United States Department of Health and Human Services

Office of the Assistant Secretary for Preparedness and Response

Project BioShield Annual Report to Congress

January 2011 – December 2011

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Foreword

The medical countermeasures pipeline has never held more promise than it does today. Innovation, enhanced partnerships and collaboration, and sustained investments throughout the last decade have resulted in the addition of eight new countermeasures in the Strategic National Stockpile (SNS), able to treat the effects of anthrax, botulism, smallpox, and radiological and nuclear agents. These countermeasures were procured by the Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response using the Special Reserve Fund and the authorities of the Project BioShield (PBS) program.

The PBS Special Reserve Fund is a critical component of the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE), which, over the last three years, has implemented a set of strategic initiatives to support an end-to-end approach in developing, procuring, and distributing medical countermeasures. These include enhancements to the governance and decision-making structure of the PHEMCE, a regular series of portfolio reviews, in process reviews with developers, implementation of recommendation of the 2010 Secretary's Countermeasure Review, and release of the 2012 PHEMCE Strategic Plan. An accompanying implementation plan will be released in the fall of 2012. In addition, PHEMCE partners developed policies to: guide medical countermeasure investments; strengthen assets of the Strategic National Stockpile (SNS); and, evaluate the use of distribution plans guiding medical countermeasures during public health and medical emergencies. PHEMCE partners are working to implement initiatives to enhance the capability of nascent biotechnology companies to bring multi-purpose products for biodefense to both the commercial and government markets by providing financial support and business management acumen to companies with promising technology. Complimenting this effort are Centers for Innovation in Advanced Development and Manufacturing, for which awards were made in June, 2012. These Centers will significantly expand our manufacturing base and will be capable of developing and manufacturing a variety of products quickly to respond to large-scale emergencies.

Across the PHEMCE we are coordinating better with our partners and have aligned limited resources to best support promising medical countermeasure candidate products. It is critical to note, however, that without the past investments of the Special Reserve Fund and PBS our current level of preparedness would be greatly diminished; we would have far fewer medical countermeasure candidates in the pipeline, reduced private sector partners developing medical countermeasures, and a SNS with limited products for response.

And, without an ongoing Special Reserve Fund, we risk losing the base of industrial partners we depend on for the development and manufacture of biodefense products. Despite our progress since 2004, we continue to face serious threats that could have catastrophic consequences to our public and medical health. With the continued dedication of our partners and support for investment in novel technologies and products, our national health security will continue to improve and our communities will become more resilient in the face of public health and medical incidents.

Nicole Lurie, MD, MSPH

Assistant Secretary for Preparedness and Response
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1.0 Project BioShield Authorities & Reporting Requirements

THE PROJECT BIOSHIELD ACT OF 2004 (PROJECT BIOSHIELD; Public Law [P.L.] 108-276 (The PBS Act)) was designed to provide additional and more flexible authorities and funding to financially support the development and procurement of medical countermeasures against chemical, biological, radiological, and nuclear (CBRN) threat agents. It was also designed to provide the government with the authority to quickly authorize their use during emergencies. PBS authorities were further delineated, clarified, and enhanced by the Pandemic and All-Hazards Preparedness Act of 2006 (P.L. 109-417), the legislation that authorized the establishment of the Biomedical Advanced Research and Development Authority (BARDA). The Project BioShield Act requires an annual report to describe use of specific provisions within the following authorities:

- **Research and Development of Qualified Medical Countermeasures** – Section Two 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. Reporting is required on use of limited competition, expedited peer review, and increased simplified acquisition thresholds.
- **Security Countermeasure Procurements and Special Reserve Fund** – Section Three authorized the appropriation of up to $5.593 billion over the period of fiscal year (FY) 2004 through FY 2013 in a Special Reserve Fund (SRF) for the procurement of security countermeasures for the strategic national stockpile (SNS). The Act specified that up to $3.4 billion could be obligated from FY 2004 through FY 2008, with the balance available from FY 2009 through FY 2013. Furthermore, it also authorized the use of simplified acquisition procedures and the modified use of other than full and open competition, and payment of premiums in multiple-award contracts. Reporting is required on use of simplified acquisition procedures, limited competition, and premium provisions in multiple-award contracts.
- **Emergency Use Authorization for Medical Countermeasures** –Section Four allows the Secretary of Health and Human Services (HHS), after declaring that an emergency determined by the Secretary, or by the Secretary of Defense or Homeland Security justifies use of an unapproved product or unapproved use of an approved product, to issue an Emergency Use Authorization (EUA), permitting the use of a medical countermeasure that is not currently approved, cleared, or licensed by the Food and Drug Administration (FDA) for such usage. The HHS Secretary has delegated the authority to issue an EUA to the FDA Commissioner. Reporting is required on emergency uses of certain drugs and devices, declarations of an emergency, and conditions on authorization.

Specifically, the Act requires the report to include the following information for each use of the specific provisions within these authorities:

- The particular actions taken under each authority, including the identification of the threat agent, emergency, or medical countermeasure;
- The particular actions taken under each authority, including the identification of the threat agent, emergency, or medical countermeasure;
- The reasons underlying each action, including, if applicable, a description of options considered for each action;
- The number and nature of entities that received or were denied a grant, cooperative agreement, or contract; and
- Whether each countermeasure acquisition that required presidential approval resulted in a contract that was entered into within one year of such approval (the President has delegated the authority to approve acquisitions to the Director of the Office of Management and Budget [OMB]).

The Act also requires a separate summary of National Institutes of Health (NIH) activities relating to the use for research and development of (a) the increased micro-

purchase threshold, (b) authority for personal services contracts, and (c) streamlined personnel authority for NIH positions. NIH did not use any of these authorities during the 2011 reporting period.

1.1 Authority Usage

In 2011, HHS used three of the PBS authorities that require annual reporting: procurement of security countermeasures, procedures other than full and open competition, and issuance of Emergency Use Authorizations.

HHS did not utilize the additional authorities of expedited peer review authority, simplified acquisition procedures, or premium provision in multiple-award contracts. The standard Federal Acquisition Regulation (FAR) practices were deemed adequate for all but one acquisition activity during the 2011 reporting period.

1.2 Expedited Peer Review

The National Institute of Allergy and Infectious Diseases (NIAID) within the NIH did not use its expedited peer review authority during the 2011 reporting period.

1.3 Security Countermeasure Procurement

HHS through BARDA extended in April 2011 the current inventory of botulinum antitoxin through 2026 by providing additional funding to Cangene on an existing PBS contract. Funded activities ($63 M) included storage of bulk plasma sera from hyperimmune persons at the vendor and delivery of fill-finished product (heptavalent antitoxin) to the SNS as needed to maintain current stockpile inventory (**Table 1**). These efforts provided another mechanism to stockpile medical countermeasures (MCMs) and provide additional surge capacity as needed.

HHS, through BARDA, added another medical countermeasure under Project BioShield (**Table 1**) by awarding a contract ($433 M) in May 2011 to SIGA Technologies, Inc. under Project BioShield for late-stage development and acquisition of the smallpox antiviral drug ST-246. Support for early development of this MCM began at the NIH, transitioned to BARDA for advanced development, and matured to a PBS contract for late stage development and acquisition. This antiviral marks another MCM to make the transition from early development to PBS within the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE).[1] In the absence of other Offerors that met program and contract time delivery requirements under Project BioShield for a smallpox antiviral drug, and to ensure industrial mobilization, engineering, research and development capabilities as specified under FAR 6.302-3 (**Table 2**), HHS elected to use a Justification for Other than Full Competition (JOFOC) for this procurement action.

The Tables below outline cumulatively PBS solicitations and acquisition contracts that were initiated, completed, or continued in 2011. Only the most recent contract awarded to SIGA Technologies, Inc utilized limited competition as detailed above. All other contracts listed on the table below followed the standard acquisition process.

[1]Under the leadership of the Department of Health and Human Services (HHS) the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) is the coordinating body for the federal agencies in charge of protecting the civilian population from potential adverse health

Table 1: Project BioShield Acquisition Contracts

Countermeasure Area/Product	Date of Contract Award	Delivery to Strategic National Stockpile	Contract Recipient	Status at the Close of CY 2011	Total Funding (Millions)	Reason for Use of Authority
Anthrax Therapeutics						
Monoclonal Antibody (Raxibacumab®, formerly Abthrax))	9/2005 (Base)	Completed (2008)	HGS	20,000 doses delivered; NDA filed with FDA (2008) & additional studies required by FDA (2009)	$174	Raxibacumab is an antitoxin used to treat anthrax and, along with vaccines and antibiotics, is part of a three-pronged approach taken by the U.S. Government to prepare for and respond to an anthrax attack. $8M was added to the contract to support studies required by the FDA.
	7/2009 (Option)	Ongoing	HGS	37,102 doses delivered of 45,000 contracted	$152 (2009) $8 (2011)	
Anthrax Immune Globulin (AIG)	9/2005 (Base)	Completed (2011)	Cangene	10,000 doses delivered	$144 (2011)	AIG® is an antitoxin used to treat anthrax and, along with vaccines and antibiotics, is part of a three-pronged approach taken by the U.S. Government to prepare for and respond to an anthrax attack.
Anthrax Vaccines						
AVA (BioThrax®, Anthrax Vaccine Absorbed)	5/2005	Completed (2006)	Emergent (formerly BioPort)	10 million doses delivered	$243	BioThrax® is the U.S.-licensed vaccine for anthrax and, along with antitoxins and antibiotics, is part of a three-pronged approach taken by the U.S. Government to prepare for and respond to an anthrax attack.
AVA (BioThrax®, Anthrax Vaccine Absorbed)	9/2007	Completed (2008)	Emergent	18.75 million doses delivered	$448	
rPA (Recombinant Protective Antigen)	11/2004	N/A	VaxGen	Terminated 12/19/05	$2	Contract terminated
Botulism Therapeutics						
Botulinum Antitoxin (hBAT) Therapeutic	9/2006	Ongoing	Cangene	107,560 doses delivered of 200,000 contracted In addition plasma was delivered under the new contract modification	$415 (2006) $61 (2011)	Equine-derived polyclonal sera to multiple strains of (A-G) of *C. botulinum* used as a therapeutic for botulism. Reevaluation of the requirement led to a decrease in the number of doses necessary in the SNS. Thus, HHS/BARDA has met the requirement. The contract was modified and $61 M in additional funds were added to maintain the horse herd, stockpile plasma and continue stability testing of plasma and product in the SNS. This contract modification will ensure preparedness out to 2026.

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Table 1: Project BioShield Acquisition Contracts *continued from page 4*

Countermeasure Area/Product	Date of Contract Award	Delivery to Strategic National Stockpile	Contract Recipient	Status at the Close of CY 2011	Total Funding (Millions)	Reason for Use of Authority
Smallpox Vaccine						
Imvamune® MVA, (Modified Vaccinia Ankara) Smallpox Vaccine	6/2007	Ongoing	Bavarian Nordic	5.9 million delivered of 20 million contracted	$505	Imvamune® is an attenuated smallpox vaccine designated for immunocompromised persons as part of the overall strategy using vaccines and antiviral drugs for preparedness to and response to a smallpox attack
ST-246	5/2011	TBD	SIGA Tech. Inc.	0 out of 1.7 M treatment courses	$433	The SNS formulary currently contains smallpox vaccine for the general population, smallpox vaccine for immunocompromised individuals and vaccinia immune globulin (VIG) to treat adverse reactions to the vaccine for the general population. ST-246 will be used to treat those individuals who are symptomatic with disease; for which the vaccine has no efficacy. Late stage development and procurement of this drug compliments the HHS formulary of MCMs to provide an appropriate response after a smallpox incident. In addition, this contract works toward the USG goal of developing two smallpox antivirals.
Medical Countermeasures for Radiological, Nuclear, and Chemical Threats						
Potassium Iodide (Thyroshield)	3/2005	Complete	Fleming	4.8 million doses, deliveries complete	$18	Provides capability for pediatric treatment
IV Calcium/Zinc DTPA (Diethylene triamine pentaacetic acid)	12/2005	Complete	Akorn	473,710 doses, deliveries complete	$22	Decorporation agent for radio-nuclear treatment

Table 2. Limited Competition Utilization

Threat Agent/MCM	Actions Taken Under Authority	Reason for Use of Authority	Number/Nature of Recipients of Awards or Contract	Number/Nature of Applicants Turned Down
Limited competition under the FAR in support of procurement of medical countermeasures				
smallpox (Variola)/ smallpox antiviral drug for treatment	Justification for Other than Full and Open Competition published December 13, 2010 Supplement to JOFOC published May 3, 2011 Solicitation RFP-11-100-SOL-00007 published May 3, 2011 Contract awarded May 13, 2011	A sole source justification was used based on FAR6.302-3 Industrial mobilization; engineering, development, or research capability; or expert services. Sub section (a) Authority section (2i) To maintain a facility, producer, manufacturer, or other supplier available for furnishing supplies or services in case of a national emergency or to achieve industrial mobilization	Single contract awarded to SIGA Technologies, Inc. (May 2011)	No applicants turned down. This was a sole source contract award.

Table 3: Project BioShield Solicitation

Name	URL	Pre-solicitation	Draft Solicitation	Final Solicitation	Closing Date	Expected Award Date	Reason for Use of Authority
Smallpox Antiviral Drug							
RFP 11-100-SOL-00007		March 2011	N/A	March 2011	March 2011	May 2011	HHS is pursuing development & procurement of smallpox antiviral drugs to treat symptomatic individuals.

Additionally, BARDA did publish two sources sought notices (SSN) during CY 2011.

One SSN was to discern current information on pharmaceutical products, vendors, regulatory status, and manufacturing capacity of recombinant cytokine products to treat neutropenia associated with acute radiation syndrome (ARS) following acute radiation exposure. The second SSN was to gather information on the current status of anthrax antitoxin candidate products. Both SSNs will be used to determine potential acquisition strategies moving forward in 2012-2013.

1.4 Emergency Use Authorization

Statutory Authority

In an emergency, potentially useful products may be available, but are not yet FDA approved or approved for the particular use contemplated. Section 564 of the Federal Food, Drug, and Cosmetic (FD&C) Act (2 1 U.S.C. 360bbb-3), as amended by section 4 of the PBS Act of 2004, permits the Secretary to issue an Emergency Use Authorization (EUA) to authorize the use of an unapproved medical product, or to authorize an unapproved use of an approved medical product, during an emergency declared by the HHS Secretary justifying the authorization.[2] Such an emergency declaration may be issued based on a determination (a) by the Secretary of Homeland Security of a domestic emergency or a significant potential for a domestic emergency involving a heightened risk of attack with a specified CBRN agent; (b) by the Secretary of Defense of a military emergency or a significant potential for a military emergency involving a heightened risk to U.S. military forces of attack with a specified CBRN agent; or (c) by the HHS Secretary of a public health emergency that affects or has a significant potential to affect national security and that involves a specified CBRN agent or a specified disease or condition that may be attributable to such agent or agents. In July 2007, FDA published a guidance document on FDA's policies for authorizing the emergency use of medical products under section 564 of the FD&C Act.[2]

Anthrax Preparedness

During the 2011 reporting period, the FDA Commissioner issued two Emergency Use Authorizations (EUAs) to authorize certain unapproved uses of the antimicrobial drug doxcycyline for post-exposure prophylaxis of inhalational anthrax in the event of a domestic emergency involving B. anthracis, the biological agent that causes anthrax. FDA issued these EUAs to facilitate pre-event planning, stockpiling, and preparedness efforts, including federal agency activities occurring under Executive Order 13527.[3]

On July 20, 2011, the Secretary of HHS renewed the declaration originally issued in 2008 justifying the authorization of the emergency use of doxycycline hyclate tablets for post-exposure prophylaxis of inhalational anthrax.[4] The declaration was amended so that it applies to all oral formulations of doxycycline products.

In accordance with the amended declaration, on July 21, 2011, the FDA Commissioner issued an EUA for all FDA-approved oral formulations of doxycycline products, including capsule, tablet, and liquid, where not contraindicated, for the post-exposure prophylaxis of inhalational anthrax.[5] The EUA allows certain aspects of emergency distribution, dispensing, and use of oral formulations of doxycycline products, which would otherwise violate the FD&C Act. The EUA allows public health authorities to stockpile doxycycline, so that, among other things, in the event of an anthrax emergency, they could mass dispense the authorized drugs with emergency use information and without individual prescriptions.

In addition, also in accordance with the amended declaration, on October 14, 2011, the FDA Commissioner issued an amendment to an EUA originally issued in 2008. As described in the 2008, 2009 and 2010 BioShield Annual Reports, FDA issued an EUA on October 3, 2008, for the prepositioning of doxycycline hyclate tablet emergency kits for inhalational anthrax with United States Postal Service (USPS) participants and their household members as part of the Cities Readiness Initiative (CRI). Through the CRI, HHS addresses various approaches for providing antimicrobial drugs to every person within a target geographic area – which could be the entire metropolitan area – within 48 hours of the decision to do so. Section 2 of EO 13527 directed the establishment of a national USPS model for residential delivery of antibiotics following a biological attack. The resulting National Postal Model

[2]Pursuant to section 1003 of the FD&C Act and existing delegations of authority, the Secretary has delegated the authority to issue a EUA under section 564 to the FDA Commissioner.

[3]http://edocket.access.gpo.gov/2010/pdf/2010-38.pdf.

[4]Declaration of Emergency Pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 360bbb-3(b) (Oct. 1, 2008); renewed October 1, 2009 (74 Fed. Reg. 51,279) (Oct. 6, 2009); renewed October 1, 2010 (75 Fed. Reg. 61,489) (Oct. 5, 2010); renewed July 20, 2011 (76 Fed. Reg. 44,926) (July 27, 2011).

[5]*Authorization of Emergency Use of Oral Formulations of Doxycycline; Availability*, 76 Fed. Reg. 47,197 (Aug. 4, 2011).

sets forth the method for establishing USPS MCM distribution and delivery to residential addresses, guiding local planning for venue-specific Postal Plans. The USPS EUA allows these volunteers to execute this critical mission.

Specifically the USPS EUA is limited to allowing doxycycline hyclate tablet emergency kits to be distributed to and stored by eligible USPS employee volunteers and their household members so that the participants are ready at the outset of an emergency to distribute post-exposure prophylaxis to the affected population. The EUA has been previously amended two times (on February 25, 2009 and August 23, 2010). On October 14, 2011, FDA once again amended this EUA to accommodate programmatic and operational changes and updates.[6]

FDA Pre-emergency Activities

As part of emergency preparedness activities, FDA continues to review and provide feedback on pre-EUA submissions for multiple products across all medical product lines.

[6]*Amended Authorization of Emergency Use Doxycycline Hyclate Tablet Emergency Kits for Eligible United States Postal Service Participants and Their Household Members; Availability,* 76 Fed. Reg/ 72,935 (Nov. 28, 2011).

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