United States Department of Health and Human Services

Office of the Assistant Secretary for Preparedness and Response

Project BioShield Annual Report

January 2013 – December 2013

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1.0 PROJECT BIOSHIELD AUTHORITIES & REPORTING REQUIREMENTS

The Project BioShield Act of 2004 [Project BioShield (PBS); Public Law [P.L.] 108-276] amended the Public Health Service (PHS) Act and the Federal Food, Drug, and Cosmetic (FD&C) Act to provide additional and more flexible authorities and funding to support financially 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. These authorities were further delineated, clarified, expanded, and extended by the Pandemic and All-Hazards Preparedness Act (PAHPA) of 2006 (P.L. 109-417) and the Pandemic and All-Hazards Preparedness Reauthorization Act (PAHPRA) of 2013 (P.L. 113-5).

Section 5 of the PBS Act (42 U.S.C. 247d-6) required the Secretary of the Department of Health and Human Services (HHS) to submit to Congress an annual report describing the use of specific provisions within the following authorities:

- **Research and Development of Qualified Medical Countermeasures –** Section 2 of the PBS Act enacted Section 319F-1 of the PHS Act (42 U.S.C. 247d-6a), authorizing 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 the use of limited competition, expedited peer review, and increased simplified acquisition thresholds.
- **Security Countermeasure Procurements and Special Reserve Fund** – Section 3 of the PBS Act enacted section 510 of the Homeland Security Act (6 U.S.C. 321j) to authorize the appropriation of up to $5.593 billion over the period of FY 2004 through FY 2013 in a Special Reserve Fund (SRF) for the procurement of security countermeasures that may be placed in 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, section 3 of the PBS Act enacted section 319F-2 of the PHS Act, which authorizes the use and reporting of simplified acquisition procedures, the modified use of other than full and open competition, and the payment of premiums in multiple-award contracts.
- **Emergency Use Authorization for Medical Countermeasures** – Section 4 of the PBS Act enacted section 564 of the FD&C Act, which allows the HHS Secretary to issue an Emergency Use Authorization (EUA) after determining circumstances exist that justify the authorization based on one of four declarations or determinations by the Secretaries of Defense, Homeland Security, or HHS. This EUA declaration justifies the use of a U.S. Food and Drug Administration (FDA) approved, licensed, or cleared product for an unapproved indication or an unapproved product for an indication pending approval, licensure, or clearance, or until the emergency ceases. The HHS Secretary has delegated the authority to issue an EUA to the FDA Commissioner. Reporting is required on emergency uses of certain biologicals, drugs and devices, emergency declarations, and conditions of authorization.

In 2013, Congress repealed section 5 of the PBS Act, and instead required reporting on these same PHS Act and FD&C Act authorities as part of the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan, enacted by PAHPRA as section 2811(d) of the PHS Act (42 U.S.C. 300hh-10). Accordingly, the Office of the Assistant Secretary for Preparedness and Response (ASPR) will include the required information in the PHEMCE Strategy and Implementation Plan provided to Congress in accordance with section 2811(d) of the PHS Act. In the meantime, this separate Project BioShield Report is provided as a courtesy, to inform Congress of the actions taken to implement these authorities through FY 2013, the final year of the initial appropriation to the SRF. Thus, in this report, HHS has included information on uses of the authorities in FY 2013 and a summary of uses of the PBS authorities from its initial authorization, 2004-2013.

1.1 AUTHORITY USAGE

In 2013, HHS used two of the authorities: one for the procurement of security countermeasures and the second, for the issuance of EUAs. HHS did not utilize the additional authorities of expedited peer review, simplified acquisition procedures, or premium provision in multiple-award contracts. The standard Federal Acquisition Regulation (FAR) practices were deemed adequate for the majority of the acquisition activity during 2013. New to HHS, the use of other transactional authority (OTA) was employed for one project within the Biomedical Advanced Research and Development Authority (BARDA) portfolio.

Over the course of the first 10 years of PBS, HHS has used all of the authorities granted under the PHS Act and the FD&C Act as enacted by the PBS Act and amended by PAHPA and PAHPRA. Each section below includes the historical use of authorities along with the current year activities.

1.2 EXPEDITED PEER REVIEW

The National Institute of Allergy and Infectious Diseases (NIAID) within the National Institutes of Health (NIH) did not use its expedited peer review authority during the 2013 reporting period.

From 2004-2010, NIAID used the expedited peer review process 11 times to award grants and contracts for research toward the development of medical countermeasures for illnesses caused by the highest priority bioterrorism agents and against radiological or nuclear terrorist attacks. **Table 1** lists these instances by medical countermeasure threat area.

Table 1: NIAID Awards by Medical Countermeasure Threat Area

Threat Agent/Emergency/ Medical Countermeasure	Actions Taken Under Authority	Reason for Use of Authority	Number/Nature of Recipients of Awards or Contract	Number/Nature of Applicants Turned Down
Therapeutics for Category A agents	23-Jul-04: NOT-AI-04-044 Response date: 23-Sep-04 68 applications received	There is a continued threat of accidental or deliberate exposure to biodefense priority pathogens, but few medical countermeasures exist. In addition, the regular review process takes a long time.	12 grants awarded Recipients: 3 universities, 3 pharmaceutical companies/corporations, 2 non-profit research institutes, 2 biotech companies, 1 biopharmaceutical company, 1 hospital	56 turned down
Development and production of antibodies that protect against botulinum toxin type A	NIH-NIAID-DMID-PR01-01 Response date: 05-Nov-04 3 proposals received	There is a continued threat of accidental or deliberate exposure to biodefense priority pathogens, but few medical countermeasures exist. In addition, the regular review process takes a long time.	1 proposal funded Recipient: 1 biotech company	2 turned down
Production of a vaccine candidate against botulinum toxin type E	7-Oct-04: NIH-NIAID-DMID-PR04-02 Response date: 05-Nov-04 2 proposals received	There is a continued threat of accidental or deliberate exposure to biodefense priority pathogens, but few medical countermeasures exist. In addition, the regular review process takes a long time.	1 proposal funded Recipient: 1 biotech company	1 turned down

Table 1: NIAID Awards by Medical Countermeasure Threat Area *continued*

Threat Agent/Emergency/ Medical Countermeasure	Actions Taken Under Authority	Reason for Use of Authority	Number/Nature of Recipients of Awards or Contract	Number/Nature of Applicants Turned Down
Assays for influenza therapeutics	17-Jun-05: NOT-AI-05-045 Response date: 01-Sep-05 21 applications received	Influenza is both a major public health threat and a biodefense priority pathogen. Current therapeutics are limited, and antiviral resistance is a potential concern. In addition, the regular review process takes a long time.	8 grants awarded Recipients: 5 universities, 2 biotech companies, 1 not-for-profit research institute	13 turned down
Protecting the immune system against radiation	23-Jul-04: NOT-AI-04-044 Response date: 23-Sep-04 27 proposals received	Although the threat of radiological/nuclear attacks or events continues, few medical countermeasures exist. In addition, the regular review process takes a long time.	4 grants awarded in Aug-05 Recipients: 2 universities, 1 biotech company, 1 research institute	23 turned down
Development of improved DTPA for radionuclide chelation	06-May-05: NOT-AI-05-041 Response date: 08-Jun-05 7 proposals received	Although the threat of radiological/nuclear attacks or events continues, few medical countermeasures exist. In addition, the regular review process takes a long time.	3 contracts awarded in Sep-05 Recipients: 1 university, 1 research institute, 1 biotech company	4 turned down
Radionuclide de-corporation agents for radiation/nuclear emergencies	30-Mar-06: NIAID RFA-AI-06-030 Response date: 15-May-06 11 applications received	Although the threat of radiological/nuclear attacks or events continues, few medical countermeasures exist. In addition, the regular review process takes a long time.	5 grants awarded to 4 organizations in Aug-Sep-06 Recipients: 2 national labs and 2 universities	6 turned down
Medical countermeasures to restore gastrointestinal function after radiation exposure	29-Dec-06: NIAID RFA-AI-07-013 Response date: 19-Apr-07 44 applications received	Although the threat of radiological/nuclear attacks or events continues, few medical countermeasures exist. In addition, the regular review process takes a long time.	10 grants awarded in Sep-07 Recipients: 1 non-profit organization, 8 universities, and 1 biotech company	34 turned down

Table 1: NIAID Awards by Medical Countermeasure Threat Area *continued*

Threat Agent/Emergency/ Medical Countermeasure	Actions Taken Under Authority	Reason for Use of Authority	Number/Nature of Recipients of Awards or Contract	Number/Nature of Applicants Turned Down
Medical countermeasures to enhance platelet regeneration and increase survival following radiation exposure	27-Sep-07: NIAID RFA-AI-07-036 Response date: 9-Jan-08 26 applications received	Although the threat of radiological/nuclear attacks or events continues, few medical countermeasures exist. In addition, the regular review process takes a long time.	7 grants awarded in Jul-Sep-08 and Sep-09 Recipients: 1 non-profit organization, 4 universities, and 2 biotech companies	19 turned down
Medical countermeasures to mitigate and/or treat ionizing radiation-induced pulmonary injury	18-Dec-07: NIAID RFA-AI-07-040 Response date: 11-Mar-08 34 applications were received	Although the threat of radiological/nuclear attacks or events continues, few medical countermeasures exist. In addition, the regular review process takes a long time.	9 grants awarded in Sep-08, Sep-09, and summer 2010 Recipients: 6 universities, 1 hospital, 1 non-profit organization, and 1 biotech company	25 turned down
Medical countermeasures to mitigate and/or treat ionizing radiation-induced cutaneous injury	27-Dec-07: NIAID RFA-AI-07-037 Response date: 11-Mar-08 31 applications received	Although the threat of radiological/nuclear attacks or events continues, few medical countermeasures exist. In addition, the regular review process takes a long time.	4 grants awarded in Sep-08 Recipients: 4 universities	27 turned down

1.3 SECURITY COUNTERMEASURE PROCUREMENT

PBS was initiated in 2004 with the passage of the PBS Act, which authorized the appropriation of $5.6 billion in the SRF from FY 2004 through FY 2013 to support the late-stage development and procurement of critical medical countermeasures used against CBRN threat agents. The original SRF appropriation expired on September 30, 2013, by which time all funds invested in the SRF for use through FY 2013 had been obligated. These funds were used to procure 12 new medical countermeasures for inclusion in the SNS and to build a robust portfolio of candidate products under BARDA's advanced research and development (ARD).

PAHPA enacted section 319L of the PHS Act (42 U.S.C. 247d-7e), establishing BARDA with the mission of supporting the ARD of medical countermeausures against CBRN, pandemic influenza, and emerging infectious disease threats. BARDA's investments in ARD were intended to bridge the "valley of death" between early development and FDA licensure, approval or clearance for needed medical countermeasures. Since its establishment in 2006, BARDA has invested just over $2.2 billion of the SRF in ARD for CBRN medical countermeasures, in accordance with annual appropriations Acts that have made amounts from the SRF available for this purpose. Since 2007, BARDA's ARD portfolio has grown from eight acute radiation syndrome (ARS)-focused products to over 80 products addressing nearly the full spectrum of CBRN threats----supporting the development of vaccines or therapeutics for anthrax, smallpox, botulism, plague, tularemia, and burkholderia; the development of biodosimetry and biothreat diagnostic devices; treatments for radionuclide exposure; therapeutics for hematopoietic, skin, lung and gastrointestinal injury caused by exposure to ionizing radiation; products for field use and definitive care of thermal and radiation burns; and antidotes for selected chemical agents.

Over its first 10 years, PBS procurements have added 12 new products to the SNS. These products address anthrax, smallpox, botulism, radiological, nuclear and chemical threats. Nine of the products acquired under PBS are licensed for biodefense or closely related indications, and two of these medical countermeasures, an anthrax antitoxin to treat individuals exposed to anthrax and a heptavalent botulinum antitoxin to treat individuals symptomatic with botulism intoxication, were approved or licensed under the FDA "animal rule". These are the first products supported under PBS and the first novel products to achieve this milestone. Three products added to the SNS - Anthrax Immune Globulin (AIG), tecovirimat (an antiviral medication for treatment of smallpox disease), and the Modified Vaccinia Ankara (MVA) smallpox vaccine - have not yet been licensed or approved for any indication. However, these and several other products that have not yet been licensed or approved for their specific intended biodefense indication could be administered under an EUA when justified.

Calendar Year 2013

The end of FY 2013 represented the conclusion of the original appropriation to the PBS program. Highlights of the 2013 SRF procurements and ARD portfolio activities follow.

In March 2013, BARDA exercised a $110 million option with Bavarian Nordic to procure four million additional doses of its smallpox vaccine, MVA. This program was the first PBS award to utilize advance and milestone payments. With support from BARDA, Bavarian Nordic was able to generate data to support the potential use of the product under an EUA. MVA deliveries to the SNS began in 2010 and the originally contracted amount of 20 million doses was delivered to the SNS by November 2013. Furthermore, in November Bavarian Nordic initiated deliveries of the four million doses under the option executed earlier in 2013, maintaining the existing inventory level in the SNS. MVA might be used under an EUA in individuals for whom the current licensed vaccine ACAM2000 is ordinarily contraindicated. This subset of patients includes individuals with human immune deficiency virus (HIV) or those with atopic dermatitis. MVA may be given to pediatric patients and nursing or pregnant women afflicted with either condition. This medical countermeasure is one of several supported by BARDA that addresses a mandate under the PHS Act to develop medical countermeasures for "at risk" populations.

The additional procurement of the liquid frozen product will maintain the current level of preparedness for the MVA vaccine and serve as a bridge until BARDA can transition to a new lyophilized (freeze-dried) formulation of the MVA vaccine that over time will offer significant cost savings to the United States Government (USG). The new

lyophilized formulation will have a longer shelf-life than the current product, can be stored at warmer temperatures, and can be deployed without the need for freezing during shipment. BARDA anticipates the new lyophilized product will be ready for procurement in 2016, allowing for a smooth transition from the current liquid frozen to the lyophilized product as the liquid frozen product in the SNS expires.

Also in March 2013, the FDA licensed the heptavalent botulism antitoxin (BAT), manufactured by Cangene Corporation, under the "animal rule". The product was licensed to treat individuals symptomatic with botulism following documented or suspected exposure to all known serotypes (A-G) of botulism neurotoxin in adults and pediatric patients. This product has been used to treat naturally occurring cases of botulism in infant, pediatric, adult, and elderly patients in the United States and Mexico. BAT is the only licensed product available in the SNS to treat botulism and its licensure represents a significant achievement for BARDA, ASPR and the PHEMCE. With the PBS procurements, BARDA has fulfilled the established national requirement for BAT. BARDA continues to collect additional plasma from the hyperimmune horse herd, which provides the starting material for BAT. As doses currently in the SNS begin to expire, collection and storage of the plasma with subsequent manufacturing beginning in 2016 will ensure preparedness for this critical medical countermeasure to 2025. BAT was the second novel PBS product to be licensed/approved under the FDA's "animal rule", the first being raxibacumab, a monoclonal anthrax antitoxin, in December 2012.

ST-246 (Tecovirimat), an antiviral medication for the treatment of smallpox disease, initiated deliveries to the SNS in March 2013. Development of ST-246 has been a true USG partnership, with development activities being funded by NIH/NIAID, the Department of Defense (DoD), and BARDA. BARDA's continued support under PBS has allowed SIGA Technologies to generate the data necessary for the potential use of the product under an EUA to treat individuals symptomatic with smallpox disease. Initial deliveries to the SNS were made under a CDC-held contingency use IND and the CDC has submitted the pre-EUA package to the FDA for review. BARDA continues to support the late stage development of ST-246 under the PBS program to generate additional data necessary to support FDA approval of the product.

In May 2013, BARDA entered into an agreement with GlaxoSmithKline (GSK) for $40 million of ARD funds to support development of a portfolio of novel antimicrobial products. The agreement, executed under BARDA's OTA, is the first use of this authority by BARDA. The agreement provides a flexible partnership in which drug candidates can be moved in or out of the portfolio based on their development stage and other technical considerations, as assessed during joint semi-annual portfolio reviews. The approach balances the business risk for both the federal government and GSK. Supporting the simultaneous development of multiple drug candidates increases the likelihood that one or more will advance to the level at which the company can apply for FDA approval.

In July 2013, BARDA reissued its Broad Agency Announcement (BAA) seeking proposals for the development of medical countermeasures to treat, prevent, or diagnose the medical consequences of CBRN attacks under ARD. In addition, BARDA issued the Strategic Science and Technology Division (SSTD) BAA for the second time (Table 4). The CBRN and SSTD BAAs reflect the medical countermeasure priorities highlighted in the PHEMCE Strategy and Implementation Plan (2012) and will remain open for two years. These vehicles are the mechanism BARDA uses to build a robust pipeline of candidate products that have the potential to transition to PBS funding for procurement.

In September 2013, BARDA made multiple awards under PBS to maintain anthrax antitoxin preparedness and to add medical countermeasures to the SNS for the treatment of ARS and exposure to chemical nerve agents.

To enhance the nation's preparedness to respond to an anthrax attack, BARDA awarded contracts to five companies developing anthrax antitoxins: Elusys (Pine Brook, NJ), Emergent BioSolutions (Gaithersburg, MD), PharmAthene (Annapolis, MD), Cangene (Winnipeg, Canada) and GSK (Research Triangle Park, NC). Each base contract was valued at $100,000 and provided the opportunity for each company to bid on task orders to deliver cell banks (as a risk mitigation strategy), monoclonal anthrax antitoxin, or plasma to manufacture polyclonal anthrax antitoxin. Under separate task orders to deliver cell banks used in manufacturing monoclonal products, awards were made to Emergent BioSolutions ($353,000), PharmAthene ($980,000), and GSK ($299,000). Under a task order to deliver monoclonal anthrax antitoxins, a single award valued at $196.4 million was made to GSK to deliver 60,000 doses of raxibacumab over four years. This acquisition will maintain the stockpile at the current level, replenishing expiring doses. Under a task order to deliver plasma to be stored in bulk and manufactured at a later date to replenish polyclonal AIG as the current product in the SNS expires, a $63.3 million contract was awarded to Cangene to reinitiate the program to collect and store plasma from individuals vaccinated with anthrax vaccine. The goal of these awards was two-fold. The first goal, obtaining the cell banks used to manufacture monoclonal anthrax antitoxins, serves as a risk mitigation strategy for the USG. In the event that any of the companies that currently manufacture monoclonal antibodies are no longer able to manufacture those products, the USG would have the cell banks necessary to produce these products if and as circumstances warrant. The cell banks could be used, for example, by the Centers for Innovation and Advanced Development and Manufacturing (CIADM) to manufacture the products to supplement the SNS stockpiles if needed. The second goal is to maintain the current SNS formulary for anthrax antitoxins at 60,000 doses of monoclonal and 10,000 doses of polyclonal products. These awards will maintain the current levels of these anthrax antitoxin products until 2017 and 2018, respectively.

The second set of PBS awards add new cytokine products to the SNS to treat neutropenia, one of the subsyndromes of ARS that may result from exposure to high doses of ionizing radiation following a nuclear detonation. There are currently four products approved by the FDA to treat neutropenia associated with cancer therapy and these products have the potential to be used under an EUA to treat the neutropenic subsyndrome of ARS. Under the solicitation, base contracts, each valued at $500,000, were awarded to Amgen (Thousand Oaks, CA) and Sanofi-Aventis (Bridgewater, NJ). In addition, Sanofi-Aventis was provided $23.3 million for the late stage development of their product (Leukine) to support the ARS indication. Awards were made under separate task orders to Amgen for the immediate delivery of 35,203 treatment courses of their product Neupogen ($157 million) and to Sanofi-Aventis for the delivery of 4,340 treatment courses of Leukine ($14 million). Both products will be maintained under vendor managed inventory (VMI). Under VMI, the products will rotate through the commercial market. This means that the products will not be stockpiled in the SNS, where they would eventually expire over time, but instead will be in constant rotation and held by the manufacturers, with the USG having access to the product when needed.

The third 2013 PBS contract will add a new product to the SNS to treat seizures resulting from exposure to chemical nerve agents. This contract award, valued at $61 million, was made to Meridian Medical Technologies (Columbia,

MD) for the late stage development and procurement of 2.3 million doses of midazolam. Midazolam has been shown to be faster acting and easier to administer than the current anticonvulsant, diazepam. The SNS currently stockpiles diazepam in forward deployed CHEMPACKs. As the diazepam expires, it will be replaced with midazolam at a one-to-one ratio.

The tables below outline cumulatively PBS acquisition contracts and solicitations that were initiated, completed, or continued in 2013 (**Table 2**), a breakdown of how the SRF has been expended from 2004-2013 (**Table 3**), and the CBRN and SSTD BAA for ARD (**Table 4**).

Table 2: Project BioShield Acquisition Contracts

Countermeasure Area/Product	Date of Contract Award	Delivery to Strategic National Stockpile	Contract Recipient	Status at the Close of CY 2012	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 USG 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)	Completed (2012)	HGS	45,000 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 (2005) $16.6 (2012)	AIG® is an antitoxin used to treat anthrax and, along with vaccines and antibiotics, is part of a three-pronged approach taken by the USG to prepare for and respond to an anthrax attack.
Replenishment of Anthrax Antitixins	9/2013	N/A	Elusys	N/A	$0.1	Base award only
	9/2013	N/A	Emergent	Cell bank will be delivered to CIADMs in 2014	$0.45	Procurement of cell bank used to manufacture monoclonal anthrax antitoxins as a risk mitigation strategy
	9/2013	N/A	Pharm-Athene	Cell bank will be delivered to CIADMs in 2014	$1.08	Procurement of cell bank used to manufacture monoclonal anthrax antitoxins as a risk mitigation strategy
	9/2013	TBD	Glaxo-Smith-Kline	0 delivered of the 60,000 treatment courses. Cell bank will be delivered to CIADM in 2014	$196.8	60,000 treatment courses of Raxibacumab to maintain current preparedness to 2017 and procurement of cell bank
	9/2013	TBD	Cangene	0 liters of plasma delivered	$63.4	10,000 treatment course equivalents of plasma to be collected and stored as plasma to maintain preparedness to 2018

Table 2: Project BioShield Acquisition Contracts *continued*

Countermeasure Area/Product	Date of Contract Award	Delivery to Strategic National Stockpile	Contract Recipient	Status at the Close of CY 2012	Total Funding (Millions)	Reason for Use of Authority
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 USG 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 (2008) $8.7 (2012)	
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	138,749 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 million 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 2025.
Smallpox Vaccine						
Imvamune® MVA, (Modified Vaccinia Ankara) Smallpox Vaccine	6/2007 (Base)	Completed (2013)	Bavarian Nordic	20 million delivered of 20 million contracted	$505 (2007) $37 (2013)	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.
Imvamune® MVA, (Modified Vaccinia Ankara) Smallpox Vaccine Option to deliver 4 million doses	3/2013 (Option)	Ongoing	Bavarian Nordic	864,000 delivered of 4 million contracted	$110 (2013)	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.

Table 2: Project BioShield Acquisition Contracts *continued*

Countermeasure Area/Product	Date of Contract Award	Delivery to Strategic National Stockpile	Contract Recipient	Status at the Close of CY 2012	Total Funding (Millions)	Reason for Use of Authority
ST-246	5/2011	Ongoing	SIGA Tech. Inc.	920,000 out of 1.7 million treatment courses	$433 (2011)	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 may 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 complements the HHS formulary of medical countermeasures 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 Note: the PHEMCE reduced this requirement and the SNS does not currently maintain this product
IV Calcium/Zinc DTPA (Diethylene triamine pentaacetic acid)	12/2005	Complete	Akorn	473,710 doses, deliveries complete	$22	Decorporation agent for radio-nuclear treatment
G-CSF cytokine for neutropenia associated with exposure to ionizing radiation	9/2013	TBD	Amgen	0/35,203 treatment courses Note: this product will be maintained as Vendor Managed Inventory (VMI)	$157.7	Neutropenia is one of the subsyndromes associated with exposure to ionizing radiation. Amgen's Neupogen® is approved by the FDA to treat neutropenia resulting from chemotherapy treatment and can be used under EUA for neutropenia associated with exposure to ionizing radiation.

Table 2: Project BioShield Acquisition Contracts *continued*

Countermeasure Area/Product	Date of Contract Award	Delivery to Strategic National Stockpile	Contract Recipient	Status at the Close of CY 2012	Total Funding (Millions)	Reason for Use of Authority
GM-CSF cytokine for neutropenia associated with exposure to ionizing radiation	9/2013	TBD	sanofi-aventis	0/4,340 treatment courses Change Note: this product will be maintained as Vendor Managed Inventory (VMI)	$36.8	Neutropenia is one of the sub-syndromes associated with exposure to ionizing radiation. Sanofi-aventis' Leukine is approved by the FDA to treat neutropenia resulting from chemotherapy treatment. Funding will provide late stage development for additional non-clinical studies that may be necessary to use under an EUA. Sanofi-aventis will be pursuing approval for the ARS indication as well.
Midazolam to treat seizures associated with exposure to chemical nerve agents	9/2013	TBD	Meridian (Pfizer)	0/2.3 million treatment courses	$60.8	Midazolam offers advantages over the current product in the SNS CHEMPACKs, diazepam. Midazolam is faster acting, longer acting and can be administered intramuscularly as opposed to intravenous for diazepam. Midazolam will replace diazepam as it expires in the CHEMPACKs. Funding will also support approval for status epilepticus in adults and pediatrics and seizures resulting from exposure to chemical nerve agents in adults and pediatrics.

Table 3: Expenditure of the Special Reserve Fund (in millions)

Original Appropriation	**$5,593**
Less FY2004 and FY05 Rescissions	**-$25**
Less FY2009 Transfers	**-$412**
Less FY2010 Transfers	**-$609**
Less FY2011 ARD Obligations	**-$408**
Less FY1202 ARD Obligations	**-$368**
Less FY2013 ARD Obligations	**-$469**
Less Total obligated to-date under PBS	**-$3,299**
Lapsed Available Funds	**$3**

Table 4: Open Advanced Research and Development (ARD) Broad Agency Announcement Solicitations

Name	URL	Pre-solicitation	Draft Solicitation	Final Solicitation	Closing Date	Expected Award Date	Reason for Use of Authority
CBRN MCM Development-BAA-CBNR-BAA-12-100-SOL-00011 "Rolling BAA"	https://www.fbo.gov/index?s=opportunity&mode=form&id=045ee83b87a8e95743fd68bb50e9e5a4&tab=core&_cview=1	07/2013	n/a	07/2013	Open Continuous Until 7/2015	N/A	Continue to support development of critical medical countermeasures under advanced research and development
BARDA-BAA-12-100-SOL-00014	https://www.fbo.gov/index?s=opportunity&mode=form&id=59a8bee92eb32ebd33098ec29dacc4c2&tab=core&_cview=1	07/2013	n/a	07/2013	Open Continuous Until 7/2015	N/A	Continue to support development of platform technologies with the capability to enhance both influenza and CBRN medical countermeasures

1.4 EMERGENCY USE AUTHORIZATION

Section 564 of the FD&C Act (21 U.S.C. 360bbb-3), as enacted under the PBS Act and amended under PAHPRA, enables the Commissioner of FDA to issue an EUA to authorize the use of an unapproved medical product, or to authorize an unapproved use of an approved medical product, when the HHS Secretary determines that an EUA is justified based on one of four declarations or determinations by the Secretaries of Homeland Security, Defense, or HHS. Since 2004, FDA has exercised its EUA authority numerous times to facilitate preparedness for and response to emergencies (**Table 5**).[1]

Anthrax Preparedness

FDA's first use of its EUA authority was in 2005, when the Agency issued an EUA to enable the use of Anthrax Vaccine Adsorbed (AVA) in military personnel deemed by DoD to be at heightened risk of exposure due to a potential attack with Bacillus anthracis, the causative agent of anthrax. FDA issued this EUA to enable the continued use of AVA under the DoD Anthrax Vaccine Immunization Program (AVIP) while a challenge to FDA's ruling that AVA is safe, effective, and not misbranded for the prevention of inhalational anthrax was addressed as part of a civil suit over the legality of mandatory vaccinations under the AVIP.[2] This EUA is no longer in effect.

FDA has also issued two EUAs to facilitate pre-event planning, stockpiling, and, if necessary, rapid response efforts in support of preparedness for an anthrax attack. Both EUAs remain in effect and authorize certain unapproved uses of the antimicrobial drug doxycycline for post-exposure prophylaxis of inhalational anthrax in the event of a public health emergency involving Bacillus anthracis. The first of these EUAs, issued in 2011, is focused on facilitating stakeholder mass dispensing activities by authorizing the use of all approved oral formulations of doxycycline products (where not contraindicated) for the post-exposure prophylaxis of inhalational anthrax. The EUA authorizes certain aspects of emergency stockpiling, distribution, dispensing, and use of oral formulations of doxycycline products that otherwise might violate provisions of the FD&C Act. For example, in the event of an anthrax emergency, this EUA allows public health authorities to mass dispense doxycycline at points of dispensing with emergency use information (e.g., streamlined fact sheets for recipients about how to use the product) that is not part of the product's approved labeling, without individual prescriptions, and by responders and volunteers who are not licensed health care professionals.[3]

The second EUA was originally issued in 2008 to enable 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. This EUA was amended annually from 2009 through 2011 to accommodate programmatic and operational changes and updates. The most recent amendments in 2011 authorize doxycycline hyclate tablet emergency kits to be distributed to and stored by eligible USPS employee volunteers and their household members as part of the

[1]Information on current EUAs is available at: Emergency Use Authorizations; Washington, DC: U.S. Food and Drug Administration. Available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm.

[2]Biological Products; Bacterial Vaccines and Toxoids; Implementation of Efficacy Review; Anthrax Vaccine Adsorbed; Final Order, 70 Fed. Reg. 75180 (Dec. 19, 2005).

[3]As a result of PAHPRA's establishment of new section 564A of the FD&C Act and because doxycycline is an FDA-approved medical countermeasure, an EUA is no longer needed to authorize the preparedness and response activities in the 2011 mass dispensing EUA. Instead, under section 564A of the FD&C Act, FDA can, for example, issue an emergency dispensing order and CGMP waiver, and CDC can issue emergency use instructions, to address stakeholders' doxycycline mass dispensing preparedness and response activities authorized in the EUA. Nonetheless, the doxycycline mass dispensing EUA remained in effect throughout the duration of this reporting cycle to ensure no legal preparedness gaps during the timeframe of implementation of the new PAHPRA authorities.

National Postal Model. This enables USPS participants to be ready to dispense, as a rapid strike force, post-exposure prophylaxis to the affected populations in pre-determined ZIP codes following an anthrax attack.

2009 H1N1 Influenza Pandemic Response

FDA used its EUA authority extensively in 2009 – 2010 to facilitate the nation's response to the 2009 H1N1 influenza pandemic including issuing three EUAs to enable the use of antiviral medications for the treatment and/or prophylaxis of influenza; one EUA to enable the use of certain N95 respirators to help reduce wearer exposure to pathologic biologic airborne particulates; and 18 EUAs to enable the use of in vitro diagnostic tests for the diagnosis of 2009 H1N1 influenza virus infection. These EUAs are no longer in effect.

Changes in EUA Authority under PAHPRA

One of the most significant EUA authority changes resulting from PAHPRA in 2013 is that it made it possible to issue an EUA based on the HHS Secretary's determination that there is a significant potential for a public health emergency.[4] Before an EUA can be issued, one of four specific determinations by the Secretaries of HHS, Homeland Security, or DoD must be made. Prior to PAHPRA, the HHS determination required the Secretary to declare that a public health emergency exists in accordance with section 319 of the PHS Act. Now, the HHS Secretary's determination is made under section 564 of the FD&C Act, and can be based on either an actual or a potential public health emergency, which provides greater flexibility to issue EUAs in advance of an actual emergency to support preparedness activities.

Based on this new flexibility, in 2013 and 2014 FDA issued two EUAs for in vitro diagnostic tests for the presumptive detection of the novel influenza A (H7N9) virus, which emerged in 2013. In 2013, FDA issued one EUA for an in vitro diagnostic test for the presumptive detection of Middle East Respiratory Syndrome (MERS-CoV), which emerged in 2012. These EUAs were issued based on a determination by the HHS Secretary that there was the significant potential for a public health emergency that had a significant potential to affect the national security or the health and security of U.S. citizens living abroad to facilitate preparedness for these emerging threats.

[4]Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA) Medical Countermeasure (MCM) Authorities: FDA Questions and Answers for Public Health Preparedness and Response Stakeholders. Washington D.C.: U.S. Food and Drug Administration. Available at: http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/UCM380269.pdf.

* Issuance of doxycycline emergency dispensing order, CGMP waiver, and CDC EUI (sec. 564A of the FD&C Act) would render the EUA unnecessary.

Table 5. Emergency Use Authorizations Issued by FDA

Year	Medical Countermeasure	Requester	Status
Anthrax [*Bacillus anthracis*]			
2005	Anthrax Vaccine Adsorbed (AVA)	DOD	Terminated
2008	Doxycycline hyclate tablets (USPS home & workplace kits)	HHS (ASPR/BARDA)	Amended in 2009,2010, 2011 - see National Postal Model row below
2011	All oral formulations of doxycycline (mass dispensing)	HHS (CDC)	Current*
2011	Doxycycline hyclate 100 mg oral tablets (National Postal Model home & workplace kits)	HHS (ASPR/BARDA)	Current
2009 H1N1 Influenza Pandemic [A(H1N1)pdm09]			
2009-2010	Oseltamivir (Tamiflu)	CDC	Terminated
	Zanamivir (Relenza)	CDC	
	Peramivir IV	CDC	
	CDC Swine Influenza Virus Real-time RT-PCR Detection Panel	CDC	
	CDC Human Influenza Virus Real-time RT-PCR Detection and Characterization Panel with additional specimens and reagents	CDC	
	Focus Diagnostics Influenza A H1N1 (2009) Real-Time RT-PCR	Focus Diagnostics, Inc.	
	CD C rRT-PCR Swine Flu Panel on the Joint Biological Agent Identification and Diagnostic System (JBAIDS) Instrument	DoD	
	Diatherix 2009 H1N1 Test	Diatherix Laboratories, Inc.	
	Focus Diagnostics Simplexa™ Influenza A H1N1 (2009) Test	Focus Diagnostics, Inc.	
	Prodesse ProFlu-ST Influenza A assay for the diagnosis of 2009 H1N1 Influenza virus infection	Prodesse, Inc.	
	ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR Test	Epoch BioSciences	
	Roche Real-Time ready Influenza A/H1N1 Test	Roche Applied Science	
	GeneSTAT 2009 A/H1N1 Influenza Test	DxNA, LLC	
	TessArray Resequencing Influenza A Microarray Detection Panel	TessArae, LLC	
	Cepheid Xpert® Flu A Panel for the Diagnosis of 2009 H1N1 Influenza Virus Infection	Cepheid	

Table 5. Emergency Use Authorizations Issued by FDA continued

Year	Medical Countermeasure	Requester	Status
	ViraCor 2009 H1N1 Influenza A Real-time RT-PCR	ViraCor Labs	
	Longhorn Influenza A/H1N1-09 Prime RRT-PCR Assay	Longhorn Vaccines and Diagnostics	
	Diagnostic Hybrids, Inc. D^{3} Ultra 2009 H1N1 Influenza A Virus ID Kit	Diagnostic Hybrids, Inc.	
	Qiagen *artus*® Inf. A H1N1 2009 LC RT-PCR Kit	Qiagen	
	IMDx 2009 Influenza A H1N1 Real-Time RT-PCR Assay from IntelligentMDx	IntelligentMDX	
	IQuum Liat™ Influenza A/2009 H1N1 Assay	IQuum, Inc.	
	Disposable N95 Respirators from Strategic National Stockpile	HHS (CDC)	
Novel influenza A (H7N9) Virus [Avian Influenza A(H7N9) virus]			
2013	CDC Human Influenza Virus Real- Time RT-PCR Diagnostic Panel- Influenza A/H7 (Eurasian Lineage) Assay	HHS (CDC)	Current
2014	Quidel Lyra™ Influenza A Subtype H7N9 Assay	Quidel Corp.	Current
Middle East Respiratory Syndrome Coronavirus [MERS-CoV]			
2013	CDC Novel Coronavirus 2012 Real-time RT-PCR Assay	HHS (CDC)	Current

** Issuance of doxycycline emergency dispensing order, CGMP waiver, and CDC EUI (sec. 564A of the FD&C Act) would render the EUA unnecessary.*

1.5 NIH PERSONNEL PRACTICES

During the period from 2004 to 2009, NIAID used PBS streamlined personnel authorities to hire seven individuals. The positions that were filled are listed in **Table 6**:

Table 6: NIH Personnel Authorities Used

1. One individual in the dual positions of NIAID Associate Director for Biodefense Product Development and Director of the Division of Microbiology and Infectious Diseases (DMID) Office of Biodefense Research Affairs; salary >$100,000.
2. One individual to the position of Associate Director for Product Development in the Division of Allergy, Immunology, and Transplantation (DAIT); salary >$100,000.
3. One individual to the position of Associate Director for Radiation Countermeasures Research and Emergency Preparedness in DAIT; salary >$100,000.
4. One individual to the position of Chemical, Biological, Radiological, Nuclear Scientific Advisor in the Office of the Director (OD); salary >$100,000.
5. One individual to the position of Chief for the Influenza, SARS, and other Viral Respiratory Diseases Section in the Respiratory Diseases Branch of DMID; salary >$100,000.
6. One individual to the position of Associate Director for Clinical Research in DMID; salary >$100,000.
7. One individual to the position of Associate Director for International Research Affairs in OD; salary >$100,000.

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