PROJECT BIOSHIELD

Annual Report to Congress

July 2004 through July 2006

United States Department of

Health & Human Services

Office of Public Health Emergency Medical Countermeasures

In the Office of Public Health Emergency Preparedness

Table of Contents

Table of Contents (cont.)

List of Figures

1.0 Executive Summary

The Project BioShield Act of 2004 (P.L. 108-276), also referred to as "Project BioShield" or "the Act," was enacted on July 21, 2004. This is the first Annual Report to Congress regarding Project BioShield and covers the two-year period from enactment of the Act through July 2006. Future reports will cover activities occurring within each one-year period (July to July). The Act is a critical part of a broader strategy to defend America against weapons of mass destruction. It provides the U.S. Department of Health and Human Services (HHS) with new authorities to speed the research, development, acquisition and use of priority medical countermeasures (for definition see Appendix 1) against chemical, biological, nuclear, and radiological (CBRN) threats. These authorities include the following:

- *Use of certain procedures regarding research and development activities that involve qualified medical countermeasures.* These authorities are found in Section 2 of the Project BioShield Act and insert a new section (319F-1) in the Public Health Service Act. The added section authorizes the use of a variety of streamlined procedures in awarding grants, contracts and cooperative agreements relating to the research and development of qualified countermeasures. The streamlined procedures include expedited peer review to assess the scientific and technical merit of research proposals up to $1.5 million, an increase of the simplified acquisition threshold from $100,000 to $25 million, an expedited limited competition process in some circumstances and an increase in the micropurchase threshold from $2,500 to $15,000.
- *Authority to use the Special Reserve Fund (SRF) for the acquisition of medical countermeasures for the Strategic National Stockpile.* These authorities are in Section 3 of the Project BioShield Act and create Section 319F-2 of the Public Health Service Act. The SRF, provided in the Department of Homeland Security Appropriations Act (P.L. 108-90) on October 1, 2003, makes available $5.593 billion over 10 years (FY04 to FY13) for the advanced development and purchase of security countermeasures for the Strategic National Stockpile (SNS). Of that amount, $3.4 billion may be obligated during FY04 to FY08. Section 319F-2 also authorizes the use of a number of streamlined contracting procedures for the procurement of security countermeasures. The streamlining includes the use of simplified acquisition procedures if the Secretary determines a pressing need for a specific countermeasure procurement. The procedures also provide for a limited competition process in some circumstances, as well as the ability to pay premiums in multiple award contracts to vendors based on the priority of the production and delivery of an increment of the specific medical countermeasure.
- *Emergency Use Authorization (EUA) for medical countermeasures.* This authority is in Section 4 of the Project BioShield Act and adds Section 564 of the Federal Food, Drug, and Cosmetic Act. This section permits the HHS Secretary to authorize the introduction into interstate commerce of a drug, device, or biological product intended for use in an actual or potential emergency, even if the product is not approved, cleared, or licensed by the HHS/Food and Drug Administration (FDA) or is approved, cleared, or licensed for a different use. The Secretary has delegated this authority to the HHS/FDA Commissioner. The HHS/FDA Commissioner may invoke this authority only following a declaration of emergency by the Secretary. The Secretary may issue such a declaration based on a determination of a public health emergency that affects or has the significant potential to affect national security and involves a specific threat agent, or on the basis of an attack, or heightened risk of attack, with such an agent on either the domestic population (as determined

by the Secretary of Homeland Security) or on U.S. military forces (as determined by the Secretary of Defense). Additional requirements for issuance of an EUA include the determination by the HHS/FDA Commissioner that there is no adequate and approved alternative product available to address the specific threat that is causing the emergency declaration, and that the known and potential benefits of use outweigh the known and potential risks. The EUA expires upon the termination of the emergency declaration, or earlier if the Secretary determines that the emergency has ceased. An EUA may be revoked before termination of the Secretary's declaration if the HHS/FDA Commissioner determines that the criteria for issuance of the EUA are no longer met or that revocation is appropriate to protect public health or safety.

Under the Project BioShield Act, HHS is required to submit an annual report to Congress to outline the use of these authorities. During the first two years following enactment, Project BioShield authorities exercised include the following:

- Research and Development (National Institutes of Health (NIH)/National Institute of Allergy and Infectious Diseases (NIAID))
  - Expedited Review and Award Authorities:
    - Awarded twelve grants for therapeutics for the most serious biological threats as determined by the HHS/Centers for Disease Control and Prevention (CDC);
    - Awarded a contract for development and production of antibodies that protect against botulinum toxin type A;
    - Awarded a contract for production of a vaccine candidate against botulinum toxin type E;
    - Awarded four grants and three contracts for research to lead to medical countermeasures against radiological or nuclear events;
    - Awarded eight grants for research leading to the development of high-throughput *in vitro* screening assays for influenza; and
    - Announced the availability of grants for radionuclide decorporation agents for radiation/nuclear emergencies.
  - Personnel Authorities:
    - Appointed three key Associate Directors to support HHS/NIH/NIAID biodefense and radiation/nuclear medical countermeasure initiatives.
- Acquisitions by using the SRF (Office of Public Health Emergency Preparedness (OPHEP)/ Office of Public Health Emergency Medical Countermeasures (OPHEMC; formerly the Office of Research Development and Coordination (ORDC))
  - OPHEMC has not used any special procurement procedures granted under Section 3 of the Project BioShield Act of 2004 and has used normal acquisition procedures for all procurements to date because no circumstance requiring special procedures has arisen.
  - Awarded seven contracts using the SRF, most within 15 months - 21 months of Office of Management and Budget (OMB) approval of each acquisition. Delivery to the SNS has begun (or been completed) for three of the seven products:
    - Pediatric liquid formulation of potassium iodide: $5.7 million for 1.7 million one-ounce bottles; delivery to the SNS was completed in September 2005. $11.8 million for 3.1 million additional bottles; delivery to the SNS has commenced;
    - Anthrax Vaccine Adsorbed (AVA): $122.7 million for 5 million doses; delivery to the SNS has completed. $120 million for 5 million additional doses of AVA; delivery to the SNS has commenced;

- Diethylenetriaminepentaacetate (DTPA): $21.9 M for 474,739 doses; delivery to the SNS was completed in April 2006.
- Anthrax recombinant Protective Antigen (rPA) vaccine: $877.5 million for 75 million doses.
- Anthrax Therapeutics (Monoclonal): $165.2 million for 20,001 treatment courses;
- Anthrax Therapeutics (Human Anthrax Immune Globulin): $143.2 million for 10,000 treatment courses;
- Botulinum Antitoxins: $362.6 million for 200,000 doses;

– Commenced two additional acquisition processes, following OMB approval to use the SRF, with Requests for Proposals:
  - Next-generation Modified Vaccinia Ankara (MVA) smallpox vaccine: For up to 20 million doses;
  - Therapeutics for neutropenia associated with Acute Radiation Syndrome (ARS): For up to 100,000 treatment courses

- Emergency Use Authorization (FDA)
  – Authorized the emergency use of Anthrax Vaccine Adsorbed (AVA) for prevention of inhalation anthrax in at-risk DoD personnel:
    - On January 14, 2005, HHS Secretary declared an emergency because of a determination by the Assistant Secretary of Defense of a heightened risk to deployed U.S. military forces of an anthrax attack;
    - On January 27, 2005, after consultation with HHS/CDC and HHS/NIH, the HHS/FDA Commissioner issued a six-month EUA for the use of AVA; and
    - On July 22, 2005, the HHS/FDA Commissioner extended the EUA for the duration of the declaration of emergency, which expired on January 14, 2006.

2.0 Introduction

On July 21, 2004, the President of the United States, George W. Bush, signed the Project BioShield Act of 2004 (Project BioShield) into law (Public Law 108-276) as part of a broader strategy to defend America against weapons of mass destruction. The purpose of Project BioShield is to accelerate the research, development, purchase and availability of medical countermeasures including therapeutics, vaccines, medical devices and diagnostics to protect Americans against the effects of chemical, biological, radiological, and nuclear (CBRN) agents.

In Project BioShield, Congress gave the Secretary of the U.S. Department of Health and Human Services (HHS) enhanced authorities to develop and acquire these medical countermeasures. The measure supports the recovery and response pillar of the President's *Biodefense for the 21st Century*,[1] a comprehensive blueprint for America's biodefense.

The new HHS authorities include the following:

- *Use of certain procedures regarding research and development activities that involve qualified medical countermeasures.* These authorities are found in Section 2 of the Project BioShield Act and insert a new section (319F-1) in the Public Health Service Act. The added section authorizes the use of a variety of streamlined procedures in awarding grants, contracts and cooperative agreements relating to the research and development of qualified countermeasures. The streamlined procedures include: (1) expedited peer review to assess the scientific and technical merit of research proposals up to $1.5 million; (2) an increase of the simplified acquisition threshold from $100,000 to $25 million; (3) an expedited limited competition process in some circumstances; and (4) an increase in the micropurchase threshold from $2,500 to $15,000.
- *Authority to use the Special Reserve Fund (SRF) for the acquisition of medical countermeasures for the Strategic National Stockpile.* This authority is in Section 3 of the Project BioShield Act. The SRF, provided in the Department of Homeland Security Appropriations Act (P.L. 108-90) on October 1, 2003, makes available $5.593 billion over 10 years (FY04 to FY13) for the advanced development and purchase of priority medical countermeasures for the Strategic National Stockpile (SNS). Of that amount, $3.4 billion may be obligated during FY04 to FY08.
- *Additional Authorities Regarding the Procurement of Security Countermeasures.* These procurement authorities are found in Section 3 of the Project BioShield Act and add Section 319F-2 of the Public Health Service Act. This section authorizes the use of a number of streamlined contracting procedures for the procurement of security countermeasures. The streamlining includes the use of simplified acquisition procedures if the Secretary determines a pressing need for a security countermeasure procurement. The procedures also provide for a limited competition process in some circumstances, as well as the ability to pay premiums in multiple award contracts to vendors based on the priority of the production and delivery of an increment of the security countermeasure.
- *Emergency Use Authorization (EUA) for medical countermeasures.* This authority is in Section 4 of the Project BioShield Act and adds Section 564 of the Federal Food, Drug, and Cosmetic Act. This section permits the HHS Secretary to authorize the introduction into interstate commerce of a drug, device, or biological product intended for use in an actual or

[1] *Biodefense for the 21st Century.* April 28, 2004. http://www.whitehouse.gov/homeland/20040430.html.

potential emergency, even if the product is not approved, cleared, or licensed by the HHS/Food and Drug Administration (FDA) within HHS or is approved, cleared, or licensed for a different use. The Secretary has delegated this authority to the HHS/FDA Commissioner. The FDA Commissioner may invoke this authority only following a declaration of emergency by the Secretary. The Secretary may issue such a declaration based on a determination of a public health emergency that affects or has the significant potential to affect national security and involves a specific threat agent, or on the basis of an attack, or heightened risk of attack, with such an agent on either the domestic population (as determined by the Secretary of Homeland Security) or on U.S. military forces (as determined by the Secretary of Defense). Additional requirements for issuance of an EUA include the determination by the HHS/FDA Commissioner that there is no adequate and approved alternative product available to address the specific threat that is causing the emergency declaration, that the known and potential benefits of use outweigh the known and potential risks, and that it is reasonable to believe the product may be effective. The HHS/FDA Commissioner also may establish conditions on an EUA that he finds necessary or appropriate to protect the public health. This section requires the FDA Commissioner (to the extent practicable, given the circumstances of the emergency) to establish certain conditions on an EUA and permits the Commissioner to establish certain other conditions. The EUA expires upon the termination of the emergency declaration, or earlier if the Secretary determines that the emergency has ceased. An EUA may be revoked before termination of the Secretary's declaration if the HHS/FDA Commissioner determines that the criteria for issuance of the EUA are no longer met or that revocation is appropriate to protect public health or safety.

The Project BioShield Act of 2004 requires an annual report to Congress to outline the use of these new authorities. This first report provides details of the research and development, acquisition, personnel management, and Emergency Use Authorization (EUA) authorities exercised from enactment of the Project BioShield Act on July 21, 2004 through July 2006.

Additionally, on 16 March 2006, before the Senate Committee on Health, Education, Labor and Pensions, Secretary Leavitt announced his intention to establish a dedicated strategic planning function and to streamline and improve the interagency Project BioShield governance process. This report will also discuss these efforts.

3.0 Restructuring the Office of Public Health and Emergency Preparedness (OPHEP)

The restructuring of the Office of Public Health Emergency Preparedness (OPHEP) was accomplished and announced in the Federal Register Notice on July 6, 2006.[2] It served to realign the functions of OPHEP in order to delineate more clearly responsibilities for the missions of advanced research and development and acquisition of medical countermeasures, and emergency preparedness and response. These missions are in keeping with the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, the Project BioShield Act of 2004, and the President's Directive *Biodefense for the 21st Century*.

Under the reorganized structure, on behalf of the Secretary, the Office of Public Health Emergency Preparedness (OPHEP) leads the Federal public health and medical response to acts of terrorism or nature, and other public health and medical emergencies. OPHEP is a component of the Public Health Service (PHS) and is responsible for ensuring a one-department approach to developing public health and medical preparedness and response capabilities and leading and coordinating the relevant activities of the HHS Operating Divisions (OPDIVs).

The principal areas of program emphasis are:

- Enhancement of State and local public health and medical preparedness—primarily health departments and hospitals;
- Development and use of National and Departmental policies and plans relating to the response to public health and medical threats and emergencies;
- Coordination with relevant entities inside and outside HHS, such as State, local, and Tribal public health and medical officials, the private sector, the Departments of Homeland Security (DHS), Defense (DoD), Veterans Affairs (VA), Justice (DOJ), the Homeland Security Council (HSC) and National Security Council (NSC), other ESF 8 partner organizations, and others within the National security community;
- Rapid public health and medical support to Federal, State, local, and Tribal governments who may be responding to incidents of national significance or public health and medical emergencies;
- Coordination, support of, and participation in research, development, and procurement activities related to public health emergency medical countermeasures destined for the Strategic National Stockpile, including under Project BioShield;
- Leadership in international programs, initiatives, and policies that deal with public health and medical emergency preparedness and response related to naturally occurring threats such as infectious deceases and deliberate threats from biologic, chemical, nuclear and radiation sources; and
- Leadership and oversight on medical, science, and public health policies, issues, and programs.

[2] Federal Register/Vol. 71, No. 129 / Thursday, July 6, 2006 / Notices

OPHEP is headed by the Assistant Secretary for Public Health Emergency Preparedness (ASPHEP), who reports directly to the Secretary, and includes the following components:

- Immediate Office of the ASPHEP
- Office of the Public Health Emergency Medical Countermeasures
- Office of Preparedness and Emergency Operations
- Office of Medicine, Science and Public Health
- Office of Policy and Strategic Planning

Functions

Immediate Office of the ASPHEP

The Immediate Office of the ASPHEP (IO/ASPHEP) provides executive and administrative direction to all OPHEP components. The ASPHEP is the principal advisor to the Secretary on matters relating to public health and medical emergencies, whether resulting from acts of nature, accidents, or terrorism. The ASPHEP coordinates interagency interfaces between HHS, the Homeland Security Council, the National Security Council, other Federal Departments and Agencies, State, local and Tribal public health and medical entities and the private sector. The ASPHEP directs and coordinates the Department's activities relating to protecting the U.S. population from acts of terrorism and other public health and medical threats and emergencies. The ASPHEP provides leadership in the coordination of activities for public health and medical emergency preparedness and represents the Department in working closely with DHS, DOD, VA, and other Federal Departments and Agencies.

The Office of Public Health Emergency Medical Countermeasures (OPHEMC; formerly the Office of Research and Development Coordination (ORDC))

The Office of Public Health Emergency Medical Countermeasures (OPHEMC) is headed by a Director and is responsible for coordination of the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE). The PHEMCE is a coordinated interagency effort to:

- Define and prioritize requirements for public health medical emergency countermeasures;
- Coordinate research, early and late stage product development and procurement activities addressing the requirements; and
- In support of the work of the PHEMCE, set deployment and use strategies for medical countermeasures held in the Strategic National Stockpile.

OPHEMC undertakes public health modeling of population exposures to assist in determining requirements and assessing deployment and utilization strategies, supports late-stage medical countermeasure research and development to address prioritized requirements for addressing the health effects of naturally occurring infectious diseases and deliberately released biologic, chemical, and radiological/nuclear threats that could cause a public health emergency. It facilitates collaboration among the Department of Health and Human Services agencies, relevant industries, academia, and others with respect to advanced product research and development, facilitates contacts between interested persons and companies interested in requirements set by the Food and Drug Administration regarding such products, and procures targeted medical

countermeasures destined for the Strategic National Stockpile, including vaccines, antivirals, and diagnostics authorized under the Project BioShield Act of 2004 (P. L. 108–276).

OPHEMC is responsible for coordinating, supporting, and providing leadership and expert advice with respect to public health medical countermeasure late stage advanced development and procurement. OPHEMC supports the ASPHEP by working with all scientific agencies of the Department, including the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), and the Food and Drug Administration (FDA), as well as other Governmental, private, and nonprofit scientific entities.

Office of Preparedness and Emergency Operations (OPEO; formerly the Offices of Emergency Operations (OEOSP) and Security Programs and Mass Casualty Planning (OMCP))

The Office of Preparedness and Emergency Operations (OPEO) is headed by a Director and is responsible for developing operational plans and analytical products, and developing and participating in training and exercises to ensure the preparedness of the Office, the Department, the Government, and the public to respond to domestic and international public health and medical threats and emergencies. OPEO is also responsible for ensuring that OPHEP has the systems, logistical support, and procedures necessary to coordinate the Department's operational response to acts of terrorism and other public health and medical threats and emergencies.

OPEO leads the HHS and interagency planning and response activities required to fulfill HHS responsibilities under ESF #8 of the *National Response Plan* (NRP) and Homeland Security Presidential Directive 10, *Biodefense for the 21st Century* (HSPD #10). OPEO:

- Manages the Secretary's Operations Center (SOC);
- Trains and manages the Incident Response Coordination Team (IRCT);
- Plans, implements, and evaluates Departmental and interagency response exercises and the HHS Continuity of Operations (COOP) and Continuity of Government (COG) programs;
- Maintains a regional planning and response coordination capability:

  Has operational responsibility for HHS functions related to the National Disaster Medical Systems (NDMS) and is also the primary operational liaison to emergency response entities within HHS (e.g., FDA, HRSA, SAMHSA, CDC), within the interagency community (e.g., HDS, VA, DoD), and the public. OPEO manages the continued planning for capabilities to meet public health and medical response missions, including development of Federal Medical Stations (FMS) and other mobile medical units. OPEO works to integrate mass casualty preparedness activities, through its surge capacity efforts, across local, State and Federal levels consistent with the National Incident Management System (NIMS) and the National Response Plan Catastrophic Incident Annex;
- Coordinates preparedness grant activities across the Department in collaboration with DHS in compliance with HSPD 8 and the National Preparedness Goal;
- Serves as the primary OPHEP liaison with the Health Resources and Services Administration (HRSA) regarding its programs for hospital bioterrorism preparedness, volunteer health professionals, and terrorism-related preparedness and response education and training for health care professionals; and

- Coordinates with CDC on public health preparedness issues and consults with the HHS scientific community on the inclusion of newly acquired countermeasures into response plans.

Office of Medicine, Science and Public Health (OMSPH)

The Office of Medicine, Science and Public Health (OMSPH) is headed by a Director and is responsible for providing expert medical, scientific, and public health advice on domestic and international medical preparedness policies, programs, initiatives, and activities of OPHEP. OMSPH serves as the OPHEP liaison to health and science professional organizations for domestic and international issues. It carries out special scientific and public health-related projects directly and works with others to establish activities, programs, policies, and standards to protect the public from acts of terrorism, naturally occurring infectious disease threats, and other natural or man-made public health threats.

OMSPH coordinates OPHEP's overall influenza pandemic effort and works closely with HHS components (e.g., National Vaccine Program Office, Office of Global Health Affairs, CDC, NIH, and FDA), and other agencies and offices, such as the Department of State, the U.S. Department of Agriculture (USDA), and the World Health Organization (WHO) to ensure that programs and plans for dealing with avian influenza and pandemic influenza are as effective as possible.

OMSPH oversees the development of medical policies related to providing access to medical products, including those needed on an emergency basis as medical countermeasures to counteract terrorism or naturally occurring biological, chemical or radiological/nuclear threats. These policies and their implementation include:

- Use of investigational and emergency use authorities;
- Serving as the focal point in HHS for biosafety, biosecurity, and dual use technology issues; and
- Liaising to the National Science Advisory Board on Biosecurity and to the State Department on the Biological and Chemical Weapons Convention.

In addition to domestic issues and programs, OMSPH is the OPHEP focal point for all international activities related to public heath emergency preparedness. It supports the Early Warning Infectious Disease Surveillance (EWIDS) program at the national borders with Mexico and Canada and works with other nations and multilateral organizations (e.g., WHO) in combating public health threats, emergencies, and bioterrorism by establishing bilateral and multilateral international arrangements to develop early warning surveillance and response capability for infectious disease outbreaks, including those involving potential bioterrorism agents.

OMSPH provides leadership in the activities of regional and multilateral groups, including the Global Health Security Action Group (GHSAG), the Security and Prosperity Partnership (SPP), and the implementation of the WHO International Health Regulations (IHR), in coordination with the Office of Global Health Affairs.

Office of Policy and Strategic Planning (OPSP)

The Office of Policy and Strategic Planning (OPSP) is headed by a Director and is responsible for policy formulation, analysis, coordination, and evaluation for preparedness, response, and strategic planning. In coordination with other OPHEP and Departmental offices, OPSP analyzes proposed policies, Presidential directives, and regulations. OPSP also develops short- and long-term policy and strategic objectives for OPHEP, and leads in the development and implementation of an integrated OPHEP approach to policy, strategy, and long-term, planning processes.

On behalf of the ASPHEP, OPSP serves as the focal point for HSC/NSC policy coordination activities and represents the ASPHEP, as appropriate, in interagency meetings. The office undertakes studies of preparedness and response issues, identifying gaps in policy and initiating policy planning and formulation to fill these gaps. It takes the lead on special projects, initiatives, and policy analysis and evaluation as tasked by the ASPHEP.

4.0 Public Health Emergency Medical Countermeasures Enterprise

Also announced in the HHS Federal Register Notice of July 6, 2006 was the establishment of the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE). The PHEMCE has the overarching mission to: (1) define and prioritize requirements for public health medical emergency countermeasures, (2) coordinate research, early and late stage product development, and procurement activities addressing the requirements, and (3) set deployment and use strategies for medical countermeasures held in the Strategic National Stockpile. In support of this mission are the:

- Project BioShield Act of 2004
- Development of the HHS Public Health Emergency Medical Countermeasures Enterprise Strategy and the HHS Implementation Plan (Refer to Section 5.0)
- Pandemic Influenza Strategic Plan (Refer to Section 9.1 and reference #2 of this report)

The roles of key HHS agencies in the PHEMCE are detailed below.

The Office of Public Health Emergency Preparedness (OPHEP) directs and coordinates HHS efforts on behalf of the Secretary with respect to preparedness for and response to bioterrorism and other public health emergencies, and coordinates activities within HHS and with other Departments and Agencies with responsibility for emergency preparedness. The Office of Public Health Emergency Medical Countermeasures (OPHEMC; formerly the Office of Research and Development) within OPHEP is responsible for coordinating the process of research, development, purchase, and availability of effective countermeasures against agents of bioterror or other public health emergencies. The Office of Medicine, Science and Public Health (OMSPH) within OPHEP supports this effort by overseeing the development of medical policies related to providing access to medical products, including those needed on an emergency basis as medical countermeasures to counteract terrorism or naturally occurring biological, chemical or radiological/nuclear threats. These policies and their implementation include use of investigational and emergency use authorities.

The National Institutes of Health (NIH) is the lead agency within HHS for conducting and supporting biomedical and behavioral research relating to causes, diagnosis, treatment, control and prevention of diseases, disorders, and impairments of mankind. The National Institute of Allergy and Infectious Diseases (NIAID), a component of the NIH, conducts and supports research on allergic and immunologic diseases and disorders and infectious diseases, including research on and development of countermeasures to agents of bioterrorism. NIAID had an R&D

budget in FY06 of $1.6 billion and has primary responsibility for biodefense research within the United States Government.

The Centers for Disease Control and Prevention (CDC) has a lead role for the USG in public health surveillance and operates HHS' Strategic National Stockpile (SNS), which contains large quantities of medicine and medical supplies to protect the American public if there is a public health emergency severe enough to cause local supplies to run out. Furthermore, CDC is responsible for recommending utilization policies for these medical countermeasures and synthesizing public health surveillance data to assist in determining when stockpiled products should be deployed during significant public health events. CDC also supports biodefense research and development but to a significantly lesser degree than NIH. OPHEP/OPEO has a role in determining how the SNS gets deployed and utilization strategies for the SNS content.

The Food and Drug Administration (FDA) is charged with ensuring the safety and effectiveness of medical countermeasures, including drugs and devices, and plays a vital regulatory role in product development and post-market surveillance. In addition, it serves a technical support role in the development of assays, animal models, etc. to support medical countermeasure development. The HHS Secretary has also delegated the authority to issue Emergency Use Authorizations (EUAs) to the FDA Commissioner. An EUA allows the use of unapproved medical countermeasures or unapproved uses of approved countermeasures in a declared emergency if certain criteria are met and there are no adequate, approved, or available alternatives.

5.0 The HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy for Chemical, Biological, Radiological, and Nuclear (CBRN) Threats

The HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) *Strategy for Chemical, Biological, Radiological, and Nuclear (CBRN) Threats* (the PHEMCE *Strategy*) establishes the principles and processes for identifying priority threat areas and requirements for medical countermeasure development and acquisition, including those medical countermeasures to be developed or acquired under the authorities of the Project BioShield Act of 2004. The PHEMCE *Strategy* is being developed to describe the HHS approach to most effectively develop and acquire the needed MCs for the highest priority deliberate threats. It will also outline the critical roles played by HHS agencies and other federal government partners, as well as private industry. The PHEMCE *Strategy* is anticipated for submission to the *Federal Register* in September 2006, and will be a key feature of the BioShield Stakeholders Workshop to be held on September 25 – 26, 2006.

The PHEMCE *Strategy* will provide a framework for future U.S. Government planning efforts that is consistent with the President's *21st Century Strategy for Biodefense*, and the *National Strategy to Combat Weapons of Mass Destruction.*

It recognizes that preparing for and responding to CBRN events is not strictly a federal responsibility, but relies significantly on other key stakeholders including the industrial, academic and governmental biomedical research and development community, federal, state and local governments, public health authorities, first responders, Congress, and the public.

The PHEMCE *Strategy* is the first in a two-stage HHS process. The HHS PHEMCE *Implementation Plan*, step 2, will analyze the input data (including population exposure assessments and threat scenarios from DHS, medical/public health consequences from HHS, and medical countermeasures technology assessment from the interagency and industry) to establish and prioritize requirements. The result will be a prioritized plan with near-, mid-, and long-term goals for research, development, and acquisition of medical countermeasures that is consistent with the guiding principles and priority-setting criteria defined in the PHEMCE *Strategy*. It is anticipated that the PHEMCE *Strategy* will be finalized along with the Implementation Plan in early 2007.

Pillars of the Draft PHEMCE *Strategy*

The four pillars of the draft PHEMCE *Strategy* are:

- Threat Identification and Prioritization

  - HHS will consider the best available intelligence and scientific information to identify and prioritize CBRN threats; and
  - HHS's public health consequences assessments and corresponding medical countermeasure priorities and requirements will be informed by the DHS Material Threat Determinations, which—as defined in the Project BioShield Act—identify agents that present a material threat sufficient to affect national security.

- Medical/Public Health Consequence Assessment: HHS will utilize modeling, where available, to complement the subject matter experts' evaluation of the effectiveness of various medical countermeasure strategies and response capabilities.
- Establishment and Prioritization of Medical Countermeasures Requirements
  - HHS will establish baseline requirements based on unmitigated consequence assessments;
  - HHS will assess the status of medical countermeasures available and in development. HHS will establish Concept of Operations including maintenance, utilization policies and deployment plans for each medical countermeasure in the context of all available consequence mitigation strategies;
  - Gap analysis: HHS will assess medical countermeasure requirements vs. candidate and available medical and non-medical countermeasures; and
  - HHS will define specific medical countermeasure requirements, including product specifications consistent with USG storage plans and operational capabilities for deployment and utilizations by federal, state and local authorities.
- Establish and Prioritize Near-Term (FY07 – 08), Mid-Term (FY09 – 13), and Long-Term (FY14 – 23) Development, Acquisition, Stockpiling and Maintenance Strategies
  - HHS will establish a research and development portfolio to address medical countermeasure gaps and to meet future acquisition targets (align requirements with priorities);
  - HHS will identify and support critical infrastructure that enables medical countermeasure development such as biocontainment facilities, animal models, workforce training, production, etc.; and
  - HHS will establish short-, mid-, and long-term acquisition strategies that incorporate all relevant cost elements for acquisition, storage, maintenance, deployment and utilization of the medical countermeasure.

6.0 The Project BioShield Process for Acquisition of Medical Countermeasures

Project BioShield seeks to accelerate research, development, purchase and availability of priority security countermeasures against CBRN threats. It charges the HHS Secretary, in collaboration with other federal agencies, to develop and provide countermeasures to protect the civilian population from the health effects that would follow CBRN events.

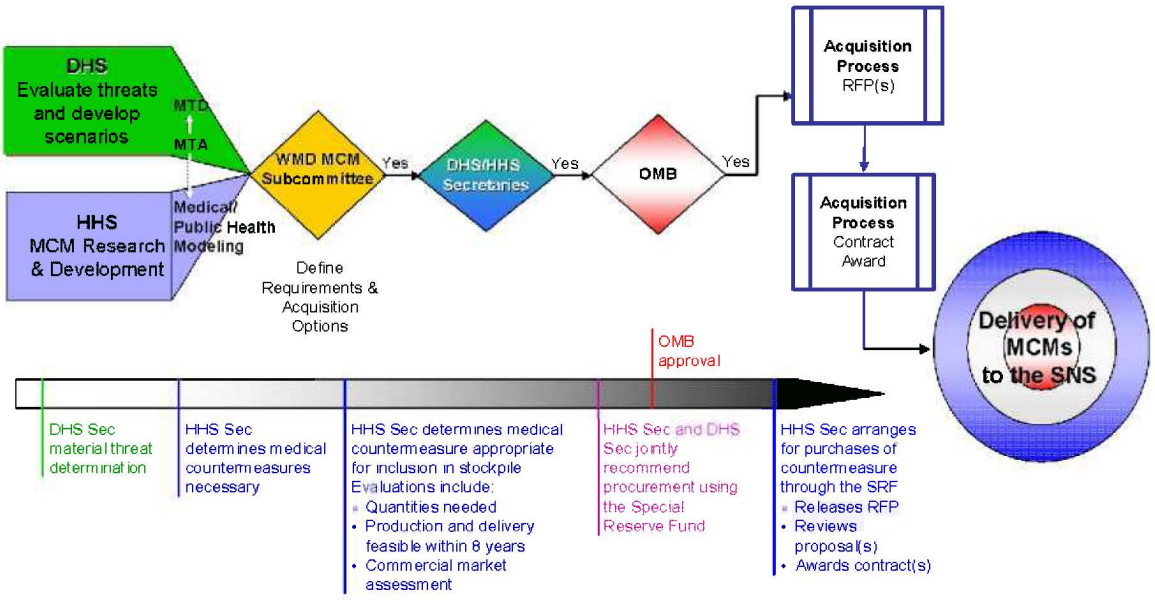
Underlying the Project BioShield process are several critical activities, including assessments and determinations of material threats, prioritization of these threats, assessment of the need for and availability of medical countermeasures given this prioritization, and balanced investment in security countermeasures that are commensurate with the threat and within the limits of the SRF.

Project BioShield Oversight

Release of the funds from the SRF is subject to interagency and presidential approval. The Secretary of Homeland Security (DHS), in consultation with the HHS Secretary and the heads of other federal agencies as appropriate, must determine that there is a material threat, and the HHS Secretary must determine that a security countermeasure is necessary to address that threat in order to protect the public health. The HHS Secretary 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 FDA requirements for licensure (vaccines and biologics), approval (drugs), or clearances (devices and diagnostics) within eight years; therefore, products must be in advanced development to be eligible for acquisition under Project BioShield. Additionally, the determination is also based on consideration of the existence or lack of a significant commercial market for the product; this consideration has not precluded any acquisition to date.

The HHS and DHS Secretaries must jointly recommend to the President use of the Special Reserve Fund to acquire a countermeasure. The President can approve the use of the Special Reserve Fund. This authority was delegated to the Director of the Office of Management and Budget (OMB) (**Figure 1**).[3] Only then does the HHS Secretary procure a medical countermeasure through OPHEP/OPHEMC, which manages Project BioShield acquisitions and executes contracts with manufacturers. Like other federal programs, Project BioShield is subject to government-wide competition requirements as outlined in Federal Acquisition Regulations (FAR) and the Health and Human Services Acquisition Regulations (HHSAR). OPHEMC makes contract awards utilizing the SRF following a full and open competition, unless the HHS Secretary determines that this requirement would seriously impair the mission of the Project BioShield program, or unless generally applicable exceptions to competition apply. In such situations, a Justification for Other than Full and Open Competition (JOFOC) is used.

[3] The President delegated authority to approve the use of the SRF for Project BioShield procurements to OMB in a Memorandum to the OMB Director dated October 21, 2004.



(WMD MCM Subcommittee = Weapons of Mass Destruction Medical Countermeasures Subcommittee)

Figure 1: Project BioShield Process

Importantly, as stated in section 319F-2(c)(7)(c)(ii) of the Project BioShield Act, no payments are made "until delivery has been made of a portion, acceptable to the Secretary, of the total number of units contracted for," unless "the Secretary determines…that an advance payment is necessary to ensure success of a project…" The statute limits such advance payments to 10 percent of the contract amount. Project BioShield allows discounted payments for unlicensed/unapproved products. Under the discounted payment authority, the vendor must seek FDA approval, clearance or licensure of the product, with additional payment rendered once the product has met the full regulatory requirements. Project BioShield procurement contracts are typically awarded for a period not to exceed five years. The only exception is where the Secretary makes a determination at the time of contract award that complexities or difficulties in performance justify an extension to no more than a total of eight years. In addition, the contract must be renewable for additional periods, none of which may exceed five years. The SRF authorized by Project BioShield can be utilized for the shipping, handling, storage, and related costs of the biomedical product. As with all medical products, the FDA (Center for Biologics Evaluation and Research for vaccines and biologics; Center for Drug Evaluation and Research for drugs and some biologics; Center for Devices and Radiological Health for devices and diagnostics) is responsible for regulatory oversight of medical countermeasures.

Requirements Determination for Project BioShield Acquisitions

The need for products that would ameliorate the effects of CBRN exposures demands a deliberative approach to defining requirements and setting priorities. The interagency Weapons of Mass Destruction Medical Countermeasures (WMD MCM) Subcommittee serves this purpose. This Subcommittee also assesses acquisition options, identifies gaps in the product development pipeline, and makes recommendations for addressing these gaps.

The President's *National Security Presidential Directive-17/Homeland Security Presidential Directive-4* (NSPD-17/HSPD-4) created the Counterproliferation Technology Coordination

Committee (CTCC), which is charged with the coordination and strategic direction of cutting edge technology aimed at non- and counterproliferation of weapons of mass destruction. The WMD MCM Subcommittee was first convened in March 2003 under the authorities of the Office of Science and Technology Policy, the Homeland Security Council (HSC) and the National Security Council, and reported through the CTCC to the Deputies Council.

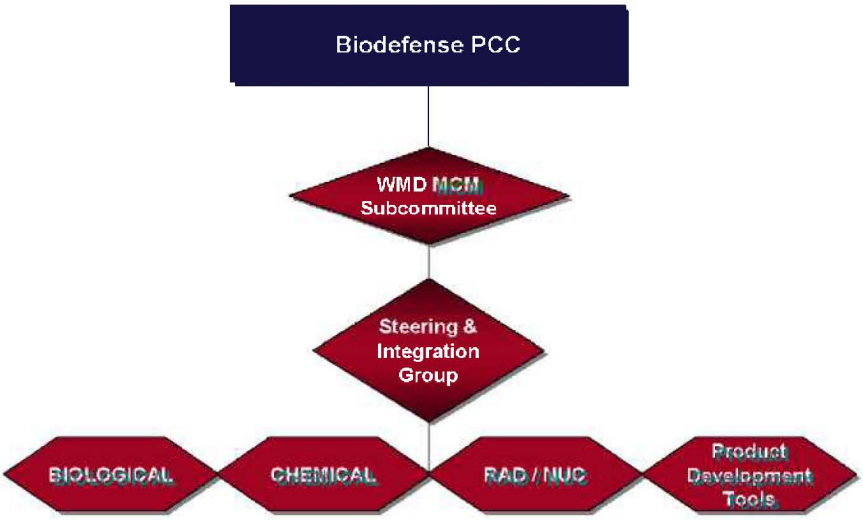


Figure 2: Project BioShield: Interagency Coordination Structure

The original charter was modified and the Subcommittee was reconvened in early 2005 (**Figure 2**). The Subcommittee now reports to the Homeland Security Council's Biodefense Policy Coordinating Committee (PCC) and Deputies Committee (DC) for informational and decisional briefings as necessary. The Subcommittee and its subordinate Working Groups include members from various Executive Branch agencies (**Figure 3**) and consider both civilian and military needs in their assessments. Appendix 2 provides a more in-depth description of the Subcommittee and its activities.

Department of Health and Human Services	Department of Veterans Affairs
• Centers for Disease Control and Prevention	Environmental Protection Agency
• Food and Drug Administration	Intelligence Community (FBI, CIA)
• National Institutes of Health	Homeland Security Council
Department of Homeland Security	National Security Council
Department of Defense	Office of the Vice President
Department of Agriculture	Office of Science and Technology Policy
Nuclear Regulatory Commission	Office of Management and Budget*
Department of Energy	

* *serves as ex officio observer*

Figure 3: Stakeholder Agencies Represented in the WMD MCM Subcommittee Process

The WMD MCM Subcommittee is responsible for evaluating the potential medical and public health impact of medical countermeasures on exposed populations. It achieves this by reviewing

modeling scenarios of medical consequences and the effectiveness of medical response. Researchers use mathematical models to estimate casualties from an attack and its impact on the health care system. These models assess the effectiveness of various medical countermeasures, such as pre-event vaccination, post-exposure vaccination, post-exposure therapeutics, quarantine, and isolation. This process identifies knowledge gaps and helps to inform the medical countermeasures research agenda. The value of these models depends on the validity of the assumptions, which are highly sensitive to estimates of factors, such as immunity, infectious doses, transmission rates and incubation periods. Initially, the three most critical Category A biological threats (see Appendix 1)—anthrax, botulism, and smallpox—were assessed. The WMD MCM Subcommittee developed the necessary requirements and acquisition options to support medical countermeasure acquisition decisions. Then, the Subcommittee selected the best acquisition options. After reviewing all materials, the Secretaries of HHS and DHS jointly recommended procurement using the Special Reserve Fund. The formal Presidential/OMB approval process to utilize the Special Reserve Fund under Project BioShield followed this joint recommendation. (Note: the responsibilities of the WMD MCM Subcommittee have now been transferred to the HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Governance Board).

Coordination of HHS Research, Development, and Acquisition Activities

OPHEMC coordinates with DHS, DoD, and other federal agencies on issues relating to medical countermeasure research, development, acquisition and use. OPHEMC manages the acquisition of priority security countermeasures for the Strategic National Stockpile using the Special Reserve Fund. **Figure 4** depicts organizational relationships within HHS regarding medical countermeasures.

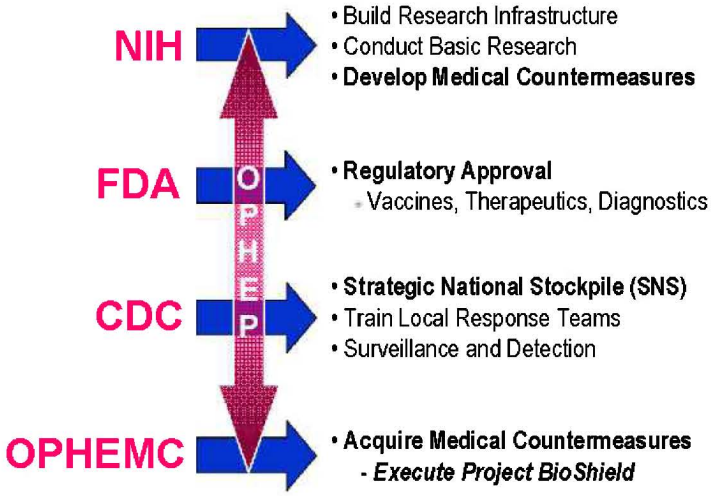


Figure 4: Organizational Relationships within HHS

The NIH is responsible for government-funded research and the development of medical countermeasures to provide a pipeline of effective products eligible for Project BioShield procurement. The FDA provides regulatory oversight for product development, approval and ongoing shelf life requirements. The CDC manages the stockpile of medical countermeasures and provides critical input for determining the optimal stockpiling and deployment product characteristics. OPHEMC works with all these HHS agencies to coordinate the transitions between product development at NIH, procurement by OPHEMC, regulatory approval and

oversight by FDA, and stockpiling by CDC. For each contract awarded for acquisition of countermeasures, OPHEMC sets up coordination teams that include experts from various USG agencies to coordinate the transition of the particular countermeasure from the manufacturer to the Strategic National Stockpile. OPHEMC hosts Risk Management Meetings, which bring together decision-makers from stakeholder agencies to identify and address general risk management issues related to the development, acquisition and use of medical countermeasures for CBRN threats.

Funding available through the NIH biodefense budget provides a major incentive for researchers to develop medical countermeasures. This "push" complements the "pull" of the Project BioShield Special Reserve Fund, which brings security countermeasures through the final stages of development (including acquisition) of the research and development pipeline (**Figure 5**).

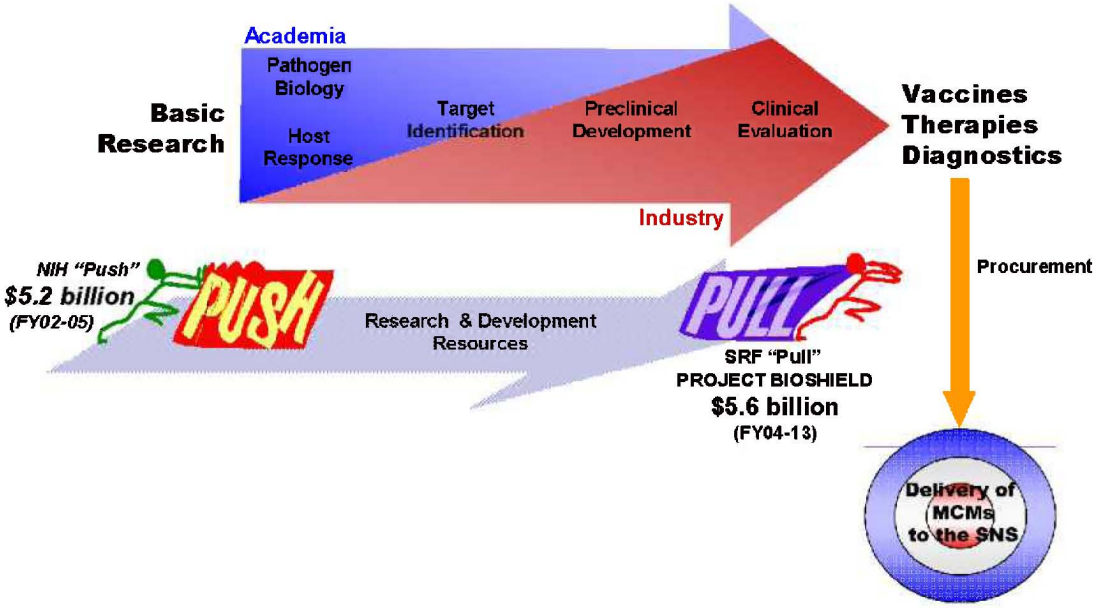


Figure 5: Medical Countermeasures Pipeline

7.0 Report on Exercises of Authorities: Office of Public Health Emergency Medical Countermeasures (formerly Office of Research and Development Coordination)/Office of Public Health Emergency Preparedness

Following is an overview of eight Project BioShield acquisitions in accordance with the reporting criteria from Section 5(a)(1)(A) of the Act. The products are recombinant protective antigen (rPA) anthrax vaccine, anthrax vaccine adsorbed (AVA), anthrax therapeutics, a liquid pediatric formulation of potassium iodide (KI), Modified Vaccinia Ankara (MVA) smallpox vaccine, botulinum antitoxin, therapeutics for acute radiation syndrome, and DTPA for radionuclide removal. HHS has not yet used the special procurement procedures to be reported under Section 5(a)(1)(A) of the Act (e.g., expanded availability of simplified acquisition procedures, and limiting competition to sources responding to a request for information). Normal acquisition procedures have been used for all procurements to date because no circumstance requiring special procedures has arisen. It is possible that they may be required for future acquisitions. All eight acquisitions used or are expected to use the Special Reserve Fund. A summary of completed and on-going acquisitions is in **Figure 6**, and a detailed account is in Section 8.0.

Threat Agent/ Acquisition Program	Date Use of SRF Was Approved	Award Date	Delivery Status	Awardee	Quantity	Cost
Anthrax						
Recombinant Protective Antigen (rPA) anthrax vaccine	August 12, 2004	November 4, 2004	–	VaxGen, Inc.	75 million doses (25 million treatment courses)	$878 M
Anthrax Vaccine Absorbed (AVA)	December 7, 2004	May 4, 2005	Delivery to the SNS has been completed.	BioPort Corporation	5 million doses	$123 million
		May 4, 2006	Delivery to the SNS has commenced.	BioPort Corporation	Additional 5M doses	$120 million
Anthrax therapeutics	August 12, 2004	June 19, 2006	–	Human Genome Sciences	20,001 treatment courses	$165.2 M
		February 24, 2006 (50 doses)	–	Cangene Corporation	50 doses	$0.6M (non-SRF)
		July 27, 2006 (9,950 treatment courses)		Cangene Corporation	10,000 treatment courses	143.8 M

Threat Agent/ Acquisition Program	Date Use of SRF Was Approved	Award Date	Delivery Status	Awardee	Quantity	Cost
Anthrax						
Radiological/ Nuclear						
Pediatric liquid potassium iodide	December 7, 2004	3/18/05	Delivery to the SNS has been completed.	Fleming & Company Pharmaceuti-cals	1.7 million bottles plus retrofitting original purchase with child-proof packaging	$5.7 M plus $1.5 M
		2/8/06	Delivery to the SNS has commenced.	Fleming & Company Pharmaceuticals	3.1 million bottles	$10.3 M
DTPA	January 3, 2006	February 13, 2006	Delivery to the SNS was completed in April 2006	Akorn, Inc.	390,000 doses of Ca-DTPA and 60,000 doses of Zn-DTPA	$22 M
		April 2006	Delivery to the SNS was completed in April 2006	Akorn, Inc.	Contract modification for an additional 5,370 doses of Ca-DTPA and 19,369 doses of Zn-DTPA	$32,500
Therapeutics to mitigate or treat neutropenia associated with Acute Radiation Syndrome (ARS)	January 3, 2006	This award is in progress.				
Smallpox						
Modified Vaccinia Ankara (MVA) smallpox vaccine	December 7, 2004	This award is in progress.				

Threat Agent/ Acquisition Program	Date Use of SRF Was Approved	Award Date	Delivery Status	Awardee	Quantity	Cost
Anthrax						
Botulism						
Botulinum antitoxin	August 17, 2004	June 1, 2006	–	Cangene Corporation	200,000 doses	$363 M

Figure 6: Current Project BioShield Acquisitions

8.0 OPHEMC Utilization of Authority Pertaining to the Acquisition of Medical Countermeasures

8.1 Anthrax Medical Countermeasures—Vaccines

OPHEMC has awarded contracts to procure two anthrax vaccines for the Strategic National Stockpile: Anthrax Vaccine Adsorbed (AVA) and recombinant Protective Antigen (rPA) vaccine.

Threat

Bacillus anthracis, the microorganism causing anthrax, is a leading bioterrorist threat. Among the six leading biological threats, known collectively as Category A Agents[4], only anthrax has actually been used as a terrorist weapon against the U.S. to date. An aerosol anthrax attack could result in hundreds of thousands to millions of casualties. During the 2001 anthrax attacks, 5 of 11 (45%) of the persons who developed symptomatic inhalational anthrax died despite medical intervention and treatment with antibiotics. Anthrax spores released at the time of an attack can persist in the environment and pose a continued risk for infection, particularly for workers who decontaminate an affected area.

On January 20, 2004, the Secretary of DHS determined that anthrax was a material threat to the U.S. population sufficient to affect national security.

Medical Countermeasures

Vaccines, antibiotics, and therapeutics to neutralize anthrax toxins in the body are all necessary to prevent and treat anthrax infection. Use of vaccines before exposure can prevent disease. Concomitant use of anthrax vaccines along with antibiotics is a treatment strategy after exposure, but these cannot neutralize the anthrax toxins once they are released into the bloodstream. Therapeutic products that can inactivate anthrax toxins would be required for symptomatic individuals (See Section 8.1.2).

Options Considered

The WMD MCM Subcommittee, previously described in Section 6.0 and detailed in Appendix 2, established national anthrax vaccine requirements and proposed ways to address them. The Subcommittee estimated the numbers of persons requiring protection in various threat scenarios to determine how many doses to acquire. The Institute of Medicine report *Anthrax Vaccine: Is It Safe? Does It Work?*[5] stated that the nation needs a next-generation anthrax vaccine to replace the existing anthrax vaccine adsorbed. Consequently, the Subcommittee recommended acquisition of the next-generation rPA anthrax vaccine to protect 25 million people. The Subcommittee also recommended a five-million-dose AVA procurement for the stockpile while development and manufacturing of the rPA anthrax vaccine was being completed.

[4] Category A is one of three categories of agents defined by the Centers for Disease Control and Prevention (see Appendix 3).
[5] http://www.iom.edu/report.asp?id=4324

8.1.1 Recombinant Protective Antigen (rPA) Anthrax

On November 4, 2004, HHS awarded VaxGen, Inc. of Brisbane, California a contract to supply 75 million doses of rPA anthrax vaccine (to protect 25 million people) for the SNS. On May 5, 2006, VaxGen, Inc. received a unilateral contract modification from HHS that extends the deadlines by which VaxGen is required to complete various milestones and provide product to the government.

Background

On January 20, 2004, in consultation with the Secretary of DHS, the Secretary of HHS, pursuant to the provisions of Section 319F-2(c)(5) of the Public Heath Service Act, determined that rPA vaccine was appropriate for inclusion in the Strategic National Stockpile (SNS).

Rationale Underlying Decision to Acquire

Given the seriousness of a possible anthrax attack, the development of a next-generation anthrax vaccine is among the top priorities of HHS. The Institute of Medicine report *Anthrax Vaccine: Is It Safe? Does It Work?* concluded "that a new [anthrax] vaccine, developed according to modern principles of vaccinology, is urgently needed." The developmental status of rPA anthrax vaccines is mature enough for a Project BioShield acquisition utilizing the SRF. Evidence of this acquisition-ready state includes more than ten years of development by DoD laboratories, a progress assessment by vaccine developers funded by the NIAID Biodefense Budget, and industry's response to the August 14, 2003 Request for Information (RFI)(RFI-ORDC-03-01) published by HHS. The response identified companies capable of producing at least 25 million doses delivered in a way that could meet FDA regulatory requirements and that could be easily deployed and administered in a public health emergency.

Approval

Following a joint request from the Secretaries of DHS and HHS, the President approved the acquisition of 75 million doses of rPA anthrax vaccine (to protect 25 million people) for the SNS on August 12, 2004.

Acquisition Process

On February 9, 2004, the Secretary of HHS released a Request for Proposal (RFP)(RFP-HHS-ORDC-04-01) for the acquisition of rPA anthrax vaccine. On April 16, 2004, the RFP closed. Following review by an expert Technical Review Panel (TRP) and subsequent site visits to manufacturing facilities, HHS awarded VaxGen, Inc. of Brisbane, CA a contract to deliver 75 million doses of rPA vaccine to protect 25 million people. The negotiated pricing for the rPA anthrax vaccine assumes delivery of the vaccine to the SNS with additional payments for (1) approval of the Biologics License Application (BLA) for the general use population, (2) approval of the BLA for Post-Exposure Prophylaxis (PEP), and (3) demonstration of 18-month real-time stability of the vaccine. The vaccine must comply with all contract terms to qualify for delivery to the SNS. Criteria required for delivery of a product to the SNS prior to licensure are defined in the contract.

Acquisition Authorities Used

Authority for this procurement was granted under 41 U.S.C. 253(a)(1)(A) as implemented in FAR subpart 6.1. OPHEMC proceeded with a full and open competition, instead of using special

acquisition authorities, in order to maximize competition. Ultimately, economies of scale and satisfaction of technical criteria dictated that the award go to a single manufacturer.

Contract Status

In accordance with Section 319F-2(c)(6) of the Public Health Service Act as added by Section 3 of the Project BioShield Act, Presidential approval to proceed with an acquisition was received on August 12, 2004, and a contract was awarded on November 4, 2004. The contract calls for delivery of 75 million doses of rPA vaccine at a cost of $877.5 million. On May 5, 2006, VaxGen, Inc. received a unilateral contract modification from HHS that extends the deadlines by which VaxGen is required to complete various milestones and provide product to the government. Completed acquisition milestones for the rPA project are in **Figure 7**.

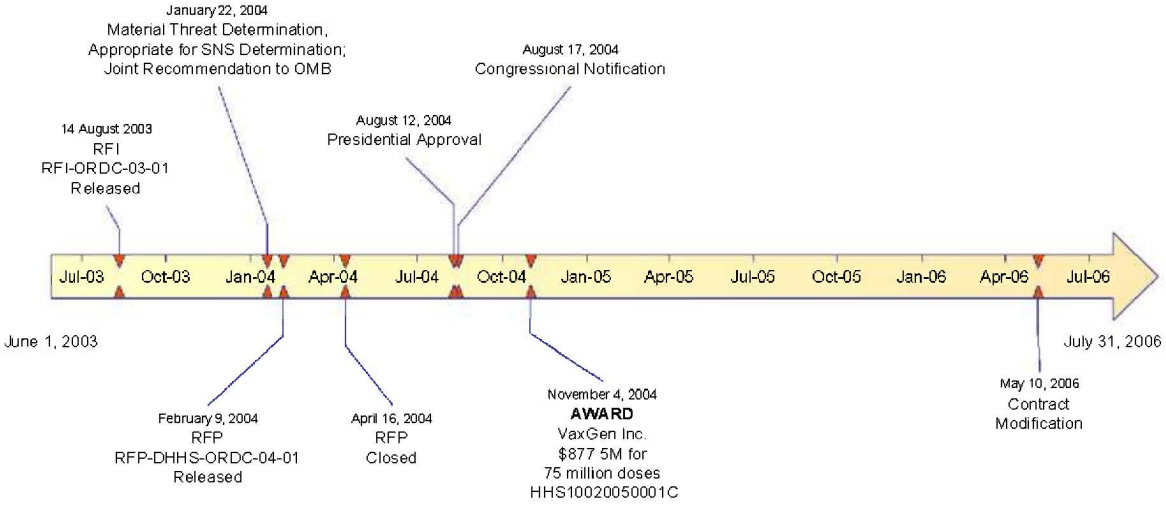


Figure 7: rPA Anthrax Vaccine Acquisition Milestones

8.1.2 Anthrax Vaccine Adsorbed (AVA)

On May 5, 2005, HHS awarded BioPort Corporation of Lansing, Michigan, a sole source contract to supply the SNS with 5 million doses of Anthrax Vaccine Adsorbed. On May 5, 2006, options were exercised under the original BioPort contract for 5 million additional doses of AVA.

Background

On October 19, 2004, in consultation with the Secretary of DHS, the Secretary of HHS, pursuant to the provisions of Section 319F-2(c)(5) of the Public Health Service Act determined that the Anthrax Vaccine Adsorbed was appropriate for inclusion in the SNS.

Rationale Underlying the Decision to Acquire

While the Institute of Medicine stated that a new anthrax vaccine based on modern manufacturing technologies was needed, the next-generation rPA anthrax vaccine is still in late-stage development. As anthrax is a critical, high priority threat, HHS pursued the acquisition of 5 million doses of AVA, which will increase immediate national preparedness until the rPA anthrax vaccine is available.

Approval

Following a joint recommendation request from the Secretaries of DHS and HHS, OMB (under delegated authority from the President) approved the acquisition of 5 million doses of AVA on December 7, 2004.

Acquisition Process and Entities Considered – Justification for Other than Full and Open Competition (JOFOC)

On November 3, 2004, OPHEMC indicated its intent to negotiate a sole source procurement with BioPort Corporation, in Presolicitation Notice 200-2005-11811-01. The special Justification for Other than Full and Open Competition (JOFOC) authority granted under Project BioShield was not necessary for this action, as the procurement met the requirement of only one responsible source to support a JOFOC under FAR 6.302-1. OPHEMC awarded the contract for 5 million doses of AVA to BioPort Corporation (Lansing, Michigan), a privately held U.S. company that is the sole licensed manufacturer of AVA, on May 5, 2005.

Contract Status

In accordance with Section 319F-2(c)(6) of the Public Health Service Act as added by Section 3 of the Project BioShield Act, Presidential approval via authority delegated to OMB was received on December 7, 2004. HHS awarded a contract on May 5, 2005, less than a year after receiving Presidential approval for AVA to be added to the SNS. The contract called for delivery of 5 million doses of AVA at a cost of $122.7 million. Final delivery of the original AVA acquisition to the SNS was completed in February 2006. To support HHS preparedness efforts and to address the additional gap resulting from delays in the VaxGen rPA contract, the Secretaries of HHS and DHS jointly recommended the acquisition of 5 million additional doses of AVA. On April 11, 2006, the Office of Management and Budget (OMB) (under delegated authority from the President) approved this acquisition. On May 5, 2006, options were exercised under the original BioPort contract for 5 million additional doses of AVA at a cost of $120 million. Delivery to the Strategic National Stockpile was initiated in May 2006. **Figure 8** shows the acquisition timeline.

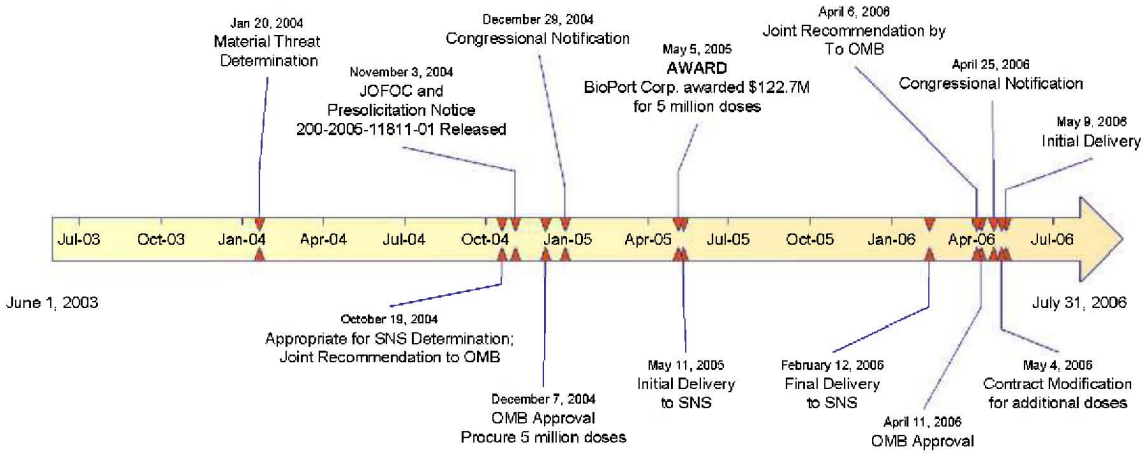


Figure 8: AVA Acquisition Milestones

8.1.3 Anthrax Medical Countermeasures—Anthrax Therapeutics

HHS evaluated proposals for Acquisition of Therapeutic Products for Treatment of Inhalational Anthrax Disease for the SNS. On September 23, 2005, HHS awarded two contracts to Human Genome Sciences, Inc. of Rockville, Maryland, and Cangene Corp. of Winnipeg, Manitoba, using non-Project BioShield funds to acquire ten grams of therapeutic products for testing regarding the treatment of inhalational anthrax disease. These contracts contained options to purchase 10,000 – 100,000 doses of product with Project BioShield funds. These contract options were exercised in June and July of 2006.

Background

On June 14, 2004, in consultation with the Secretary of DHS, the Secretary of HHS, pursuant to the provisions of Section 319F-2(c)(5) of the Public Health Service Act, determined that anthrax therapeutics were appropriate for inclusion in the SNS.

Rationale Underlying Decision to Acquire

The research and development of products that could neutralize anthrax toxin is mature enough for a Project BioShield acquisition utilizing the SRF. Evidence of this acquisition-ready state is based on consultation with government scientists and responses received from industry to an HHS-posted RFI (RFI-65-1 Request for Information for Anthrax Therapeutics) on March 31, 2004.

The HHS RFI requested information on the availability of commercial products or products in advanced development for immune-based antitoxin treatments or drug therapies effective against anthrax toxins. OPHEMC received information on 14 products, including monoclonal antibodies, immunoglobulins, and small molecules. Although none was as mature in the development process as the rPA anthrax vaccines, several products could potentially meet the criteria for a Project BioShield SRF acquisition. HHS proceeded with the acquisition because of the critical need for anthrax therapeutic products.

Approval

Following a joint request from the Secretaries of DHS and HHS, the President approved the acquisition of anthrax therapeutics to treat up to 200,000 persons on August 17, 2004.

Acquisition Process

RFP DHHS 2004-N-01385 for Acquisition of Therapeutic Products for Treatment of Inhalational Anthrax Disease for the Strategic National Stockpile was issued August 18, 2004. The RFP described the need for 10,000 to 200,000 anthrax therapeutic treatments. A technical review panel evaluated proposals received by October 26, 2004. HHS posted a second RFI (ORDC-05-04) on February 23, 2005, essentially repeating the request from RFI [65-1]. Information gathered may result in the release of additional RFPs.

Eligibility for placement of products in the SNS is contingent upon successful animal testing to demonstrate likely efficacy and testing in healthy human volunteers to demonstrate safety. In September 2005, OPHEMC made an award using non-Project BioShield funds to purchase small quantities of anthrax therapeutic products from two separate manufacturers for the animal testing.

Options for acquisition of up to 100,000 doses of product in these contracts would utilize the SRF.

Entities Considered – Full and Open Competition

HHS held a full and open competition because multiple competitors were anticipated. Four companies responded to the RFP, including two U.S. privately held companies, a publicly held U.S. company and a publicly held Canadian company.

Contract Status

In accordance with Section 319F-2(c)(6) of the Public Health Service Act as added by Section 3 of the Project BioShield Act, OMB approval to use the SRF was received on December 7, 2004. HHS awarded two contracts on September 26, 2005, using non-Project BioShield funds to acquire ten grams of product for testing. The contracts also contained options to purchase 10,000-100,000 doses of product with Project BioShield funds. The contracts were awarded a little over one year after receiving Presidential approval for anthrax therapeutics to be added to the SNS. On June 19, 2006, HHS modified its existing contract with Human Genome Sciences of Rockville, Maryland, to include the purchase of 20,001 treatment courses of ABthrax™, an anthrax therapeutic treatment, for a total of $165.2 million. On July 28, 2006, HHS modified its existing contract with Cangene Corporation of Winnipeg, Manitoba, to purchase 10,000 therapeutic courses of treatment of Anthrax Immune Globulin (AIG). The acquisition timeline for anthrax therapeutics is shown in **Figure 9**.

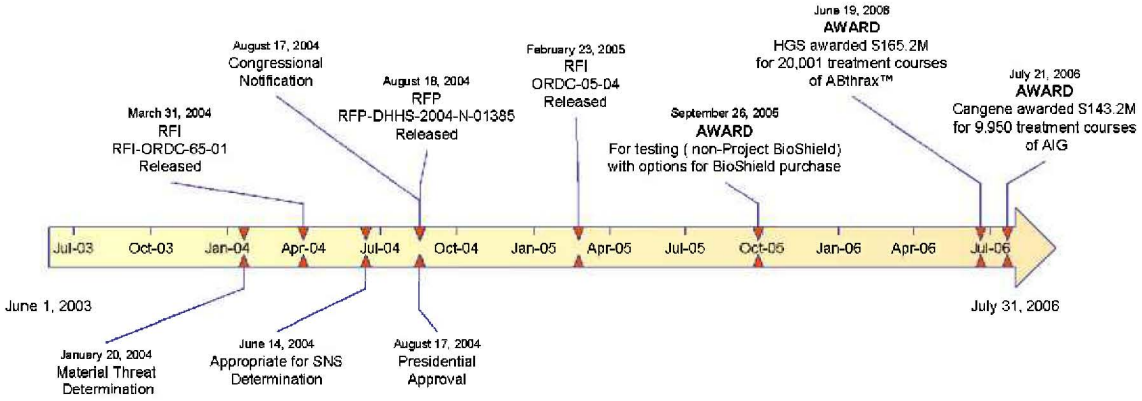


Figure 9: Anthrax Therapeutics Acquisition Milestones

8.2 Smallpox Medical Countermeasures—Modified Vaccinia Ankara (MVA) Vaccine

On August 15, 2005, HHS published an RFP to manufacture and deliver to the SNS up to 20 million doses of MVA. The RFP closed on 3 October 2005, and this award is in progress.

Threat

On September 23, 2004, the Secretary of DHS determined that the smallpox virus is a material threat to the U.S. population sufficient to affect national security.

There are no specific treatments for smallpox disease, and the only preventive measure is vaccination. The vaccine licensed in the United States can have serious side effects, and is potentially unsafe for persons with impaired immune systems, such as some cancer patients, organ transplant recipients, and HIV-infected patients.

Medical Countermeasure

Attenuated vaccinia viruses have the potential to act as safer smallpox vaccines because they appear to have a more limited capacity to reproduce in humans. Early clinical trial data in a limited number of human subjects suggest that the Modified Vaccinia Ankara (MVA) vaccine may be safe and immunogenic in humans. Animal studies demonstrate MVA vaccine protects monkeys and mice from smallpox-like viruses.

Options Considered

Three procurement options for a next-generation smallpox vaccine were proposed. Vaccine cost per dose and the size of the targeted population were major considerations.

The WMD MCM Subcommittee recommended the initial purchase of MVA for the protection of 10 million immunocompromised persons, and endorsed efforts to continue the development of next-generation smallpox vaccines for other target populations.

Background

On October 19, 2004, in consultation with the Secretary of DHS, the Secretary of HHS, pursuant to the provisions of Section 319F-2(c)(5) of the Public Health Service Act, determined that the MVA vaccine was appropriate for inclusion in the SNS.

Rationale Underlying Decision to Acquire

RFI-ORDC-03-01 for Large-Scale Manufacturing Capabilities for Next Generation Anthrax Vaccines (e.g., Anthrax Recombinant Protective Antigen) and Safer Attenuated Vaccinia Vaccines was posted August 14, 2003. Three companies commented specifically on safer smallpox vaccines, and provided information to indicate that MVA met the criteria for a Project BioShield SRF acquisition.

Approval

Following the joint request from the Secretaries of DHS and HHS, OMB approved the acquisition of 10 million immunization courses (20 million doses) of the attenuated smallpox vaccine, MVA on December 7, 2004.

Acquisition Process

HHS issued a draft RFP for industry comment (HHS-ORDC-V&B-05-06 for Acquisition of Modified Vaccinia Ankara [MVA] Vaccine for the Strategic National Stockpile) on May 13, 2005. OPHEMC received three responses by May 31, 2005. A Presolicitation Announcement was posted June 28, 2005, and the final RFP was released on August 15, 2005. The RFP closed on October 3, 2005.

Entities Considered – Full and Open Competition

HHS utilized a full and open competition for this procurement. Three companies responded to the RFI and draft RFP, and two companies responded to the final RFP, which was released on August 15, 2005. This indicates there is more than one responsible source.

Contract Status

In accordance with Section 319F-2(c)(6) of the Public Health Service Act as added by Section 3 of the Project BioShield Act, OMB approved the use of the SRF on December 7, 2004. This award is in progress. **Figure 10** shows the acquisition timeline.

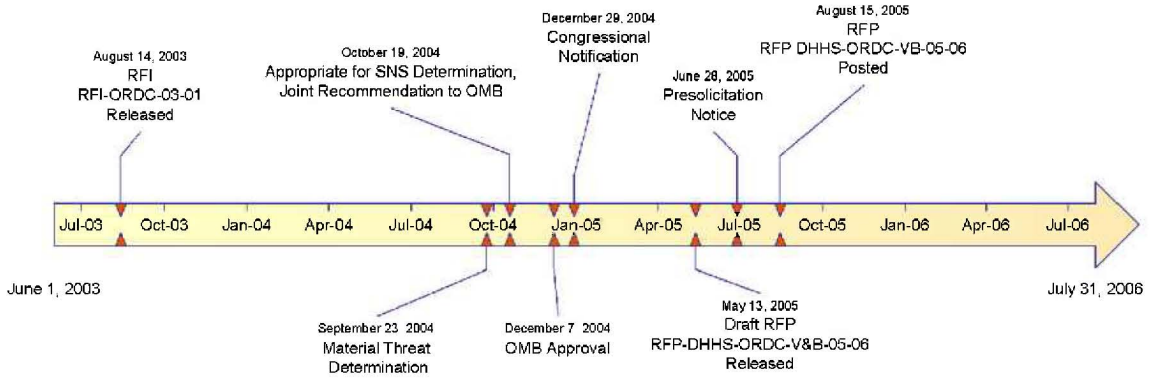


Figure 10: MVA Acquisition Milestones

8.3 Botulism Medical Countermeasures—Botulinum Antitoxin

On September 14, 2004, HHS released a presolicitation notice for acquisition of 200,000 doses of Heptavalent Botulinum Immune Globulin (BIG) via a sole source contract to Cangene Corporation of Winnipeg, Canada. A JOFOC was approved in accordance with the FAR provision in December 2004. A contract was awarded on June 1, 2006, to Cangene Corporation for 200,000 doses of Heptavalent Botulism Antitoxin.

Threat

Botulism is a serious paralytic illness caused by a neurotoxin produced by several *Clostridium botulinum* strains. Exposure to the toxin can lead to death due to respiratory failure. Scenarios used in government preparedness and response planning indicate that hundreds of thousands of casualties could occur following an attack using botulinum toxin.

On June 9, 2004, the Secretary of DHS determined that botulinum toxin (derived from the *Clostridium* species) is a material threat to the U.S. population sufficient to affect national security.

Medical Countermeasure

Use of the appropriate antitoxin within 12 to 36 hours of intoxification can prevent worsening of the effects of botulinum toxin. Antitoxins for the seven known subtypes of toxin produced by *Clostridium* species already exist. A combination of all seven antitoxins is effective against the toxins.

Options Considered

The WMD MCM Subcommittee, previously described in Section 3, established the requirement and proposed options to address those requirements. The options analyzed included four types of products to prevent or treat illness from botulinum toxin and two different dose requirements. Botulinum antitoxin derived from immune globulin was the only product thought suitable for Project BioShield acquisition based on post-exposure effectiveness and maturity of this product's development. The Subcommittee recommended the option to acquire 200,000 doses of heptavalent equine botulinum antitoxin.

Background

On June 14, 2004, in consultation with the Secretary of DHS, the Secretary of HHS, pursuant to the provisions of Section 319F-2(c)(5) of the Public Health Service Act, determined that Investigational Despeciated Heptavalent Botulinum Immune Globulin was appropriate for inclusion in the SNS.

Rationale Underlying Decision to Acquire

The Department of Defense acquired heptavalent equine botulinum antitoxin through the mid-1990s and maintains a limited stockpile of these products. Additionally, CDC had previously awarded a competitive contract to process existing bulk equine antitoxin to augment the limited national supply. In FY04, $50 million was obligated from the SRF for support of the botulinum antitoxin program prior to enactment of the Project BioShield legislation. These initial funds were used to establish the horse farms needed to provide equine plasma containing antitoxin for further processing for human use.

Approval

Following a joint request from the Secretary of DHS and HHS, the President approved the acquisition of 200,000 doses of botulinum antitoxin on August 17, 2004.

Acquisition Process Entities Considered – Justification for Other than Full and Open Competition (JOFOC)

OPHEMC posted Presolicitation Notice 2004-N-01183 titled "HHS and CDC has a Requirement for 200,000 Doses of Heptavalent Botulinum Immune Globulin" on September 14, 2004. A JOFOC was approved in accordance with the FAR provision in December 2004.

Contract Status

In accordance with Section 319F-2(c)(6) of the Public Health Service Act as added by Section 3 of the Project BioShield Act, presidential approval was received on August 12, 2004. The contract award timing was contingent upon the horses showing evidence of high enough antibody titers against botulinum toxins to begin processing their plasma for human use. A contract was awarded on June 1, 2006, to Cangene Corporation for 200,000 doses of Heptavalent Botulism Antitoxin at a cost of $363 million. **Figure 11** shows the acquisition timeline.

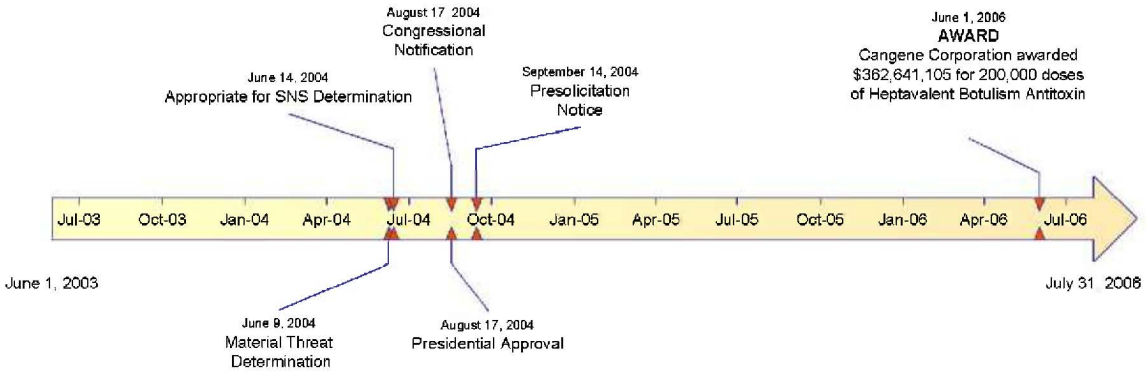


Figure 11: Botulinum Antitoxin Acquisition Milestones

8.4 Radiological and Nuclear Medical Countermeasures

8.4.1 Liquid Potassium Iodide (KI)

On March 18, 2005, HHS awarded Fleming and Company Pharmaceuticals of Fenton, Missouri, a sole source contract to supply the SNS with 1.7 million one-ounce bottles of liquid formulation potassium iodide(KI) for pediatric use. On February 8, 2006, the original contract with Fleming & Company Pharmaceuticals Inc. was modified to acquire 3.1 million additional bottles of pediatric KI.

Threat

On September 23, 2004, the Secretary of DHS determined that radiological and nuclear agents were material threats to the U.S. population sufficient to affect national security.

A nuclear detonation or reactor accident could disperse radioactive isotopes, including radioactive iodine (radioiodine) into the environment. Radioiodine poses a threat because any form of absorbed iodine is concentrated in the thyroid gland. Exposure of the thyroid gland to radioiodine can lead to either thyroid cancer or the destruction of the thyroid gland. Because the thyroid gland is most active in young children, they are at greatest risk of developing adverse effects following exposure to radioiodine.

Medical Countermeasure

One strategy to prevent incorporation of radioiodine into the thyroid gland is to saturate the gland with potassium iodide (KI). KI acts as a blocking agent to counter the effects of radioiodine. The FDA has approved KI in tablet form as a nonprescription drug; however, the American Academy of Pediatrics recommended delivery of KI to children in a liquid preparation because children under 10 years of age may find it difficult to swallow the tablets[6].

Options Considered

HHS considered several acquisition options for the protection of children from radioiodine exposure. All involved a liquid formulation of KI, and primarily differed as to the number of doses required under different scenarios. The final recommended option was to purchase sufficient doses of a liquid formulation of KI to protect children within a 0-20 mile radius of nuclear power plants, in those States with approved KI distribution programs.

Background

On October 19, 2004, in consultation with the Secretary of DHS, the Secretary of HHS, pursuant to the provisions of Section 319F-2(c)(5) of the Public Heath Service Act, determined that liquid potassium iodide was appropriate for inclusion in the SNS.

Rationale Underlying Decision to Acquire

The WMD MCM Subcommittee recommended acquiring sufficient doses of liquid KI to protect children under the age of 10 who live within a 0–20-mile radius of nuclear power plants. This was based on offering the liquid KI for forward deployment in those States with approved KI distribution programs. As other States developed KI programs, their liquid KI procurement requirements would also be considered.

[6] http://www.gnyha.org/eprc/general/nbc/nuclear_radiological/Radiation_Speaking_Points.pdf

Approval

Following a joint request from the Secretaries of DHS and HHS, the OMB approved the acquisition on December 7, 2004.

Acquisition Process and Entities Considered – Justification for Other than Full and Open Competition (JOFOC)

The acquisition of the pediatric liquid formulation of KI was through a sole source contract. Fleming and Company Pharmaceuticals, a privately held U.S. company, manufactures KI in tablet form. The company submitted an Abbreviated New Drug Application to the FDA for the liquid formulation. As Fleming and Company Pharmaceuticals is the sole manufacturer of this formulation, the normal FAR provisions for a JOFOC applied and the special authority granted under Project BioShield was not necessary.

Contract Status

In accordance with Section 319F-2(c)(6) of the Public Health Service Act as added by Section 3 of the Project BioShield Act, OMB approved on December 7, 2004, and a contract was awarded on March 18, 2005, for the delivery of 1.7 million one-ounce bottles at a cost of $5.7 million. Delivery to the stockpile was completed in September 2005, less than a year after OMB approval was received. On February 8, 2006, the original contract with Fleming & Company Pharmaceuticals Inc. was modified to acquire 3.1 million additional bottles of pediatric KI at a cost of $10.3 million. **Figure 12** shows the acquisition timeline.

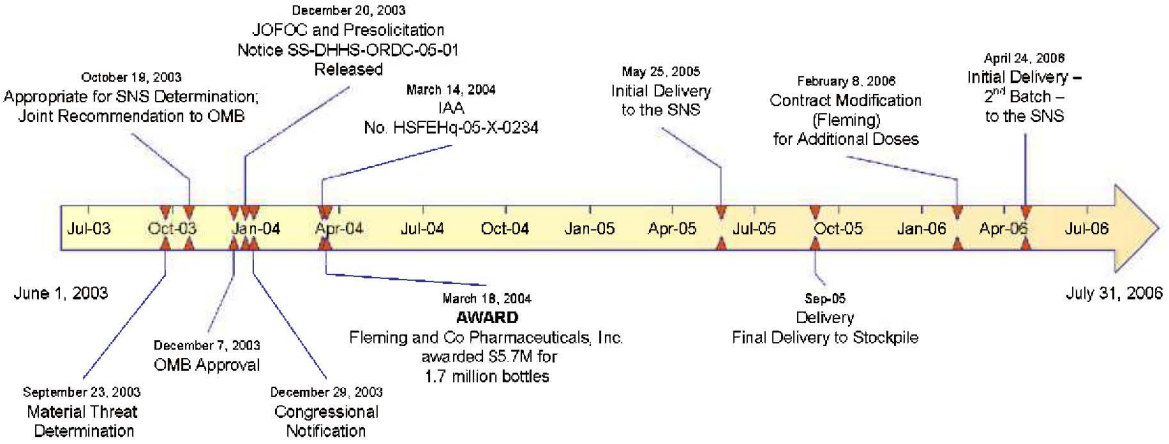


Figure 12: Pediatric Potassium Iodide Acquisition Milestones

8.4.2 Therapeutics/Mitigators for Acute Radiation Syndrome (ARS)

On December 9, 2005, HHS published an RFP to manufacture and deliver to the SNS up to 100,000 treatment courses of a medical countermeasure to mitigate or treat the neutropenia associated with ARS alone or in combination with co-morbidities.

Threat

On January 20, 2004, the Secretary of DHS determined that radiological and nuclear agents were material threats to the U.S. population sufficient to affect national security. DHS subsequently

analyzed in depth the specific threats caused by both radiological materials and so-called "fissile materials." These studies resulted in a Material Threat Assessment of radiological materials (sent to HHS in February of 2005) and a special study on fissile materials sent to HHS in May of 2005.

A radiological or nuclear explosive event could cause high fatality rates and acute and long-term adverse health effects and poses the danger of long-term environmental persistence. Certain forms of radioactive materials could also be delivered by either aerosolization or through food or water contamination.

The health effects following a radiological/nuclear event can be attributed to either whole body radiation exposure and/or uptake of radioactive particles. Whole or significant partial body exposure to radiation can cause radiation sickness, also known as acute radiation syndrome or ARS. ARS describes a range of health effects that indicate there has been severe damage to specific organs. There are separate components of ARS, reflecting the dose absorbed, the rate at which that dose was received, and the organs targeted. One of the most pressing needs of survivors exposed to levels of radiation likely to be experienced in a radiological/nuclear event is mitigation or treatment addressing their decrease in the blood cells needed to protect against infection (the neutropenia associated with ARS). Other important components of the ARS include thrombocytopenia (low platelets) and anemia (lower red blood cells) that can be associated with bleeding, the gastrointestinal syndrome associated with severe diarrhea, an increased risk of life-threatening bacteremia (bloodstream infection), and cerebrovascular syndrome (affecting the brain and blood vessels).

Rationale Underlying Decision to Acquire

Neutropenia is a profound decrease in the number of infection-fighting blood cells (neutrophils), and is an important component of ARS. A decrease in these neutrophils can lead to serious or fatal infections within weeks of high radiation exposure. Medical countermeasures that mitigate or treat this neutropenia and demonstrate improved survival in animal efficacy studies could greatly decrease the risk of death from infection in ARS patients. Additionally, medical products that can mitigate or treat other components of ARS in combination with neutropenia are also important.

The WMD MCM Subcommittee recommended acquisition of 200,000 treatment courses of a medical countermeasure to mitigate and/or treat the neutropenia associated with ARS. The interim requirement for up to 100,000 treatment courses released in the RFP took into account that all products anticipated to be advanced enough for acquisition must be given by injection, either into muscle or under the skin, and must be given as multiple doses over a number of days. The ideal countermeasure—one that could be either taken orally or applied to the skin with a device such as a patch—does not currently exist; hence, deployment of any products acquired under the proposed solicitation will pose challenges.

Status

A draft RFP for medical countermeasures to mitigate or treat the neutropenia associated with ARS was published for industry comment on September 30, 2005. This draft RFP closed on November 2. On November 18, 2005, HHS/DHS jointly submitted a recommendation to OMB that the Project BioShield Special Reserve Fund be utilized to acquire security countermeasures to mitigate or treat the neutropenia associated with ARS for the SNS. A pre-solicitation synopsis of this acquisition was also published on November 18, and HHS posted the final RFP for

medical countermeasures that mitigate and/or treat the neutropenia associated with ARS, alone or in combination with other co-morbidities, on December 9, 2005, contingent on availability of funds. OMB approved the acquisition using the Special Reserve Fund on January 3, 2006 and the RFP closed on February 23, 2006. An award is in progress. **Figure 13** shows the acquisition timeline.

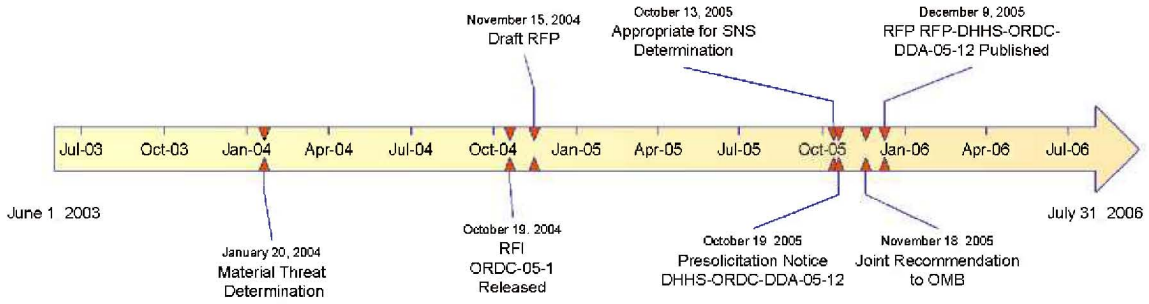


Figure 13: Acute Radiation Syndrome (ARS) Medical Countermeasures Acquisition Milestones

8.4.3 Calcium and Zinc Diethylenetriaminepentaacetate (Ca- and Zn-DTPA)

On October 7, 2005, HHS published an RFP to manufacture and deliver to the SNS 450,000 doses of DTPA (390,000 doses of Calcium-DTPA and 60,000 doses of Zinc-DTPA). A contract was awarded on December 30, 2005. On February 13, 2006, HHS awarded a contract to Akorn, Inc. of Buffalo Grove, Ill., for the manufacture and delivery of 390,000 doses of Ca-DTPA and 60,000 doses of Zn-DTPA. This contract was modified on April 13, 2006, to purchase an additional 5,370 doses and 19,369 doses, respectively.

Threat

On January 20, 2004, the Secretary of DHS determined that radiological and nuclear agents were material threats to the U.S. population sufficient to affect national security. DHS subsequently analyzed in depth the specific threats caused by both radiological materials and so-called "fissile materials." These studies resulted in a Material Threat Assessment of radiological materials (sent to HHS in February of 2005) and a special study on fissile materials sent to HHS in May of 2005.

The release of radiological or nuclear agents could involve high fatality rates, acute and long-term adverse health effects, and the potential for long-term environmental persistence. Certain forms of radioactive materials may also be easy to obtain and deliver by aerosolization or through food or water contamination.

Particulate radiation can be absorbed into the body by inhalation, ingestion or wound contamination. Radioactive isotopes in these particles can then be absorbed, transported via the blood, and later incorporated into the bones, liver or lymph nodes. The radioactive isotopes emit radiation to surrounding tissues, and may cause cell death, organ dysfunction or cancer. Rapid removal of the particles can greatly reduce exposure.

Rationale Underlying Decision to Acquire

Two drugs, calcium diethylenetriaminepentaacetate (Ca-DTPA) and zinc diethylenetriamine-pentaacetate (Zn-DTPA), have been approved by FDA for treating internal contamination with

plutonium, americium, and curium. These two forms of DTPA enhance the body's ability to expel certain radioactive particles. An improved form of DTPA would enhance excretion of the radionuclides that are likely to be ingested or inhaled after a radiological or nuclear event.

The WMD MCM Subcommittee recommended acquisition of 450,000 doses of DTPA to treat such internal contamination.

Status

On September 14, 2005, OPHEMC released a Synopsis expressing the intent to purchase DTPA through a sole source contract under the FAR. An RFP was released on October 7, 2005, contingent on the availability of funds, and closed on October 18, 2005. On November 18, 2005, HHS/DHS jointly submitted a recommendation to OMB that the Project BioShield SRF be utilized to acquire both zinc and calcium DTPA for the Strategic National Stockpile and OMB approved the acquisition on January 3, 2006. On February 13, 2006, HHS announced the award of a $21.9 million contract to Akorn, Inc. of Buffalo Grove, Ill., for the manufacture and delivery of 390,000 doses of Ca-DTPA (Pentetate Calcium Trisodium Injection Sterile Solution) and 60,000 doses of Zn-DTPA (Pentetate Zinc Trisodium Injection Sterile Solution). This contract was modified on April 13, 2006, to purchase an additional 5,370 doses of Ca-DTPA and 19,369 doses of Zn-DTPA. In April 2006, delivery was made of 395,370 doses of Ca-DTPA and 79,369 doses of Zn-DTPA. **Figure 14** shows the acquisition timeline.

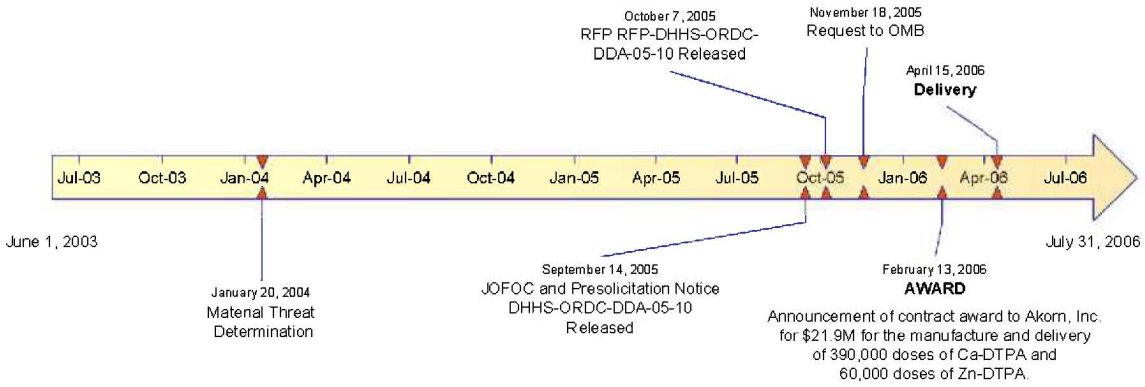


Figure 14: DTPA Acquisition Milestones

8.5 Chemical Medical Countermeasures

8.5.1 Human Butyrl-Cholinesterase (Hu-BChE)

HHS is currently formulating an acquisition strategy

Threat

Nerve agents include organophosphorous insecticides, soman, sarin, tabun, VX, and nontraditional agents. Human butyrl-cholinesterase (Hu-BChE), an enzyme found in human plasma, has been demonstrated to prevent nerve agent-induced mortality and morbidity. The government is interested in identifying sources of Hu-BChE and developing capabilities for the licensure of Hu-BChE for treatment by injection. DHS has been working on a Material Threat Assessment for nerve agents, which will provide estimates of the size of the potential threat that these agents pose to the U.S. population.

Status

Proof-of-principle animal studies are complete. Eventual licensure will depend on, among other things, additional animal studies. OPHEMC invited interested parties to respond to RFI-ORDC-05-03 (Development and Manufacture of Plasma Derived Human Butyrl-Cholinesterase [Hu-BChE] as a Prophylactic/Therapeutic for Exposure to Nerve Agents; posted December 6, 2004, by HHS). This RFI is to identify potential sources of Hu-BChE that is manufactured under a commercial-scale GMP process and tested for effectiveness in animal models and for safety in human volunteers. The RFI closed on January 14, 2005. The data from this RFI and modeling of outcomes of exposure scenarios will be used to determine requirements and elaborate options needed to make decisions for an appropriate acquisition strategy.

9.0 Report on Exercises of Authorities: National Institutes of Health (NIH)

9.1 NIH Utilization of Authority Pertaining to Medical Countermeasures Research and Development

Actions Taken to Date

(1) NIAID has used Project BioShield authorities to award grants and contracts for research toward the development of medical countermeasures for illnesses caused by the highest priority bioterrorism agents:

- Therapeutics for CDC Category A agents
- Development and production of antibodies that protect against botulinum toxin type A
- Production of a vaccine candidate against botulinum toxin type E
- Development of assays for the high-throughput screening of candidate therapeutics for influenza

(2) NIAID has used Project BioShield authorities to award grants and contracts for research leading to medical countermeasures against radiological or nuclear terrorist attacks:

- Protecting the Immune System against Radiation: Project BioShield Accelerated Product Development
- Development of Improved Diethylenetriaminepentaacetate (DTPA) for Radionuclide Chelation

(3) NIAID has used Project BioShield authorities to announce the availability of grants for the development of radionuclide decorporation agents for radiation/nuclear emergencies.

Rationale Underlying the Decision to Use the Authority

The urgent need for medical countermeasures against accidental or deliberate exposure to the highest priority bioterrorism agents (CDC Category A agents, which include anthrax, smallpox, tularemia, plague, botulism, and viral hemorrhagic fevers) underlies NIAID's use of these authorities in each of the first three instances described subsequently (*a, b, c*). These initiatives also follow the findings in the *NIAID Biodefense Research Agenda for Category A Agents* (http://www3.niaid.nih.gov/Biodefense/Research/biotresearchagenda.pdf), as articulated by the Blue Ribbon Panel on Bioterrorism and its Implications for Biomedical Research, convened by NIAID in 2002.

Therapeutics for Category A Agents is a high-priority initiative based on an assessment of medical countermeasure needs and the state of the existing science. This initiative has the potential for the broadest impact in advancing candidates toward eligibility for possible procurement under Project BioShield. With regard to the botulinum toxin initiatives, both the vaccine candidate against serotype E and the monoclonal antibodies against serotype A were advanced enough to enable NIAID to undertake specific developmental activities towards eligibility for possible procurement by OPHEMC with Project BioShield funds.

NIAID exercised the new and expanded authorities granted under Project BioShield to expedite research and development of critical medical countermeasures against accidental or deliberate radiation exposure through the next two projects described subsequently (*d* and *e*). The threat of such attacks has grown in recent years; however, few medical countermeasures currently exist. The programs for which these authorities were used are components of the *NIH Strategic Plan and Research Agenda for Medical Countermeasures against Radiological and Nuclear Threats,* a comprehensive program of basic and translational research, with a strong emphasis on product development.

Finally, NIAID is using Project BioShield authorities to expedite the development of assays for the high-throughput screening of candidate therapeutics for influenza. Influenza is both a major public health threat and an NIAID Biodefense Category C priority pathogen. The influenza therapeutics currently available are limited, and antiviral resistance is a potential concern. New options for treating influenza are a high priority for the nation to address this threat, as articulated by the *National Strategy for Pandemic Influenza* (http://www.whitehouse.gov/homeland/pandemic-influenza.html) and the HHS *Pandemic Influenza Response and Preparedness Plan* (http://www.hhs.gov/pandemicflu/plan/).

Descriptions of NIAID Project BioShield Initiatives

(a) *Therapeutics for Category A Agents*
This grant program supports the design and/or preclinical development of a discrete step or milestone in the process of advancing new therapeutic modalities directed against CDC Category A agents, with potentially broad-spectrum activity.

(b) *Development and Production of Antibodies That Protect against Botulinum Toxin Type A*
The intent of this contract is to manufacture clinical-grade material of human monoclonal antibodies. This could eventually lead to a safer treatment for exposure to botulinum neurotoxins than the currently recommended therapy, polyclonal equine antitoxin, which carries a significant risk of adverse reactions. These manufactured antibodies will allow the performance of animal efficacy studies that are required by the FDA and, subsequently, a Phase 1 clinical trial to establish the safety of the monoclonal antibodies in humans.

(c) *Production of a Vaccine Candidate against Botulinum Toxin Type E*
The intent of this contract is to support further development of the manufacturing information for a recombinant type E botulinum neurotoxin vaccine. Contracted services include development and production of cell banks, and a variety of other projects. This contract will develop the manufacturing information needed to determine how best to make a recombinant type E botulinum neurotoxin vaccine and will support future development of new multivalent vaccines for botulinum neurotoxins.

(d) *Protecting the Immune System against Radiation: Project BioShield Accelerated Product Development*
These grants will support research projects focused on practical methods for pre-exposure protection of the immune system against damage by radiological or nuclear terrorist attacks and/or practical methods to replace hematopoietic stem cells, their progeny, or mature cells of the immune system following exposure to immunosuppressive radiation.

(e) *Development of Improved DTPA for Radionuclide Chelation*
These contracts will support the discovery and demonstration of proof-of-concept of prodrugs (see Appendix 1) or alternative (oral, inhalation, or transdermal) formulations of DTPA that deliver plasma levels sufficient to enhance excretion of certain transuraninc radionuclides that people are likely to ingest or inhale after a radiological or nuclear event.

(f) *Assays for Influenza Therapeutics*
These grants support research projects focused on the development of high-throughput *in vitro* screening assays incorporating validated, high-priority biochemical targets. Of particular interest are assays that allow selection of lead compounds with the potential to be effective against a broad spectrum of influenza strains, including newly emergent influenza strains.

(f) *Radionuclide Decorporation Agents for Radiation/Nuclear Emergencies*
Research supported by these grants will include the development of radionuclide decorporation agents that increase the rates of radionuclide elimination and offer broader ranges of radionuclide decorporation, and the evaluation of various routes of administration to facilitate their use with mass casualties.

Other Options Considered and Rejected

NIAID first considered using the normal NIH review and award process; however, because this process averages 18 months from the conception of an initiative to award, the NIAID rejected this option. Instead, because the Project BioShield mechanism shortens the award process timeframe to approximately nine months, NIAID elected to utilize Project BioShield authorities to expedite these high-priority programs.

Nature and Number of Grants and Contracts Awarded; Nature and Number of Persons/Entities Receiving Awards

To date, NIAID has awarded the following grants and contracts under Project BioShield authorities:

(a) *Therapeutics for Category A Agents*
Twelve grants awarded to research hospitals and institutions, universities, and biotechnology companies:

- The Scripps Research Institute, La Jolla, California: identification of drugs that reverse paralysis caused by botulinum toxin
- Apath LLC, St. Louis, Missouri: development of new antiviral drugs for Ebola infection
- Veterans Affairs San Diego Healthcare System, San Diego, California: development of a new antiviral drug against smallpox
- Arizona State University, Tempe, Arizona: optimization of smallpox vaccine's protective effect when given after exposure to the virus
- NovoBiotic Pharmaceuticals LLC, Cambridge, Massachusetts: development of new drugs against the bacterium that causes anthrax
- Children's Hospital Oakland Research Institute, Oakland, California: development of antibodies to be used as post-exposure anthrax therapy

- Nanotherapeutics Inc., Alachua, Florida: development of single-dose disposable inhalers of two antibiotics for immediate, post-exposure protection against pneumonic plague and tularemia
- University of Chicago, Chicago, Illinois: development of a therapy that blocks the action of anthrax edema toxin, which produces severe swelling in human cells
- MaxThera, Inc., Reading, Massachusetts: identification of new antibacterial agents against a broad spectrum of potential bioterror pathogens
- Veritas Inc., Rockville, Maryland: development of several tests used to screen tens of thousands of drugs to identify those that inhibit the activity of botulinum toxin
- Oncovir, Inc., Washington, DC: development of a drug for prophylaxis and early treatment of Ebola virus infection
- New York University School of Medicine, New York, NY: evaluation of a new antibacterial class of agents that targets a novel pathway for growth and toxin production

(b) Development and Production of Antibodies that Protect against Botulinum Toxin Type A
One contract awarded to a biotechnology company:

- XOMA US LLC, Berkeley, California

(c) Production of a Vaccine Candidate against Botulinum Toxin Type E
One contract awarded to a biotechnology company:

- DynPort Vaccine Company, Frederick, Maryland

(d) Protecting the Immune System against Radiation: Project BioShield Accelerated Product Development
Four grants were awarded in August 2005:

- Cleveland BioLabs, Inc., Cleveland, OH
- Fred Hutchinson Cancer Research Center, Seattle, WA
- University of Illinois at Chicago, Chicago, IL
- University of Maryland School of Medicine, Baltimore, MD

(e) Development of Improved DTPA for Radionuclide Chelation
Three contracts were awarded in September 2005:

- SRI International, Menlo Park, CA
- University of Kentucky, Lexington, KY
- Nanotherapeutics Inc., Alachua, FL

(f) Assays for Influenza Therapeutics

NIAID released the initiative on June 17, 2005, and the receipt date for applications was September 1, 2005. Eight grants were awarded to research institutions, universities, and biotechnology companies:

University of Cambridge, Cambridge, United Kingdom

Integral Molecular, Inc., Philadelphia, PA

University of Colorado, Boulder, CO

University of Virginia, Charlottesville, VA (two awards)

Virion Systems, Inc., Rockville, MD

Northwestern University, Evanston, IL

Southern Research Institute, Birmingham, AL

(g) *Radionuclide Decorporation Agents for Radiation/Nuclear Emergencies*
NIAID released the initiative on March 30, 2006, and the receipt date for applications was May 15, 2006. NIAID plans to award the grants in FY2006.

Application Pool

(a) *Therapeutics for Category A Agents*
NIAID received applications from 68 research hospitals and institutions, universities, and biotechnology companies, and have funded 12.

(b) *Development and Production of Antibodies That Protect against Botulinum Toxin Type A*
NIAID received proposals from three biotechnology companies and funded one.

(c) *Production of a Vaccine Candidate against Botulinum Toxin Type E*
NIAID received proposals from two biotechnology companies and funded one.

(d) *Protecting the Immune System against Radiation: Project BioShield Accelerated Product Development*
NIAID received applications from 27 academic and commercial institutions and awarded four grants.

(e) *Assays for Influenza Therapeutics*
NIAID received applications from 21 research institutions, universities, and biotechnology companies and awarded eight grants.

(f) *Development of Improved DTPA for Radionuclide Chelation*
NIAID received proposals from seven academic and commercial institutions and awarded three contracts.

(g) *Radionuclide Decorporation Agents for Radiation/Nuclear Emergencies*
NIAID received applications from 11 academic and commercial institutions. NIAID plans to award five grants in FY2006.

9.2 Summary of Personnel Authorities (Sec. 5 (a)(2))

Number of Appointments/Types of Job Positions Relating to Streamlined Personnel Authority

To date, NIAID has used Project BioShield authorities to hire three individuals. The positions filled are:

- One individual in the dual positions of NIAID Associate Director for Biodefense Product Development and Director of the Division of Microbiology and Infectious Diseases' Office of Biodefense Research Affairs; salary >$100,000.
- One individual to the position of Associate Director for Product Development in the Division of Allergy, Immunology, and Transplantation; salary >$100,000.
- One individual to the position of Associate Director for Radiation Countermeasures Research and Emergency Preparedness, in the Division of Allergy, Immunology, and Transplantation; salary >$100,000.

10.0 Report on Exercises of Authorities: Food and Drug Administration (FDA)

FDA Utilization of Authority Pertaining to Medical Products for Use in Emergencies (Section 564, Federal Food, Drug, and Cosmetic Act)

To date, the FDA has issued one EUA under Section 564 of the Food, Drug and Cosmetic (FD&C) Act, as added by Section 4 of the Project BioShield Act. On January 27, 2005, the FDA Commissioner authorized the emergency use of AVA for prevention of inhalation anthrax for individuals between 18 and 65 years of age who are deemed by the DoD to be at heightened risk of exposure due to attack with anthrax.[7]

The FDA issued the EUA for AVA following a determination on December 10, 2004, by the Deputy Secretary of Defense that there is a significant potential for a military emergency involving a heightened risk to U.S. military forces of attack with anthrax.[8] Based on this determination, the Secretary of HHS, on January 14, 2005, declared an emergency justifying the authorization of the emergency use of AVA. After consulting with the NIH and the CDC and concluding that the criteria for issuance of an authorization under Section 564 (c) of the Act was justified, the FDA Commissioner, on January 27, 2005, authorized the emergency use of AVA for prevention of inhalation anthrax, subject to certain conditions of authorization.[9]

Under the EUA, DoD is to provide to each potential AVA recipient information designed to ensure that he or she is informed that FDA has authorized the emergency use of AVA for preventing inhalation anthrax. Potential recipients must receive information about the benefits and risks of the emergency use of AVA. They have the option to refuse or accept administration of AVA. They must receive information about alternatives to AVA that are available, and of their benefits and risks. The letter of authorization further states that individuals who refuse anthrax vaccination will not be punished. Refusal may not be grounds for any disciplinary action under the Uniform Code of Military Justice or for any adverse personnel action. There may be no penalty or loss of entitlement for refusing anthrax vaccination.

As a condition of authorization, DoD is required, to conduct an educational program for health care providers. Other conditions of authorization include requirements for adverse event reporting and recordkeeping on administration of AVA.

The EUA for AVA was originally issued for six months on the request of DoD. Under the Act an EUA can be extended within the duration of the declaration of emergency if the criteria under Section 564 (c) of the FD&C Act for issuance of such authorization are still met. On July 22,

[7] As the result of an October 27, 2004, order from the United States District Court for the District of Columbia (the Court) (see 70 Fed. Reg. 5452 (Feb. 2, 2005)), the use of AVA by the DoD for the prevention of inhalation anthrax under the Anthrax Vaccine Immunization Program (AVIP) is deemed an unapproved use of an approved product for purposes of Section 564 (a) (2) of the FD&C Act. But for the Court's order, the FDA would not consider the use of AVA for inhalation anthrax to be an unapproved use.

[8] A December 22, 2004, letter from the Assistant Secretary of Defense to the FDA Commissioner requesting the issuance of an EUA for AVA states that the Deputy Secretary of Defense has assigned authority from the Secretary of Defense to make the statutory determination under Section 564 (b) (1) (B) of the FD&C Act.

[9] Notices of the declaration of emergency and determination and the authorization were published in the Federal Register on February 2, 2005.

2005, the FDA Commissioner extended the EUA for the duration of the declaration of emergency, which terminated on January 14, 2006. On December 19, 2005, FDA issued a Final Order concluding that AVA is safe and effective for its labeled indication, to protect individuals at high risk for anthrax disease.

11.0 Conclusion

During the first 24 months of Project BioShield, HHS has used the provisions of this legislation to initiate major acquisition programs for medical countermeasures to biological and radiological/nuclear threats. To establish a pipeline for future medical countermeasure acquisitions, HHS has used Project BioShield authorities to expedite the award of grants and contracts for research to identify and develop medical countermeasures to protect the U.S. population from chemical, biological, radiological, and nuclear threat agents. HHS will continue to work with its interagency partners in the development and prioritization of security countermeasure requirements and acquisition plans.

Specifically, HHS agencies have used their Project BioShield authorities as follows:

- OPHEMC has acquired eight security countermeasures utilizing the Special Reserve Fund authorized under Project BioShield. Contracts were awarded for: vaccines against anthrax (two contracts), therapeutics for anthrax-induced toxemia (two contracts), antitoxins to treat botulism, a liquid formulation of a drug to protect children from radioactive iodine exposure following nuclear events, and two chelating agents to remove radionuclide particles (one contract). Two additional procurements are under way to provide smallpox vaccine for immunocompromised individuals and security countermeasures to mitigate or treat the neutropenia associated with acute radiation syndrome.
- NIH has used its Project BioShield authorities to initiate grants and contracts for research on therapeutics and a vaccine candidate directed against CDC Category A biological agents; to expedite the development of assays for the high-throughput screening of candidate therapeutics for influenza; and to expedite research and development of critical medical countermeasures against accidental or deliberate radiation exposure.
- FDA has issued an EUA for AVA to protect individuals deemed by DoD to be at heightened risk of exposure to anthrax. It has also issued draft guidance to explain its policies for issuing EUAs and currently is finalizing this guidance.

The Project BioShield authorities, process, and structure provide a strategic approach for identifying the greatest threats and acquiring medical countermeasures to address those threats. HHS, under Secretary Leavitt, will continue to work to strategically plan for the research, development, acquisition, and utilization of critical medical countermeasures to protect the American people from the highest priority threats.

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Appendix 1 – List of Abbreviations and Glossary

Abbreviation/Term	Definition
Animal Efficacy Rule	Provides for approval of certain new drug (21 CFR 314 Subpart I) and biological products (21 CFR 601 Subpart H) based on animal data when adequate and well-controlled efficacy studies in humans cannot be ethically conducted because the studies would involve administering a potentially lethal or permanently disabling toxic substance or organism to healthy human volunteers and field trials are not feasible prior to approval.
ARS	Acute Radiation Syndrome
AVA	Anthrax Vaccine Adsorbed
BLA	Biologics License Application
BSL-3 or BSL-4	Biosafety Level 3 or 4, Biosafety levels are guidelines of engineering controls, management policies, and work policies and procedures developed for microbiological and biomedical laboratories that provide increasing levels of personnel and environmental protection.
Category A Agents	Biological agents classified as high-risk by the Centers for Disease Control and Prevention (CDC) because of their relative ease in dissemination and transmission, high infectivity and mortality rates, impact on public order, and requirement of unique and extraordinary public health preparedness and response. These are the causative agents of anthrax, botulism, plague, smallpox, tularemia, and viral hemorrhagic fevers.
CBER	Center for Biologics Evaluation and Research
CBRN	Chemical, biological, radiological, nuclear
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
cGCP	current Good Clinical Practices
cGLP	current Good Laboratory Practices
cGMP	current Good Manufacturing Practices
CY	Calendar year
HHS	Department of Health and Human Services
DHS	Department of Homeland Security

Abbreviation/Term	Definition
DTPA	Diethylenetriaminepentaacetate
DoD	Department of Defense
EPZ	Emergency Planning Zone
EUA	Emergency Use Authorization
FAR	Federal Acquisition Regulation
FBI	Federal Bureau of Investigation
FDA	U.S. Food and Drug Administration
FD&C	Food, Drug, and Cosmetic (Act)
FY	Fiscal year
GCP	Good Clinical Practices
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
HHSAR	Health and Human Services Acquisition Regulation
Hu-BChE	Human Butyrl-Cholinesterase
HSC	Homeland Security Council
IAA	Interagency agreement
IND	Investigational New Drug application
JOFOC	Justification for other than full and open competition
KI	Potassium iodide
Medical Countermeasure	Medical countermeasure (used interchangeably with security countermeasure (SC))as defined in Section (3) of the Project BioShield Act of 2004, Section 319F-2 of the Public Health Service Act (PHS Act.): a drug (as that term is defined by section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act [FDCA] (21 U.S.C. 321 (g)(1))), biological product (as that term is defined by section 351(i) of PHS (42 U.S.C. 262(i))), or device (as that term is defined by section 201 (h) of the Federal FDCA (21 U.S.C. 321 (h))) that the Secretary of HHS determines to be a priority (consistent with sections 302(2) and 304(a) of the Homeland Security Act of 2002) to treat, identify, or prevent harm from any biological, chemical, radiological or nuclear agent identified as a material threat under paragraph (2)(A)(ii), or to treat, identify, or prevent harm from a condition that may result in adverse health consequences or death and may be caused by administering a drug, biological product, or device against such an agent;

Abbreviation/Term	Definition
	the Secretary determines under Section 319F-2(c)(2)(B)(ii) of the PHS Act to be a necessary countermeasure, and is a countermeasure for which the Secretary determines that sufficient and satisfactory clinical experience or research data (including data, if available, from pre-clinical and clinical trials) support a reasonable conclusion that the countermeasure will qualify for approval or licensing within eight years after the date of a determination under paragraph (5) of Section 319F-2(c) or is approved or cleared under chapter V of the FDCA or licensed under section 351 of the PHS Act; or is authorized for emergency use under section 564 of the FDCA.
MTA	Material Threat Assessment refers to an official estimate of the magnitude and severity of the threat that a specfic CBRN agent poses to the U.S. population, based on scientific evidence and classified intelligence information of plausible worse case scenarios.
MTD	Material Threat Determination refers to an official statement that a specific CBRN agent has been determined to pose a material threat to the U.S. population sufficient to affect national security.
MVA	Modified Vaccinia Ankara
NHP	Nonhuman primate
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NSC	National Security Council
NSTC	National Science and Technology Council
NTA	Non-traditional agents
OMB	Office of Management and Budget
OASPHEP	Office of the Assistant Secretary for Public Health Emergency Preparedness, now named Office of Public Health Emergency Preparedness
OPHEMC	Office of Public Health Emergency Medical Countermeasures
OPHEP	Office of Public Health Emergency Preparedness
ORDC	Office of Research and Development Coordination, now named Office of Public Health Emergency Medical Countermeasures
PDT	Product Development Tools
PEP	Post-Exposure Prophylaxis
Prodrug	A compound that, on administration, must undergo chemical conversion by metabolic processes before becoming the pharmacologically active drug for which it is a prodrug.

Abbreviation/Term	Definition
Project BioShield	Project BioShield Act of 2004 (P.L.108-276)
Qualified Countermeasure	A countermeasure that qualifies for purchase under the terms of Section 2 of the Project BioShield Act and insert a new section (319F-1) in the Public Health Service Act.
RFI	Request for Information
RFP	Request for Proposal
rPA	Recombinant protective antigen
Security Countermeasure	The technical term for a countermeasure that qualifies for purchase under the terms of Section 2 of the Project BioShield Act in the Public Health Service Act.
SRF	Special Reserve Fund as defined in P.L. 108-90. The appropriations for Project BioShield were included in the Department of Homeland Security (DHS) Appropriations Act, 2004 (P.L. 108-90), which appropriated $5.593 billion for FY2004 to FY2013. This is an advance appropriation for the entire 10-year cost of Project BioShield. This act specifies that $890 million are available to be obligated in FY2004 and $3.418 billion are available for obligation in FY2004 to FY2008. Obligation is the promising of the money through a contract as opposed to the spending of the money, which would occur upon delivery of the countermeasures at some later date.
SNS	Strategic National Stockpile. The federal cache of pharmaceuticals, vaccines, medical supplies, equipment, and other items to augment local supplies of critical medical care targeted to high-priority diseases and conditions (based on the CDC Category A agents). Also refers to the program and support staff managing and operating this cache. Formerly known as the National Pharmaceutical Stockpile (NPS).
STIG	Steering and Integration Group
TPR	Technical Progress Report
TRP	Technical Review Panel
TSWG	Technical Support Working Group
VX	Lethal nerve agent O-ethyl-S-(2-iisopropylaminoethyl) methylphosphonothiolate
WMD MCM	Weapons of Mass Destruction Medical Countermeasures

Appendix 2 – The Weapons of Mass Destruction Medical Countermeasures (WMD MCM) Subcommittee

HHS has a leadership role in the WMD MCM Subcommittee. This Subcommittee is the focal point for U.S. Government interagency efforts to prioritize and coordinate medical countermeasure acquisition programs. The WMD MCM Subcommittee considers a wide range of variables in their deliberations. These include the credibility and immediacy of the threat as determined by DHS material threat assessments (MTAs) and models of potential target populations and the settings in which the medical countermeasure would be used. It also evaluates the availability and suitability of current medical countermeasures and the products in the research and development pipeline. It considers utilization policies for potential medical countermeasures including the dosing schedule, the feasibility of deployment in a public health emergency and product shelf life and storage requirements. These factors, with others, form the basis of the U.S. Government's requirements.

The Subcommittee is made up of Assistant Secretary-level officials from HHS, DoD, and DHS. Four Working Groups and a Steering Group serve the Subcommittee; these are the Chemical, Biological, Radiological/Nuclear, and Product Development Tools Working Groups and the Steering and Integration Group (STIG).

The Chemical, Biological, and Radiological/Nuclear Working Groups collect and evaluate information in their areas of expertise in order to:

- develop findings and recommendations regarding a scenario-based prioritization of threats;
- report the status of medical countermeasure research and development; to include both publicly and privately funded research;
- identify research gaps and provide recommendations for federally supported research and development; and
- develop acquisition strategy options.

The Working Groups provide their recommendations to the STIG for review within the overall CBRN context. These recommendations are then presented to the Subcommittee. The Working Groups also provide an ongoing "Technology Watch" and will report the findings to the STIG annually.

The mission of the Product Development Tools Working Group is to ensure availability of the tools required for producing medical countermeasures to CBRN threat agents. This Working Group examines the availability of biocontainment facilities, animal stocks, animal models, validated experimental protocols, and validated animal assays to support medical countermeasure development. It also proposes recommendations and cost estimates of identified gaps and drafts a Requirements Options paper for closing each of the identified gaps.

The STIG serves as a coordination mechanism across the Working Groups. The STIG provides the Subcommittee with requisite information to make informed decisions regarding the development and acquisition of medical countermeasures. The STIG serves as the single point of contact for the WMD MCM Subcommittee and all subordinate working groups to ensure that

documents drafted from these working groups address all the essential aspects that need to be considered by the Subcommittee.

The STIG is co-chaired by HHS (OPHEP's ORDC Director) and DHS (Biological Countermeasures Portfolio Manager, Science and Technology Directorate). Membership in the STIG includes co-chairs from each Working Group and representatives from the OPHEP, NIH, CDC, FDA, DoD, the Department of Veterans Affairs, DHS, the Department of Commerce, and the Department of Agriculture, and organizations within the Executive Office of the President.

The work of the WMD MCM Subcommittee is critical to the Project BioShield acquisition process. The WMD MCM Subcommittee is responsible for evaluating the potential medical and public health impact of medical countermeasures on exposed populations. It achieves this by reviewing modeling scenarios of medical consequences and the effectiveness of medical response. Researchers use mathematical models to estimate casualties from an attack and its impact on the health care system. These models assess the effectiveness of various medical countermeasures, such as pre-event vaccination, post exposure vaccination, post exposure therapeutics, quarantine and isolation. This process identifies knowledge gaps and helps to inform the medical countermeasures research agenda. The value of these models depends on the validity of the assumptions, which are highly sensitive to estimates of factors, such as immunity, infectious doses, transmission rates and incubation periods.

The appropriate Working Group then considers these models, along with its own expert knowledge, to determine the medical countermeasure requirements to address those threat agents identified in the Material Threat Assessments developed by DHS. The Working Group also develops acquisition options to meet those requirements. Both the requirement and acquisition options are presented to the STIG and then to the Subcommittee, which issues its recommendations to the DHS and HHS Secretaries. These recommendations are considered by the Secretaries in their decision as to the pursuit of an acquisition under Project BioShield.

Appendix 3 – Categories of Hazardous Diseases/Agents

The Centers for Disease Control and Prevention classifies potential dangers to public health and safety by dividing them into three categories, based on their potential for harm.

Category A Diseases/Agents

The U.S. public health system and primary healthcare providers must be prepared to address various biological agents, including pathogens that are rarely seen in the United States. High-priority agents include organisms that pose a risk to national security because they

- can be easily disseminated or transmitted from person to person;
- result in high mortality rates and have the potential for major public health impact;
- might cause public panic and social disruption; and
- require special action for public health preparedness.

Category B Diseases/Agents

Second highest priority agents include those that

- are moderately easy to disseminate;
- result in moderate morbidity rates and low mortality rates; and
- require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance.

Category C Diseases/Agents

Third highest priority agents include emerging pathogens that could be engineered for mass dissemination in the future because of

- availability;
- ease of production and dissemination; and
- potential for high morbidity and mortality rates and major health impact.