BARDA Industry Day was held on August 3, 2007, and provided an opportunity for stakeholders to demonstrate the operation and effectiveness of relevant countermeasure technologies that will be repeated in conjunction with future Stakeholder Workshops. ASPR will continue to engage with stakeholders regarding the implementation of the PAHPA legislation, and our next stakeholder meeting is scheduled for November 8.

National Biodefense Science Board

On May 24, 2007, the Secretary established the National Biodefense Science Board (NBSB) to provide expert advice and guidance to the Secretary on scientific, technical and other matters of special interest to HHS regarding activities to prevent, prepare for and respond to adverse health effects of public health emergencies resulting from current and future CBRN agents, whether naturally occurring, accidental, or deliberate. Th NBSB will convene twice a year, and will be employed as a mechanism to engage stakeholders, to provide a forum for the discussion and collaboration on controversial issues, and to enhance transparency and credibility to the decision making process. Moreover, consistent with the Pandemic and All-Hazards Preparedness Act, the NBSB will include broad membership, including from industry, academia, the healthcare professional and consumer advocacy communities.

Lessons Learned and Path Forward

HHS has incorporated valuable lessons from the three years of BioShield and has applied these perspectives to the current and future medical countermeasure

development and acquisition projects. While we have achieved successes, we have also learned valuable lessons. The discovery and development of new medical countermeasures is complex and an inherently risky endeavor. The termination of the contract to procure an rPA anthrax vaccine exemplifies the multi-factorial challenges encountered in the implementation of Project BioShield. There are three particular lessons to be gained from recent Project BioShield procurements:

- First, for the most part, experienced and well-resourced companies have not responded to BioShield, and contract terms dictated by the BioShield statute were challenging, particularly for less experienced companies.
- Second, it is critical that developers establish effective relationships with the FDA early, to gain a clear understanding of the regulatory requirements with respect to their product for the stockpile.
- Finally, absence of a robust Advanced Development program placed too much risk on BioShield procurement programs.

Funding

The fiscal year (FY) 2008 request for advanced development will help to bridge the gap between NIH research and development programs and Project BioShield, and it is critical to BARDA implementation. The Department has established a framework to build medical countermeasure advanced development programs, critical to the evaluation of promising drug candidates and to their approval and licensure.

It is helpful to review briefly the development and acquisition of public health medical countermeasures, which involve three broad steps. First, in the research phase, early studies are conducted to discover how disease occurs, and to identify candidate products to prevent or treat it. Second, during the development stage candidate products must successfully navigate animal studies, several stages of clinical studies for safety and efficacy, and manufacturing scale-up leading to approval and licensure of a product. Third is acquisition, the stage in which a product is purchased by the federal government through Project BioShield.

Traditionally, basic research activities have been supported by research grants and contracts, primarily through the NIH. Procurement is supported by the Special Reserve Fund (SRF) under Project BioShield and traditional SNS procurement mechanisms.

It is important to understand that prior to the enactment of PAHPA, the SRF payment was conditioned upon delivery of a product to the stockpile, and there were limited mechanisms to support advanced development. For small biotechnology companies, this stage of development, an inherently risky endeavor, usually relies on funding from venture capital or stock offerings where a commercial market exists . Unfortunately, for biodefense medical products this stage has often proved challenging. The President's budget request included $189 million to help to fill this gap and support advanced development of promising biodefense product candidates in FY08.

BioShield Implementation

HHS recognizes that BioShield procurements must be made more swiftly. To help achieve this, HHS and the Department of Homeland Security (DHS) have established an interagency agreement to expedite the implementation of BioShield by clarifying roles and responsibilities and by establishing mechanisms to improve efficiencies. We have also secured direct funding for Project BioShield management and are building a highly qualified and accomplished workforce of acquisition specialists and scientists. Furthermore, HHS continues to seek ways to more effectively manage and streamline the time between the release of an RFP and the award of a contract

Because the process of product development can be fraught with unexpected complications and delays, it is nearly impossible to know the exact specifications for a product at the beginning of a Project BioShield acquisition. To address this challenge, HHS now requires that companies awarded Project BioShield contracts communicate with the Food and Drug Administration (FDA) early and often to ensure the success of each acquisition program.

Transparency and Outreach

The Department continues to work to make the BioShield process more transparent to stakeholders. The PHEMCE Strategy and Implementation Plan are the result of significant input from industry and other BioShield stakeholders, and provide insight into HHS countermeasure acquisition requirements and priorities. The PHEMCE Strategy and Implementation Plan reaffirms and further identifies our commitments to the development and acquisition of anthrax vaccines, anthrax antitoxins and therapeutics for radiological and nuclear threats. It also identifies the need for the continued development and acquisition of broad spectrum antibiotics, antivirals, and diagnostics against high priority threats. The end-to-end PHEMCE process has also increased our understanding of the challenging operational conditions that medical countermeasures must be designed for.

This outreach is critical to providing the visibility into BARDA programs necessary to ensure a mutual understanding between HHS and industry stakeholders, and to maximize participation. HHS is continually refining these processes to ensure that stakeholders receive accurate, consistent, and timely information and to facilitate the participation of the largest number of biotechnology and pharmaceutical manufacturers.

Conclusion

Thank you for the opportunity to present the progress HHS has made in national preparedness for biological threats to public health. We have made substantial progress. The threat remains real, and we have much left to do to ensure that we meet our mission of a Nation prepared for a public health emergency. This concludes my testimony. I will be happy to answer any questions.

United States Government Accountability Office

GAO

Testimony
Before the Committee on Homeland Security and Governmental Affairs, U.S. Senate

For Release on Delivery
Expected at 10:00 a.m. EDT
Tuesday, October 23, 2007

PROJECT BIOSHIELD

Actions Needed to Avoid Repeating Past Mistakes

Statement of Keith Rhodes, Chief Technologist
Center for Technology and Engineering,
Applied Research and Methods

GAO-08-208T

October 23, 2007

GAO
Accountability · Integrity · Reliability
Highlights

Highlights of GAO-08-208T, a testimony before the Committee on Homeland Security and Governmental Affairs, U.S. Senate

PROJECT BIOSHIELD

Actions Needed to Avoid Repeating Past Mistakes

Why GAO Did This Study

The anthrax attacks in September and October 2001 highlighted the need to develop medical countermeasures. The Project BioShield Act of 2004 authorized the Department of Health and Human Services (HHS) to procure countermeasures for a Strategic National Stockpile. However, in December 2006, HHS terminated the contract for a recombinant protective antigen (rPA) anthrax vaccine because VaxGen failed to meet a critical contractual milestone. Also, supplies of the licensed BioThrax anthrax vaccine already in the stockpile will start expiring in 2008.

GAO was asked to testify on its report on Project BioShield, which is being released today. This testimony summarizes (1) factors contributing to the failure of the rPA vaccine contract and (2) issues associated with using the BioThrax in the stockpile. GAO interviewed agency and industry officials, reviewed documents, and consulted with biodefense experts.

What GAO Recommends

GAO recommended that the HHS Secretary ensure that (1) for future procurements the concept of use and all critical requirements for medical countermeasures are clearly articulated at the outset, (2) expired stockpile vaccines are destroyed, and (3) the HHS and the Department of Defense (DOD) Secretaries develop an integrated stockpile for BioThrax with rotation based on a first-in, first-out principle. HHS and DOD generally concurred with GAO's recommendations.

To view the full product, including the scope and methodology, click on GAO-08-208T. For more information, contact Keith Rhodes, (202) 512-6412 or rhodesk@gao.gov.

What GAO Found

Three major factors contributed to the failure of the first Project BioShield procurement effort for an rPA anthrax vaccine. First, HHS's Office of the Assistant Secretary for Preparedness and Response (ASPR) awarded the procurement contract to VaxGen, a small biotechnology firm, while VaxGen was still in the early stages of developing a vaccine and had not addressed many critical manufacturing issues. This award preempted critical development work on the vaccine. Also, the contract required VaxGen to deliver 25 million doses of the vaccine in 2 years, which would have been unrealistic even for a larger manufacturer. Second, VaxGen took unrealistic risks in accepting the contract terms. VaxGen officials told GAO that they accepted the contract despite significant risks due to (1) the aggressive delivery time line for the vaccine, (2) VaxGen's lack of in-house technical expertise—a condition exacerbated by the attrition of key company staff as the contract progressed—and (3) VaxGen's limited options for securing any additional funding needed.

Third, important Food and Drug Administration (FDA) requirements regarding the type of data and testing required for the rPA anthrax vaccine to be eligible for use in an emergency were not known at the outset of the procurement contract. In addition, ASPR's anticipated use of the rPA anthrax vaccine was not articulated to all parties clearly enough and evolved over time. Finally, according to VaxGen, the purchase of BioThrax for the stockpile as a stopgap measure raised the bar for the VaxGen vaccine. All these factors created confusion over the acceptance criteria for VaxGen's product and significantly diminished VaxGen's ability to meet contract time lines. ASPR has announced its intention to issue another request for proposal for an rPA anthrax vaccine procurement but, along with other HHS components, has not analyzed lessons learned from the first contract's failure and may repeat earlier mistakes. According to industry experts, the lack of specific requirements is a cause of concern to the biotechnology companies that have invested significant resources in trying to meet government needs and now question whether the government can clearly define future procurement contract requirements.

GAO identified two issues related with the use of the BioThrax in the Strategic National Stockpile. First, ASPR lacks an effective strategy to minimize the waste of BioThrax. Starting in 2008, several lots of BioThrax in the Strategic National Stockpile will begin to expire. As a result, over $100 million per year could be lost for the life of the vaccine currently in the stockpile. ASPR could minimize such potential waste by developing a single inventory system with DOD—a high-volume user of BioThrax—with rotation based on a first-in, first-out principle. DOD and ASPR officials identified a number of obstacles to this type of rotation that may require legislative action. Second, ASPR planned to use three lots of expired BioThrax vaccine in the stockpile in the event of an emergency. This would violate FDA rules, which prohibit using an expired vaccine, and could also undermine public confidence because the vaccine's potency could not be guaranteed.

Mr. Chairman and Members of the Committee:

We are pleased to be here to discuss our findings on Project BioShield's first major procurement contract and the potential for waste in the Strategic National Stockpile. My statement is based on our report, which we are releasing today.[1]

In 2002, in response to the anthrax attacks, the National Institute of Allergy and Infectious Diseases (NIAID) within the National Institutes of Health (NIH) launched an effort to rapidly develop a second generation recombinant protective antigen (rPA) anthrax vaccine. While there was already a licensed anthrax vaccine (BioThrax), it is given in six doses over 18 months followed by an annual booster. NIAID wanted to have a vaccine that could be administered in an immunization series of not more than three doses.

In 2002 and 2003, NIAID awarded development contracts for rPA vaccines to two companies—VaxGen and Avecia. VaxGen was a small U.S. biotechnology company. According to NIAID, one of the objectives was to demonstrate how manufacturing efforts might be increased to support creation of a stockpile of medical countermeasures.

The Project BioShield Act of 2004 formalized this initiative and authorized the Secretary of Health and Human Services (HHS) to acquire and ensure the management of and accounting for a stockpile of medical countermeasures.[2] The Secretary, in turn, entrusted this responsibility to the Office of the Assistant Secretary for Preparedness and Response (ASPR). Among other medical countermeasures, this stockpile contained, as of June 2007, about 10 million doses of BioThrax, the licensed anthrax vaccine. Since doses of BioThrax, like other vaccines, have an expiration date, these doses will be disposed of if they are not used before that date. The only other large user of BioThrax vaccine is the Department of Defense (DOD), which has procured its own inventory of the vaccine.

[1] *Project BioShield: Actions Needed to Avoid Repeating Past Problems with Procuring New Anthrax Vaccine and Managing the Stockpile of Licensed Vaccine*, GAO-08-88 (Washington, D.C.: October 23, 2007).

[2] The Strategic National Stockpile, formerly known as the National Pharmaceutical Stockpile, contains pharmaceuticals, vaccines, medical supplies, and medical equipment to respond to terrorist attacks and other emergencies.

In November 2004, ASPR awarded VaxGen a procurement contract for $877.5 million for the manufacture and delivery of 75 million doses of its rPA anthrax vaccine to the stockpile. Two years later, in December 2006, ASPR terminated VaxGen's contract for failure to meet a critical contractual milestone. The failure of this procurement effort raised larger questions regarding the country's ability to develop a new anthrax vaccine and a robust and sustainable biodefense medical countermeasure industry by building a partnership between pharmaceutical and biotechnology firms and the government. The biotech industry has raised concerns about whether the government can clearly define its requirements for future procurement contracts.

Today, my testimony will focus on the following two issues that you asked us to address: (1) factors that contributed to the failure of ASPR's first Project BioShield procurement effort with VaxGen for an rPA anthrax vaccine and (2) issues associated with using the licensed anthrax vaccine, BioThrax, in the Strategic National Stockpile.

Scope and Methodology

To respond to these questions, we interviewed agency and industry officials, reviewed documents, and consulted with biodefense experts. We conducted our review from June 2007 through August 2007 in accordance with generally accepted government auditing standards.

Summary

Three major factors contributed to the failure of the first Project BioShield procurement effort.

- First, ASPR awarded the first BioShield procurement contract to VaxGen when its product was at a very early stage of development.
- Second, VaxGen took unrealistic risks in accepting the contract terms.
- Third, important Food and Drug Administration (FDA) requirements regarding the type of data and testing required for the rPA anthrax vaccine to be eligible for use in an emergency were not known—to FDA, NIAID, ASPR, and VaxGen—at the outset of the procurement contract.

Since ASPR and other HHS components involved have not completed any formal lessons-learned exercise from the first procurement's failure, they may repeat their mistakes in the absence of a corrective plan. According to industry experts, the lack of clear requirements is a cause of concern to

companies asked to partner with the government since they invest significant resources in trying to meet government needs and now question whether the government can clearly define its requirements for future procurement contracts.

We identified two issues related to using the licensed anthrax vaccine, BioThrax, in the Strategic National Stockpile:

- ASPR lacks an effective strategy to minimize waste.[3] Vaccine valued at more than $12 million has already expired and is no longer usable. Without an effective management strategy in the future, over $100 million per year could be lost for the life of the licensed anthrax vaccine currently in the stockpile. ASPR could minimize such potential waste by developing a single inventory system for BioThrax with DOD, with rotation based on a first-in, first-out principle.

- ASPR plans to use expired vaccine in violation of FDA's current rules. According to CDC, ASPR told CDC not to dispose of three lots of BioThrax vaccine that expired in 2006 and 2007. ASPR officials told us that the agency's decision was based on the possible need to use these lots of vaccines in an emergency. However, FDA rules prohibit the use of expired vaccine.[4] Thus, ASPR's planned use of expired vaccine would violate FDA's current rules and could undermine public confidence because ASPR would be unable to guarantee the potency of the vaccine.

The report that we are issuing today makes three recommendations. To help ensure the success of future medical countermeasures procurement, the Secretary of HHS direct ASPR, NIAID, FDA, and CDC to ensure that the concept of use and all critical requirements for such procurements are clearly articulated at the outset.

To ensure public confidence and comply with FDA's current rules, we recommend that the Secretary of HHS direct ASPR to destroy the expired BioThrax vaccine in the stockpile.

[3]All vaccines will eventually expire. However, when there is a large volume user for stockpile products, not having an effective strategy to ensure stockpile products would be used constitutes waste.

[4]FDA regulations do allow the extension of the expiration date of a vaccine under certain limited circumstances. See 21 C.F.R. 610.53.

To minimize waste of the BioThrax anthrax vaccine in the stockpile, we recommend that the Secretaries of HHS and DOD develop a single integrated inventory system for the licensed anthrax vaccine, with rotation based on a first-in, first-out principle.

HHS and DOD generally concurred with our recommendations. In addition, with regard to our recommendation on integrated stockpile, they identified legal challenges to developing an integrated inventory system for BioThrax in the stockpile, which may require legislative action. Although HHS and DOD use different authorities to address BioThrax liability issues, both authorities could apply to either DOD or HHS; consequently, indemnity does not appear to be an insurmountable obstacle for future procurements.

Background

Project BioShield

The Project BioShield Act of 2004 (Public Law 108-276) was designed to encourage private companies to develop civilian medical countermeasures by guaranteeing a market for successfully developed countermeasures.

The Project BioShield Act (1) relaxes some procedures for bioterrorism-related procurement, hiring, and research grant awarding; (2) allows for the emergency use of countermeasures not approved by FDA; and (3) authorizes 10-year funding (available through fiscal year 2013) to encourage the development and production of new countermeasures for chemical, biological, radiological, or nuclear agents. The act also authorizes HHS to procure these countermeasures for the Strategic National Stockpile.

Agency Roles in Developing, Procuring, and Stockpiling of Medical Countermeasures

Project BioShield procurement involves actions by HHS (including ASPR, NIAID, FDA, and the Centers for Disease Control and Prevention (CDC)) and an interagency working group.

HHS's role

Various offices within HHS fund the development research, procurement, and storage of medical countermeasures, including vaccines, for the Strategic National Stockpile.

ASPR's role: ASPR is responsible for the entire Project BioShield contracting process, including issuing requests for information and requests for proposals, awarding contracts, managing awarded contracts, and determining whether contractors have met the minimum requirements for payment. ASPR maintains a Web site detailing all Project BioShield solicitations and awards.

ASPR has the primary responsibility for engaging with the industry and awarding contracts for large-scale manufacturing of licensable products, including vaccines, for delivery into the Strategic National Stockpile. With authorities recently granted, the Biomedical Advanced Research and Development Authority (BARDA) will be able to use a variety of funding mechanisms to support the advanced development of medical countermeasures and to award up to 50 percent of the contract as milestone payments before purchased products are delivered.

NIAID's role: NIAID is the lead agency in NIH for early candidate research and development of medical countermeasures for biodefense. NIAID issues grants and awards contracts for research on medical countermeasures exploration and early development, but it has no responsibility for taking research forward into marketable products.

FDA's role: Through its Center for Biologics Evaluation and Research (CBER), FDA licenses many biological products, including vaccines, and the facilities that produce them. Manufacturers are required to comply with current Good Manufacturing Practices regulations, which regulate personnel, buildings, equipment, production controls, records, and other aspects of the vaccine manufacturing process. FDA has also established the Office of Counterterrorism Policy and Planning in the Office of the Commissioner, which issued the draft *Guidance on the Emergency Use Authorization of Medical Products* in June 2005. This guidance describes in general terms the data that should be submitted to FDA, when available, for unapproved products or unapproved uses of approved products that HHS or another entity wishes FDA to consider for use in the event of a declared emergency. The final emergency use authorization (EUA) guidance was issued in July 2007.

CDC's role: Since 1999, CDC has had the major responsibility for managing and deploying the medical countermeasures—such as antibiotics and vaccines—stored in the Strategic National Stockpile.

DOD's Role

DOD is not currently a part of Project BioShield. Beginning in 1998, DOD had a program to vaccinate all military service members with BioThrax. DOD's program prevaccinates personnel being deployed to Iraq, Afghanistan, and the Korean peninsula with BioThrax. For other deployments, this vaccination is voluntary. DOD also has a program to order, stockpile, and use the licensed anthrax vaccine. DOD estimates its needs for BioThrax doses and bases its purchases on that estimate.

The Licensed Vaccine for Anthrax

An FDA-licensed anthrax vaccine, BioThrax, has been available since 1970. The vaccine has been recommended for a variety of situations, for example, laboratory workers who produce anthrax cultures. The BioShield program stockpiled BioThrax for the Strategic National Stockpile for postexposure use in the event of a large number of U.S. civilians being exposed to anthrax. ASPR had already acquired 10 million doses of BioThrax from Emergent BioSolutions by 2006 and recently purchased an additional 10 million doses.

Three Factors Contributed to the Failure of ASPR's First Project BioShield Effort to Produce an rPA Anthrax Vaccine

Three major factors contributed to the failure of the first Project BioShield procurement effort. First, ASPR awarded the first BioShield procurement contract to VaxGen when its product was at a very early stage of development and many critical manufacturing issues had not been addressed. Second, VaxGen took unrealistic risks in accepting the contract terms. Third, key parties did not clearly articulate and understand critical requirements at the outset.

HHS Awarded the Contract Too Soon

ASPR's decision to launch the VaxGen procurement contract for the rPA anthrax vaccine at an early stage of development, combined with the delivery requirement for 25 million doses within 2 years,[5] did not take the complexity of vaccine development into consideration and was overly aggressive. Citing the urgency involved, ASPR awarded the procurement contract to VaxGen several years before the planned completion of earlier

[5]The contract called for 75 million doses overall, but only 25 million were required to be delivered within 2 years of award.

and uncompleted NIAID development contracts with VaxGen and thus preempted critical development work.

NIAID awarded VaxGen two development contracts, neither of which was near completion when ASPR awarded the procurement contract. However, on November 4, 2004, a little more than a year after NIAID awarded VaxGen its second development contract, ASPR awarded the procurement contract to VaxGen for 75 million doses of its rPA anthrax vaccine. At that time, VaxGen was still at least a year away from completing the Phase 2 clinical trials under the second NIAID development contract. Moreover, VaxGen was still finishing up work on the original stability testing required under the first development contract.

At the time of the award, ASPR officials had no objective criteria, such as Technology Readiness Levels (TRL), to assess product maturity.[6] They were, however, optimistic that the procurement contract would be successful. One official described its chances of success at 80 percent to 90 percent. However, a key official at VaxGen told us at the same time that VaxGen estimated the chances of success at 10 percent to 15 percent. When we asked ASPR officials why they awarded the procurement contract when they did, they pointed to a sense of urgency at that time and the difficulties in deciding when to launch procurement contracts.

According to industry experts, preempting the development contract 2 years before completing work—almost half its scheduled milestones—was questionable, especially for vaccine development work, which is known to be susceptible to technical issues even in late stages of development. NIAID officials also told us it was too early for a BioShield purchase. At a minimum, the time extensions for NIAID's first development contract with VaxGen to accommodate stability testing should have indicated to ASPR that development on its candidate vaccine was far from complete.

After ASPR awarded VaxGen the procurement contract, NIAID canceled several milestones under its development contracts undermining VaxGen's ability to deliver the required number of doses within the 2-year time frame.

[6]TRLs have been used by federal agencies (DOD, the National Aeronautics and Space Administration, and others) to assess the maturity of evolving technologies prior to incorporating that technology into a system or subsystem. The primary purpose of using TRLs is to help management make decisions concerning the development and transitioning of technology.

VaxGen Took Unrealistic Risks in Accepting the Procurement Contract

VaxGen officials told us that they understood their chances for success were limited and that the contract terms posed significant risks. These risks arose from aggressive time lines, VaxGen's limitations with regard to in-house technical expertise in stability and vaccine formulation—a condition exacerbated by the attrition of key staff from the company as the contract progressed—and its limited options for securing additional funding should the need arise.

Industry experts told us that a 2-year time line to deliver 75 million filled and finished doses of a vaccine from a starting point just after phase 1 trials is a near-impossible task for any company. VaxGen officials told us that at the time of the procurement award they knew the probability of success was very low, but they were counting on ASPR's willingness to be flexible with the contract time line and work with them to achieve success. In fact, in May 2006, ASPR did extend the contract deadlines to initiate delivery to the stockpile an additional 2 years. However, on November 3, 2006, FDA imposed a clinical hold on VaxGen's forthcoming phase 2 trial after determining that data submitted by VaxGen were insufficient to ensure that the product would be stable enough to resume clinical testing.[7] By that time, ASPR had lost faith in VaxGen's technical ability to solve its stability problems in any reasonable time frame. When VaxGen failed to meet a critical performance milestone to initiate the next clinical trial, ASPR terminated the contract.

According to VaxGen's officials, throughout the two development contracts and the Project BioShield procurement contract, VaxGen's staff peaked at only 120, and the company was consistently unable to marshal sufficient technical expertise. External expertise that might have helped VaxGen better understand its stability issue was never applied. At one point during the development contracts, NIAID—realizing VaxGen had a stability problem with its product—convened a panel of technical experts in Washington, D.C. NIAID officials told us that at the time of the panel meeting, they offered to fund technical experts to work with the company, but VaxGen opted not to accept the offer. Conversely, VaxGen officials reported to us that at the time NIAID convened the panel of experts, NIAID declined to fund the work recommended by the expert panel.

[7]A clinical hold is the mechanism that FDA uses to stop a study when it finds that the study should not proceed because of an identified deficiency.

Finally, VaxGen accepted the procurement contract terms even though the financial constraints imposed by the BioShield Act limited its options for securing any additional funding needed. In accordance with this act, payment was conditional on delivery of a product to the stockpile, and little provision could be made, contractually, to support any unanticipated or additional development needed—for example, to work through issues of stability or reformulation.[8] Both problems are frequently encountered throughout the developmental life of a vaccine. This meant that the contractor would pay for any development work needed on the vaccine. VaxGen, as a small biotechnology company, had limited internal financial resources and was dependent on being able to attract investor capital for any major influx of funds. However VaxGen was willing to accept the firm, fixed-price contract and assume the risks involved. VaxGen did so even though it understood that development on its rPA vaccine was far from complete when the procurement contract was awarded and that the contract posed significant inherent risks.

Key Parties Did Not Clearly Articulate and Understand Critical Requirements

Important requirements regarding the data and testing required for the rPA anthrax vaccine to be eligible for use in an emergency were not known at the outset of the procurement contract. They were defined in 2005 when FDA introduced new general guidance on EUA. In addition, ASPR's anticipated use of the rPA anthrax vaccine was not articulated to all parties clearly enough and evolved over time. Finally, according to VaxGen, purchases of BioThrax raised the requirement for use of the VaxGen rPA vaccine. All of these factors created confusion over the acceptance criteria for VaxGen's product and significantly diminished VaxGen's ability to meet contract time lines.

Guidance on Emergency Use Authorization Appeared Midcontract and Created Confusion

After VaxGen received its procurement contract, draft guidance was issued that addressed the eventual use of any unlicensed product in the stockpile. This created confusion over the criteria against which VaxGen's product would be evaluated, strained relations between the company and the government, and caused a considerable amount of turmoil within the

[8]Under Project BioShield, advance payments of up to 10 percent of the contract value could be made if the HHS Secretary deemed it necessary for the success of the program. ASPR officials told us that VaxGen did request such a payment, but ASPR did not grant it.

company as it scrambled for additional resources to cover unplanned testing.

In June 2005, FDA issued draft EUA guidance, which described for the first time the general criteria that FDA would use to determine the suitability of a product for use in an emergency.[9] This was 7 months after the award of the procurement contract to VaxGen and 14 months after the due date for bids on that contract.

Since the request for proposal for the procurement contract was issued and the award itself was made before the EUA guidance was issued, neither could take the EUA requirements into consideration. The procurement contract wording stated that in an emergency, the rPA anthrax vaccine was to be "administered under a 'Contingency Use' Investigational New Drug (IND) protocol" and that vaccine acceptance into the stockpile was dependent on the accumulation and submission of the appropriate data to support the "use of the product (under IND) in a postexposure situation." However, FDA officials told us they do not use the phrase "contingency use" under IND protocols.

When we asked ASPR officials about the requirements for use defined in the contract, they said that the contract specifications were consistent with the statute and the needs of the stockpile. They said their contract used "a term of art" for BioShield products. That is, the contractor had to deliver a "usable product" under FDA guidelines. The product could be delivered to the stockpile only if sufficient data were available to support emergency use. ASPR officials told us that FDA would define "sufficient data" and the testing hurdles a product needed to overcome to be considered a "usable product."

According to FDA, while VaxGen and FDA had monthly communication, data requirements for emergency use were not discussed until December 2005, when VaxGen asked FDA what data would be needed for emergency use. In January 2006, FDA informed VaxGen, under its recently issued draft EUA guidance, of the data FDA would require from VaxGen for its product to be eligible for consideration for use in an emergency. The draft

[9]FDA is ultimately responsible for determining if available products (unapproved products or approved products for unapproved usage) in the stockpile can be used in an emergency. The data FDA needs to determine whether a product can be used in an emergency are critical to manufacturers to adequately plan and estimate the time and resources required for generating the data.

guidance described in general FDA's current thinking concerning what FDA considered sufficient data and the testing needed for a product to be considered for authorization in certain emergencies.

Because the EUA guidance is intended to create a more feasible protocol for using an unapproved product in a mass emergency than the term "contingency use" under an IND protocol that ASPR used in the procurement contract, it may require more stringent data for safety and efficacy. Under an IND protocol, written, informed consent must be received before administering the vaccine to any person, and reporting requirements identical to those in a human clinical trial are required.[10] The EUA guidance—as directed by the BioShield law—eased both informed consent and reporting requirements. This makes sense in view of the logistics of administering vaccine to millions of people in the large-scale, postexposure scenarios envisioned. Because EUA guidance defines a less stringent requirement for the government to use the product, it correspondingly may require more testing and clinical trial work than was anticipated under contingency use.

Several of the agencies and companies involved in BioShield-related work have told us the EUA guidance appears to require a product to be further along the development path to licensure than the previous contingency use protocols would indicate. VaxGen officials told us that if the draft EUA guidance was the measure of success, then VaxGen estimated significant additional resources would be needed to complete testing to accommodate the expectations under this new guidance. NIAID told us that the EUA guidance described a product considerably closer to licensure (85 percent to 90 percent) than it had assumed for a Project BioShield medical countermeasure (30 percent) when it initially awarded the development contracts.

The Concept of Use for the rPA Vaccine Was Not Clearly Articulated to All Parties

FDA considers a vaccine's concept of use important information to gauge the data and testing needed to ensure the product's safety and efficacy. According to FDA, data and testing requirements to support a product's use in an emergency context may vary depending on many factors, including the number of people to whom the product is expected to be administered. The current use of an unlicensed product involves assessing potential risks and benefits from using an unapproved drug in a very small

[10]It also requires an approval from the Institutional Review Board.

number of people who are in a potentially life-threatening situation. In such situations, because of the very significant potential for benefit, safety and efficacy data needed to make the risk benefit assessment might be lower than in an emergency situation where an unlicensed vaccine might be offered to millions of healthy people. This distinction is critical for any manufacturer of a product intended for use in such scenarios—it defines the level of data and testing required. Product development plans and schedules rest on these requirements.

However, in late 2005, as VaxGen was preparing for the second phase 2 trial and well into its period of performance under the procurement contract, it became clear that FDA and the other parties had different expectations for the next phase 2 trial. From FDA's perspective, the purpose of phase 2 trials was to place the product and sponsor (VaxGen) in the best position possible to design and conduct a pivotal phase 3 trial in support of licensure[11] and not to produce meaningful safety and efficacy data to support use of the vaccine in a contingency protocol under IND as expected by VaxGen, ASPR, and CDC. This lack of a clear understanding of the concept of use for VaxGen's product caused FDA to delay replying to VaxGen until it could confer with ASPR and CDC to clarify this issue. Thus, we conclude that neither VaxGen nor FDA understood the rPA anthrax vaccine concept of use until this meeting.

Purchase of BioThrax for the Stockpile Raised Requirements for Use of rPA Vaccine

The introduction of BioThrax into the stockpile undermined the criticality of getting an rPA vaccine into the stockpile and, at least in VaxGen's opinion, forced FDA to hold it to a higher standard that the company had neither the plans nor the resources to achieve. ASPR purchased 10 million doses of BioThrax in 2005 and 2006 as a stopgap measure for post-exposure situations. The EUA guidance states that FDA will "authorize" an unapproved or unlicensed product—such as the rPA anthrax vaccine candidate—only if "there is no adequate, approved and available alternative." [12]According to the minutes of the meeting between FDA and VaxGen, in January 2006, FDA reported that the unlicensed rPA anthrax vaccine would be used in an emergency after the stockpiled BioThrax, that is, "when all of the currently licensed [BioThrax] had been deployed." This

[11]In commenting on the draft report, FDA indicated that the purpose of the phase 2 trial is to collect additional safety and, when possible, efficacy data, as well as to determine the dose, route, and schedule for administration.

[12]This is a requirement of the BioShield law.

diminished the likelihood of a scenario where the rPA vaccine might be expected to be used out of the stockpile and, in VaxGen's opinion, raised the bar for its rPA vaccine.

ASPR Lacks an Effective Strategy to Minimize Waste in the Strategic National Stockpile and Plans to Use Expired Anthrax Vaccine

We identified two issues related to using the BioThrax in the Strategic National Stockpile. First, ASPR lacks an effective strategy to minimize waste. As a consequence, based on current inventory, over $100 million is likely to be wasted annually, beginning in 2008. Three lots of BioThrax vaccine in the stockpile have already expired, [13] resulting in losses of over $12 million. According to the data provided by CDC, 28 lots of BioThrax vaccine will expire in calendar year 2008. ASPR paid approximately $123 million for these lots. For calendar year 2009, 25 additional lots—valued at about $106 million—will reach their expiration dates. ASPR could minimize the potential waste of these lots by developing a single inventory system with DOD—which uses large quantities of the BioThrax vaccine—with rotation based on a first-in, first-out principle.[14]

Because DOD is a high-volume user of the BioThrax vaccine, ASPR could arrange for DOD to draw vaccine from lots long before their expiration dates. These lots could then be replenished with fresh vaccine from the manufacturer. DOD, ASPR, industry experts, and Emergent BioSolutions (the manufacturer of BioThrax) agree that rotation on a first-in, first-out basis would minimize waste.

DOD and ASPR officials told us that they discussed a rotation option in 2004 but identified several obstacles. In July 2007, DOD officials believed they might not be able to transfer funds to ASPR if DOD purchases BioThrax from ASPR. However, in response to our draft report, DOD informed us that funding is not an issue. However, ASPR continues to believe that the transfer of funds would be a problem. DOD stated smallpox vaccine (Dryvax) procurement from HHS is executed under such an arrangement. Further, DOD and ASPR officials told us that they use different authorities to indemnify the manufacturer against any losses or problems that may arise from use of the vaccine. According to DOD, this area may require legislative action to ensure that vaccine purchased by ASPR can be used in the DOD immunization program. Finally, since DOD

[13]These lots contained 167,990; 168,130; and 183,990 doses of vaccine, respectively.

[14]In 1999, CDC created a stockpile of licensed medical products. CDC officials told us that CDC had a strategy to rotate products in that stockpile on a first-in, first-out principle with other high-volume users, such as the Department of Veterans Affairs.

vaccinates its troops at various locations around the world, there may be logistical distribution issues. A DOD official acknowledged that these issues could be resolved.

Second, ASPR plans to use expired vaccine from the stockpile, which violates FDA's current rules.[15] Data provided by CDC indicated that two lots of BioThrax vaccine expired in December 2006 and one in January 2007. CDC officials stated that their policy is to dispose of expired lots since they cannot be used and continuing storage results in administrative costs. FDA rules prohibit the use of expired vaccine.

Nevertheless, according to CDC officials, ASPR told CDC not to dispose of the three lots of expired BioThrax vaccine. ASPR officials told us that ASPR's decision was based on the possible need to use these lots in an emergency. ASPR's planned use of expired vaccine would violate FDA's current rules and could undermine public confidence because ASPR would be unable to guarantee the potency of the vaccine.

Conclusions

The termination of the first major procurement contract for rPA anthrax vaccine raised important questions regarding the approach taken to develop a new anthrax vaccine and a robust and sustainable biodefense medical countermeasure industry by bringing pharmaceutical and biotechnology firms to form a partnership with the government. With the termination of the contract, the government does not have a new, improved anthrax vaccine for the public, and the rest of the biotech industry is now questioning whether the government can clearly define its requirements for future procurement contracts.

Since HHS components have not completed a formal lessons-learned exercise after terminating VaxGen's development and procurement contracts, these components may repeat the same mistakes in the future in the absence of a corrective plan. Articulating concepts of use and all critical requirements clearly at the outset for all future medical countermeasures would help the HHS components involved in the anthrax procurement process to avoid past mistakes. If this is not done, the government risks the future interest and participation of the biotechnology industry.

[15]See footnote 4.

Given that the amount of money appropriated to procure medical countermeasures for the stockpile is limited, it is imperative that ASPR develop effective strategies to minimize waste. Since vaccines are perishable commodities that should not be used after their expiration dates, finding other users for the stockpile products before they expire would minimize waste. Because DOD requires a large amount of the BioThrax vaccine on an annual basis, it could use a significant portion of BioThrax in the stockpile before it expires.

Recommendations for Executive Action

The report that we are issuing today makes three recommendations. To avoid repeating the mistakes that led to the failure of the first rPA procurement effort, we recommend that the Secretary of HHS direct ASPR, NIAID, FDA, and CDC to ensure that the concept of use and all critical requirements are clearly articulated at the outset for any future medical countermeasure procurement.

To ensure public confidence and comply with FDA's current rules, we recommend that the Secretary of HHS direct ASPR to destroy the expired BioThrax vaccine in the stockpile.

To minimize waste of the BioThrax vaccine in the stockpile, we recommend that the Secretaries of HHS and DOD develop a single integrated inventory system for the licensed anthrax vaccine, with rotation based on a first-in, first-out principle.

HHS and DOD generally concurred with our recommendations. In addition, with regard to our recommendation on integrated stockpile, they identified legal challenges to developing an integrated inventory system for BioThrax in the stockpile, which may require legislative action. Although HHS and DOD use different authorities to address BioThrax liability issues, both authorities could apply to either DOD or HHS; consequently, indemnity does not appear to be an insurmountable obstacle for future procurements.

Mr. Chairman, this concludes my remarks. I will be happy to answer any questions you or other members may have.

Contacts and Acknowledgements

For questions regarding this testimony, please contact Keith Rhodes at (202) 512-6412 or rhodesk@gao.gov. GAO staff making major contributions to this testimony included Noah Bleicher, William Carrigg, Barbara Chapman, Crystal Jones, Jeff McDermott, Linda Sellevaag, Sushil Sharma, and Elaine Vaurio.

Center for Biosecurity

UPMC | University of Pittsburgh Medical Center

United States Senate
Committee on Homeland Security and Governmental Affairs
"Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?"

Testimony of Tara O'Toole, MD, MPH
Director, Center for Biosecurity of UPMC
October 23, 2007

Mr. Chairman, Senator Collins and members of the committee, thank you for the opportunity to address the vital issue of biodefense and the difficult challenges surrounding the U.S. government's efforts to protect civilians against bioattacks.

My name is Tara O'Toole. I am the Director and CEO of the Center for Biosecurity of the University of Pittsburgh Medical Center and professor of medicine at the University of Pittsburgh Medical School. The Center for Biosecurity is a non-profit, multidisciplinary organization that includes physicians, public health professionals and biological and social scientists located in Baltimore. The Center is dedicated to understanding the threat of large-scale lethal epidemics due to bioterrorism and to natural causes, and has studied the bioweapons threat, biodefense strategies, and the government's biopreparedness efforts since 1998. My colleagues and I are committed to the development of policies and practices that would help prevent bioterrorist attacks or destabilizing natural epidemics, and, should prevention fail, to mitigate the destructive consequences of such events.

My testimony will address two aspects of preparedness for bioterrorist attacks: the status of the Department of Health and Human Services' (HHS) programs to acquire medicines and vaccines against likely bioweapons threats; and the efforts by the Department of Homeland Security (DHS) to establish environmental/aerosol sensor systems and information technology designed to establish adequate surveillance to detect and help manage large-scale public health emergencies.

First, however, I will review the nature of the bioterrorism threat. Six years after anthrax was mailed to members of the U.S. Congress and to media organizations, the immediacy and potentially strategic significance of the bioweapons threat is not widely appreciated, nor is the country prepared to cope with the consequences of major bioattacks. This is the case in spite of the extensive efforts to improve U.S. biodefense capabilities, including important contributions by this committee, to catalyze and oversee the agencies and programs involved in response to large-scale bioattacks and pandemics.

621 East Pratt Street, Suite 210 | Baltimore, MD 21202 | 443-573-3304
www.upmc-biosecurity.org

Bioterror Threat is Urgent, Potentially Destabilizing

A June 2001 report by The Defense Science Board noted that there are no technical barriers to large-scale bioattacks.

"...major impediments to the development of biological weapons – strain availability, weaponization technology, and delivery technology – have been largely eliminated in the last decade by rapid, global spread of biotechnology."
– Defense Science Board, *Biological Defense*, June 2001; p.18.

Dozens of government and technical reports since 9/11 and the October 2001 anthrax mailings have affirmed the viability of terrorist groups wielding biological weapons that could cause death, suffering and social and economic disruption on calamitous scales. The National Academy of Sciences has published at least a dozen reports on bioterrorism in the past six years.

The Robb-Silverman Report on WMD Intelligence Capabilities documented that "Al Qaeda had a major bioweapons effort [in Afghanistan]" as of 2003. We do not know what became of this program, but we do know that Al Qaeda representatives have asserted their right to kill up to four million Americans and issued a 2003 fatwa authorizing the use of biological, chemical and nuclear weapons against non-Muslims, and we know that Al Qaeda in Iraq has call for scientists to join the jihad for the purpose of producing "WMD." Almost two years ago the National Intelligence Council noted that:

"Our greatest concern is that terrorists might acquire biological agents, or less likely, a nuclear device, either of which could cause mass casualties."
-National Intelligence Council 2020 Project, *Mapping the Global Future;* Jan. 2005

More recently, analysts in and out of government have written that Al Qaeda has regrouped to become "stronger and more resilient" and presents a greater threat to the U.S. than at any time since before 9/11. [Ref: Reidel, B. *Foreign Affairs*]. Key judgments of a July 2007 National Intelligence Estimate include the assessment that:

"...al-Qa'ida will continue to try to acquire and employ chemical, biological, radiological or nuclear material in attacks and would not hesitate to use them..."

Yet, in spite of all these sobering reports and expert findings, progress in preparing the country to mitigate the consequences of a bioattack has been slow and modest. There have been accomplishments to be sure, thanks, in large part, to highly skilled civil servants in federal and state governments who have worked long hours, some almost continuously since 9/11 to fund, staff and manage vital biodefense programs. The nation should be especially grateful for the dedication of Drs. Gerry Parker, Carol Linden, Monique Mansoura and Jerry Donlon who have done much to get these programs started.

But it is highly disturbing that six years after the 2001 attacks, and in the face of continuous documentation of the seriousness of the biothreat, we face the following realities:

- There is no conduct of operations plan to guide national or local response to an anthrax attack
- The country has inadequate supplies of anthrax vaccine stockpiled; it would require years at present production capacity to produce enough to immunize the military or the civilian population.
- Only a handful of cities or states could distribute the SNS in a timely manner.
- The country is unprepared to cope with the medical demands of a mass casualty event.
- There are no approved, point-of-care diagnostic tests that physicians could use to diagnose (and rule out) anthrax or any other bioterror threat agent – this is critical in a context of scarce, potentially life-saving resources.
- Should there be a covert biological attack on U.S. civilians, it is highly unlikely that the national command structure, or governors or mayors would have even rudimentary situational awareness during a bioattack.

As we have learned, building an effective civilian biodefense capability is a much larger and more difficult proposition than was recognized in 2001. The scale of our ambitions and the level of federal funding have not been equal to the challenges we face. The level of leadership attention – in both the executive and legislative branches, and at both the federal and state levels – has been inadequate.

Last week, the White House released Homeland Security Presidential Directive 21, establishing a national strategy for public health and medical preparedness for catastrophic events. This document, which reflects a wealth of input from medical and public health practitioners, and experts in disaster response, begins to display the extent and complexity of what it will take to construct a robust biodefense. Creating a homeland defense that secures the country against devastating bioattacks will be the work of a generation. If we do it correctly, we will create the capacity to eliminate bioweapons as agents of mass lethality and take a major national security threat off the table. Moreover, if we approach this vital defense strategy with imagination and vision, we could greatly relieve the suffering and premature death from naturally occurring infectious disease in the U.S. and globally.

Medical Countermeasures

A Snapshot of What's Wrong with BioShield

In 2002, it was officially determined that anthrax attacks represented a "material threat" to the U.S. HHS then established a requirement for 75 million doses of "second generation" anthrax vaccine, to be delivered in 2008. It was not until two years after HHS determined that it needed such a countermeasure that the contract to produce this vaccine was awarded. Four years later, in December 2006, HHS canceled the contract, reportedly because of FDA concerns about the vaccine's stability. It took HHS another nine months to conclude a contract to acquire 18.75 million doses of the original, "first generation" anthrax vaccine. So, instead of anticipating delivery of second generation anthrax vaccine next year, the country is starting over in its quest

for such vaccine. We currently have enough first generation anthrax vaccine in the stockpile to immunize about three million people – not enough to immunize a single, small city.

How did we get to this point? There is a broad consensus among representatives of the biopharma industry and outside observers as to what is wrong with the BioShield program, created in 2004 to allow development and acquisition of essential medical countermeasures for the Strategic National Stockpile (SNS), and how to fix it. The problems and proposed solutions were well documented in the record leading up to the 2006 passage of the Pandemic and All Hazards Preparedness Act. The critical problems with BioShield are these:

Not Enough Money for Critical Biodefense Countermeasures

There is not enough money in the BioShield Special Reserve Fund to cover the costs of developing and purchasing even the most high priority countermeasures. HHS has operated under the assumption that it must satisfy the requirements for *all* countermeasures for *all* credible CBRN threats – not just biothreats – with the $5.6B fund appropriated in 2004. (Approximately $3.6 B remains.) When one considers that the average cost of drug *development* is $800 billion – and this is before a single pill or vaccine is purchased – it is obvious that $5.6B is not sufficient to protect the nation against the range of potential biothreats, let alone chemical or radiological or nuclear threats.

HHS staff are conscientiously trying to develop and purchase countermeasures against all of the 14 Material Threats thus far identified by DHS – and we are just at the start of the analysis of material threats. DHS's 2006 Biothreat Assessment, (the full version is classified), identified more than a dozen pathogens which, if released in a single attack, could plausibly kill thousands of people. It is important to understand that the number and variability of potential bioweapons agents will increase as bioengineering techniques become more accessible – this is happening at a rapid pace all over the globe. HHS' "Public Health Emergency Medical Countermeasures Enterprise" (PHEMCE) strategy, published in March 2007, recognizes this expanding "threat space" and proposes development of "broad spectrum" countermeasures which could be used to treat or prevent more than a single bioweapons agent. This "flexible defense strategy" is a rational way to go, but it must be recognized that development of such new drugs traditionally takes ten years or more.

It should also be understood that the inadequate funding has also resulted in an extremely low tolerance for risk in the BioShield program. This risk-aversion was reinforced by the failure of the VaxGen second generation anthrax vaccine contract – the first and so far biggest BioShield contract. While it is appropriate to work to avoid failure, the reality is that medicine and vaccine development is an extraordinarily risky endeavor. It has been estimated that of 5000 compounds identified by basic research as potential new drugs, only five enter clinical trials, and only one of those five survive testing and become FDA approved. Expecting HHS to pick a winner with every countermeasure development project is not realistic and will result in an even more conservative approach by HHS, which will in turn have the unintended consequence of dissuading biopharma companies from engaging with government.

To make decisions about what contracts should proceed and how much of a countermeasure should be stockpiled even more complicated, HHS staff have to weigh the value of acquiring products that are available today against the delay and possible development failures of investing in a less mature, but potentially more desirable product.

Moreover, medical countermeasures degrade over time – they have shelf lives, and must be renewed periodically. The traditional approach to vaccine and drug manufacture is to build facilities dedicated to the production of a single product. FDA licensure is linked to approval of manufacturing processes in that particular plant for that product. For many of the products in the SNS – anthrax vaccine for example – the government is the only customer. Thus, maintaining the manufacturing capacity to ensure periodic refreshment of the SNS requires maintaining a "warm base" – an entire manufacturing plant that exists only to supply the U.S. government's needs. This is an expensive proposition.

Flawed Contracting Processes

The result of all this is that HHS has taken a long time to make decisions. The mean time from HHS' receipt of a Material Threat Determination to RFP to BioShield award is *27 months*. This long delay is at odds with the business realities of the biopharma business. Small biotech companies in particular are unable to wait this long for decisions. These time frames have seriously eroded the willingness of companies and of private capital to participate in biodefense work. If HHS does not soon exhibit a more aggressive determination to pursue success, fewer and fewer companies will agree to participate, and HHS's investment choices will wither. Furthermore, such delays in the contracting process translate into long gaps of years during which essential countermeasures are unavailable.

When BioShield began, there were only a handful of staff at HHS dedicated to the program and few had experience in drug or vaccine development. That has changed – approximately 100 federal officials are now dedicated to the program and more and more have industry backgrounds. This is crucial for the program's success.

The Alliance for Biosecurity was formed in 2005 to build a strong partnership between government and private sector biotech and pharmaceutical companies engaged in biodefense work. The Center for Biosecurity was an organizer of and is a participant in the Alliance, which on numerous occasions provided Congressional Testimony and authored letters to Congress and to HHS describing procedural problems with BioShield and possible solutions. Greater transparency on HHS's part, including more precise and more timely target product profiles, more opportunities for direct interaction and discussion between industry and government, and more skilled staff in HHS who understand the realities of the drug and vaccine business figure prominently in these suggestions. I am happy to say that HHS has welcomed these comments and made clear efforts to respond constructively.

Advanced Development and Innovation is essential to success, but has been neglected

BARDA, The Biodefense Advanced Research and Development Authority written into the PAHPA legislation is seen by most observers and by industry as key to BioShield's success, and

passage of the bill in December 2006 was seen as a signal of the government's ongoing commitment to biodefense. BARDA was intended to improve coordination of BioShield activities across government agencies and to bridge the gap between early stage basic research and drug target "discovery" and late-stage product development and procurement. This gap, encompassing advanced development and clinical testing activities, is sometimes refereed to as the "valley of death" because drug and vaccine development is so difficult, time-consuming and risky. Smaller companies are at high risk of going under during this period.

Congress authorized $1.07B for BARDA in FY06-08 – this was seen at the time as the start of what will be needed to accomplish BARDA's long term goals. However, no money was appropriated for BARDA in FY06, and only $99M was given to BARDA in the FY07 supplemental appropriation. The Administration has requested $189M for BARDA in FY08. Both the House and Senate versions of the Labor-HHS appropriations bills contain less than the President's request ($135.5M is proposed in the House, while the Senate version contains $159M). It is important to understand that biotech and pharmaceutical companies read these relatively small numbers as evidence that the U.S. Congress is not serious about biodefense and does not intend to invest in the development of medicines and vaccines against bioterror threats. Are these companies wrong?

Biosurveillance: Detection of Bioattacks and Situational Awareness during Public Health Emergencies

Biodefense programs within the DHS Directorate of Science and Technology have been become more coherent and mature over time, thanks in part to the dedication and leadership of Undersecretary Cohen and Dr. John Vitko. BioWatch technologies have improved since they were first deployed and some serious operational flaws have been addressed.

Clearly, it would be highly desirable to have a near-real time understanding of critical facts and operational realities during public health emergencies or other biological crises such as the Foot and Mouth Disease outbreak that occurred in England earlier this year. I am skeptical however, that a significant expansion or technology upgrade of the BioWatch program is warranted at this time. In addition, I do not think it is in the best strategic interests of U.S. biodefense to invest significant funds in constructing the National Biological Informational System until we know what, exactly we are building and how it will work. The initial proposal for such a system (in HSPD-9 and 10) was, I believe, based on erroneous assumptions about the availability of digitalized health information, overly optimistic expectations of what data could be collected and analyzed by the federal government, and how meaningful such data would be to decision-makers.

As I have done in previous testimony before other committees, I urge that DHS initiate a strategic examination of the current state of "biosurveillance" and develop a five year strategy for biosurveillance, in collaboration with other federal agencies and key stakeholders. The current trajectory of biosurveillance programs is understandable in historical context, but I strongly believe that the country could make different, and more useful and cost-effective investments in biosurveillance than are currently planned.

Historically, Detection Emphasized Over Situational Awareness

There has been a strong federal focus on surveillance initiatives designed to *detect* bioattacks or natural epidemics. This is a desirable goal – it is one of the holy grails of public health – but it is very difficult to achieve. Now, after six years of significant federal and state investment in a range of environmental sensor systems, syndromic surveillance and a panoply of local attempts to build surveillance systems of all types, is a good time to stand back and examine the nation's overall surveillance strategy. There is a need for a longer-term strategy that balances investments in detection against the need to assure situational awareness during an event; that assures collaboration between DHS and the various agencies within HHS that deal with aspects of surveillance, and better coordination between federal and local efforts. There is also a pressing need to consider the long-term maintenance costs of these programs, which can be considerable.

In my view, we have not paid sufficient attention to the need to provide decision-makers at all levels with adequate situational awareness during a public health disaster. This is a major strategic issue, and it is not clear who in government, or even which agency "owns" it. There is, I believe, a mistaken assumption that a great deal of health data will be available – for example, the number of people who are ill or admitted to hospitals with certain diagnoses or the availability and local of critical resources such as available hospital beds, equipment, drugs, etc. But the health care industry is a decade behind the rest of the economy in digitalizing its business functions and the clinical side of health care. Thus there are likely to be dangerous delays in gathering the basic information that will be needed to manage the crisis. It may well be that rapid, point-of-service diagnostic tests and better physician education would provide critical situational awareness during public health crises, but thus far, these matters have not been examined from a strategic perspective.

NBIS may be intended to address this issue, at least in part, though it is difficult to find clear statements of what NBIS will accomplish, what data will be collected from where, how it will be analyzed, who will use the output, how it will work or how much it will cost. The main flaw in NBIS as it is now described is the apparent assumption that there are lots of data sources available to be collated and analyzed. This is not the case, and a careful appraisal of what fundamental sources and types of data are needed and available is essential.

Moreover, recent experience across the federal government has shown that large, ambitious electronic information systems are difficult to build and most such programs fail. GAO has documented many reasons for these failures, including unclear goals, rapid turnover in and inadequately skilled project managers, failure to consult appropriately with stakeholders, inadequate funding, etc. Both the DHS's planned NBIS and CDC's BioSense programs are likely victims of such ills. Moreover, it is not at all evident that these ambitious electronic information systems will serve their intended purpose.

Specifically, I would suggest that *national investments in rapid diagnostic tests and in electronic health records and digital links between hospitals and public health agencies will yield more benefits – for both routine use and in emergencies – than additional investments in environmental sensors or syndromic surveillance technologies.* We should not have to decide

between electronic health data or environmental sensors, but there must be a coherent, long term strategy for biosurveillance.

BioWatch – Environmental Sensor Technologies for Detecting Bioterror Attacks

The governing concept of BioWatch, a collection of environmental sensors located in cities and critical locales across the U.S. and designed to detect specific airborne bioweapons agents, is that early detection of bioweapons pathogens in the air will enable an earlier "response" and thus save lives. DHS first deployed the BioWatch in some cities just before U.S. troops entered Iraq in 2003, and has expanded the number of sensors and improved aspects of the technology and its management since then.

BioWatch is intended to supply "early warning" of an aerosolized bioattack. While early warning is desirable, there are a number of practical, operational and strategic questions that deserve examination before additional investments are committed to the BioWatch program. It is not clear thus far, based on detection of natural organisms in the environment that were previously not known to be there, that BioWatch information alone is "actionable". That is, in several incidents of BioWatch detectors accurately signaling the presence of a pathogen, public health officials were reluctant to take decisive action – to act as though an attack were underway – without confirmatory clinical data. This raises questions about whether BioWatch truly shortens "response time".

Other important questions about BioWatch include the following:

- Will the turn-around time for BioWatch samples – the time required to collect the samples from the sensors, transport them to labs and analyze the filters –shorten the time needed to detect an attack large enough to be picked up by the sensors, or will astute clinicians recognize the attack just as quickly? Would cheap, rapid, point-of-service clinical diagnostic tests be a more cost-effective investment than the next generation BioWatch?

- Does it make sense to invest limited biodefense funds in more advanced BioWatch technology even as we cut funds for public health personnel needed to analyze BioWatch data, as we are now doing? Many public health professionals at the March 15 White House meeting noted that assessment of BioWatch data requires limited public health resources that might be otherwise employed to greater effect.

- State and local public health officials – the "users" of these technologies who are the ones who must decide to act on BioWatch data – have repeatedly complained, at the March meeting and in Congressional hearings and roundtables about lack of coordination and poor information flows. What is DHS doing to address these local concerns?

- Environmental sensor technologies are now being marketed to individual companies for installation in privately owned buildings. Will DHS develop commercial standards or regulations to ensure that such systems be are reliable and maintained properly? Should

public health agencies be required to assess every warning signal ("hit") registered by privately owned sensors? Should public health agencies be reimbursed for such assessments?

- Would we improve detection more cost-effectively by focusing on raising clinician's awareness of bioweapons-related disease or by investments in point-of-care diagnostic tests, which could not only detect bioweapons agents but would help sort out attack victims once an attack occurs?
- Would digital connections between hospitals and public health agencies be more cost-effective and more widely useful that environmental sensors in detecting natural disease outbreaks and bioattacks? Such connections, which are now rare, would certainly be valuable in ascertaining situational awareness once an epidemic is underway.

- What are the long-term plans for BioWatch deployments? Thinking enemies are likely to learn which jurisdictions are covered by BioWatch and which areas of the country are less thoroughly monitored. The JASONS calculated that sensor coverage of the entire country would cost $40 per person per year – $12B/year for all 300M Americans [Ref: Biodetection Architectures, JASON, the Mitre Corporation, Feb. 2003]. Is BioWatch expansion a smart use of limited biodefense resources? What are the operational advantages of deploying a third generation technology as DHS proposes?

These are complicated questions. I want to acknowledge that DHS personnel have worked extremely hard to deploy BioWatch and to improve its technical performance and to coordinate response scenarios with local public health officials and first responders. However, I remain skeptical about the overall value of the program.

It is the assessment of the Center for Biosecurity of UPMC that digital links between hospitals and large HMOs and local public health agencies, and investments in interoperable electronic health records – which authorities agree would improve health care quality and lower health care costs on a routine basis – would be far more cost-effective than funds spent on future generations of BioWatch.

Most advanced countries have electronic health records – the UK's system, for example, makes it much easier for British hospitals and doctors to communicate in real time during crises such as the London metro bombings. President Bush has advocated the adoption of electronic health records and set a ten year timeline for establishing such systems, but does not anticipate the federal government providing capital for such efforts. Investments in electronic health records – an electronic health information highway system – could render the country safer from devastating bioattacks while simultaneously making the nation stronger on a daily basis.

The United States – for now – has the world's best scientific research base and the most powerful technological prowess, but our technical imagination has to be matched by strategic thinking and wise choices. We have made some progress in the past six years, but our activities to date do not reflect a commitment to a national security priority. It is time to think anew about the biothreat and what we should do about it.

Question#:	1
Topic:	NBIS
Hearing:	Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?
Primary:	The Honorable Susan M. Collins
Committee:	HOMELAND SECURITY (SENATE)

Post-Hearing Questions for the Record
Submitted to the Honorable Jay M. Cohen
From Senator Susan M. Collins

Question: The National Biosurveillance Integration System (NBIS) was created to provide early recognition of a biological event and enhanced situational awareness by integrating information on the health of humans, animals, and plants, with air, food and water monitoring data, as well as threat and intelligence information. NBIS began in your Directorate then moved to another Directorate and then finally landed in the Office of Health Affairs. The DHS IG report released July 26, 2007, found that NBIS has suffered from poor management and a lack of direction as it moved from one department to another at DHS on almost a yearly basis. Do you believe that NBIS has now found its correct placement within the DHS at the Office of Health Affairs?

Answer: Yes, I believe the National Biosurveillance Integration System (NBIS) is correctly placed within the Office of Health Affairs (OHA). OHA has the responsibility for integrating all of DHS' operational biodefense activities and for advising the Secretary on biodefense issues. Section 1101 of the "Implementing Recommendations of the 9/11 Commission Act of 2007" (Public Law 110-53) clarified and recognized the roles and responsibilities for the National Biosurveillance Integration Center (NBIC). As part of NBIC activities, OHA established information sharing MOUs with six Federal partners. Five additional MOUs are in progress. OHA has also begun interagency detailing of individuals, with the first Centers for Disease Control and Prevention (CDC) detailee having arrived in October and additional biosurveillance support detailed from Defense Intelligence Agency(DIA)/Armed Forces Medical Intelligence Center (AFMIC) to DHS/Intelligence and Analysis (I&A) to assist in the overall biosurveillance mission.

Question#:	1
Topic:	NBIS
Hearing:	Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?
Primary:	The Honorable Susan M. Collins
Committee:	HOMELAND SECURITY (SENATE)

The placement of NBIS within OHA is providing the medical expertise and oversight needed to take major steps forward in ensuring the integration of information streams on the state of health of people, animals and plants, with environmental monitoring data on air, food and water for better situational awareness for decision-makers. In addition, OHA's management of NBIS is enabling the development of processes to make this integrated information available and accessible to its critical partners in a timely manner for future bio-events.

Question#:	2
Topic:	strategic national stockpile
Hearing:	Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?
Primary:	The Honorable Susan M. Collins
Committee:	HOMELAND SECURITY (SENATE)

Question: I imagine that Biothrax is not the only medical countermeasure we are stocking in the Strategic National Stockpile that could be useful at DoD as well. And according to the GAO report, part of the problem is sharing the supply between HHS and DoD lies in different indemnity provisions, one from DHS and one from DoD. What steps has DHS taken to assist HHS and DoD sort out the indemnity protections so that we can effectively manage our resources in the Strategic National Stockpile?

Answer: This question would be best answered by the Department of Health and Human Services (HHS) and the Department of Defense (DoD). We believe considerations regarding the indemnity and other liability-limiting authorities lie with these respective Departments and their Secretaries. DHS is ready to assist HHS and DoD as needed.

Question#:	3
Topic:	BioWatch
Hearing:	Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?
Primary:	The Honorable Susan M. Collins
Committee:	HOMELAND SECURITY (SENATE)

Question: Your office is responsible for BioWatch, technology designed to detect the release of biological agents in the air through a comprehensive protocol of monitoring and laboratory analysis. BioWatch is currently operational in 30 cities. As I understand it, developmental efforts continue in the S&T Directorate toward the development of the third generation of technology for BioWatch. This new technology would automate systems to shorten the time for issuing an alert from 12-36 hours to just 4-6 hours. It would also allow for cost savings with less labor involved; and increase the number of cities with coverage. When does S&T estimate that this new technology will be ready to transfer to OHA for operation?

Answer: Based on the current timeline, it is the intent of the S&T Directorate to transition prototype Gen 3 BioWatch detectors to the Office of Health Affairs in FY 2009 for operational test and evaluation.

Question#:	4
Topic:	anthrax
Hearing:	Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?
Primary:	The Honorable Daniel K. Akaka
Committee:	HOMELAND SECURITY (SENATE)

Post-Hearing Questions for the Record
Submitted to the Honorable Jay M. Cohen
From Senator Daniel K. Akaka

Question: Anthrax remains the only biological pathogen to be used against the American people. It remains the most likely biological threat. The original requirement of 200,000 treatments was issued in 2004. Are we vulnerable to an anthrax attack and should we be procuring antidotes more quickly?

Answer: Because of the seriousness of a possible anthrax attack, it is critical that we continue to prepare. The Nation is pursuing a multi-pronged medical countermeasure strategy consisting of antibiotics, vaccines that can be used in conjunction with antibiotics, and therapeutics (anti-toxins) that can be used to neutralize toxins in the body. Currently there are enough antibiotics in the Strategic National Stockpile to prophylaxis individuals against multiple, large-scale anthrax attacks. The Department of Health and Human Services (HHS) has procured and stockpiled millions of doses of the current anthrax vaccine. Additional details regarding ongoing and future procurements of anthrax countermeasures could best be provided by HHS. In addition, HHS, DHS and other interagency partners continue to develop and test novel countermeasure distribution strategies.

Question#:	5
Topic:	MDR anthrax
Hearing:	Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?
Primary:	The Honorable Daniel K. Akaka
Committee:	HOMELAND SECURITY (SENATE)

Question: Multi-drug resistant anthrax was included in the Public Health Emergency Medical Countermeasures Enterprise Top Priority Chemical, Biological, Radiological, and Nuclear threats. How real is the threat of MDR anthrax and should we be procuring potential antidotes against MDR anthrax now?

Answer: Multi-drug resistant (MDR) anthrax is considered a real threat. MDR anthrax was one of 28 agents evaluated by DHS in its 2006 Bioterrorism Risk Assessment (BTRA) and was deemed a significant enough threat for the Secretary of Homeland Security to issue a Material Threat Determination, hence its inclusion in the Public Health Emergency Medical Countermeasures Enterprise Top-Priority Chemical, Biological, Radiological, and Nuclear (PHEMCE) list. The Department of Health and Human Services (HHS) Centers for Disease Control and Prevention (CDC) and the Department of Homeland Security (DHS) are taking steps to address the MDR anthrax threat. This includes stocking the Strategic National Stockpile with more than one type of antibiotic for treating anthrax (HHS); developing and acquiring novel anthrax countermeasures to be used in such a situation (HHS); and developing a new laboratory technique for rapidly determining (in about 6 hours after acquiring a pure culture isolate) whether an anthrax sample is antibiotic resistant or not – thereby rapidly informing the response process (DHS and CDC).

Question#:	6
Topic:	2008 iCBRN
Hearing:	Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?
Primary:	The Honorable Daniel K. Akaka
Committee:	HOMELAND SECURITY (SENATE)

Question: Are the baseline results on track for the 2008 iCBRN? The biological risk assessments were to be completed by early September and the final report is due to the White House in February of next year. Do these results support the need for enhanced near-term procurement of anthrax countermeasures?

Answer: Yes, we are on track to complete the iCBRN as required by HSPD-18 by June 2008. The S&T Directorate has completed the biological risk analysis and it is currently undergoing internal review prior to its socialization with our interagency partners and subsequent delivery to the White House. While all the results are not yet finalized, it is clear that anthrax continues to be very high-priority threat and that the on-going and planned anthrax medical countermeasure development and acquisition programs need to continue.

Post-Hearing Questions for the Record
Submitted to Gerald W. Parker
From Senator Daniel K. Akaka

"Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?"
October 23, 2007

1. Six years after the Senate was hit with the anthrax letter attack, HHS has only entered into contracts to procure 30,000 treatments. Given that there are other promising anthrax therapies available, why is the Administration moving so slowly in this area?

As identified in the *HHS Public Health Emergency Medical Countermeasures Enterprise Implementation Plan*, anthrax therapeutics are a high priority component of the overall HHS strategy for public health preparedness in the event of an anthrax attack. While there are some anthrax medical countermeasures currently available for acquisition and stockpiling, the next generation of anthrax drugs in the development pipeline is not mature. HHS is executing a staged development and acquisition program that balances near-term preparedness needs with mid- and long-term programs that will support the development of products further upstream.

Near-term:
HHS has two current acquisition contracts for procurement of 30,000 antitoxin treatment courses. Under one of these contracts, the Cangene Corporation has already begun delivery of product to the Strategic National Stockpile.

Mid-term:
Investments in advanced development programs are critical to mitigating risks in Project BioShield. As identified in the *HHS PHEMCE Implementation Plan*, HHS anticipates a mid-term acquisition of additional anthrax therapeutics. To support this developmental pipeline, in September 2007, BARDA and NIAID awarded $55 million in funding awards to support the advanced development of three additional candidate anthrax therapeutic products. The timing of the next anthrax therapeutic RFP is directly related to the maturation of candidate products in the pipeline. HHS is closely monitoring the progress of these products.

2. If there is a release of a biological agent, would doctors be equipped to handle the scores of people coming into an emergency department? How long under the current reporting system would it take to notify the state and federal governments?

Through the Hospital Preparedness Program administered through HHS States and hospitals have been addressing various aspects of all-hazards planning and response. Specific activities that would help in biologic outbreaks include purchasing personal protective equipment (and the associated training), purchasing and storing pharmaceutical caches, exercising of surge capacity plans, training and education activities in recognition

and treatment of various agents, increasing the isolation capacity of hospitals and at regional facilities, and planning for use of Alternate Care Sites.

We call call the National Operations Center at DHS on the phone – a few minutes at best to notify, send out a note via Epi-X or through the Health Alert Network. Time-wise it would take several minutes to an hour to get the notice out. We work through state operations centers to notify of events.

3. I am concerned that the timeframe between Request For Proposal submission and award has, in some cases, taken several years. How do you plan to reduce these time lines in the future?

HHS and DHS signed an MOU in September 2006 streamlining the process for transferring funds once a BioShield contract has been awarded. BARDA is working to reduce the time between releasing an RFP and awarding a contract through improving acquisition infrastructure, increasing our acquisition staff, and implementing best acquisition management practices from DoD and other federal agencies.

4. Although the Biomedical Advanced Research and Development Authority (BARDA) at HHS was established in December 2006, it still does not have a director. How has this affected BARDA activities, including the issuance of Requests for Proposals and the awarding of contracts for both advanced development and procurements?

The Department stood up BARDA in April 2007, with Dr. Carol Linden serving as Acting Director. Under her leadership, BARDA has continued to perform its mission and to implement activities under the Pandemic and All-Hazards Preparedness Act as demonstrated by the following accomplishments:

- The PHEMCE Strategy and Implementation plans were released in 2007, as well as the Draft BARDA Strategy.
- The 2nd Annual PHEMCE Stakeholder's Workshop was held in July 2007.
- Advanced development funding was received in May 2007 and was awarded in partnership with NIAID in September 2007. These advanced development awards were consistent with BARDA's priorities.
- A contract for the purchase of MVA vaccine was awarded to Bavarian Nordic in June 2007 and the advance and first milestone payments have been approved by HHS for the company's completion of specified milestones.
- Deliveries to the stockpile of Anthrax Vaccine Adsorbed (AVA), a pediatric formulation of potassium iodide (KI), and diethylene triamine pentaacetate (DTPA).
- A draft RFP for recombinant protective antigen (rPA) anthrax vaccine was released on November 26, 2007..

An offer was made to a highly qualified candidate, but unfortunately that individual was not able to accept the position. The Department of Health and Human Services continues to conduct a rigorous nation-wide search for the strongest candidate possible to serve as BARDA Director. HHS is carefully and thoroughly considering candidates according to Federal hiring principles, and the flexibilities afforded in PAHPA.

5. Of the total $3.4 billion in BioShield funds available through FY 08, HHS has only obligated approximately $1.9 billion. The Implementation Plan only targets two additional purchases in the near-term – anthrax vaccine and acute radiation syndrome therapy. Does HHS anticipate that these acquisitions will account for the remaining $1.5 billion?

Yes, HHS anticipates that it will spend the remaining $1.5 billion in BioShield funds available through FY08. However, although HHS has prepared Independent Government Cost Estimates (IGCE) for both of these acquisitions, the prices for these medical countermeasures will not be known until proposals are received and negotiated and contracts awarded. To promote competition, we do not publicly disclose the IGCEs for individual acquisitions.

6. HHS has identified 8 items for mid-term acquisitions, which are to occur in the FY 09 to FY 13 timeframe, including diagnostics, broad spectrum antibiotics, and anthrax anti-toxins. Does HHS anticipate that all of these acquisitions can be made with the $2.2 billion remaining in the BioShield budget?

During the discussions leading up to the development of the PHEMCE Implementation Plan, HHS and interagency partners discussed the prioritization of products for the remaining BioShield funds. Using very conservative estimates with the following assumptions, the remaining BioShield funds were allocated:

- The product pipeline for all of these threats will be fully supported with advanced development funding. Project BioShield's Special Reserve Fund will be used only for acquiring products, and not for supporting advanced development activities.
- The Division of Strategic National Stockpile (DSNS) funding will be leveraged to procure those items that are also licensed, such as broad spectrum antibiotics.
- At least one candidate supported in advanced development would meet the technical criteria to be considered ready for acquisition.

HHS understands the limitations to these assumptions and the projections regarding the future status of the developmental medical countermeasures and future BARDA budgets needed to support advanced development prior to acquisition. HHS will revisit the PHEMCE Implementation Plan every two years, with more refined data about product pipelines and costs and resources associated with advanced development and acquisition.

7. According to the Implementation Plan, mid-term acquisitions are planned in the FY 09 to 13 timeframe. This is a long time. I understand from OMB that there is no barrier to issuing RFPs in advance of funding as long as the RF-P awards are predicated on the availability of funds. This is routinely done at NIH. Can you tell me when you expect to procure additional anthrax anti-toxins?

In September 2007, BARDA and NIAID issued funding awards to support the advanced development of three additional anthrax therapeutic products. By supporting a robust advanced development program, HHS hopes to be able to have additional product(s) available for acquisition using the Project BioShield SRF in the 2009 – 2013 timeframe. The timing of the next anthrax antitoxin RFP will depend on the maturation of candidate products that are currently in development, which HHS is closely monitoring.

8. Given the historically lengthy time period between RFP and actual award, does HHS plan to issue an RFP, particularly in the anthrax anti-toxin area prior to FY 09 to allow for procurement immediately upon availability of funds?

HHS could issue an RFP prior to 2009 if the products currently supported by BARDA advanced development funds are deemed appropriate for acquisition.

Post-Hearing Questions for the Record
Submitted to Gerald W. Parker
From Senator Mark L. Pryor

"Six Years after Anthrax: Are We Better Prepared to Respond to Bioterrorism"
October 23, 2007

1) In light of the problems with the first contract awarded to VaxGen under the Project BioShield Act of 2004,

a) (How) have your contracting practices changed since that contract was terminated in 2006?

Biomedical Advanced Research and Development Authority has increased the acquisition management workforce and enhanced transparency with industry in an effort to improve overall efficiency in our acquisitions. A rigorous acquisition management system is under development to better manage the complex life cycle of medical countermeasure development. This system includes performance parameters that will allow us to evaluate and monitor the progress of medical countermeasure development against established baselines.

- To enhance transparency, HHS has worked proactively to inform industry of our priorities and opportunities.
    - The HHS Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) Strategy and Implementation plans provide important transparency for product developers and manufacturers by identifying the medical countermeasure programs that will be our highest priorities for development and acquisition in the near-, mid- and long-term.
    - The Annual Enterprise Stakeholders Workshops have afforded us the opportunity to communicate with industry, educate industry on our processes, and receive constructive feedback that has been incorporated in our strategies and plans.
    - In August 2007, BARDA held its first Industry Day that provided an open forum for companies interested in working with the Federal Government to display technological advances in medical countermeasures.
    - Also in August 2007, HHS launched a new internet-based portal site (MedicalCountermeasures.gov) that will serve as the "one stop shop" for any company with a medical countermeasure product of potential interest to HHS.
    - BARDA staff will continue their ongoing efforts to engage with stakeholders regarding the implementation of the BARDA legislation. ASPR and BARDA leadership have already participated in roundtable discussions with the following organizations and groups: Center for Biosecurity of the University of Pittsburgh Medical Center (March, 2007),

McKenna, Long and Aldridge (May, 2007) and the Biotechnical Industry Organization (BIO) (May, 2007).

b) What are the specific criteria used to select contract recipients?

All offerors are subject to the evaluation criteria that can be found in section M of each Request For Proposal (RFP). Evaluation criteria typically include the following:

a. Technical Approach
b. Personnel
c. Facilities & Equipment
d. Project Management
e. Risk Mitigation
f. Licensure Plan
g. Security
h. Past Performance

RFPs can be found at the following web addresses:

http://www.hhs.gov/aspr/barda/procurement/cbrnactivities.html

http://www.hhs.gov/aspr/barda/mcm/panflu/activities.html

c) What are the factors HHS considers in addition to production time and cost estimates? Does HHS examine the history of the manufacturer to determine whether the company has the qualified staff and necessary technological resources to successfully carry out the contract?

HHS will consider all of the factors that are listed in section M of each respective RFP.

HHS does examine the past performance and history of the manufacturer to determine whether the company has the qualified staff and necessary technological resources to successfully perform the contract.

2) Amid reports that DHS is using steel imported from China to build the fence along the southern border of the United States, it is important to consider whether there are circumstances under which we should give preference to American manufacturers.

a) Do you believe it is important that vaccines for combating bioterrorism be manufactured in the United States?

Location of manufacture is not a selection factor. HHS conducts its acquisitions in order to comply with statutory requirements pertaining to full and open competition and trade agreements, which require that we consider offers from foreign sources.

b) How do you balance cost and speed of production with loyalty to American companies if a foreign company can do the job more quickly at lower cost?

The company that offers the best value (considering price, technical, and other factors) will win the award irrespective of their domestic or foreign distinction consistent with laws and regulations that guide acquisition for HHS.

3) What are the national security implications of various anthrax vaccine production options?

HHS is seeking a diversity of products in the strategic national stockpile from various manufactures to avoid a single point of failure.

a) What percentage of our national stockpile of anthrax vaccine is produced outside the country? Do we have agreements in place with other countries and/or foreign manufacturers to determine how many vaccines we will be allowed to purchase in the event of an emergency?

None. The contents of the Strategic National Stockpile are dictated by our current acquisition contracts. To date, all acquisition contracts for anthrax vaccine have been awarded to Emergent BioSolutions of Gaithersburg, MD. The vaccine is manufactured in Michigan. HHS will continue to work diligently to acquire sufficient anthrax vaccines to meet our requirements; however, at this time we do not have any agreements with foreign countries or overseas manufacturers.

b) What percentage of our national stockpile is produced by public versus private enterprises? Do we have advance pricing agreements with private manufactures to prevent them from marking up vaccine prices in a crisis?

As noted above, the current anthrax vaccine stockpile consists solely of Anthrax Vaccine Adsorbed (AVA, BioThrax), which is produced by a private company. Emergent BioSolutions. The current contract does not include any advance pricing agreements.

Post-Hearing Questions for the Record
Submitted to Gerald W. Parker
From Senator Susan M. Collins

"Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?"
October 23, 2007

1. The failure of the VaxGen Contract means that six years later and $877 million down the drain, we do not have an anthrax vaccine. I understand that your office is about the issue a new RFP for an anthrax vaccine since the contract with VaxGen failed. What steps has your office taken to ensure that HHS does not repeat the same mistakes that were made with VaxGen?

To clarify, the Project BioShield Act requires that payment be conditioned on delivery of product. As such, because VaxGen did not deliver product, the company did not receive payment under their BioShield contract, aside from $1.5M expended to cover security costs that HHS required under the contract. The $877.5 million was de-obligated and remains available under the Project BioShield Special Reserve Fund.

HHS continues to move forward to improve its medical countermeasure development and acquisition programs as the result of lessons learned from Project BioShield acquisitions to date, including the VaxGen contract, which was the subject of both external and internal reviews.

First, using new authorities made available in December 2006 under the Pandemic and All-Hazards Preparedness Act, HHS is providing advanced development support for top priority medical countermeasure programs to mitigate the risk of procurement of medical countermeasures under Project BioShield. For FY2007, the office of the Biomedical Advanced Research and Development Authority has dedicated over $30M of its $99M advanced development budget to support important manufacturing and product development activities for an rPA vaccine candidate. BARDA and NIAID recently released a Broad Agency Announcement (BAA) for Biodefense Vaccine Enhancement that will fund development of next generation anthrax vaccines featuring additional improvements to the route of delivery, schedule of administration, storage conditions, and shelf life.

Second, HHS is using every contracting tool available to maximize transparency with medical countermeasure manufacturers for the rPA anthrax vaccine acquisition. HHS began this May by releasing a Sources Sought Notice that allowed manufacturers to submit information on their current research and development programs. On November 26, HHS released a draft Request for Proposals (RFP) that will allow our industry partners to examine the requirements and objectives of the upcoming solicitation, evaluate changes that have been made since the Sources Sought Notice, and provide feedback on the feasibility of these objectives before the final RFP is released. The draft RFP has a 30 day comment period, and HHS expects to release the final RFP soon after considering any comments that are received.

Finally, open communication with the FDA is an essential part of the success of any medical product, and HHS has emphasized this by establishing receipt of FDA's current thinking as the sole mandatory criterion for eligibility of the draft RFP. Both the Sources Sought Notice and the draft RFP contain a requirement for potential offerors to obtain current thinking from the Food and Drug Administration (FDA) on anthrax vaccine development.

Post-Hearing Questions for the Record
Submitted to Gerald W. Parker
From Senator Norm Coleman

"Six Years After Anthrax: Are We Better Prepared to Respond To Bioterrorism?"
October 23, 2007

1. Can you assure me that HHS is fully taking into account both long-term AND short-term approaches to bioterrorism, specifically anthrax? Are there technologies available that could be implemented today, even as we continue to press ahead with longer term solutions?

   The events of October 2001 made it very clear that bioterrorism is a serious threat to our Nation and the world. HHS has made substantial progress in the development and acquisition of Medical Countermeasures for known biological threats such as anthrax threat while recognizing that public health threats and emergencies can ensue from multiple other causes, both naturally-occurring and man-made, and that many of the preparedness activities HHS is pursuing will have cross-cutting value. Bioterrorism preparedness is not an insular activity for HHS but rather a critical component integrated within an all-hazards readiness program.

   HHS and CDC are working closely with state and local public health officials on public health and bioterrorism preparedness and have invested nearly $8 billion to States and territories through cooperative agreements since 2001. HHS' anthrax preparedness and response mission includes surveillance and detection activities and coordination with State and local partners in the delivery and distribution of medical countermeasures. HHS specifically invested close to $60 million in 2006-2007 in the Cities Readiness Initiative (CRI). CRI provides funding to states, whose CRI jurisdictions cover 500 counties. This means that 56% of the US population lives within a CRI jurisdiction. CRI aids state and local officials in developing plans that support mass dispensing drugs to 100% of the identified population within 48 hours of a decision to do so.

   Development, acquisition and deployment of safe, effective medical countermeasures to mitigate illness and death in the event of a bioterrorist attack are critically important in the overall strategy for public health emergency preparedness efforts by HHS. Although much remains to be done, we have made substantive progress in building our Strategic National Stockpile from where it was pre-9/11to what we have available today. In the near term, antibiotics remain a cornerstone of our response strategy to anthrax and demonstrate the dramatic improvements to our readiness. In December 2000, we only had enough 60-day regimens to provide post-exposure prophylaxis for approximately 137,000 people. Today we could provide this antibiotic regimen to over 40 million individuals. HHS has also built upon its efforts to maintain and improve preparedness for

anthrax including obligating over $1.1 billion for anthrax vaccines and in 2006 issued two contracts for development and delivery of a total of 30,000 treatment courses of anthrax antitoxin therapeutics. Under the Project BioShield vaccine and therapeutic contracts, both Emergent Biosolutions and Cangene have already made deliveries of BioThrax and Anthrax Immune Globulin, respectively, to the SNS.

In the Spring of 2007, HHS released the *HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan for CBRN threats.* These documents provide a comprehensive intra-agency framework to guide near, mid and long-term development and acquisition of vaccines, therapeutics, and diagnostics for top priority medical countermeasure programs, including anthrax, both within and beyond Project BioShield.

In the mid-term HHS is committed to supporting the research, development, and acquisition of next-generation anthrax vaccines and enhanced antitoxin products. The requirement for a next-generation vaccine serves these important goals: (a) to maintain the most effective stockpile possible in light of scientific, medical, and technological developments, as feasible under budgetary considerations; and (b) to broaden the manufacturing base for an essential medical countermeasure. Multiple sources can expedite fulfillment of requirements and mitigate the risk associated with only having a single supplier.

Support for the development of enhanced anthrax antitoxins is critical for increasing the treatment capabilities for the toxemia that can develop after anthrax exposure. The timing of the next generation anthrax vaccine and antitoxin RFPs will depend on the maturation of candidate products that are currently in development and that we are closely monitoring. HHS recently released an rPA draft RFP and anticipates releasing the actual RFP in early 2008. In September 2007, HHS made three contract awards for FY07 joint BARDA and NIAID advanced development totaling over $55 million will support next generation anthrax antitoxins.

In addition to these near and mid-term approaches, HHS will also be investing in improving long-term preparedness by supporting research and development on innovative approaches and platform technologies. These technologies will facilitate rapid identification and characterization of novel threat agents, thereby creating the capability to rapidly produce relevant medical countermeasures. This policy is aligned with the National Strategy for *Medical Countermeasures against Weapons of Mass Destruction* which targets the use of existing, proven approaches for developing medical countermeasures to address challenges posed by traditional CBRN agents while calling for a flexible capability to develop new medical countermeasures. These latter activities emphasize the need to capitalize upon the development of innovative and future technologies that will enhance our ability to respond swiftly and effectively to potential, emerging, and future unknown CBRN threats. This will require targeted, balanced, and sustained investments to support fundamental basic research to discover new technologies

and update platforms as well as applied research for technology development to deliver new medical capabilities and countermeasures.

2. Would U.S. preparedness against an anthrax attack be better served if HHS focused its anthrax vaccine investment on acquiring additional doses of the current U.S. manufactured anthrax vaccine over the next few years as opposed to investing in foreign based production of an experimental anthrax vaccine that is years away from FDA approval, if that?

   HHS is pursuing a comprehensive anthrax vaccine strategy to maximize our near-term preparedness by procuring available vaccines while also supporting the research and development of next-generation anthrax vaccines for the mid- and long-term. Both of these activities are necessary in parallel for us to maintain and improve our anthrax vaccine stockpile. A comprehensive advanced development program is essential for supporting the scientific and technological advances that will lead to the next generation of vaccines with improved storage conditions, more rapid production and mechanisms for delivery.

   To address near-term preparedness needs, since 2005 HHS has signed contracts to acquire nearly 30 million doses of Anthrax Vaccine Adsorbed (AVA, BioThrax), the only currently available anthrax vaccine, manufactured by Emergent Biodefense Operations of Lansing, Michigan.

   Due to concerns regarding production capacity and homeland security, HHS strives to establish a diversified manufacturing base for anthrax vaccines and to address shortcomings of the AVA vaccine identified in the 2002 Institute of Medicine report. To achieve this goal, HHS is pursuing the development and acquisition of a recombinant protective antigen (rPA) anthrax vaccine, and will be seeking proposals from any industry partner that has the ability to develop, produce, and deliver such a vaccine safely, securely, and reliably. Because government acquisitions are performed through full and open competition, HHS cannot predetermine if an rPA vaccine manufacturer will be based in the United States. If a non-domestic source proves to be the most appropriate, HHS will pursue every opportunity to meet our anthrax vaccine requirement for protecting 25 million people.

3. Should HHS focus its resources in the short term on the domestically produced vaccine and in the long term on the development of a third generation anthrax vaccine that can be self administered by a patch or tablet and which would require only one dose?

   To meet our medical countermeasure requirements, HHS is building a complete portfolio of programs that address near-, mid- and long-term needs. HHS takes a comprehensive, multifaceted approach to medical countermeasure development and acquisition to maximize public health preparedness against an anthrax attack, as set forth in the *HHS Public Health Emergency Medical Countermeasures*

Enterprise Strategy and *Implementation Plan.* These documents have been informed by world-renowned technical experts and developed at the highest levels of leadership in the Department taking into account dozens of comments received from stakeholders throughout industry, the public health community and academia. The Department works diligently (a) to obtain the most effective medical countermeasures currently available, for current and near-term needs; (b) to support advanced development of new products, such as the second generation (rPA) anthrax vaccine, that will be the most effective in addressing our requirements in the future, as current supplies expire and as science, medicine, and technology advance; and (c) to seek the most appropriate medical countermeasures to address our requirements wherever they can be obtained, both from current supplies and for future development, with due regard for the integrity, security, and reliability of the source.

Post-Hearing Questions for the Record
Submitted to Gerald W. Parker
From Senator Tom Coburn

"Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?"
October 23, 2007

1. **It has been 10 months since the Pandemic and All-Hazards Preparedness Act was signed into law creating BARDA and there has still not been a Director selected by the Secretary. When will you put someone in charge of this critical mission?**

An offer was made to a highly qualified candidate, but that individual was unfortunately not able to accept the position. The Department of Health and Human Services continues to conduct a rigorous nation- wide search for the strongest candidate possible to serve as BARDA Director. HHS is carefully and thoroughly considering candidates according to federal hiring principles, and the flexibilities afforded in PAHPA.

2. **What has HHS done to improve BioShield by streamlining it and making its priorities more transparent?**

HHS has engaged in multiple activities to streamline the process of BioShield acquisitions and to make HHS' priorities more transparent.

Streamlining processes:

- HHS and DHS signed an MOU in September 2006 streamlining the process for transferring funds once a BioShield contract has been awarded.

- BARDA is working to reduce the time between releasing an RFP and awarding a contract through improved acquisition infrastructure, increasing our acquisition staff and implementing best acquisition management practices from DoD and other federal agencies.

Transparency:

- The *HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan for Chemical, Biological, Radiological and Nuclear (CBRN) Threats* were released in Spring 2007 and provide a comprehensive intra-agency framework to guide the development and acquisition of vaccines, therapeutics, and diagnostics, both within and beyond Project BioShield. The Strategy presents the principles used in prioritizing our efforts to increase medical countermeasure preparedness against the most serious CBRN threats, while the Implementation Plan identifies specific near-, mid-, and long-term goals for research, development and acquisition of critical medical countermeasures. Both are available on the HHS website at www.hhs.gov/aspr/barda/phemce/enterprise/strategy/.

- The Draft BARDA Strategy published on the BARDA website outlines how BARDA Advanced Development authorities and funding will be used to bridge the gap between R&D funding and acquisition.
- The Annual HHS PHEMCE Stakeholder's Workshop has brought together government, industry, and other stakeholders to discuss processes and to understand the mutual challenges we face in developing, licensing, and acquiring medical countermeasures to enhance preparedness.
- ASPR hosted the 2007 BARDA Industry Day on August 3, 2007. This inaugural event provided an open forum for biotechnology and pharmaceutical companies and for academia to showcase technological advances in emergency medical countermeasures for major intentional, accidental, and naturally occurring threats to the nation's public health.
- BARDA participated in a series of roundtable discussions with important stakeholder groups hosted by McKenna, Long, and Aldridge, the Center for BioSecurity at the University of Pittsburgh, and the Biotechnology Industry Organization (BIO). During these dialogues, ASPR and BARDA staff discussed a wide range of issues with interested stakeholders, including the *HHS PHEMCE Strategy and Implementation Plan,* implementation of the Pandemic and All-Hazards Preparedness Act, and the future of the Project BioShield program.
- BARDA seeks additional opportunities to dialogue with industry including with our PHEMCE partners to address issues and challenges, and help set the course for the future.
- BARDA will use acquisition tools such as draft RFPs and pre-proposal conferences to increase transparency and expedite the RFP process.
- BARDA will work to ensure that companies are fully knowledgeable of FDA's current thinking on regulatory requirements for product safety, efficacy, and manufacturing.

3. The Administration requested $189 million for BARDA. $159 million was included in the underlying Labor/HHS/Education Appropriations bill, and just yesterday the Senate accepted by UC a fully offset amendment from Senator Burr to bring that amount up the full $189 million request. What will HHS do with the $189 million you have requested to support countermeasure advanced research and development?

HHS will fund advanced development in priority areas consistent with the PHEMCE Implementation Plan:

- Medical countermeasures for biological threat agents including anthrax vaccines, broad spectrum medical countermeasures, smallpox antivirals, and viral hemorrhagic fever medical countermeasures.
- Medical countermeasures for radiological and nuclear threat agents including treatments for acute radiation syndrome (neutropenia and cell therapies), skin and lung injury, radionuclide facilities for animal testing and licensure of medical countermeasures, improved formulations of decorporating/chelating agents to remove radionuclides from the body, and biodosimetry for measuring exposure.
- Chemical countermeasures include development and licensure of the nerve agent antidote Midazolam to replace the existing nerve agent antidote in the Enterprise CHEMPACK.

4. **Tell me where we are as a country when it comes to being able to actually distribute these medical countermeasures in a timeframe that will save lives after an attack.**

The U.S. Government is working to be better prepared to rapidly distribute medical countermeasures as exemplified by programs like the Cities Readiness Initiative (CRI). This federally funded effort began in 2004 with a purpose to prepare major U.S. cities and metropolitan areas to effectively respond to a large scale bioterrorist event. The CRI goal is focused on developing capacity to dispense antibiotics to an identified city or MSA population within 48 hours of the decision to do so. Cities and MSAs are selected based on population, geographical location, and potential vulnerability to a bioterrorism threat. Participation in CRI has grown from an initial 21 to 72 cities.

CRI has enhanced communication and collaboration across state and local boundaries resulting in optimal use of shared resources. It has also increased availability of federal resources to local areas, and aid state and local officials in developing plans that support mass dispensing of prophylaxis to 100% of the identified population, within 48 hours of a decision to do so.

5. **What should we be doing to enable faster distribution of medical countermeasures - for example working with retail pharmacies as points of distribution (PODs), rather than setting up huge free standing PODs at schools, etc?**

Dispensing plans may employ several methodologies. Some project areas under CRI have received special funding to assist them in developing comprehensive dispensing campaigns. Regardless of the funding streams, all project areas should be able to employ different modalities to provide medicine to the affected population as quickly as possible. Some of those modalities could include:

- Purchasing and managing localized caches of antibiotics or a plan to use initial shipments of antibiotics, so project areas can dispense first to critical response personnel and their families.
- Delivering antibiotics to homes with the assistance of the U.S. Postal Service. With this modality, mail carriers could deliver antibiotics to the homes in selected zip codes. The postal option is entirely voluntary for the employees of the Postal Service and only available to the jurisdictions with an approved Postal Service dispensing plan.
- Working with local businesses to use their existing infrastructure to dispense to employees and families.
- Utilizing established community structures such as local schools, churches, and civic centers to serve as additional points of dispensing.

6. **How long would it actually take us to detect an anthrax attack in the air through BioWatch, or in the hospital through BioSense?**

BioWatch:
BioWatch is a program that uses air samplers to detect for threat agents. The samplers are located in undisclosed cities and monitor the air 24 hours a day, 7 days a week. Air passes through a filter to trap organisms, including those that are considered bioterrorism threats. A select number of state public health labs that are Laboratory Response Network members also provide testing for the BioWatch program. LRN/BioWatch labs conduct tests on filters taken from these air samplers. Tests include polymerase chain reaction (PCR). PCR can detect the presence of an agent's unique DNA within three to four hours.

Under the current BioWatch program, the time required to detect and report the release of a bioterrorism agent can take as long as 36 hours and little as 8 hours. Detection depends on the time of the actual release and the time filters are retrieved from sampler, the travel time between the sampler and the nearest LRN/BioWatch lab, and the time required to run tests on the filters. BioWatch filters are tested once a day. In cities where national significant events are taking place, filters are tested twice a day.

BioSense:
It is possible that signals that might indicate an anthrax attack could be detected as soon as patients with symptoms would begin to present themselves in emergency departments connected to the BioSense system under certain scenarios. If we assume that the attack occurred in an area with hospitals sending emergency department (ED) chief complaint data to BioSense in near real-time, that a large number of people were affected, and that patients would develop symptoms and go to EDs 3 days after the attack, then data anomalies would appear in the BioSense system 3-5 days after the attack. This would not identify anthrax per se, a process that requires laboratory confirmation, but would be a warning that an outbreak was occurring, and could help in understanding the geographic extent of the outbreak and the numbers of patients affected (ie provide situational awareness).

If the patients went to a BioSense hospital that was collecting additional clinically rich data (eg, xrays, laboratory data), then smaller numbers of patients could be noticed and laboratory cultures would show evidence of anthrax 1-2 days after the patients presented to the hospital EDs.

United States Government Accountability Office
Washington, DC 20548

January 28, 2008

The Honorable Joseph Lieberman
Chairman
Homeland Security and Governmental Affairs
United Stated Senate

The Honorable Susan Collins
Ranking Member
Committee on Homeland Security and Governmental Affairs
United States Senate

The Honorable Daniel Akaka
United States Senate

The Honorable Tom Coburn
United States Senate

You asked us to respond to three post-hearing questions for the official record from the hearing on October 23, 2007, titled "Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?"

Post-Hearing Question for the Record
Submitted to Keith A. Rhodes
From Senator Susan M. Collins

1. "One of the issues that seem to come up in every review undertaken of government contracting is the amount of attention that is paid to the upfront process of acquisition planning. Please share with the Committee your findings in the GAO report regarding HHS acquisition planning for the VaxGen Contract."

GAO Response: Acquisition planning should begin as soon as the agency need is identified, and is designed to ensure that agency requirements are stable and clear, that the capabilities of commercial suppliers to meet those requirements are fully considered, and that competition among suppliers is sought to maximum extent practicable. Sound acquisition planning should integrate the efforts of all personnel responsible for significant aspects of the acquisition.

However, in the case of VaxGen's contract, as we stated in our report, important requirements regarding the data and testing required for recombinant protective antigen (rPA) anthrax vaccine to be eligible for use in an emergency were not known at the outset of the procurement contract. They were not defined until 2005 when the Food and Drug Administration introduced new general guidance on emergency use authorization. In addition, Office of the Assistant Secretary for Preparedness and Response's anticipated use of the rPA anthrax vaccine was not articulated to all parties clearly enough and evolved over time.

Post-Hearing Questions for the Record
Submitted to Keith A. Rhodes
From Senator Tom Coburn

2 and 3. "One of the major lessons that was learned from the VaxGen contract termination seems to be that HHS needed to be able to assist companies in moving products further down the development pipeline before locking into a multi-million dollar procurement contact. How is HHS using the new BARDA authorities provided by Congress last year to do this? What advice do you have for HHS in implementing BARDA in the year ahead?"

GAO Response: These questions were beyond the scope of our first report. We plan to address these questions in our next report.

If you need additional information, please do not hesitate to contact me at 202-512-2700.

Sincerely yours,

Nancy Kingsbury
Managing Director
Applied Research and Methods

Post-Hearing Questions for the Record
Submitted to Tara O'Toole
From Senator Daniel K. Akaka

"Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?"
October 23, 2007

1. **Dr. O'Toole, why do you believe so many companies such as VaxGen, Avant, and Hollis Eden have decided to leave the biodefense market?**

There are several reasons, most of which were well documented in the hearings that lead up to the BARDA legislation of 2006 and in letters to members of Congress from the Alliance for Biosecurity, and in which the Center for Biosecurity participates. These reasons include:

Large pharmaceutical companies have no interest in biodefense work, because they can make much more money developing products for which there are private markets. The government is the only customer for biodefense products. Thus, the only segment of the biopharma industry interested in making medical countermeasures (MCMs) – which include medicines and vaccines against the full spectrum of CBRN attacks – are small biotech companies, most of which have little or no experience in bringing a candidate MCM through advanced development to FDA licensure. The process of advanced development is a highly risky and complex enterprise. Thus the USG is dependent on fragile, unproven companies to develop vital MCMs for American defense.

HHS had no experience in developing drugs or vaccines before 2002 and has thus far proven to be a bad business partner. It took years for HHS to establish contracting processes, to hire knowledgeable personnel and to decide what MCMs it would invest in. The confusion and delays have had a profound effect on small companies' ability to raise capital and convince investors that .MCM development was a sound investment. Most sources of private capital will now have nothing to do with biodefense R&D and some companies claim that admitting that they are working on MCMs is actually viewed negatively by venture capitalists because of the USG's perceived unreliability.

Industry has been asking for better communication with HHS and for more leadership from the government. In past years, government officials have been severely constrained by administration policy from speaking directly with industry, making it extremely difficult for business leaders to understand exactly what HHS needs or expects. Even more importantly, HHS has not had the people needed to manage these programs and to reach out to industry, largely because Congress failed to appropriate funds for such infrastructure needs. Recently, HHS is being more open and has made efforts to hold "stakeholder" meetings, etc., modeling their approach on DOD's methods of interacting with the private sector.

The private sector is increasingly skeptical of the US government's commitment to biodefense, particularly in view of the government's failure to allocate reasonable funds for MCM development and purchase. Our Center estimates that funding products to meet all the MCM requirements already identified by Material Threat Assessments would require BARDA funding of approximately $3B. No funds were allocated last year for BARDA and only $100M has been appropriated in FY08.

2. **What are the top two or three things BARDA could do to shore up the biodefense industry and send a message that the Government is truly committed to developing and procuring countermeasures?**

First, the government must appropriate a reasonable amount of federal dollars to BARDA. When BARDA was passed in December 2007, $1B was authorized but only $99M appropriated in the FY07 Supplemental. The Bush Administration requested $189M in the FY08 budget; the actual FY08 BARDA appropriation for advanced development of medical countermeasures against all CBRN threats was $102 M

Our Center's analyses indicate that to have a 90% chance of actually developing one successful medicine or vaccine for each of the biological threats certified by DHS to constitute a "material threat" to the nation and designated in the HHS PHEMCE requirements, BARDA would need $3,180M in advanced development funds in FY09. Note that this $3B does not include advanced development funds for countermeasures against radiological or chemical threats.

These meager funding levels, and the vast gap between what it actually costs to develop a new drug or vaccine compared to what is being appropriated are interpreted by the private sector as a lack of serious government commitment to biodefense. If small biotech companies cannot get private capital to invest in MCM development, and there are no funds in the federal budget line that is designed to support advanced development, it simply does not make sense for companies to pursue MCMs. Large Pharmaceutical companies have already declined to pursue biodefense MCMs. What is happening now is that smaller biotech companies are leaving the biodefense field.

Second, the appointment of a BARDA Director of appropriate stature and experience would send a powerful message to the industry that HHS is intent on improving the program so that it can fully partner with the private sector. Today, a year after the BARDA legislation mandated such a post, HHS has yet to name a director. This failure sends a loud message that HHS has not made this recruitment a top priority. Thirdly, the Congress has to get manifestly serious about biodefense generally. It is quite amazing – and telling - that the threat which the Director of National Intelligence describes as the one "which keeps him awake at night, and which the Hart Rudmann report judged (in 1999) to represent the gravest threat to the country in the 21st Century has been the subject of few Congressional hearings or oversight. I have yet to find a member of Congress who has been briefed on the classified 2006 DHS biothreat assessment.

Third, Congress and the Administration must act as though biodefense is a top national security priority, not just another vexing public health issue. It is remarkable that so few members have been briefed on the DHS Biothreat Assessment of 2006 and how few have had any intelligence briefing on the bioterror threat facing the nation. No other national security threat is handled in the manner applied to biothreats. Since the anthrax attacks of 2001 there have been repeated affirmations from the intelligence community that bioterror is a serious national security problem. Yet important biodefense programs, such as Bioshield and BARDA are allowed to languish and fail. – without much outcry or investigation by Congress. There is still no single person in the federal government whose sole job is biodefense, no conduct of operations to guide federal or state response to a bioattack, and widespread inability at the state level to distribute the stockpile in a timely manner. Hundreds of millions of dollars have been spent since 2001 on biosurveillance efforts of all types, with no clear gain in situational awareness and no overall federal strategy for future spending, in spite of a clear record of past failures. The threat of bioterrorism is a national security issue of the highest importance – but the issue is treated as a "low probability" public health threat rather than as a top, potentially imminent and destabilizing national security issue.

Post-Hearing Questions for the Record
Submitted to Tara O'Toole
From Senator Susan M. Collins

"Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?"
October 23, 2007

1. **In 2006, Congress passed the Biodefense Advanced Research and Development Authority (BARDA) as part of the Pandemic and All-Hazards Preparedness Act. BARDA is meant to help bridge the gap between early-stage research and the ultimate procurement of products for the Strategic National Stockpile under Project BioShield by funding advanced development and research. Congress passed this legislation because it recognized that the gap between early-stage research and procurement is where many promising technologies and products have languished, the so called valley of death for biotech companies. The failure of VaxGen occurred before BARDA came into existence. Do you think BARDA will help us avoid another failed investment in vaccine development?**

2. **How important is it that the federal government provide the catalyst for vaccine development?**

The federal government has an essential role to play in catalyzing the creation of vaccines for the future – and not just for biodefense vaccines.

We are at a point in the evolution of bioscience and of drug production technologies that could enable the development of fast, inexpensive methods of vaccine development that would benefit not only biodefense, but many aspects of US health care, economic competitiveness and US foreign policy. Only the federal government can fill this role, as it did for the computer and aerospace industries a generation ago. Meanwhile, other countries, notably China and India, have recognized that bioscience will be central to future economic and defense development and have embarked on national investment strategies of their own. There is a limited window of opportunity during which the US can make use of its fleeting intellectual competitive advantage in the biosciences an harness this advantage to national purposes.

The US national security imperative to create medical countermeasures (MCMs) for use against a spectrum of CBRN attacks ought to serve as the impetus for an ambitious strategy of national investment in drug and vaccine development and manufacture. The aim ought to be to learn how to make drug and vaccine development less risky, less costly and faster. The technologies which could power such a transformation exist and could be further developed, but market forces are unlikely to promote such changes any time soon.

Vaccines are among the most cost-effective public health interventions. But while the research and development required to license and manufacture vaccines costs about the same as is required for other medicines, vaccines are much less profitable. There are several reasons for this, including the need to take vaccines only once or twice instead of every day for a lifetime; the impoverishment of many who would most benefit from vaccines, especially in the developing world; and the difficulty and costs of carrying out clinical trials for vaccines designed for use in healthy populations. Thus, market forces are reducing the number of vaccine producers worldwide, even as the need for newer, safer and cheaper vaccines grows, especially in developing countries.

Today, the US is losing its capacity to produce any countermeasure, as US biopharma firms outsource all stages of drug and vaccine R&D, mostly to Asia. (Clinical trials conducted in India cost 20% of trials carried out in the US.) Half of the antibiotics in the world are made in China, including a raw ingredient essential to the manufacture of Ciprofloxacin (made in Germany). The biotech industry is vital to national defense and the Harvard Business review has stated that biosciences will have a more profound "transformative effect" on the 21st Century economy than information technology had on business in the 20th Century. Yet the US government funds virtually no work on applied biology beyond a small fraction of DARPA's budget. Total US bioscience spending is less than half the amount of total defense spending, and the majority of bioscience appropriations is NIH funding for basic research.

The US government should consider programs such as Sematech in the context of medical countermeasure development and manufacture. When the Defense Department feared the country was losing its ability to produce semiconductor chips vital to national defense, it organized and funded an industry consortium to address the issues.

But at the least, a more considered strategy for pursuing urgently needed MCMs against top national security threats must be devised. The Bioshield legislation of 2002 is not sufficient to get the country the MCMs it needs – this was implicitly recognized with the passage of the 2006 Pandemic and Public Health Act and the creation of BARDA. The imperative of establishing a robust biodefense could be used to catalyze not only vaccine development but to spur a much wider and far reaching development of bioscience and biotechnology that would benefit the US and the world.

Post-Hearing Questions for the Record
Submitted to Tara O'Toole
From Senator Tom Coburn

"Six Years After Anthrax: Are We Better Prepared to Respond to Bioterrorism?"
October 23, 2007

1. **How much does it cost to produce a medical countermeasure? (She should answer about $800 million) How much is reasonable to expect BARDA to underwrite during product development?**

The $800M estimate is the most common, and best documented average estimate of the cost pharmaceutical company's bear for bringing a compound from the lab bench through all testing to licensure by FDA. This number includes the costs of all the failed attempts to create a new drug. Biopharma is an exceedingly risky business – only about 1 candidate drug out of 5000 actually gets licensed! The $800M encompasses development costs only however – it does not include the *purchase* of a single pill or vaccine dose. Given these facts, it is unrealistic to think that the USG can achieve the development and purchase of medicines and vaccines needed for the entire US population against all forms of CBRN attacks for the $5.6B (through 2013) that was allocated for Bioshield funds.

As this question implies, it will be extremely expensive to develop and stockpile a new drug and/or vaccine against all possible (or even just the most likely) bioagents threats using current technologies. Moreover, the spectrum of possible engineered biothreats is expanding inexorably as bioscience advances. Thus, the 2006 DHS Biorisk Threat Assessment has already listed more than a dozen different naturally occurring bioagents which it deems capable of inflicting upwards of 10,000 casualties in a single strike. Because bioweapons are self-replicating organisms, however, multiple strikes on different targets are feasible, and would create a need for millions of doses of the relevant countermeasure.

In the long run, BARDA ought to be funding technologies and approaches that greatly reduce the risk, time and cost required to develop and manufacture new medicines and vaccines. In the near term, BARDA is the only source of funding for advanced development of countermeasures.

The answer to the second question depends on Congress' estimation of the risk of a bioterror attack and the appraisal of what it would be worth to mitigate the consequences of such an attack. The current Director of National Intelligence reportedly stated that a covert anthrax attack is the threat which keeps him awake at night. The 2005 National Intelligence Estimate noted that "Our greatest concern is that terrorists might acquire biological agents, or less likely, a nuclear device, either of which could cause mass casualties." ["Mapping the Global Future, National Intelligence Council 2020 Project, Jan. 2005].

At present, the Strategic National Stockpile has sufficient anthrax vaccine to immunize approximately 3 million people. Somewhere between 10-50% of the US military is vaccinated. Given existing vaccine production capacities it would take over 100 years to manufacture enough vaccine for every American. Should the US spend more than the current appropriate of $5.6B (through FY2013) to develop and procure medicines and vaccines against all forms of CBRN attack?

The existing US strategy for obtaining countermeasures against destabilizing bioattacks is not viable and must be rethought and reorganized. We simply will not get the countermeasures we need with the current approach and funding. The Center for Biosecurity estimates that it would require about $3B in BARDA funds to bring MCMs already deemed necessary by material threat assessments through advanced development phases. The FY08 BARDA appropriation was $130M. The country simply cannot get the countermeasures the executive branch has certified to be necessary for the common defense with the present strategy and funding levels.

To provide an effective defense against bioattacks, the US must catalyze the creation of new drug and vaccine development and manufacturing processes, structure bioscience funding so that we greatly improve the predictability of drug and vaccine development – and thereby increase the speed and decrease the cost of production - and evolve more efficient regulatory processes suited to emergency situations. Faster, cheaper drug production would also, of course, have profound implications for ordinary health care costs. It would also make sense to explore sharing the costs of MCM development and manufacture with the British and other close allies.

Six years after the first anthrax attacks, the nation still does not have a second generation anthrax vaccine. The HHS' attempt to obtain such a vaccine from a small biotech company failed, largely due to the company's (and HHS') inexperience. The nation is dependent upon small biotechnology companies to develop CBRN countermeasures, companies that lack the capital or ability to attract capital needed to sustain investigation of "candidate" drugs. The "big Pharma" companies are unwilling to participate in MCM development, for reasons that are well documented – basically, there's too much risk and not enough money in it compared to other opportunities. So the small biotech firms are the only source of MCMs – and as the Vaxgen experience has demonstrated, these relatively inexperienced and fragile companies will fail without more support than was afforded by the initial Bioshield legislation.

The intended purpose of BARDA, which was strongly supported by the biotech industry, was to provide bridge funding that would allow small biotech companies to bring potential products through the initial stages of clinical testing. The reasons why Big Phama companies are uninterested in biodefense and why smaller biotech companies cannot find the capital needed to move a candidate drug through "advanced development" and testing were documented in the hearings that preceded the BARDA legislation.

Congress' failure to fund BARDA adequately has seriously eroded industry's interest in developing medical countermeasures (MCMs) and convinced many companies that the government is not serious about biodefense and has caused several companies to abandon countermeasure development.

2. **Tell me where we are as a country when it comes to being able to actually distribute these medical countermeasures in a timeframe that will save lives after an attack.**

The answer depends on where one lives. Atlanta and a handful of other cities have made considerable progress in mass distribution – largely because they have begun to enlist the private sector in the process. Other locales, such as Seattle, have spearheaded efforts to create a mosaic of approaches, including, for instance, the use of postal delivery workers to distribute the stockpile. Most cities and states have no effective means of rapidly delivering countermeasures during an emergency.

The best available analysis of mass distribution capacities is the report conducted by the Trust for America's Health, which reported most recently in December 2007 that 13 states lack the capability to deliver the stockpile. I would judge this to be quite optimistic and untested. [ref: Trust for America's Health. *Ready or Not 2007*. http://healthyamericans.org/reports/bioterror07/BioTerrorReport2007.pdf. Released December 18, 2007. Accessed December 20, 2007.]

Effective mass distribution of countermeasures will require direct participation by private sector. As was noted by a senior public health official in a March 2007 meeting held by the White House, public health agencies do not have any modern experience in mass distribution of drugs, at least not on the scale now being contemplated. For most cities staffing the "points of distribution" (PODS) envisioned by CDC will require organizing tens of thousands of people within hours – a feat that is just not realistic. New York City, which has invested considerable effort and funds in this problem, estimates that it will require 40,000 people (running 2 shifts) to staff 202 PODs. This type of people power is just not available to state and local governments. On the other hand, the private sector has lots of manpower and wide experience with delivering products efficiently and rapidly.

Congress could provide a significant boost to private sector engagement by enacting national liability waiver that protects participating companies and individuals from being sued if the countermeasures don't work or cause harm to some. In cities where the private sector has gotten engaged, the benefits to homeland security go well beyond mass distribution of countermeasures.

3. **What should we be doing to enable faster distribution of medical countermeasures - for example working with retail pharmacies as points of distribution (PODs), rather than setting up huge free standing PODs at schools, etc?**

In most places, a variety of delivery approaches will be needed. The most essential step towards achieving a mass distribution capacity is enlisting the private sector in the effort. Private companies have the people power – and often the direct experience – needed to achieve rapid distribution, first to their own employees, and then to the wider community. Some areas may be best served by receiving MCMs via postal delivery personnel – this is one way to reach shut-ins and rural populations. PODs will probably be needed, but the approach now advocated by CDC cannot work. Atlanta has pioneered a strategy that involves the local business community and has proven quite successful in drills and in minor emergencies such as the summer water shortage.

The Congress could do three important things to encourage the private sector to participate in mass distribution efforts. First, Congress could play an important role in alerting private companies to the nation's needs and in convincing business leaders that bioterrorism is a real threat. Second, legislation is needed to ensure that individuals and companies that participate in mass distribution efforts during public health emergencies cannot be sued if the MCMs don't work or cause harm. .Third, the Congress should assure multi-year funding for state distribution programs and allow these funds to be used to hire people to manage the programs. The rapid turnover that currently plagues virtually all state health departments is a major reason for lack of progress.

4. **How long would it actually take us to detect an anthrax attack in the air through BioWatch, or in the hospital through BioSense?**

BioSense

There is little chance that the Biosense project will detect anything – the CDC website does not now claim that the system is designed to detect a public health emergency, although this was a stated purpose of the program in earlier incarnations. It is very difficult to understand in any detail the current purposes or structure of CDC's Biosense program. Over the past several years, CDC has spent hundreds of millions of dollars on successive biosurveillance efforts, all of which have failed or been superseded by other programs.

The ostensible purpose of Biosense, as stated on the CDC website, is to provide "situational awareness" during a pandemic or other national health emergency, by gathering digital input from a wide variety of sources, including hospitals, clinical labs and state syndromic surveillance systems. This is a laudable and important goal, but it is not at all clear whether such data would be useful or how such data would be analyzed by CDC or to what purpose. The confusion about the intent of the program is magnified by the absence of an overall national conduct of operations plan for a bioattack or other public health emergency, which makes it hard to know what, exactly, CDC's role would be, or how it would assemble or employ "situational awareness" during such

emergencies. Biosense currently receives "data" (of what type is not clear) from only 130 of the more than 5000 hospitals in the US.

The Biosense program has been widely criticized by state health officials, in part because it initially attempted to funnel data from local hospitals directly to CDC, bypassing state and local authorities. This made little sense, given that response is local; the system also seemed to replicate efforts already underway in some states. More recent versions of the policy behind Biosense include data flows to local public health authorities, but the purpose and usefulness of this very expensive project remain murky and the large sums expended on the program might be better invested elsewhere.

My first choice for such alternative investments would be to create real-time digital links between hospitals and state health agencies – without real-time communication among these critical institutions, meaningful situational awareness is hard to conceive. If the US truly wants to assure situational awareness during public health catastrophes, we must invest in a health information highway – a nationally interoperable system of electronic health records, such as exists in all other developed countries. Electronic health records must be the foundation of any system attempting to provide situational awareness. The nation is spending hundreds of millions of dollars on untested and unproven "systems" that will supposedly improve situational awareness. It's time to examine these claims and develop a coherent biosurveillance strategy that will serve the nation's needs.

It should be understood that achieving situational awareness during a large-scale public health emergency – especially if it is a pandemic or bioattack – is a formidable task. Moreover, the USG has a terrible record of failure when it comes to developing complex computer systems. The reasons for this are well documented by GAO and others – the government awards these difficult projects to the lowest bidder, fails to hold contractors accountable, fails to hire federal employees with sufficient technical and managerial skills to manage the project and then fails to consistently appropriate the funds needed to complete the project.

Biowatch

The short – but misleading – answer to the question is: a covert aerosol attack using one of the agents that Biowatch sensors can detect could, theoretically be identified somewhere between 6-36 hours after a release. It is also quite possible that a covert attack will not be detected by Biowatch, even if the attack occurs in one of the 30 or so cities where Biowatch is deployed. More importantly and to the point, it is not at all obvious that the Biowatch system, even if it does detect the attack, will improve response.

The country is not asking the right questions about the Biowatch program. The assessment thus far has focused on the technology – it is time to reassess the overall US biosurveillance strategy and the role of Biowatch in this strategy. In my view, far too much emphasis has been placed on detecting a bioattack and far too little attention paid to

ensuring that leaders have the situational awareness they will need to manage an attack once it occurs.

Biowatch sensors – which are sited next to EPA air pollution monitors – are not necessarily placed in a manner that allows blanket coverage of the complex air flows in urban environments. So it is possible that only some or none of the Biowatch sensors in a city under attack will detect the aerosol release. The JASONS estimated it would take 150 sensor stations to adequately cover the flat terrain of Lincoln, Nebraska (0.1% of US pop.) so to cover a complex topography like New York's urban canyons or San Francisco would require many more sensors than are now deployed or contemplated. As far as I know, no city has enough sensors properly placed to allow accurate reconstruction of a release – i.e. Biowatch data cannot be relied upon to reconstruct the source and path of an attack so won't be of great help in determining who was or was not exposed.

It is quite possible that Biowatch will accurately detect an attack, but that realization of the attack will come more rapidly through the health care system's identification of sick patients. If the incubation period of the bioweapon is short – e.g. an anthrax attack will incite symptoms in some people within 24 hours of exposure. At present, there are no rapid diagnostic tests for anthrax (or any other bioagents) available to doctors, so absolute confirmation that individuals were infected with anthrax would require growing blood cultures – which takes about 24 hours. I would argue that investments in such rapid diagnostic tests are urgently needed, but there are no funds for this available – it is one of the multitude of tasks relegated to the limited Bioshield funding. The technology needed for such diagnostic tests is readily available.

Suppose Biowatch sensors detect an aerosolized bioweapon before there is any clinical evidence of an attack. All the evidence to date indicates that public health authorities will want to confirm such an attack through the identification of sick people – public health agencies will call hospital emergency departments and seek evidence of an unusually large number of patients or of unusual symptoms consistent with an attack. This checking process will take time because we currently lack real-time electronic links between hospitals and public health. Doctors will be reporting clinical impressions – because rapid diagnostic tests are not available. It is important to recognize that the attack occurred many hours earlier – by now, the victims are spread all over and only some are yet developing symptoms. Determining the source and scale of the attack will take a long time and will immediately complicate decisions about where and how to deploy the SNS. Biowatch data may help in these deliberations – or may be misleading or useless, depending on the source of the attack(s), placement of sensors, type of agent used and the predictability of the aerosol path.

The single greatest failing in US biodefense today is the absence of any conduct of operations plans for dealing with a bioattack. HHS is reportedly working on such a "play book" but seven years after the first anthrax attack, no one outside the agency has seen it. Without such a plan, it is difficult to know how the USG plans to use Biowatch data once an attack has occurred or to evaluate if other investments in biosurveillance – such as rapid diagnostic tests, digital links between hospitals and public health officials, etc. – would be more worthwhile.

It was not unreasonable to deploy Biowatch sensors in 2003 in major cities as the US military were beginning operations in Iraq and it is certainly sensible to deploy "drop-in" biosensors during important, high-profile events. But it is past time for a re-evaluation of the US biosurveillance strategy.

United States Government Accountability Office

GAO

Report to Congressional Requesters

October 2007

PROJECT BIOSHIELD

Actions Needed to Avoid Repeating Past Problems with Procuring New Anthrax Vaccine and Managing the Stockpile of Licensed Vaccine

GAO-08-88

October 2007

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Highlights

Highlights of GAO-08-88, a report to congressional requesters

PROJECT BIOSHIELD

Actions Needed to Avoid Repeating Past Problems with Procuring New Anthrax Vaccine and Managing the Stockpile of Licensed Vaccine

Why GAO Did This Study

The anthrax attacks in September and October 2001 highlighted the need to develop medical countermeasures. The Project BioShield Act of 2004 authorized the Department of Health and Human Services (HHS) to procure countermeasures for a Strategic National Stockpile. However, in December 2006, HHS terminated the contract for a recombinant protective antigen (rPA) anthrax vaccine because VaxGen failed to meet a critical contractual milestone. Also, supplies of the licensed BioThrax anthrax vaccine already in the stockpile will start expiring in 2008. GAO was asked to identify (1) factors contributing to the failure of the rPA vaccine contract and (2) issues associated with using the BioThrax in the stockpile. GAO interviewed agency and industry officials, reviewed documents, and consulted with biodefense experts.

What GAO Recommends

GAO is recommending that the HHS Secretary ensure that (1) for future procurements the concept of use and all critical requirements for medical countermeasures are clearly articulated at the outset, (2) expired stockpile vaccines are destroyed, and (3) the HHS and the Department of Defense (DOD) Secretaries develop an integrated stockpile for BioThrax with rotation based on a first-in, first-out principle.

HHS and DOD generally concurred with GAO's recommendations but identified legal challenges that may require legislative action.

To view the full product, including the scope and methodology, click on GAO-08-88. For more information, contact Keith Rhodes at (202) 512-6412 or rhodesk@gao.gov.

What GAO Found

Three major factors contributed to the failure of the first Project BioShield procurement effort for an rPA anthrax vaccine. First, HHS's Office of the Assistant Secretary for Preparedness and Response (ASPR) awarded the procurement contract to VaxGen, a small biotechnology firm, while VaxGen was still in the early stages of developing a vaccine and had not addressed many critical manufacturing issues. This award preempted critical development work on the vaccine. Also, the contract required VaxGen to deliver 25 million doses of the vaccine in 2 years, which would have been unrealistic even for a larger manufacturer. Second, VaxGen took unrealistic risks in accepting the contract terms. VaxGen officials told GAO that they accepted the contract despite significant risks due to (1) the aggressive delivery time line for the vaccine, (2) VaxGen's lack of in-house technical expertise—a condition exacerbated by the attrition of key company staff as the contract progressed—and (3) VaxGen's limited options for securing any additional funding needed.

Third, important Food and Drug Administration (FDA) requirements regarding the type of data and testing required for the rPA anthrax vaccine to be eligible for use in an emergency were not known at the outset of the procurement contract. In addition, ASPR's anticipated use of the rPA anthrax vaccine was not articulated to all parties clearly enough and evolved over time. Finally, according to VaxGen, the purchase of BioThrax for the stockpile as a stopgap measure raised the bar for the VaxGen vaccine. All these factors created confusion over the acceptance criteria for VaxGen's product and significantly diminished VaxGen's ability to meet contract time lines. ASPR has announced its intention to issue another request for proposal for an rPA anthrax vaccine procurement but, along with other HHS components, has not analyzed lessons learned from the first contract's failure and may repeat earlier mistakes. According to industry experts, the lack of specific requirements is a cause of concern to the biotechnology companies that have invested significant resources in trying to meet government needs and now question whether the government can clearly define future procurement contract requirements.

GAO identified two issues related with the use of the BioThrax in the Strategic National Stockpile. First, ASPR lacks an effective strategy to minimize the waste of BioThrax. Starting in 2008, several lots of BioThrax in the Strategic National Stockpile will begin to expire. As a result, over $100 million per year could be lost for the life of the vaccine currently in the stockpile. ASPR could minimize such potential waste by developing a single inventory system with DOD—a high-volume user of BioThrax—with rotation based on a first-in, first-out principle. DOD and ASPR officials identified a number of obstacles to this type of rotation which may require legislative action. Second, ASPR planned to use three lots of expired BioThrax vaccine in the stockpile in the event of an emergency. This would violate FDA rules, which prohibit using an expired vaccine, and could also undermine public confidence because the vaccine's potency could not be guaranteed.

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Abbreviations

ASPR	Office of the Assistant Secretary for Preparedness and Response
AVA	Anthrax Vaccine Adsorbed
AVIP	Anthrax Vaccine Immunization Program
BARDA	Biomedical Advanced Research and Development Authority
CBER	Center for Biologics Evaluation and Research
CBRN	chemical, biological, radiological, or nuclear
CDC	Centers for Disease Control
cGMP	current Good Manufacturing Practices
DHS	Department of Homeland Security
DOD	Department of Defense
EUA	emergency use authorization
FDA	Food and Drug Administration
HHS	Department of Health and Human Services
IND	investigational new drug
IOM	Institute of Medicine
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
PHEMCE	Public Health Emergency Medical Countermeasure Enterprise
PTA	population threat assessment
RFI	request for information
RFP	request for proposal
rPA	recombinant protective antigen
TRL	Technology Readiness Level

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United States Government Accountability Office
Washington, DC 20548

October 23, 2007

The Honorable Edward M. Kennedy
Chairman
Committee on Health, Education, Labor and Pensions
United States Senate

The Honorable Joseph I. Lieberman
Chairman
The Honorable Susan M. Collins
Ranking Member
Committee on Homeland Security and Governmental Affairs
United States Senate

The Honorable Richard Burr
United States Senate

The anthrax attacks in September and October 2001 highlighted major gaps in our civilian preparedness to respond to health emergencies that threaten national security. These incidents also led the Congress and the federal government to focus attention on the importance of developing new drugs, vaccines, and therapeutics to protect U.S. citizens.

In 2002, in response to the anthrax attacks, the National Institute of Allergy and Infectious Diseases (NIAID) within the National Institutes of Health (NIH) launched an effort to rapidly develop a second generation recombinant protective antigen (rPA) anthrax vaccine.[1] While there is already a licensed anthrax vaccine (BioThrax), it is given in six doses over 18 months followed by an annual booster. NIAID wanted to have a vaccine that could be administered in an immunization series of not more than three doses.[2]

[1] The vaccine based on rPA is often referred to as a second generation anthrax vaccine to differentiate it from BioThrax. Recombinant refers to a product created using a genetic engineering technology in which one or more pieces of DNA are combined together. A protective antigen is a biochemical that produces an immunologic response that then protects animals or humans against challenges from the infectious agent.

[2] National Institute of Allergy and Infectious Diseases, "Production and Testing of Anthrax Recombinant Protective Antigen (rPA) Vaccine." Request for Proposal (RFP) No. NIH-NIAID-DMID-03-29.

In the late 1980s, Department of Defense (DOD) research identified an rPA anthrax vaccine, created with a process that (1) is fully defined, quantified, and controlled in terms of protective antigens; (2) showed development potential; and (3) required fewer doses. DOD researchers developed a fully defined manufacturing process to produce highly purified rPA. The researchers found that they could protect animals using this rPA with fewer doses than the existing licensed vaccine.[3] In 2002, the Institute of Medicine (IOM) stated that although AVA—Anthrax Vaccine Adsorbed, now called BioThrax—is safe and effective for use, "it is far from optimal."[4] The IOM supported the development of a new anthrax vaccine. According to the Department of Health and Human Services (HHS), when an rPA vaccine is fully developed, it will address the shortcomings of the AVA vaccine identified in the IOM report.[5]

In 2002 and 2003, NIAID awarded development contracts for rPA vaccines to two companies—VaxGen and Avecia. VaxGen was a small U.S. biotechnology company. According to NIAID, one of the objectives was to demonstrate how manufacturing efforts might be increased to support creation of a national stockpile of medical countermeasures.

The Project BioShield Act of 2004 formalized this initiative and authorized the Secretary of HHS, who in turn entrusted the Office of the Assistant

[3] B. Ivins and others, "Immunization Studies with Attenuated Strains of *Bacillus anthracis*," *Journal of Infection and Immunity*, 52(1986):454-58. B. E. Ivins, "The Search for a New-Generation Human Anthrax Vaccine," *Clinical Immunology Newsletter*, 9(1988): 30-32; and Y. Singh and others, "Study of Immunization against Anthrax with the Purified Recombinant Protective Antigen of *Bacillus anthracis*," *Journal of Infection and Immunity*, 66(1998): 3447-48.

[4] Institute of Medicine, *The Anthrax Vaccine: Is It Safe? Does It Work?* (National Academy Press: Washington, D.C., 2002), p. 20.

[5] Stewart Simonson, Assistant Secretary, Department of Health and Human Services, Office of Public Health and Emergency Preparedness (now ASPR), testimony before the Senate Committee on Appropriations, Subcommittee on Homeland Security, April 28, 2005.

Secretary for Preparedness and Response (ASPR)[6] with responsibility for acquiring and ensuring the management of and accounting for a Strategic National Stockpile of medical countermeasures.[7] It is designed to supplement and resupply state and local public health agencies in the event of a national emergency anywhere and anytime within the United States or its territories. Among other medical countermeasures, this stockpile contained, as of June 2007, about 10 million doses of BioThrax, the licensed anthrax vaccine.[8] Since doses of BioThrax, like other vaccines, have an expiration date, these doses will be disposed of if they are not used before their expiration date.

The only other large user of BioThrax vaccine is DOD, which has procured its own inventory of the vaccine. DOD has a mandatory Anthrax Vaccine Immunization Program (AVIP) for military personnel, emergency-essential DOD civilians, and contractors, based on defined geographic areas or roles. The policy also allows personnel previously immunized against anthrax, who are no longer deployed to high-threat areas, to receive follow-up vaccine doses and booster shots on a voluntary basis.

In November 2004, ASPR awarded VaxGen a procurement contract for $877.5 million for the manufacture and delivery of 75 million doses of its rPA anthrax vaccine to the Strategic National Stockpile. Two years later, in December 2006, ASPR terminated VaxGen's contract for failure to meet a critical contractual milestone. The failure of this procurement effort

[6]The Office of the Assistant Secretary for Preparedness and Response (ASPR) is the lead agency within HHS on this issue. These offices have undergone several name changes. ASPR was formerly the Office of Public Health Emergency Preparedness (OPHEP) and was renamed pursuant to Public Law 109-417, the Pandemic and All-Hazards Preparedness Act in December 2006. The name OPHEP was created administratively in August 2004. Prior to that change, the office was called the Office of the Assistant Secretary for Public Health Emergency Preparedness (ASPHEP), pursuant to Public Law 107-188, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002. Briefly, before that change, it had been called the Office of Public Health Preparedness, which was created administratively in January 2002. In July 2006, Office of Public Health Emergency Medical Countermeasures (OPHEMC), an office within ASPR, was renamed, replacing the name Office of Research and Development Coordination. ORDC was created administratively within ASPHEP in December 2002. OPHEMC has been renamed Biomedical Advanced Research and Development Authority (BARDA).

[7] The Strategic National Stockpile, formerly known as the National Pharmaceutical Stockpile, contains pharmaceuticals, vaccines, medical supplies, and medical equipment to respond to terrorist attacks and other emergencies.

[8] The Department of Homeland Security provides indemnification to the manufacturer of BioThrax for civilian use of the vaccine.

raised larger questions regarding the country's ability to develop a new anthrax vaccine and a robust and sustainable biodefense medical countermeasure industry by building a partnership between pharmaceutical and biotechnology firms and the government. The biotech industry has raised concerns whether the government can clearly define its requirements for future procurement contracts.

In our May 2006 testimony, we concluded that ASPR's procurement strategy for rPA anthrax vaccine had been very aggressive. We stated that "it is important to understand the unique issues at stake in this early phase of implementation of the biodefense strategy. The rest of the biotechnology sector will be watching to see whether the industry and the U.S. government can make this partnership work. Issues with this contract might have an effect beyond just this individual vaccine procurement. They could have an impact on how the biotechnology industry responds to government overtures in the future for the development and procurement of medical countermeasures for the many biothreat agents still to be addressed." [9]

To assist in ongoing efforts to address these concerns, you asked that we identify (1) factors that contributed to the failure of ASPR's first Project BioShield procurement effort with VaxGen for an rPA anthrax vaccine and (2) issues associated with using the licensed anthrax vaccine, BioThrax, in the Strategic National Stockpile.

Scope and Methodology

To determine what factors contributed to the failure of ASPR's procurement effort with VaxGen, we interviewed officials from HHS's components—ASPR, NIAID, the Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention (CDC). In addition, we reviewed documents these agencies provided. We visited and interviewed the officials of the two companies—Avecia and VaxGen—that NIAID contracted with to develop the new rPA anthrax vaccine. We also talked to officials of several biotech companies that are currently working on biodefense medical countermeasures. We consulted with a small group of experts in the manufacturing of biodefense vaccines to ensure that our assessments were accurate. Finally, we reviewed scientific literature on

[9] GAO, *Anthrax: Federal Agencies Have Taken Some Steps to Validate Sampling Methods and to Develop a Next Generation Anthrax Vaccine*, GAO-06-756T (Washington, D.C.: May 9, 2006) pp. 20-21.

vaccine development, manufacturing, and safety and efficacy, including regulatory requirements for licensing.

To identify issues associated with using the licensed anthrax vaccine (BioThrax) in the stockpile, we interviewed officials from ASPR, CDC, and DOD. In addition, we reviewed documents these agencies provided and analyzed data on stockpile inventory of the licensed anthrax vaccine. We visited and interviewed officials from Emergent Biosolutions, the company that manufactures the licensed anthrax vaccine. We also talked to officials of several biotech companies that are currently working on biodefense medical countermeasures to obtain their views on ways to minimize waste in the stockpile. We conducted our review from June 2007 through August 2007 in accordance with generally accepted government auditing standards.

Results in Brief

Three major factors contributed to the failure of the first Project BioShield procurement effort. First, ASPR awarded the first BioShield procurement contract to VaxGen when its product was at a very early stage of development and many critical manufacturing issues (such as stability[10] and scale-up production[11]) had not been addressed. ASPR officials told us that they felt a sense of urgency to demonstrate to the public that a new, improved vaccine was coming; they also stated that at the time of the award, they were 80 percent to 90 percent confident about VaxGen's chances of success. These officials based this confidence level on a subjective assessment and not on objective tools to determine a product's level of maturity. This award—several years before planned completion of earlier and uncompleted NIAID development contracts with VaxGen—preempted critical development work. Similarly, the requirement to deliver 75 million doses of rPA anthrax vaccine was not based on objective data. This requirement, according to the industry experts, would have

[10] Stability refers to the physical, chemical, biological, biopharmaceutical, and microbiological characteristics of a vaccine, during and up to the end of the expiration dating period and storage periods of samples under expected handling and storage conditions. The results of stability studies are used to recommend storage conditions and to establish the shelf life and/or the release specifications.

[11] Scale-up production occurs when the decision is made to take a vaccine produced in small amounts in a pilot facility and increase production to commercial levels. This is one of the most difficult, complex, time-consuming, and resource-intensive aspects of vaccine development for manufacturers.

been unrealistic for even a large pharmaceutical firm, given that the product was at an early stage of development.

Second, VaxGen took unrealistic risks in accepting the contract terms. According to VaxGen officials, they understood that their chances of success were limited. Nonetheless, they accepted the contract terms in spite of (1) the aggressive delivery time line, (2) their lack of in-house technical expertise in stability and vaccine formulation—a condition exacerbated by the attrition of key staff from the company as the contract progressed—and (3) their limited options for securing additional funding should the need arise for additional testing required to meet regulatory requirements.

Third, important FDA requirements regarding the type of data and testing required for the rPA anthrax vaccine to be eligible for use in an emergency were not known—to FDA, NIAID, ASPR, and VaxGen—at the outset of the procurement contract. They were defined later when FDA introduced new guidance on emergency use authorization (EUA). In addition, ASPR's anticipated use of the rPA anthrax vaccine was not articulated to all parties clearly enough and evolved over time. Finally, according to VaxGen, the purchase of BioThrax for the stockpile as a stopgap measure raised the requirement for using the VaxGen rPA vaccine. All of these factors created confusion over the acceptance criteria for VaxGen's product and significantly diminished VaxGen's ability to meet contract time lines.

ASPR had announced its intention to issue another request for proposal for an rPA anthrax vaccine procurement in 2007 but had not done so at the time of this report.[12] Since ASPR and other HHS components involved have not completed any formal lessons-learned exercise from the first procurement's failure, they may repeat their mistakes in the absence of a corrective plan. According to industry experts, the lack of clear requirements is a cause of concern to companies asked to partner with the government since they invest significant resources in trying to meet government needs and now question whether the government can clearly define its requirements for future procurement contracts.

We identified two issues related to using the licensed anthrax vaccine, BioThrax, in the Strategic National Stockpile: First, ASPR lacks an

[12] HHS issued a Source Sought Notice in May 2007.

effective strategy to minimize waste.[13] Vaccine valued at more than $12 million has already expired and is no longer usable. Without an effective management strategy in the future, over $100 million per year could be lost for the life of the licensed anthrax vaccine currently in the stockpile. ASPR could minimize such potential waste by developing a single inventory system for BioThrax with DOD, with rotation based on a first-in, first-out principle. DOD and ASPR officials told us that they discussed the rotation option in 2004 but identified several obstacles. Specifically, since the funding to purchase BioThrax comes from DOD and HHS appropriations, respectively, ASPR officials believe funding transfer may be a problem. However, DOD officials told us that funding is not an issue. DOD and ASPR officials told us that they have used different authorities to indemnify the manufacturer against any losses or problems that may arise from use of the vaccine.[14] Finally, since DOD vaccinates its troops at various locations around the world, there may be logistical distribution issues. DOD officials acknowledged that these issues could be resolved.

The second issue related to use of the BioThrax in the Strategic National Stockpile is ASPR's planned use of expired vaccine in violation of FDA's current rules. According to CDC, ASPR told CDC not to dispose of three lots of BioThrax vaccine that expired in 2006 and 2007. ASPR officials told us that the agency's decision was based on the possible need to use these lots of vaccines in an emergency. However, FDA rules prohibit the use of expired vaccine.[16] Thus, ASPR's planned use of expired vaccine would violate FDA's current rules and could undermine public confidence because ASPR would be unable to guarantee the potency of the vaccine.

To help ensure the success of future medical countermeasures procurement, we recommend that the Secretary of HHS direct ASPR, NIAID, FDA, and CDC to ensure that the concept of use and all critical requirements for such procurements are clearly articulated at the outset.

[13]All vaccines will eventually expire. However, when there is a large-volume user for stockpile product, not having an effective strategy to ensure stockpile products would be used constitutes waste.

[14]Indemnification was originally granted by DOD to the manufacturer in the late 1990s because of the manufacturer's inability to get commercial insurance at a reasonable price.

[16]FDA regulations do allow the extension of the expiration date of a vaccine under certain limited circumstances. See 21 C.F.R. 610.53.

To ensure public confidence and comply with FDA's current rules, we recommend that the Secretary of HHS direct ASPR to destroy the expired BioThrax vaccine in the stockpile.

To minimize waste of the BioThrax anthrax vaccine in the stockpile, we recommend that the Secretaries of HHS and DOD develop a single integrated inventory system for the licensed anthrax vaccine, with rotation based on a first-in, first-out principle.

HHS and DOD provided written comments on a draft of this report and generally concurred with our recommendations. In addition, with regard to our recommendation on integrated stockpile, they identified funding and legal challenges to developing an integrated inventory system for BioThrax in the stockpile, which may require legislative action. Although HHS and DOD use different authorities to address BioThrax liability and funding issues, both authorities could apply to either DOD or HHS; consequently, indemnity does not appear to be an insurmountable obstacle for future procurements.

Background

Following the anthrax attacks of 2001, the federal government determined that it would need additional medical countermeasures (for example, pharmaceuticals, vaccines, diagnostics, and other treatments) to respond to an attack involving chemical, biological, radiological, or nuclear (CBRN) agents.

Project BioShield

The Project BioShield Act of 2004 (Public Law 108-276) was designed to encourage private companies to develop civilian medical countermeasures by guaranteeing a market for successfully developed countermeasures.

The Project BioShield Act (1) relaxes some procedures for bioterrorism-related procurement, hiring, and research grant awarding; (2) allows for the emergency use of countermeasures not approved by FDA; and (3) authorizes 10-year funding (available through fiscal year 2013) to encourage the development and production of new countermeasures for CBRN agents. The act also authorizes HHS to procure these countermeasures for the Strategic National Stockpile.

Project BioShield is a procurement program that allows the government to enter into contracts to procure countermeasures while they still are in development, up to 8 years before product licensure is expected. Under this program, the government agrees to buy a certain quantity of

successfully developed countermeasures for the Strategic National Stockpile at a specified price once the countermeasure meets specific requirements. The government pays the agreed-upon amount only after these requirements are met and the product is delivered to the Strategic National Stockpile. If the product does not meet the requirements within the specified time frame, the contract can be terminated without any payment to the contractor. Thus, while Project BioShield reduces the producer's market risk—that is, the possibility that no customer will buy the successfully developed product—it does not reduce the development risk to the producer—that is, the possibility that the countermeasure will fail during development.

In December 2006, the Pandemic and All-Hazards Preparedness Act (Public Law 109-417) modified the Project BioShield Act to allow for milestone-based payments before countermeasure delivery for up to half of the total award. Within HHS, the Biomedical Advanced Research and Development Authority (BARDA) has the authority to directly fund the advanced development of countermeasures that are not eligible for Project BioShield contracts.

Agency Roles in Developing, Procuring, and Stockpiling Medical Countermeasures

Project BioShield procurement involves actions by the Department of Homeland Security (DHS), HHS (including ASPR, NIAID, FDA, and CDC), and an interagency working group.

DHS's Role

The first step in the Project BioShield acquisition process is to determine whether a particular CBRN agent poses a material threat to national security. DHS performs this analysis, which is generally referred to as a population threat assessment (PTA). On the basis of this assessment, the DHS Secretary determines whether that agent poses a material threat to national security. The Project BioShield Act of 2004 requires such a written PTA for procurements using BioShield funds and authorities. This declaration neither addresses the relative risk posed by an agent nor determines the priority for acquisition, which is solely determined by ASPR. Furthermore, the issuance of a PTA does not guarantee that the government will pursue countermeasures against that agent. DHS has issued PTAs for 13 agents, including the biological agents that cause anthrax; multi-drug-resistant anthrax; botulism; glanders; meliodosis; tularemia; typhus; smallpox; plague; and the hemorrhagic fevers Ebola, Marburg, and Junin.

HHS's Role

Various offices within HHS (ASPR, NIAID, FDA, and CDC) fund the development research, procurement, and storage of medical countermeasures, including vaccines, for the Strategic National Stockpile.

ASPR's role: ASPR is responsible for the entire Project BioShield contracting process, including issuing requests for information and requests for proposals, awarding contracts, managing awarded contracts, and determining whether contractors have met the minimum requirements for payment. ASPR maintains a Web site detailing all Project BioShield solicitations and awards.

ASPR has the primary responsibility for engaging with the industry and awarding contracts for large-scale manufacturing of licensable products, including vaccines, for delivery into the Strategic National Stockpile. With authorities recently granted, BARDA will be able to use a variety of funding mechanisms to support the advanced development of medical countermeasures and to award up to 50 percent of the contract as milestone payments before purchased products are delivered.

NIAID's role: NIAID is the lead agency in NIH for early candidate research and development of medical countermeasures for biodefense. NIAID issues grants and awards contracts for research on medical countermeasures exploration and early development, but it has no responsibility for taking research forward into marketable products.

FDA's role: Through its Center for Biologics Evaluation and Research (CBER), FDA licenses many biological products, including vaccines, and the facilities that produce them. Manufacturers are required to comply with current Good Manufacturing Practices regulations, which regulate personnel, buildings, equipment, production controls, records, and other aspects of the vaccine manufacturing process. FDA has also established the Office of Counterterrorism Policy and Planning in the Office of the Commissioner, which issued the draft *Guidance on the Emergency Use Authorization of Medical Products* in June 2005. This EUA guidance describes in general terms the data that should be submitted to FDA, when available, for unapproved products or unapproved uses of approved products that HHS or another entity wishes FDA to consider for use in the event of a declared emergency. The final EUA guidance was issued in July 2007.

CDC's role: Since 1999, CDC has had the major responsibility for managing and deploying the medical countermeasures stored in the Strategic National Stockpile. The Omnibus Consolidated and Emergency

Supplemental Appropriations Act (Public Law 105-277) first provided the stockpile with a fund specially appropriated for purchases. Since then, CDC has maintained this civilian repository of medical countermeasures, such as antibiotics and vaccines.

DOD's Role

DOD is not currently a part of Project BioShield. Beginning in 1998, DOD had a program to vaccinate all military service members with BioThrax. DOD's program prevaccinates personnel for deployment to Iraq, Afghanistan, and the Korean peninsula with BioThrax. For other deployments, this vaccination is voluntary. DOD also has a program to order, stockpile, and use the licensed anthrax vaccine. DOD estimates its needs for BioThrax doses and bases its purchases on that estimate.

Interagency Working Group

Multiple agencies, including HHS and DHS, provide input on priority-setting and requirements activities. For BioShield purchases, the Secretaries of HHS and DHS prepare a joint recommendation, which requires presidential approval before HHS enters into a procurement contract. The Secretary of HHS currently coordinates the interagency process; the National Science and Technology Council previously handled the coordination.

The Nature of Anthrax and the Anthrax Vaccine

The Nature of Anthrax

Anthrax is a rare but serious acute infectious disease that must be treated quickly with antibiotics. Anthrax is caused by the spore-forming bacterium *Bacillus anthracis*. It occurs most commonly in herbivores in agricultural regions that have less effective veterinary and public health programs. Anthrax can infect humans who have been exposed to infected animals or products from infected animals such as hide, hair, or meat. Human anthrax occurs rarely in the United States from these natural causes. However, the anthrax exposures in September and October 2001 through mail intentionally contaminated with anthrax spores resulted in illness in 22 persons and the death of 5.

The Licensed Vaccine for Anthrax

An FDA-licensed anthrax vaccine, BioThrax, has been available since 1970. The vaccine has been recommended for laboratory workers who are involved in the production of cultures of anthrax or who risk repeated exposure to anthrax by, for example, conducting confirmatory or environmental testing for anthrax in the U.S. Laboratory Response Network for Bioterrorism laboratories; persons who may be required to make repeated entries into known *Bacillus anthracis* contaminated areas

after a terrorist attack, such as remediation workers; and persons who work with imported animal hides, furs, or similar materials, if the industry standards and restrictions that help to control the disease are insufficient to prevent exposure to anthrax spores.

Preventive anthrax vaccine is not recommended for civilians who do not have an occupational risk. However, in 1998, DOD began a mandatory program to administer the vaccine to all military personnel for protection against possible exposure to anthrax-based biological weapons. By late 2001, roughly 2 million doses of the vaccine had been administered, most of them to U.S. military personnel. As the vaccination program proceeded, some military personnel raised concerns about the safety and efficacy of the vaccine.[16]

The BioShield program stockpiled BioThrax for the Strategic National Stockpile for postexposure use in the event of a large number of U.S. civilians being exposed to anthrax. ASPR officials characterized the acquisition of the licensed vaccine as a "stopgap" measure as they also have been engaged in the development and purchase of a new rPA anthrax vaccine. ASPR had already acquired 10 million doses of BioThrax from Emergent BioSolutions by 2006 and recently purchased an additional 10 million doses.

The Vaccine Development Process

Vaccine research and development leading to FDA approval for use is a long and complex process. It may take 15 years and, according to FDA, cost from $500 million to $1.2 billion and require specialized expertise.

Vaccines are complex biological products given to a person or animal to stimulate an immune reaction the body can "remember" if it is exposed to the same pathogen later.[17] In contrast to most drugs, they have no simple chemical characterization. As a result, evaluating them involves measuring their effects on living organisms, and their quality can be guaranteed only through a combination of in-process tests, end-product tests, and strict controls of the entire manufacturing process.

[16]GAO, *Anthrax Vaccine: GAO's Survey of Guard and Reserve Pilots and Aircrew*, GAO-02-115 (Washington, D.C.: Sept. 20, 2002).

[17]Biological products are typically derived from living sources, such as humans, animals, bacteria, and viruses.

Vaccines are highly perishable and typically require cold storage to retain potency. Even if they are stored at the recommended temperature, most vaccines have expiration dates beyond which they are considered outdated and should not be used. A great deal of attention is directed to using the vaccine before its expiration date. For example, a recent CDC manual advises users: "Check expiration date on container" and "rotate stock so that the earliest dated material is used first." After the storage vial has been opened, the vaccine begins to deteriorate quickly in many cases, often necessitating the opened or reconstituted vaccine to be used within minutes to hours or discarded."[18] Since human challenge studies cannot be conducted for CBRN medical countermeasures, FDA requires animal efficacy data instead.

The FDA process for approving a biologic for use in the United States begins with an investigational new drug (IND) application.[19] A sponsor that has developed a candidate vaccine applies to start the FDA oversight process of formal studies, regulated by CBER within FDA. Phase 1 trials involve safety and immunogenicity studies in a small number of healthy volunteer subjects.[20] phase 2 and phase 3 trials gather evidence of the vaccine's effectiveness in ever larger groups of subjects, providing the documentation of effectiveness and important additional safety data required for licensing. If the data raise safety or effectiveness concerns at any stage of clinical or animal studies, FDA may request additional information or halt ongoing clinical studies.[21]

In vaccine development, clinical trials typically last up to 6 years. After they have been successfully completed, the sponsor applies for FDA's approval to market the product. FDA's review of the license application includes review of the manufacturing facility and process. According to FDA, this process is typically completed within 10 months for a standard

[18]Centers for Disease Control and Prevention, *Vaccine Management: Recommendations for Storage and Handling of Selected Biologicals*, (Atlanta, Georgia: January 2007).

[19]FDA will permit an investigational drug to be used under a treatment IND if there is preliminary evidence of drug efficacy and the drug is intended to treat a serious or life-threatening disease or if there is no comparable alternative drug or therapy available to treat that stage of the disease in the intended patient population.

[20]"Immunogenicity" refers to the ability of a vaccine to stimulate a protective immune response.

[21]When FDA decides to halt drug development activity, it issues a "clinical hold," which begins a series of review activities.

review and 6 months for a priority review. According to industry sources, the challenge in scaling up vaccine production from a research laboratory to a large manufacturing environment while still maintaining quality requires much skill, sophisticated facilities, and a great deal of experience.

Several Factors Contributed to the Failure of ASPR's First Project BioShield Effort for the Production of an rPA Anthrax Vaccine

Three major factors contributed to the failure of the first Project BioShield procurement effort. First, ASPR awarded the first BioShield procurement contract to VaxGen when its product was at a very early stage of development and many critical manufacturing issues had not been addressed. Second, VaxGen took unrealistic risks in accepting the contract terms. Third, key parties did not clearly articulate and understand critical requirements at the outset.

HHS Awarded the Procurement Contract Before Development Had Reached an Appropriate Level of Maturity

ASPR's decision to launch the VaxGen procurement contract for the rPA anthrax vaccine at an early stage of development, combined with the delivery requirement for 25 million doses within 2 years,[22] did not take the complexity of vaccine development into consideration and was overly aggressive. Citing the urgency involved, ASPR awarded the procurement contract to VaxGen several years before the planned completion of earlier and uncompleted NIAID development contracts with VaxGen and thus preempted critical development work. (For a time line of events for the first rPA anthrax vaccine development and procurement effort, see appendix I).

In response to the anthrax attacks of 2001, NIAID was assigned responsibility for developing candidate vaccines leading up to licensure, purchase, and storage in the stockpile. NIAID envisioned a strategy of minimizing risk by awarding contracts to multiple companies to help ensure that at least one development effort would be successful. NIAID's strategy was appropriate since failure is not uncommon in vaccine development. Toward this end, NIAID designed a sequence of two contracts—one to follow the other—to advance pilot lots of rPA anthrax vaccine through early characterization work, phase 1 and phase 2 clinical trials, accelerated and real-time (long-term) stability testing, and tasks to evaluate the contractor's ability to manufacture the vaccine in large

[22] The contract called for 75 million doses overall, but only 25 million were required within 2 years of award.

quantities according to current Good Manufacturing Practices (cGMP).[23] Additionally, these contracts were cost reimbursable, an appropriate contracting mechanism when uncertainties involved in contract performance do not permit cost to be estimated with sufficient accuracy to use a fixed-price contract. VaxGen was one of the awardees. The other awardee was Avecia, Ltd., of Manchester, United Kingdom. NIAID's development effort with Avecia to prepare a candidate rPA anthrax vaccine for potential purchase for the stockpile is ongoing.

VaxGen's first development contract, awarded in September 2002, had three major requirements: characterize the chemical composition of the pilot lot; conduct phase 1 clinical trials to determine the basic safety profile of the vaccine; and produce a feasibility plan to manufacture, formulate, fill and finish, test, and deliver up to 25 million doses of cGMP vaccine. The initial period of performance for this first contract was 15 months, to be completed in September 2003. However, NIAID twice extended the period of performance to accommodate problems, including stability testing. The final completion date of the contract was December 2006.

The second development contract was awarded to VaxGen in September 2003 to continue development of its vaccine. This contract covered 36 months and was scheduled to end in October 2006. Three of the major requirements were to (1) manufacture, formulate, fill, finish, release, and deliver 3 million to 5 million doses of vaccine from at least three different lots that met cGMP requirements; (2) develop, implement, and execute accelerated and real-time stability testing programs to ensure the safety, sterility, potency, and integrity of the vaccine; and (3) conduct phase 2 clinical trials.

This second development contract covered especially critical steps in the development cycle. For example, only during the phase 2 trials is the vaccine given to a large enough number of human subjects to further project its safety. Under the contract, phase 2 clinical trials, which were to determine the optimum dose and dosing regimen, were expected to take 2 years to complete.[24] This second contract also covered accelerated and

[23] Pharmaceutical and biotech firms follow the cGMP to ensure that the products produced meet specific requirements for identity, strength, quality, and purity. FDA regulates these industries to ensure cGMPs are being followed.

[24] Industry experts told us that even this time scale is very optimistic.

real-time stability testing programs to ensure the safety, sterility, potency, and integrity of the vaccine. Vaccines, especially those intended to be stockpiled, need to exhibit the necessary stability to ensure they will remain safe and potent for the required storage period.

In early 2004, VaxGen's product entered particularly critical stages of development and scale-up production. According to industry officials we talked to, the challenge in scaling up vaccine production from a research pilot lot to a large manufacturing environment while still maintaining quality is not trivial. It requires a great deal of skill, sophisticated facilities, and experience. The officials also stated that work on the vaccine at this point would have been expected to take multiple years to complete, during which time the contractor would work back and forth with FDA in evaluating, testing, and then reworking both its product and manufacturing capability against criteria for eventual licensure.

However, on November 4, 2004, a little more than a year after NIAID awarded VaxGen its second development contract, ASPR awarded the procurement contract to VaxGen for 75 million doses of its rPA anthrax vaccine. At that time, VaxGen was still at least a year away from completing the Phase 2 clinical trials under the second NIAID development contract. Moreover, VaxGen was still finishing up work on the original stability testing required under the first development contract.

ASPR officials at the time of the award had no objective criteria, such as Technology Readiness Levels (TRL), to assess product maturity.[25] They were, however, optimistic the procurement contract would be successful. One official described its chances of success at 80 percent to 90 percent. However, a key official at VaxGen told us at the same time that VaxGen estimated the chances of success at 10 percent to 15 percent. ASPR now estimates that prior to award, the rPA vaccine was at a TRL rating of 8. According to industry experts, a candidate vaccine product at such a level

[25]TRLs have been used by federal agencies (DOD, the National Aeronautics and Space Administration, and others) to assess the maturity of evolving technologies prior to incorporating that technology into a system or subsystem. The primary purpose of using TRLs is to help management in making decisions concerning the development and transitioning of technology.

is generally expected to be 5-8 years away from completion and to have only a 30 percent chance of development into a successful vaccine.[26]

When we asked ASPR officials why they awarded the procurement contract when they did, they pointed to a sense of urgency at that time and the difficulties in deciding when to launch procurement contracts. However, November 2004 was 3 years after the anthrax attacks in 2001, and while the sense of urgency was still important, it could have been tempered with realistic expectations. According to industry experts, preempting the development contract 2 years before completing work—almost half its scheduled milestones—was questionable, especially for vaccine development work, which is known to be susceptible to technical issues even in late stages of development. NIAID officials also told us that, in their opinions, it was too early for a BioShield purchase. At a minimum, the time extensions for NIAID's first development contract with VaxGen to accommodate stability testing should have indicated to ASPR that development on its candidate vaccine was far from complete.

After ASPR awarded VaxGen the procurement contract, NIAID canceled several milestones under its development contract with VaxGen to free up funds for earlier milestones that VaxGen was having trouble meeting. However, this undermined VaxGen's ability to refine product development up to the level needed to ensure delivery within the 2-year time frame required under the procurement contract.

VaxGen Took an Unrealistic Risk in Accepting the Procurement Contract, Knowing Its Own Technical and Financial Limitations

VaxGen officials told us that they understood their chances for success were limited and that the contract terms posed significant risks. These risks arose from aggressive time lines, VaxGen's limitations with regard to in-house technical expertise in stability and vaccine formulation—a condition exacerbated by the attrition of key staff from the company as the contract progressed—and its limited options for securing additional funding should the need arise.

Industry experts told us that a 2-year time line to deliver 75 million filled and finished doses of a vaccine from a starting point just after phase 1 trials is a near-impossible task for any company. VaxGen officials told us that at the time of the procurement award they knew the probability of

[26]In December 2006, at the time the contract was terminated, according to ASPR officials, the TRL level was still at 8.

success was very low, but they were counting on ASPR's willingness to be flexible with the contract time line and work with them to achieve success. In fact, in May 2006, ASPR did extend the contract deadlines to initiate delivery to the stockpile an additional 2 years. However, on November 3, 2006, FDA imposed a clinical hold on VaxGen's forthcoming phase 2 trial after determining that data submitted by VaxGen were insufficient to ensure that the product would be stable enough to resume clinical testing.[27] By that time, ASPR had lost faith in VaxGen's technical ability to solve its stability problems in any reasonable time frame. When VaxGen failed to meet a critical performance milestone of initiating the next clinical trial, ASPR terminated the contract.

According to VaxGen's officials, throughout the two development contracts and the Project BioShield procurement contract, VaxGen's staff peaked at only 120, and the company was consistently unable to marshal sufficient technical expertise. While it is not known how a larger pharmaceutical company might have fared under similar time constraints, we believe more established pharmaceutical companies have staff and resources better able to handle the inevitable problems that arise in vaccine development and licensure efforts. For example, according to industry experts, a large firm might be able to leverage an entire internal department to reformulate a vaccine or pursue solutions to a stability issue, while a smaller biotechnology company like VaxGen would likely be unable to use more than a few full-time scientists. In such situations, the smaller company might have to contract out for the necessary support, provided it can be found within a suitable time frame.

External expertise that might have helped VaxGen better understand its stability issue was never applied. At one point during the development contracts, NIAID—realizing VaxGen had a stability problem with its product—convened a panel of technical experts in Washington, D.C.

[27]A clinical hold is the mechanism that FDA uses to stop a study when it finds that the study should not proceed because of an identified deficiency. When the deficiency is identified in FDA's initial review of the IND application, FDA contacts the sponsor within 30 days of submission of the IND. FDA may also impose a clinical hold on an ongoing study based on its review of newly submitted protocols and amendments, safety reports, or other information. When a clinical hold is issued, a sponsor must address the issue before the hold is removed. FDA has issued a regulation that identifies the deficiencies that provide the basis for a clinical hold. A clinical hold may be imposed, as in this case, because a plan or a protocol for the investigation is clearly deficient in design to meet its stated objectives. All clinical holds are reviewed by FDA management to ensure consistency and quality in FDA's clinical hold decisions.

NIAID officials told us that at the time of the panel meeting, they offered to fund technical experts to work with the company, but VaxGen opted not to accept the offer. Conversely, VaxGen officials reported to us that at the time NIAID convened the panel of experts, NIAID declined to fund the work recommended by the expert panel.

The lack of available technical expertise was exacerbated when key staff at the company began leaving. A senior VaxGen official described the attrition problem as "massive." Of special significance, VaxGen's Senior Vice President for Research and Development and Chief Scientific Officer left during critical phase 2 trials. An official at VaxGen described this person's role as key in both development of the assays and reformulation of the vaccine.[28]

Finally, VaxGen accepted the procurement contract terms even though the financial constraints imposed by the BioShield Act limited its options for securing any additional funding needed. In accordance with this act, payment was conditional on delivery of a product to the stockpile, and little provision could be made, contractually, to support any unanticipated or additional development needed—for example, to work through issues of stability or reformulation.[29] Both problems are frequently encountered throughout the developmental life of a vaccine. This meant that the contractor would pay for any development work needed on the vaccine. VaxGen, as a small biotechnology company, had limited internal financial resources and was dependent on being able to attract investor capital for any major influx of funds.

In such a firm, fixed-price contractual arrangement, the contractor assumes most of the risk because the price is not subject to any adjustment based on the contractor's cost experience. Thus, even if the contractor costs go up, the delivery price does not. We believe these contracts are appropriate in situations where there are no performance uncertainties or the uncertainties can be identified and reasonable estimates of their cost impact can be made, but this was not the situation in the VaxGen procurement contract. VaxGen had to be willing to accept

[28]An assay is a laboratory test or procedure carried out in order to measure the amount of a substance present in a product and/or to measure its activity.

[29]Under Project BioShield, advance payments of up to 10 percent of the contract value could be made if the HHS Secretary deemed it necessary for the success of the program. ASPR officials told us that VaxGen did request such a payment, but ASPR did not grant it.

the firm, fixed-price contract and assume the risks involved. VaxGen did so even though it understood that development on its rPA vaccine was far from complete when the procurement contract was awarded and that the contract posed significant inherent risks.

Key Parties Did Not Clearly Articulate and Understand Critical Requirements

Important requirements regarding the data and testing required for the rPA anthrax vaccine to be eligible for use in an emergency were not known at the outset of the procurement contract. They were defined in 2005 when FDA introduced new general guidance on EUA. In addition, ASPR's anticipated use of the rPA anthrax vaccine was not articulated to all parties clearly enough and evolved over time. Finally, purchase of BioThrax raised the requirement for use of the VaxGen rPA vaccine. All of these factors created confusion over the acceptance criteria for VaxGen's product and significantly diminished VaxGen's ability to meet contract time lines.

Guidance on Emergency Use Authorization Appeared Midcontract and Created Confusion

Criteria for product acceptance need to be clearly articulated and understood by all parties before committing to a major procurement. Terms of art that leave critical requirements unclear are problematic in contract language. After VaxGen received its procurement contract, draft guidance was issued that addressed the eventual use of any unlicensed product in the stockpile. This created confusion over the criteria against which VaxGen's product would be evaluated, strained relations between the company and the government, and caused a considerable amount of turmoil within the company as it scrambled for additional resources to cover unplanned testing.

In June 2005, FDA issued draft EUA guidance, which described for the first time the general criteria that FDA would use to determine the suitability of a product for use in an emergency.[30] This was 7 months after the award of the procurement contract to VaxGen and 14 months after the due date for bids on that contract.

Since the request for proposal for the procurement contract was issued and the award itself was made before the EUA guidance was issued,

[30]FDA is ultimately responsible for determining if available products (unapproved products or approved products for unapproved usage) in the stockpile can be used in an emergency. The data FDA needs to determine whether a product can be used in an emergency are critical to manufacturers to adequately plan and estimate the time and resources required for generating the data.

neither could take the EUA requirements into consideration. The procurement contract wording stated that in an emergency, the rPA anthrax vaccine was to be "administered under a 'Contingency Use' Investigational New Drug (IND) protocol" and that vaccine acceptance into the stockpile is dependent on the accumulation and submission of the appropriate data to support the "use of the product (under IND) in a postexposure situation." FDA officials told us they do not use the phrase "contingency use" under IND protocols.

When we asked ASPR officials about the requirements for use defined in the contract, they said that the contract specifications were consistent with the statute and the needs of the stockpile. They said their contract used "a term of art" for BioShield products. That is, the contractor had to deliver a "usable product" under FDA guidelines. The product could be delivered to the stockpile only if sufficient data were available to support emergency use. ASPR officials told us that FDA would define "sufficient data" and the testing hurdles a product needed to overcome to be considered a "usable product."

While VaxGen and FDA had monthly communication, according to FDA, data requirements for emergency use were not discussed until December 2005, when VaxGen asked FDA what data would be needed for emergency use. In January 2006, FDA informed VaxGen, under its recently issued draft EUA guidance, of the data FDA would require from VaxGen for its product to be eligible for consideration for use in an emergency. The draft guidance described in general FDA's current thinking concerning what FDA considered sufficient data and the testing needed for a product to be considered for authorization in certain emergencies.

Because the EUA guidance is intended to create a more feasible protocol for using an unapproved product in a mass emergency than the term "contingency use under an IND protocol" that ASPR used in the procurement contract, it may require more stringent data for safety and efficacy. Under an IND protocol, written, informed consent must be received before administering the vaccine to any person, and reporting requirements identical to those in a human clinical trial are required.[31] The EUA guidance—as directed by the BioShield law—eased both informed consent and reporting requirements. This makes sense in terms of the logistics of administering vaccine to millions of people in the large-scale,

[31]It also requires an approval from the Institutional Review Board.

postexposure scenarios envisioned. Because EUA guidance defines a less stringent requirement for the government to use the product, it correspondingly may require more testing and clinical trial work than was anticipated under contingency use.

Several of the agencies and companies involved in BioShield-related work have told us the EUA guidance appears to require a product to be further along the development path to licensure than the previous contingency use protocols would indicate. VaxGen officials told us that if the draft EUA guidance was the measure of success, then VaxGen estimated significant additional resources would be needed to complete testing to accommodate the expectations under this new guidance. NIAID told us that the EUA guidance described a product considerably further along the path to licensure (85 percent to 90 percent) than it had assumed for a Project BioShield medical countermeasure (30 percent) when it initially awarded the development contracts.

The Concept of Use for the rPA Vaccine Was Not Clearly Articulated to All Parties

FDA considers a vaccine's concept of use important information to gauge the data and testing needed to ensure the product's safety and efficacy. Under the EUA statute, FDA must determine on the basis of the specific facts presented whether it is necessary and appropriate to authorize use of a specific product in an emergency. According to FDA, data and testing requirements to support a product's use in an emergency context may vary depending on many factors, including the number of people to whom the product is expected to be administered. The current use of an unlicensed product involves the assessment of potential risks and benefits from use of an unapproved drug in a very small number of people who are in a potentially life-threatening situation. In such situations, because of the very significant potential for benefit, safety and efficacy data needed to make the risk benefit assessment might be lower than in an emergency situation where an unlicensed vaccine might be offered to millions of healthy people. This distinction is critical for any manufacturer of a product intended for use in such scenarios—it defines the level of data and testing required. Product development plans and schedules rest on these requirements.

In late 2005, as VaxGen was preparing for the second phase 2 trial and well into its period of performance under the procurement contract, its officials participated in meetings, primarily with FDA but also with ASPR and NIAID representatives, to receive FDA comments on its product development plans and responses to specific requests for regulatory advice. VaxGen needed to have a clear understanding of FDA's data and testing requirements for the rPA vaccine for the upcoming phase 2 trial to

be able to plan for and implement the necessary clinical and nonclinical work to generate that data. Without it, VaxGen did not have adequate means to determine how far along it was toward meeting FDA's requirements.

However, in these meetings, it became clear that FDA and the other parties had different expectations for the next phase 2 trial. FDA officials concluded from the discussion that VaxGen, ASPR, and CDC anticipated the next phase 2 trial to produce meaningful safety and efficacy data to support use of the vaccine in a contingency protocol under IND. However, FDA officials stated that this was a new idea to the agency.[32] From FDA's perspective, the purpose of phase 2 trials was to place the product and sponsor (VaxGen) in the best position possible to design and conduct a pivotal phase 3 trial in support of licensure.[33] The lack of a definition of concept of use caused FDA to delay replying to VaxGen until it could confer with ASPR and CDC to clarify this issue. Thus, we conclude that neither VaxGen nor FDA understood the rPA anthrax vaccine concept of use until this meeting.

Purchase of BioThrax for the Stockpile Raised Requirements for Use of rPA Vaccine

The introduction of BioThrax into the stockpile undermined the criticality of getting an rPA vaccine into the stockpile and, at least in VaxGen's opinion, forced FDA to hold it to a higher standard that the company had neither the plans nor the resources to achieve. ASPR purchased 10 million doses of BioThrax in 2005 and 2006 as a stopgap measure for post-exposure situations. After discussions between VaxGen and FDA, VaxGen concluded that this raised the bar for its rPA vaccine. Although BioThrax is currently licensed for use in pre-exposure, and not postexposure, scenarios, the draft EUA guidance states that FDA will evaluate each EUA candidate's safety and efficacy profile. The EUA guidance states that FDA will "authorize" an unapproved or unlicensed product—such as the rPA anthrax vaccine candidate—only if "there is no adequate, approved and available alternative."[34] According to the minutes of the meeting between FDA and VaxGen, in January 2006, FDA reported that the unlicensed rPA anthrax vaccine would be used in an emergency after the stockpiled BioThrax, that is, "when all of the currently licensed [BioThrax] had been

[32] See FDA's minutes of the December 2005 meeting with VaxGen.

[33] In commenting on the draft report, FDA indicated that the purpose of the phase 2 trial is to collect additional safety and, when possible, efficacy data, as well as to determine the dose, route, and schedule for administration.

[34] This is a requirement of the BioShield law.

deployed." This diminished the likelihood of a scenario where the rPA vaccine might be expected to be used out of the stockpile.

ASPR Lacks an Effective Strategy to Minimize Waste in the Strategic National Stockpile and Plans to Use Expired Anthrax Vaccine

We identified two issues related to using the BioThrax in the Strategic National Stockpile. First, ASPR lacks an effective strategy to minimize waste. As a consequence, based on current inventory, over $100 million is likely to be wasted annually, beginning in 2008. Three lots of BioThrax vaccine in the stockpile have already expired,[35] resulting in losses of over $12 million. According to the data provided by CDC, 28 lots of BioThrax vaccine will expire in calendar year 2008. ASPR paid approximately $123 million for these lots. For calendar year 2009, 25 additional lots—valued at about $106 million—will reach their expiration dates. ASPR could minimize the potential waste of these lots by developing a single inventory system with DOD—which uses large quantities of the BioThrax vaccine—with rotation based on a first-in, first-out principle.[36]

Because DOD is a high-volume user of the BioThrax vaccine, ASPR could arrange for DOD to draw vaccine from lots long before their expiration dates. These lots could then be replenished with fresh vaccine from the manufacturer. DOD, ASPR, industry experts, and Emergent BioSolutions (the manufacturer of BioThrax) agree that rotation on a first-in, first-out basis would minimize waste.

DOD and ASPR officials told us that they discussed a rotation option in 2004 but identified several obstacles. In July 2007, DOD officials believed they might not be able to transfer funds to ASPR if DOD purchases BioThrax from ASPR. However, in response to our draft report, DOD informed us that funding is not an issue. However, ASPR continues to believe that transfer of funds would be a problem. DOD stated smallpox vaccine (Dryvax) procurement from HHS is executed under such an arrangement. Further, DOD and ASPR officials told us that they use different authorities to indemnify the manufacturer against any losses or problems that may arise from use of the vaccine. According to DOD, this area may require legislative action to ensure that vaccine purchased by ASPR can be used in the DOD immunization program. Finally, since DOD

[35]These lots contained 167,990, 168,130, and 183,990 doses of vaccine respectively.

[36]In 1999, CDC created a stockpile of licensed medical products. CDC officials told us that CDC had a strategy to rotate products in that stockpile on a first-in, first-out principle with other high-volume users, such as the Department of Veterans Affairs.

vaccinates its troops at various locations around the world, there may be logistical distribution issues. A DOD official acknowledged that these issues could be resolved.

Second, ASPR plans to use expired vaccine from the stockpile, which violates FDA's current rules.[37] Data provided by CDC indicated that two lots of BioThrax vaccine expired in December 2006 and one in January 2007. CDC officials stated that their policy is to dispose of expired lots since they cannot be used and continuing storage results in administrative costs. FDA rules prohibit the use of expired vaccine.

Nevertheless, according to CDC officials, ASPR told CDC not to dispose of the three lots of expired BioThrax vaccine. ASPR officials told us that ASPR's decision was based on the possible need to use these lots in an emergency. ASPR's planned use of expired vaccine would violate FDA's current rules and could undermine public confidence because ASPR would be unable to guarantee the potency of the vaccine.

Conclusions

The termination of the first major procurement contract for rPA anthrax vaccine raised important questions regarding the approach taken to develop a new anthrax vaccine and a robust and sustainable biodefense medical countermeasure industry by bringing pharmaceutical and biotechnology firms to form a partnership with the government. With the termination of the contract, the government does not have a new, improved anthrax vaccine for the public, and the rest of the biotech industry is now questioning whether the government can clearly define its requirements for future procurement contracts.

Since HHS components have not completed a formal lessons-learned exercise after terminating VaxGen's development and procurement contracts, these components may repeat the same mistakes in the future in the absence of a corrective plan. Articulating concepts of use and all critical requirements clearly at the outset for all future medical countermeasures would help the HHS components involved in the anthrax procurement process to avoid past mistakes. If this is not done, the government risks the future interest and participation of the biotechnology industry.

[37]See footnote 15.

Given that the amount of money appropriated to procure medical countermeasures for the stockpile is limited, it is imperative that ASPR develop effective strategies to minimize waste. Since vaccines are perishable commodities that should not be used after their expiration dates, finding other users for the stockpile products before they expire would minimize waste. Because DOD requires a large amount of the BioThrax vaccine on an annual basis, it could use a significant portion of BioThrax in the stockpile before it expires.

Recommendations for Executive Action

To avoid repeating the mistakes that led to the failure of the first rPA procurement effort, we recommend that the Secretary of HHS direct ASPR, NIAID, FDA, and CDC to ensure that the concept of use and all critical requirements are clearly articulated at the outset for any future medical countermeasure procurement.

To ensure public confidence and comply with FDA's current rules, we recommend that the Secretary of HHS direct ASPR to destroy the expired BioThrax vaccine in the stockpile.

To minimize waste of the BioThrax vaccine in the stockpile, we recommend that the Secretaries of HHS and DOD develop a single integrated inventory system for the licensed anthrax vaccine, with rotation based on a first-in, first-out principle.

Agency Comments and Our Evaluation

We provided a draft of this report to the Department of Health and Human Services and the Department of Defense for review and comment. HHS and DOD provided written comments on our draft, which are reprinted in appendixes II and III, respectively. Both agencies also provided technical comments, which we have addressed in the report text as appropriate.

HHS and DOD generally concurred with our recommendations. However, with regard to our recommendation on an integrated stockpile, they identified funding and legal challenges to developing an integrated inventory system for BioThrax in the stockpile, which may require legislative action. Although HHS and DOD use different authorities to address BioThrax liability and funding issues, both authorities could apply to either DOD or HHS; consequently, indemnity does not appear to be an insurmountable obstacle for future procurements.

HHS also disagreed with a number of our specific findings. We have addressed these areas of disagreement in detailed comments in appendix II.

We are sending copies of this report the Secretary of the Department of Defense and the Secretary of the Department of Health and Human Services. We are also sending a copy of this report to other interested congressional members and committees. In addition, the report will be available at no charge on GAO's Web site at http://www.gao.gov.

If you or your staffs have any questions about this report or would like additional information, please contact me at (202) 512-6412 or rhodesk@gao.gov, or Sushil K. Sharma, Ph.D., Dr.PH, at (202) 512-3460 or sharmas@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report.

GAO staff who made major contributions to this report included Noah Bleicher, William Carrigg, Barbara Chapman, Crystal Jones, Jeff McDermott, and Linda Sellevaag.

Keith Rhodes, Chief Technologist
Center for Technology and Engineering
Applied Research and Methods

Appendix I: Time Line of Events in the First rPA Anthrax Vaccine Development and Procurement Effort

Year	Month	Event
2001	Oct.–Nov.	Letters contaminated with anthrax spores sent through U.S. Postal Service, resulting in death of five persons.
2002	April	National Institute of Allergy and Infectious Diseases (NIAID) issues first rPA anthrax vaccine request for proposal (RFP).
	Sept.	NIAID awards rPA contracts to Avecia and VaxGen for first RFP.
2003	May	NIAID issues second rPA anthrax vaccine RFP.
	Aug.	Health and Human Services (HHS) issues request for information (RFI) for large-scale manufacturing capabilities for next generation anthrax vaccines.
	Oct.	NIAID awards Avecia and VaxGen contracts for second rPA RFP.
2004	Mar.	HHS issues Strategic National Stockpile rPA anthrax vaccine RFP.
	July	President George W. Bush signs Project BioShield into law.
	Nov.	HHS awards Strategic National Stockpile contract to VaxGen for rPA anthrax vaccine procurement.
2005	May	HHS awards Emergent Strategic National Stockpile contract for 5 million doses of BioThrax Vaccine.
	June	Food and Drug Administration (FDA) issues draft *Guidance for Emergency Use Authorization of Medical Products.*
2006	June	NIAID issues RFP for third-generation anthrax vaccine.
	Sept.	HHS issues broad RFI regarding Technology Readiness Levels for medical countermeasures.
		HHS issues draft *Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) Strategy.*
	Nov.	FDA issues clinical hold notice on Vaxgen's trial.
		HHS issues "cure" notice on VaxGen.
	Dec.	HHS terminates contract with VaxGen for rPA anthrax vaccine.
2007	Feb.	NIAID cancels RFP for third-generation anthrax vaccine.
	Mar.	HHS issues PHEMCE Strategy.
	Apr.	HHS issues PHEMCE Implementation Plan.
	Apr.	Biomedical Advanced Research and Development Authority (BARDA) releases presolicitation notice for BioThrax.
	May	BARDA releases sources sought notice for rPA vaccine.

Source GAO

Appendix II: Comments from the Department of Health and Human Services

Note: GAO comments supplementing those in the report text appear at the end of this appendix.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Assistant Secretary for Legislation

Washington, D.C. 20201

OCT 4 2007

Mr. Keith Rhodes
Director/Chief Technologist
Center for Technology and Engineering
U.S. Government Accountability Office
Washington, DC 20548

Dear Mr. Rhodes:

Enclosed are the Department's comments on the U.S. Government Accountability Office's (GAO) draft report entitled, "Actions Needed to Avoid Repeating Past Problems with Procuring New Anthrax Vaccine and Managing Stockpile of Licensed Vaccine" (GAO-08-88).

The Department has provided several technical comments directly to your staff.

The Department appreciates the opportunity to review and comment on this draft before its publication.

Sincerely,

Rebecca Hennard

for Vincent J. Ventimiglia
Assistant Secretary for Legislation

GENERAL COMMENTS FROM THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE U.S. GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT: "PROJECT BIOSHIELD: ACTIONS NEEDED TO AVOID REPEATED PAST PROBLEMS WITH PROCURING NEW ANTHRAX VACCINE AND MANAGING STOCKPILE OF LICENSED VACCINE" (GAO-08-88)

The U.S. Department of Health and Human Services (HHS) is grateful for the opportunity to comment on the draft report from the U.S. Government Accountability Office (GAO) entitled *Project BioShield: Actions Needed to Avoid Repeated Past Problems with Procuring New Anthrax Vaccine and Managing Stockpile of Licensed Vaccine.*

Overview

Anthrax remains a top priority for the ongoing public health emergency preparedness efforts at HHS, and the Department is committed to developing and acquiring a robust portfolio of medical countermeasures against this threat. This prioritization is reflected in the discussion of anthrax medical countermeasures in the *HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Implementation Plan for Chemical, Biological, Radiological, and Nuclear (CBRN) Threats (HHS PHEMCE Implementation Plan)*, providing a road map for future medical countermeasure development and acquisition activities throughout HHS.

The Department continues to pursue a comprehensive strategy for the development and acquisition of products to respond to the threat of anthrax. Antibiotics represent the first line of defense to protect the nation following an anthrax attack. We currently have over 40 million courses of antibiotics in the Strategic National Stockpile (SNS). Anthrax vaccines are also an essential element of our national preparedness. Vaccines may be given as post-exposure prophylaxis in combination with antibiotics to potentially provide longer-term protection; this combination may also allow for a reduction in the duration of the antibiotic regimen. HHS has awarded contracts for the acquisition of nearly 30 million doses of anthrax vaccine since 2005, including the recent contract award of 18.75 million doses of Anthrax Vaccine Adsorbed (AVA, BioThrax™). In addition, antitoxins are necessary to treat individuals with advanced stages of infection, and may contribute to a more successful therapeutic outcome. HHS has awarded contracts to two manufacturers to deliver antitoxins sufficient for treating 30,000 people. These vaccine and antitoxin contracts were awarded under the authorities of the Project BioShield Act of 2004.

Maintaining a diversified medical countermeasure program requires a number of concurrent initiatives to improve near-term preparedness while also supporting the development of next-generation products. For example, while procuring currently available anthrax vaccine, HHS is using authorities made available under the Pandemic and All-Hazards Preparedness Act of 2006 to invest over $40 million in the continued development of an rPA anthrax vaccine. This investment complements the rPA vaccine program that has been ongoing at the National Institute of Allergy and Infectious Diseases (NIAID) since 2002. In addition, the Office of the Biomedical Advanced Research and Development Authority (BARDA) and NIAID released a Broad Agency Announcement in September 2007 that is designed to support multiple third generation anthrax vaccine candidates.

See comment 1.

This GAO report does not accurately and completely reflect the anthrax vaccine programs at the Department of Health and Human Services. Evaluations regarding past procurement activities

1

GENERAL COMMENTS FROM THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE U.S. GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT: "PROJECT BIOSHIELD: ACTIONS NEEDED TO AVOID REPEATED PAST PROBLEMS WITH PROCURING NEW ANTHRAX VACCINE AND MANAGING STOCKPILE OF LICENSED VACCINE" (GAO-08-88)

See comment 2.

must be considered in the context of the sense of urgency felt in the aftermath of the 2001 anthrax attacks, and the authorities available to HHS at the time. We are also concerned that the draft report fails to recognize the many important strides made in the transparency and effectiveness of medical countermeasure initiatives at HHS. The process of developing the *HHS PHEMCE Strategy* and the *HHS PHEMCE Implementation Plan*, published in the spring of 2007, brought together experts from across the federal government to come to a consensus on priorities for medical countermeasure development and acquisition. This process was also informed by substantial input solicited at the 2006 BioShield Stakeholders Workshop, and in response to the publication of the draft *HHS PHEMCE Strategy* in September 2006. In addition, the public release of these documents provided a clear signal of the path forward to our external stakeholders. We continue to improve transparency and foster strong relationships with product developers through the Enterprise Stakeholder Workshops, BARDA Industry Day, and MedicalCountermeasures.gov, and through continued dialogue with the public through other meetings and forums. Feedback about these initiatives from our stakeholders has been universally positive and encouraging.

Below, we have repeated each of the draft recommendations, and responded to each.

Responses to GAO Recommendations

Recommendation: To avoid repeating the mistakes that led to the failure of the first rPA procurement effort, we recommend that the Secretary of HHS direct ASPR, NIAID, FDA, and CDC to ensure that the concept of use and all critical requirements are clearly articulated at the outset for any future medical countermeasure procurement.

Response: HHS agrees with the importance of clearly establishing and articulating the concept of use and critical requirements for each medical countermeasure. For this reason, many of the Requests for Proposal (RFP) issued through BioShield are preceded by a Request for Information (RFI) or draft RFP, to ensure that the final RFP is informed by the best scientific and industry expertise possible. In furtherance of this goal, HHS has published the *HHS PHEMCE Implementation Plan*, which provides guidance concerning the priorities and requirements for future medical countermeasures.

See comment 3.

With respect to the rPA procurement process, the concept of use and critical requirements for anthrax vaccine have not changed, and are clearly articulated in many public documents from HHS, including the *HHS PHEMCE Implementation Plan*. Anthrax vaccine is to be used in combination with antibiotics as post-exposure prophylaxis. However, more specific requirements for the formulation, dosage, and studies necessary to achieve regulatory approval must be made on the basis of each individual product, through the process of direct communication with FDA that is undertaken by every medical product developer. Given that the Project BioShield legislation provides for a time period of eight years during which products must achieve licensure and that the process of product development can be fraught with unexpected complications and delays, it is nearly impossible to know the exact regulatory specifications for a product at the beginning of this process. Nonetheless, HHS has encouraged,

See comment 4.

2

GENERAL COMMENTS FROM THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE U.S. GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT: "PROJECT BIOSHIELD: ACTIONS NEEDED TO AVOID REPEATED PAST PROBLEMS WITH PROCURING NEW ANTHRAX VACCINE AND MANAGING STOCKPILE OF LICENSED VACCINE" (GAO-08-88)

and now requires potential bidders to demonstrate early engagement with FDA and understanding of regulatory requirements based upon those discussions.

Recommendation: To ensure public confidence and comply with FDA's current rules, we recommend that the Secretary of HHS direct ASPR to destroy the expired BioThrax vaccine in the stockpile.

See comment 5.

Response: HHS agrees with GAO that expired vaccines cannot be used. The Department has never planned to use any expired products in an emergency, and we strongly disagree with the claim that the Department "planned to use three lots of expired BioThrax vaccine in the stockpile in the event of an emergency". HHS fully understands the regulations surrounding the use of expired medical products, and has no such plans to administer expired doses of BioThrax. The expired vaccine in question is being quarantined until a decision on disposition is made. HHS continues to develop comprehensive life cycle plans for all medical countermeasures in the SNS.

Recommendation: To minimize waste of the BioThrax vaccine in the stockpile, we recommend that the Secretaries of HHS and DOD develop a single integrated inventory system for the licensed anthrax vaccine with rotation based on a first-in, first-out principle.

See comment 6.

See comment 7.

See comment 8.

Response: HHS agrees with the importance of an inventory management strategy to minimize attrition of BioThrax vaccine doses in the SNS resulting from expiration of the product. The Department is engaged in a broad effort to develop comprehensive life cycle management plans for all medical countermeasures in the SNS. To this end, HHS and the Department of Defense (DOD) are currently exploring a number of inventory management strategies that would include potential exchange of BioThrax between the HHS and DOD stockpiles. However, there are important liability issues and funding differences between DOD and HHS contracts that currently preclude this exchange. These issues are currently the focus of work by both Departments. The efficient transfer of short-dated vaccine from HHS to DOD could save the US Government up to $25 million per year. The report inaccurately claims that the amount of money lost is "over $100 million per year".

The very nature of these products dictates that they have a fixed dating period. If not used during an event, all medical countermeasures will eventually expire and will need to be properly discarded. HHS continues to work diligently as an effective steward of its investments, and seeks to limit unnecessary spending as much as possible, but it is inaccurate to suggest that all expired product represents wasted or lost investments.

HHS Response to GAO Findings

In addition to our response to specific GAO recommendations above, we would like to correct several particular misconceptions and inaccuracies contained in the draft report.

3

GENERAL COMMENTS FROM THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE U.S. GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT: "PROJECT BIOSHIELD: ACTIONS NEEDED TO AVOID REPEATED PAST PROBLEMS WITH PROCURING NEW ANTHRAX VACCINE AND MANAGING STOCKPILE OF LICENSED VACCINE" (GAO-08-88)

See comment 9.

First, HHS strongly disagrees with the assertion that VaxGen's candidate rPA vaccine was not sufficiently advanced to warrant a Project BioShield contract award. The Project BioShield Act of 2004 is intended to allow medical countermeasure contracts to be awarded that support both product development and acquisition activities. The VaxGen contract award was wholly consistent with the terms of the legislation, and this was validated through findings of an investigation by the HHS Office of the Inspector General. However, we recognize that commitments to acquiring products at early stages of development adds risk and uncertainty to the program. This risk was deemed to be appropriate given the urgency of the requirement. Additionally, HHS was continuing to support another rPA vaccine candidate through research and development contracts at NIAID. Fortunately, through modifications to the Project BioShield Act instituted in the Pandemic and All-Hazards Preparedness Act of 2006, BARDA now has the ability to include milestone payments in these contracts that will provide financial support for manufacturers as important product development activities are completed. BARDA is working to incorporate these payments into its future Project BioShield procurements, but this mechanism was not available to be used for the VaxGen rPA contract.

See comment 10.

The report also claims that the evaluation of VaxGen's rPA vaccine candidate was a subjective one. HHS maintains stringent processes to evaluate objective criteria and make the most appropriate contract awards. The determination of capabilities of the four different manufacturers who responded to the Request for Proposals (RFP) was based on a rigorous technical evaluation process. In addition, a Request for Information (RFI) for rPA vaccines was released in 2003, and those results were used to inform the requirements of the RFP in 2004. The responses to the RFI indicated that the anticipated timeline for rPA development and acquisition was achievable. The respondent to any solicitation is required to provide a full and honest assessment of their technical and financial capabilities. At the time of contract award, VaxGen provided the government with comprehensive project plans and timelines that projected a successful vaccine development and manufacturing process.

See comment 11.

It is also important to note that, contrary to that stated in the draft report, the VaxGen Project BioShield award did not pre-empt other support for product development that was being provided to VaxGen through its NIAID contract. Simultaneously, HHS continued to support development programs by other anthrax vaccine manufacturers with grants administered by NIAID.

See comment 12.

Next, it is inaccurate to state that "the purchase of BioThrax for the stockpile as a stopgap measure raised the bar for the VaxGen vaccine." The minimum amount of data and information needed to consider VaxGen's rPA vaccine potentially "usable" under either a "Contingency Use" IND or, subsequently, an EUA, did not change because there was a stockpile of BioThrax. Although the necessary data and information to support the use of the rPA vaccine in an emergency did not change, the likelihood of using the rPA in an emergency was reduced given ASFR's decision to first use the licensed BioThrax. Furthermore, using this logic, HHS could never buy existing medical countermeasures while next-generation products were in

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GENERAL COMMENTS FROM THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE U.S. GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT: "PROJECT BIOSHIELD: ACTIONS NEEDED TO AVOID REPEATED PAST PROBLEMS WITH PROCURING NEW ANTHRAX VACCINE AND MANAGING STOCKPILE OF LICENSED VACCINE" (GAO-08-88)

development. Maintaining a robust product pipeline requires concurrent efforts to improve near-term preparedness by acquiring available products while also supporting the development of improved next-generation products. More specifically, we do not see any particular characteristics of the BioThrax products that would adversely impact the expectations for an rPA vaccine.

See comment 13.

The draft report claims that HHS changed the requirements for the VaxGen rPA vaccine. However, the requirement for the acquisition of 25 million courses of anthrax vaccine was established following medical consequence modeling and input from public health experts. Since the Project BioShield legislation provides for up to eight years of development prior to achieving licensure, it is very difficult to predict when a contract is awarded exactly what the required studies and specific characteristics of each product will be. To resolve this problem, HHS is very clear that any companies interested in responding to a solicitation will be in frequent contact with the Food and Drug Administration (FDA) to keep the FDA up-to-date with their progress and to maintain a clear understanding of the studies that will be required for their product to achieve licensure. It is now a requirement of Project BioShield contracts that companies communicate with FDA early and often to ensure the success of each acquisition program.

In the field of medical product development, it is the responsibility of all manufacturers to be responsive to and communicative with FDA, and to incorporate regulatory feedback into their product development plans. Over the course of the VaxGen rPA contract, HHS was similarly responsive to the evolution of the candidate product. VaxGen experienced a failure in its Phase 2 clinical trial in 2004 that produced results that could not be interpreted. As a result of this and other product development delays, HHS instituted a contract modification that extended VaxGen's delivery schedule for an additional three years. It is not clear that VaxGen made equivalent efforts to remain aware of FDA guidance. There are no regulated or mandated timelines for development of a new product. The interactions of FDA's Center for Biologics Evaluation and Research (CBER) with VaxGen were typical of those with any sponsor during the IND stages of development of any product, especially during early stages, prior to VaxGen getting the BioShield contract. Post-contract award, November 2004, VaxGen, CBER and other HHS agencies had frequent meetings and extensive technical discussions to aid in development of this important product. VaxGen did not request information regarding the specific data and information needed by CBER to potentially allow use under a "Contingency Use" IND, as specified in the RFP, until December 2005, so they could more appropriately account for development costs, predict manufacturing and delivery timelines and have a clear understanding of the criteria which would make their product considered "usable (term used by HHS)" and thus appropriate for acquisition and stockpiling. CBER provided this information in January 2006.

See comment 14.

One of the central claims of this report is that product requirements were not known to VaxGen at the outset of the procurement contract. As with any medical product development program, it is the responsibility of the manufacturer to engage effectively with FDA. It is also unclear what GAO is trying to convey by the following two sentences: "This confused FDA officials and

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GENERAL COMMENTS FROM THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE U.S. GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT, "PROJECT BIOSHIELD: ACTIONS NEEDED TO AVOID REPEATED PAST PROBLEMS WITH PROCURING NEW ANTHRAX VACCINE AND MANAGING STOCKPILE OF LICENSED VACCINE" (GAO-08-88)

caused them to balk at replying to VaxGen until it could meet with ASPR and CDC to clarify this issue. As a result, VaxGen was placed in a position where it had to respond to different requirements." The meeting referenced occurred in December 2005. It is also CBER's impression that VaxGen wanted the next Phase II trial to support use of the vaccine in a "contingency use" protocol under IND. However, the purpose of Phase II trials, in order to position the product for the pivotal Phase III trial in support of licensure, is to collect additional safety, and when possible efficacy data, as well as to determine the dose, route and schedule for administration. Since VaxGen had not previously requested information regarding the specific data and information needed by CBER to potentially allow use under a "Contingency Use" IND, as specified in the RFP, it appears that VaxGen may not have clearly understood that the data needed to support this use should be gathered using final drug product administered by the dose, route and schedule determined to be most immunogenic and safe in the Phase II trials. Since CBER was asked the question regarding use during an emergency during this meeting, CBER needed time to respond and provided the information in January 2006.

See comment 15.

The report also makes inaccurate statements regarding Emergency Use Authorization guidance from FDA. The draft guidance "Emergency Use Authorization of Medical Products" which was issued in June 2005, and published as final guidance in July 2007, was drafted directly from and intended to provide information regarding the Agency's current thinking concerning one way to meet the statutory requirements defined in Section 564 of the Federal Food, Drug, and Cosmetic Act, as it was amended by the Project BioShield Act of 2004. Section 564 is self-executing and does not require implementing regulations or guidance. As stated in the guidance "The document is intended to inform industry, government agencies, and FDA staff of the Agency's general recommendations and procedures for issuance of EUAs." It goes on to clarify that the amount of data and information needed will be determined on a case-by-case basis and that this document summarizes the types of data that FDA would recommend submitting. The EUA guidance also discusses the conditions that must be met to authorize use of a product under an EUA, as well as other conditions of authorization that may be imposed. In discussing these issues, the guidance clarifies that the exact type and amount of data may vary depending on the nature of the declared emergency and the product under consideration.

ee comment 16.

HHS is dedicated to building a comprehensive stockpile of medical countermeasures that would be available in the case of a public health emergency. The very nature of these products dictates that they have a fixed dating period. If not used during an event, all medical countermeasures will eventually expire and will need to be properly discarded. However, all expired product does not represent wasted or lost investments, and it is disingenuous to suggest as much. HHS continues to serve as a responsible and effective steward of its investments as it works to achieve our mission to prevent, prepare for, and respond to the adverse health effects of public health emergencies.

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The following are GAO's comments on the Department of Health and Human Services' letter dated October 4, 2007.

GAO Comments

1. Our draft report acknowledged the Office of the Assistant Secretary for Preparedness and Response's (ASPR) sense of urgency to develop an rPA anthrax vaccine following the 2001 attack. However, our report also stated that by November 2004, ASPR had had sufficient time and opportunity to thoroughly evaluate contractual risks and issues without being overly influenced by the sense of urgency. By November 2004, it was clear that significant manufacturing issues needed to be overcome and that a 2-year time scale to produce 25 million doses was accordingly unrealistic.

2. We agree that ASPR has taken several steps to develop and communicate its strategy and plans to acquire medical countermeasures to potential manufacturers. In addition, HHS has conducted several workshops to stimulate discussion with potential manufacturers. However, these steps were taken just before or after VaxGen's procurement contract was terminated. While we reviewed the HHS Public Health Emergency Medical Countermeasures Enterprise Strategy and Implementation Plan for Chemical, Biological, Radiological, and Nuclear Threats, we did not find these documents to be relevant to our evaluation of ASPR's performance with regard to VaxGen's procurement contract.

3. ASPR's definition of the concept of use refers, as expressed in its comments, to the anthrax vaccine in combination with antibiotics as post-exposure prophylaxis. However, our report discusses the potential use of the unlicensed rPa vaccine in the stockpile when the licensed anthrax vaccine was already available. We cite the Food and Drug Administration's position that it would give preference to the licensed vaccine over the unlicensed vaccine.

With regard to critical requirements, HHS acknowledged that critical requirements would change for different products. Therefore, HHS should have known the consequences of changing requirements for a fixed-price contract with a 2-year time limit.

4. We agree with HHS that it is not always possible to know the exact regulatory specifications for a product at the beginning of the procurement process. However, ASPR failed to recognize that changing requirements under a fixed-price procurement contract could significantly affect the finances and the 2-year delivery time line it established.

5. The acting director of ASPR told us that the principal deputy of ASPR had decided not to destroy the expired lots in case they were needed for use in an emergency. However, using the expired vaccine would violate the FDA rule. In response to the draft of this report, HHS now states that it is quarantining the expired lots until a decision can be made regarding disposal. We do not understand HHS's rationale for continuing to hold the vaccine in quarantine for nearly a year and the justification for the administrative expenses involved.

6. Although HHS and the Department of Defense (DOD) use different authorities to address BioThrax liability and funding issues, both authorities could apply to vaccines purchased by either DOD or HHS; consequently, indemnity does not appear to be an insurmountable obstacle for future procurements. As indicated in our report, DOD and HHS should continue to explore the legal implications of different indemnity authorities and present a legislative proposal to Congress if they determine that a statutory change is required to establish a joint inventory.

7. Since, as ASPR acknowledges, it does not have a strategy to minimize waste, we calculated the potential $100 million annual wastage based on expiration dates of the current vaccine inventory. ASPR stated that the annual saving would only be up to $25 million per year but did not provide any basis for this estimate. However, according to DOD, in contract year 2006, it purchased BioThrax valued at about $55 million, a savings of more than double ASPR's estimate.

A strategy to minimize waste in the stockpile should include not only integration of inventory based on a first-in, first-out principle but also reexamination of requirements derived from consequence modeling with regard to the size of the inventory. Such a strategy would result in savings closer to $100 million.

8. We did not mean to suggest that all expired products represent waste or lost investment. We clarified our definition of waste in the report. When there is a large-volume user for the stockpile product, not having an effective strategy to ensure that stockpile product would be used constitutes waste. However, since DOD is a large user of BioThrax, unnecessary waste will result from ASPR not making an effort to ensure that to the extent possible, DOD uses the vaccine in the stockpile.

9. We did not question the legality of the contract award to VaxGen but rather the rationale underlying the contract's requirement for 25 million doses in 2 years.

10. ASPR officials told us that they did not have tools to assess product maturity at the time of the contract award, and that they were guided by a sense of urgency. On the basis of these statements, we concluded that their assessment was subjective.

11. We disagree that the VaxGen Project BioShield award did not preempt other support for product development that was being provided to VaxGen through its National Institute of Allergy and Infectious Diseases contract. According to our analysis of the contract document and discussions with NIAID officials, funding under the development contract largely ceased once the procurement contract was awarded.

12. We clarified the report text to attribute to VaxGen officials the statement that the purchase of BioThrax for the stockpile as a stopgap measure raised the bar for the VaxGen vaccine.

13. Our draft report did not say that HHS changed the requirements for the VaxGen rPA vaccine. However, we have clarified the text to state that purchase of BioThrax for the stockpile raised the requirement for the use of rPA anthrax vaccine.

14 We clarified the report text to indicate that neither FDA nor VaxGen understood the concept of use prior to January 2006.

15. We clarified the report text to indicate that ASPR officials told us that FDA would define "sufficient data" and the testing hurdles a product needed to overcome to be considered a "usable product."

16. See our response to comment 8.

Appendix III: Comments from the Department of Defense

Note: GAO comments supplementing those in the report text appear at the end of this appendix.

NUCLEAR AND CHEMICAL AND BIOLOGICAL DEFENSE PROGRAMS

ASSISTANT TO THE SECRETARY OF DEFENSE
3050 DEFENSE PENTAGON
WASHINGTON, DC 20301-3050

OCT 3 2007

Mr. Keith Rhodes
Director/Chief Technologist, Center for Technology and Engineering
U.S. Government Accountability Office
441 G Street, N.W.
Washington, DC 20548

Dear Mr. Rhodes:

This is the Department of Defense (DoD) response to the GAO draft report 08-88, "PROJECT BIOSHIELD: Actions Needed to Avoid Repeated Past Problems with Procuring New Anthrax Vaccine and Managing Stockpile of Licensed Vaccine," dated September 20, 2007, (GAO Code 460590).

The Department partially concurs with the GAO recommendation. Our position on this recommendation is explained in the enclosure.

My point of contact for this matter is Dr. Robert Borowski, who can be reached at (703) 416-4682 or at Robert.Borowski@anser.org.

David G. Jarrett, COL, MC, USA
Deputy and Medical Director
OSA(CBD&CDP)

Enclosure

GAO Draft Report Dated SEPTEMBER 20, 2007
GAO-08-88 (GAO CODE 460590)

"PROJECT BIOSHIELD: ACTIONS NEEDED TO AVOID REPEATED PAST PROBLEMS WITH PROCURING NEW ANTHRAX VACCINE AND MANAGING STOCKPILE OF LICENSED VACCINE"

DEPARTMENT OF DEFENSE COMMENTS TO THE GAO RECOMMENDATION

RECOMMENDATION: The GAO recommends that in order to minimize waste of the BioThrax® vaccine in the stockpile, HHS and DoD develop a single integrated inventory system for the licensed anthrax vaccine with rotation based on a first-in, first-out principle. (p. 25/GAO Draft Report)

See comment 1.

DOD RESPONSE: The DoD partially concurs with the GAO recommendation.

- While the recommendations in the draft GAO report have merit, it should be underscored that there are operational, logistical, and legal challenges to implementation that may require potential legislative action to overcome.
  - Logistical challenge: The HHS stockpile is far larger than the amount DoD consumes on an annual basis and hence, if a joint stockpile is created, DoD will only be able to use a fraction of the expiring doses. It should also be noted that DoD can not distribute expiring stocks at the last minute and would require some level of lead time to distribute and dispense the soon-to-expire stocks. The DoD will also work with HHS to specifically analyze the potential cost avoidance with the proposal.
  - Legal challenge: DoD and HHS have differing methods of liability protection. DHHS plans to use the Public Readiness and Emergency Preparedness (PREP) Act provisions to limit the liability of manufacturers of medical countermeasures, versus DoD's use of P.L. 85-804 indemnification. DoD has identified this area of differing methods of liability protection as one that will require further discussion between the agencies' legal staffs. This area may require legislative action to ensure that vaccine purchased by DHHS can be used in the DoD immunization program.
- The DoD and HHS have been and will continue to coordinate the actions of this effort in the best interests of the United States Government.

The following is GAO's comment on the Department of Defense's letter dated October 3, 2007.

GAO Comment

1. Although HHS and DOD use different authorities to address BioThrax liability, both authorities could apply to vaccines purchased by either DOD or HHS; consequently, indemnity does not appear to be an insurmountable obstacle for future procurements. As indicated in our report, DOD and HHS should continue to explore the legal implications of different indemnity authorities and present a legislative proposal to Congress if they determine that a statutory change is required to establish a joint inventory.