Project BioShield: What It Is, Why It Is Needed, and Its Accomplishments So Far

Philip K. Russell
Albert B. Sabin Vaccine Institute, Washington, DC

Project BioShield is a comprehensive effort involving the US Department of Health and Human Services (HHS), its component agencies, and other partner federal agencies to speed the research, development, acquisition, and availability of medical countermeasures to improve the government’s preparedness for and ability to counter chemical, biological, radiological, and nuclear threat agents. The legislation authorizes use of the Special Reserve Fund, which makes available $5.6 billion over 10 years for the advanced development and purchase of medical countermeasures. This appropriation is intended to provide an economic incentive to the pharmaceutical industry to develop medical countermeasures for which the government is the only significant market. Acquisitions under Project BioShield are restricted to products in development that are potentially licensable within 8 years from the time of contract award. In exercising the procurement authorities under Project BioShield, HHS has launched acquisition programs to address each of the 4 threat agents, including Bacillus anthracis (anthrax), smallpox virus, botulinum toxins, and radiological/nuclear agents, originally deemed by the Department of Homeland Security to be threats to the US population sufficient to affect national security. At the time of writing, 7 contracts have been awarded: (1) recombinant protective antigen anthrax vaccine, the next-generation anthrax vaccine (contract terminated in December 2006 for default); (2) anthrax vaccine adsorbed, the currently licensed anthrax vaccine; (3) anthrax therapeutics (monoclonal); (4) anthrax therapeutics (human immune globulin); (5) the pediatric formulation of potassium iodide; (6) Ca- and Zn-diethylenetriaminepentaacetate (DTPA), chelating agents to treat ingestion of certain radiological particles; and (7) botulinum antitoxins. Additional acquisition contracts are expected to be awarded in 2007.

THE PROJECT BIOSHIELD PROGRAM

After the anthrax attacks in the fall of 2001, the US Department of Health and Human Services (HHS) placed the responsibility for the development and acquisition of medical countermeasures against biological threat agents in the newly created Office of the Assistant Secretary for Preparedness and Response (ASPR) (formerly the Office of Public Health Emergency Preparedness). Initial efforts focused on securing next-generation vaccines for 2 category A threats, anthrax and smallpox. It was soon recognized that a secure funding source would be a key component in attracting industry to meet US government requirements. To encourage the development of new medical countermeasures against biological, chemical, or radiological agents and to speed their delivery and use in the time of an attack, President George W. Bush proposed Project BioShield in his 2003 State of the Union address. Former secretary of HHS Tommy Thompson and former secretary of Homeland Security Tom Ridge jointly transmitted the Project BioShield Act of 2003 to Congress on 26 February 2003.

The bill was passed by Congress and signed into law (Public Law 108-276) on 21 July 2004. The funds had been previously appropriated, on 1 October 2003, in the first-ever appropriations bill (Public Law 108-90) for the recently created Department of Homeland Security (DHS). In response to the need for funds to stockpile medical countermeasures against the threat
of bioterrorism, Project BioShield includes a federal acquisition program. The appropriation created a $5.6 billion "Special Reserve Fund" to support the acquisition of "security countermeasures" through fiscal year 2013 and restricted spending to $3.4 billion in fiscal years 2004–2008.

In addition to the acquisition program, the Project BioShield Act of 2004 included 2 other critical elements. First, it contained provisions that increased the authority and flexibility of the National Institutes of Health to expedite research and development of "qualified countermeasures." The bill also gave the US Food and Drug Administration the authority to provide Emergency Use Authorization before licensure for medical countermeasures in the later stages of product development, in the event of an emergency need. Although the initial focus of HHS efforts had been on developing medical countermeasures for biological threats, the Project BioShield legislation expanded the scope of the BioShield program to enable the acquisition of products to protect against radiological and nuclear threats and chemical-induced injury, including antidotes to nerve gases.

The legislation specified both the conditions and the process for the release of BioShield funds. Although the funds are in the DHS appropriation, HHS was designated as the acquisition agency. The release of funds from the Special Reserve Fund requires formal determinations from the Secretaries of the DHS and HHS. To release BioShield funds, the secretary of the DHS, in consultation with the secretary of HHS and the heads of other federal agencies, as appropriate, must determine that there is a material threat, and the secretary of HHS must determine that a security countermeasure is necessary to address that threat in order to protect the public health. The secretary of HHS also determines whether a given medical countermeasure is appropriate and available for Project BioShield acquisition. This determination is based on current scientific data on prospective countermeasures, the quantities to be procured, and the feasibility of meeting Food and Drug Administration requirements for licensure within 8 years. Release of funds requires approval by the President. The approval authority was delegated by the President to the Director of the Office of Management and Budget. The Office of Management and Budget staff reviews the acquisition plans.

Previously, the interagency Weapons of Mass Destruction Medical Countermeasures Subcommittee served as the focal point for the determination of requirements and the coordination of acquisition plans for the US government. The Subcommittee was led by HHS and included senior leadership from the DHS and the Department of Defense. In July 2006, the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) was established, assuming the functions of the Weapons of Mass Destruction Medical Countermeasures Subcommittee. The PHEMCE is a coordinated, intra-agency effort led by the ASPR and includes 3 HHS internal agencies: the Centers for Disease Control and Prevention, the Food and Drug Administration, and the National Institutes of Health. The PHEMCE has the mission to define and prioritize requirements for public health medical emergency countermeasures and to coordinate research, early- and late-stage product development, and procurement activities addressing these requirements, as well as to set deployment-and-use strategies for medical countermeasures held in the Strategic National Stockpile (SNS).

It is important to recognize that the Project BioShield Act, as originally passed, defines specific contract terms. For example, it does not allow for payment to the manufacturer until at least a portion of the product has been delivered to the SNS. This has the consequence of requiring the supplier of a BioShield product to assume the financial risk and financial burden of development until the product can be delivered.

The fact that a product must be potentially licensable to qualify for a BioShield procurement effectively limits the program to contracting for products that have progressed far enough in the development process to allow a judgment on the potential for licensability to be made with some degree of confidence. In most instances, this excludes products in the preclinical stage of development.

The Pandemic and All-Hazards Preparedness Act (Public Law 109-417) provides HHS with new authorities to improve the implementation of Project BioShield. The legislation supports much needed late-stage research-and-development funding and will allow HHS to make milestone-based payments under BioShield. It also supports HHS efforts to improve coordination of preparedness and response programs across HHS.

**WHY PROJECT BIOSHIELD IS NEEDED**

The development of medical countermeasures, such as vaccines, antitoxins, and antibiotics, involves very high costs and high risks. The cost of development of a medical product in the commercial sector is estimated to be more than a billion dollars [1]. The earlier stages of development are relatively inexpensive, but costs escalate as a product progresses to large-scale manufacturing and the late stages of clinical development. The risk of failure of a product to succeed in the developmental process and achieve Food and Drug Administration licensure is also high. Approximately 8% of products entering phase 1 trials ultimately progress to licensure. Unexpected adverse effects, unpredicted adverse events in clinical trials, and lower-than-expected efficacy all contribute to a high rate of failure, often after many millions of dollars have been spent on development [2]. When markets are large, the costs and risks are acceptable to the developers, because success is rewarded with substantial profits. When the only market is the government, a high risk of failure and a low expectation of profit discourages manufacturers from investing research-and-development funds in the
Table 1. Summary of Project BioShield medical countermeasure acquisition programs.

<table>
<thead>
<tr>
<th>Threat agent, medical countermeasure</th>
<th>Quantity</th>
<th>Funds obligated/status of contract</th>
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<tbody>
<tr>
<td>Anthrax Recombinant protective antigen anthrax vaccine</td>
<td>75 million doses</td>
<td>Contract awarded in Nov 2004 to VaxGen: $879.2 million (contract terminated for default Dec 2006)</td>
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<tr>
<td>Anthrax vaccine adsorbed</td>
<td>10 million doses</td>
<td>Contract awarded in May 2005 to BioPort: $122.7 million for 5 million doses; contract options for an additional 5 million doses ($120 million) exercised in May 2006; delivery to SNS completed in early 2007</td>
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<td></td>
<td>10.4 million doses</td>
<td>Presolicitation notice issued in Apr 2007, stating intent to purchase 10.4 million doses, with an option for an additional 8.4 million doses</td>
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<tr>
<td>Anthrax therapeutics</td>
<td>20,001 treatment courses</td>
<td>Contract awarded in Jun 2006 to Human Genome Sciences for 20,001 treatment courses of ABthrax: $165.2 million</td>
</tr>
<tr>
<td></td>
<td>10,000 treatment courses</td>
<td>Contract awarded in Jul 2006 to Cangene for 9900 treatment courses of human anthrax immune globulin: $144 million</td>
</tr>
<tr>
<td>Botulinum Botulinum antitoxin</td>
<td>200,000 doses</td>
<td>Contract awarded Jun 2006 to Cangene for 200,000 doses of heptavalent botulism antitoxin: $362.6 million</td>
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<td>Radiological/nuclear Pediatric (liquid) potassium iodide</td>
<td>1.7 million 1-ounce bottles</td>
<td>Contract awarded Mar 2005 to Fleming Pharmaceuticals for 1.7 million bottles: $5.7 million; delivery to the SNS was completed in Sep 2005</td>
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<td></td>
<td>Additional 3.1 million bottles</td>
<td>Contract options exercised in Feb and May 2006, including an additional 3.1 million bottles: $11.8 million; total obligation, $17.5 million; delivery to the SNS started in May 2006</td>
</tr>
<tr>
<td>Medical countermeasures to treat/mitigate neutropenia associated with acute radiation syndrome</td>
<td>Up to 100,000 treatment courses</td>
<td>Request for proposals closed in Feb 2006 and cancelled in Mar 2007</td>
</tr>
<tr>
<td>Chelating agents Zn- and Ca-DTPA</td>
<td>~475,000 doses</td>
<td>Contract awarded Feb 2006 to Akron for delivery of &gt;390,000 doses of Ca-DTPA and &gt;60,000 doses of Zn-DTPA; total obligation, $22 million; delivery to the SNS completed in Apr 2006</td>
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NOTE. DTPA, diethylenetriaminepentaacetate; SNS, Strategic National Stockpile.
ment authorities under Project BioShield, HHS has launched acquisition programs to address each of the 4 threat agents originally deemed by the DHS to be threats to the US population sufficient to affect national security, including *Bacillus anthracis* (anthrax), smallpox virus, botulinum toxins, and radiological/nuclear agents. In September 2006, the DHS determined that 9 additional agents, including viruses causing hemorrhagic fever (Ebola, Marburg, and Junin viruses), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia), *Rickettsia prowazekii* (typhus), *Burkholderia mallei* (glanders), *Burkholderia pseudomallei* (meliodosis), and multidrug-resistant *Bacillus anthracis* (anthrax), may pose a threat to national security. Anthrax is the single most dangerous threat on the list, and we will ultimately need a vaccine in the stockpile that is stable for long periods and can be efficiently delivered to large populations. We also need other countermeasures to deal with the threat of antibiotic-resistant anthrax. The current smallpox vaccine is highly effective but has well-known safety issues, and a safer vaccine for the general population is needed, as are effective antiviral drugs. Antibiotics or other treatments to deal with threat organisms resistant to existing drugs will be needed in the future. Experimental vaccines against plague, tularemia, botulism, and Ebola and Marburg viruses are being developed with National Institutes of Health funding and would be valuable countermeasures for both civilian and military use. The BioShield program will be essential to bring some of these products through the final stages of the development process.

**ACCOMPLISHMENTS SO FAR**

Significant progress has been made in the establishment of both national requirements and acquisition strategies, as well as the procurement of pre- and postexposure countermeasures to meet the threat from anthrax, botulinum toxins, smallpox, and radiological and nuclear threats. Refer to table 1 for the details of Project BioShield acquisitions to date.

HHS has taken a number of additional steps to accomplish the goal of effectively and efficiently implementing the Project BioShield Act of 2004. HHS has reorganized the ASPR (formerly the Office of Public Health Emergency Preparedness) and established a dedicated strategic planning function that more efficiently integrates biodefense requirements and streamlines the interagency governance process. Under the reorganized structure, on behalf of the secretary of HHS, the ASPR leads the federal public health and medical response to acts of terrorism or nature and other public health and medical emergencies. As was previously mentioned, HHS announced, in the Federal Register Notice of 6 July 2006 [4], the establishment of the PHEMCE.

HHS has worked to educate the public and industry about its priorities and opportunities for biodefense, as is outlined in the PHEMCE Strategy [5]. The draft PHEMCE Strategy was published for public comment in the Federal Register on 8 September 2006 [6]. The ultimate goal of the PHEMCE Strategy is to establish the foundational elements and guiding principles that will support medical countermeasure availability and utilization for the highest-priority CBRN threats facing our nation. The PHEMCE Strategy will be followed by the PHEMCE Implementation Plan, which will outline near- (fiscal years 2007–2008), mid- (fiscal years 2009–2013), and long-term (fiscal years 2014–2023) goals for research, development, and acquisition of medical countermeasures that are consistent with the guiding principles and priority-setting criteria defined in this PHEMCE Strategy.

**DR. THEODORE E. WOODWARD**

Dr. Theodore E. Woodward maintained an interest in infectious diseases threats to the armed forces throughout his career. He conducted research on typhus in the Army during World War II and later pioneered the antibiotic treatment of scrub typhus through landmark studies in the US Army laboratory in Malaya. His interest included the threats of biological warfare, and he advised the Army on research to defend against biological agents through more than 20 years of service on the Commission on Epidemiologic Survey of the Armed Forces Epidemiologic Board and, later, as the president of the Board [7]. He was a frequent visitor to and a strong supporter of US Army and Navy research institutions and their overseas laboratories. The author trained as a resident in medicine in Dr. Woodward’s department and maintained a close professional relationship through the remainder of his career. Many of the products planned for acquisition under Project BioShield are the results of research in military laboratories, principally the US Army Research Institute of Infectious Diseases, which benefited greatly from advice and guidance provided by Dr. Woodward.

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**References**


