

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

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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, 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 the response to large-scale bioattacks and pandemics.

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 released 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 a calamitous scale. 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 called 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. January 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 materials from 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.
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- 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, large 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 \$5.6 billion fund appropriated in 2004. (Approximately \$3.6 billion remains.) When one considers that the average cost of drug development is \$800 million—and this is before a single pill

or vaccine is purchased—it is obvious that \$5.6 billion is not sufficient to protect the nation against the range of potential biotreats, let alone chemical, 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 a particular plant for a particular 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 timeframes 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 among 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 has 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 referred 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 \$1.07 billion for BARDA in FY06-08—this was seen at the time as the start of what would be needed to accomplish BARDA's long term goals. However, no money was appropriated for BARDA in FY06, and only \$99 million was given to BARDA in the FY07 supplemental appropriation. The Administration has requested \$189 million for BARDA in FY08. Both the House and Senate versions of the Labor-HHS appropriations bills contain less than the President's request (\$135.5 million is proposed in the House, while the Senate version contains \$159 million). 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, it 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 ensure situational awareness during an event; that ensures collaboration between DHS and the various agencies within HHS that deal with aspects of surveillance; and that ensures 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 healthcare 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—but 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 among 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 and emergency use—than additional investments in environmental sensors or syndromic surveillance technologies. We should not have to decide between electronic health data or environmental sensors; rather 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 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—i.e., 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 of 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 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?
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- Would we improve detection more cost-effectively by focusing on raising clinician's awareness of bioweapons-related diseases or by investments in point-of-care diagnostic tests, which not only could 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 than 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—\$12 billion/year for all 300 million Americans [Ref: Biodetection Architectures. JASON. The Mitre Corporation, February 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 among hospitals and large HMOs and local public health agencies, and investments in interoperable electronic health records—which authorities agree would improve healthcare quality and lower healthcare 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.