



U.S. Department of Health and Human Services

2016 Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan



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EXECUTIVE SUMMARY

The *2016 Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan (SIP)* describes the priorities that the United States (U.S.)

Department of Health and Human Services (HHS), in collaboration with its interagency partners, will implement over the next five years. This plan updates the *2014/2015 PHEMCE SIPs* and fulfills the annual requirement established by Section 2811(d) of the Public Health Service (PHS) Act, as amended by the Pandemic and All-Hazards Preparedness Reauthorization Act (PAHPRA). The annual *PHEMCE SIP* provides the blueprint the PHEMCE will use to enhance national health security through the procurement and effective use of medical countermeasures (MCM).

Considering the progress achieved and the remaining strategic gaps in MCM preparedness, the PHEMCE annually examines the SIP goals and objectives and re-adjusts or adds to them, as needed. The *2016 PHEMCE SIP* includes additional and revised objectives to reflect the PHEMCE's increased focus on operational challenges posed by using MCMs in large-scale public health emergencies (see Table 1 below). Specifically, the new Objective 2.3 articulates the need to expedite the development and evaluation of MCMs needed during a public health emergency. Objective 3.2 is now streamlined, while Objective 3.3 emphasizes the need for logistic and operational plans, which were previously included under Objective 3.2. By agreement across the PHEMCE agencies, a strategic review of all goals and objectives will be conducted in the *2018 PHEMCE SIP*.

The *2016 PHEMCE SIP* identifies priority activities over the next five years in the near-term (FY 2017-18), mid-term (FY 2019-20), and long-term (FY 2021 and beyond) timeframes. All activities described are contingent on available appropriations. The *2016 PHEMCE SIP* provides both a broad-based description of these priority activities, as well as a more detailed description of individual threat-based and capabilities-based approaches.

What is the PHEMCE?

The *PHEMCE* is an interagency coordinating body led by the HHS Assistant Secretary for Preparedness and Response, comprising the Centers for Disease Control and Prevention, the National Institutes of Health, the Food and Drug Administration, and interagency partners at the Departments of Veterans Affairs, Defense, Homeland Security, and Agriculture. It coordinates the development, acquisition, stockpiling, and use of medical products that are needed to effectively respond to a variety of high-consequence public health emergencies, whether naturally occurring or intentional.

Table 1: Overview of PHEMCE Strategic Goals and Objectives

Goal 1: Identify, create, develop, manufacture, and procure critical medical countermeasures.

Objective 1.1: Develop a strategic framework to prioritize PHEMCE resources and investments;

Objective 1.2: Utilize consistent approaches for medical consequence and public health response assessments and MCM requirement setting that include consideration of production, inventory management, deployment, dispensing, and administration strategies;

Objective 1.3: Ensure a robust and sustainable product pipeline for MCMs that emphasizes multi-functional capabilities rather than stand-alone outcomes (e.g., platform technologies, host-based innovations, broad-spectrum medical countermeasures) and includes consideration of viable commercial markets and/or routine public health applicability; and,

Objective 1.4: Promote effective domestic and international partnerships with developers and manufacturers and support core services.

Goal 2: Establish and communicate clear regulatory pathways to facilitate medical countermeasure development and use.

Objective 2.1: Identify scientific and regulatory issues that challenge MCM development or use during public health emergencies and coordinate activities among PHEMCE partners to address those challenges;

Objective 2.2: Assist MCM developers in working interactively with FDA during product development and regulatory review.

Objective 2.3: Establish and implement strategies to expedite the development and evaluation of MCMs during a public health emergency.

Goal 3: Develop logistics and operational plans for optimized use of medical countermeasures at all levels of response.

Objective 3.1: Promote innovative approaches to inventory management to enable a sustainable preparedness infrastructure;

Objective 3.2: Develop and communicate MCM utilization policy, guidance, and response strategies, which take into account FDA regulatory frameworks and are responsive to end-user needs;

Objective 3.3: Develop logistics and operational plans that promote innovative approaches to distribution, dispensing, and administration to ensure timely and efficient access to MCMs;

Objective 3.4: Develop and provide MCM communications, training, and education to inform all stakeholders; and,

Objective 3.5: Develop and implement strategies to assess, evaluate, monitor, and communicate MCM safety, performance, and patient adherence during and after a public health emergency response.

Goal 4: Address medical countermeasure gaps for all sectors of the American civilian population.

Objective 4.1: Develop medical consequence and public health response assessments and requirements setting for at-risk individuals;

Objective 4.2: Support MCM advanced development and procurement for at-risk individuals; and,

Objective 4.3: Develop and implement strategies, policies, and guidance to support the appropriate use of MCMs in all civilian populations during an emergency.

INTRODUCTION

The U.S. continues to face a range of serious threats to its national health security from the deliberate use or accidental release of chemical, biological, radiological, and nuclear (CBRN) agents, as well as from naturally occurring and emerging infectious diseases (EID), including pandemic influenza (see [Box 1](#) below). A failure to anticipate these threats – or the lack of a capacity to effectively respond to them – could result in substantial illness and death among the U.S. population. The nation must have the nimble, flexible capability to produce and effectively use medical countermeasures (MCM)¹ in the face of any attack or threat, whether known or unknown, novel or reemerging, natural or intentional. These capabilities must be communicated to the American public before and during an emergency. Accomplishing these goals requires coordination of MCM-related activities across federal departments. To provide this coordination, the U.S. Department of Health and Human Services (HHS) established the [Public Health Emergency Medical Countermeasures Enterprise](#) (PHEMCE)² in July 2006, to coordinate federal efforts to enhance civilian MCM preparedness. The PHEMCE is charged with coordinating the development, production, and availability of MCMs to limit potential adverse health impacts on the large and diverse U.S. civilian population. The PHEMCE works to meet the public health emergency needs of the entire civilian population, including those of groups that require special medical considerations, such as children, pregnant women, and older adults, as well as [first responders](#),³ health care personnel, and other [critical infrastructure](#) personnel, by taking a whole-of-community approach in planning, response, and recovery efforts. It also seeks to leverage and coordinate with, as appropriate, efforts to address the needs of military populations, especially where product development efforts are congruent.

¹ Medical countermeasures include both pharmaceutical medical interventions (e.g., vaccines, antimicrobials, antidotes, and antitoxins) and non-pharmaceutical medical interventions (e.g., ventilators, diagnostics, personal protective equipment, and patient decontamination) that may be used to prevent, mitigate, or treat the adverse health effects of an intentional, accidental, or naturally occurring public health emergency. They include qualified countermeasures as defined in section 319F-1(a)(2) of the Public Health Service Act (42 U.S.C. § 247d-6a(a)(2)); qualified pandemic or epidemic products as defined in section 319F-3(i)(7) of the Public Health Service Act (42 U.S.C. § 247d-6d(i)(7)), and security countermeasures as defined in section 319F-2(c)(1)(B) of the Public Health Service Act (42 U.S.C. § 247d-6b(c)(1)(B)).

² For more on the establishment of the PHEMCE, see <http://www.gpo.gov/fdsys/pkg/FR-2006-07-06/pdf/06-6004.pdf>. For more information regarding the structure and governance of the PHEMCE, refer to [Appendix 2](#) of this document.

³ This mandate includes consideration of the needs of first-responder populations who face particular risk in the course of their duties and critical infrastructure workers. The role of HHS in working with interagency partners to ensure these populations have access to needed support, including MCMs, is primarily described elsewhere. While particularly relevant activities may be called out in this document, broader efforts are not detailed here. They can be found at <http://www.phe.gov/emergency/events/sandy/Pages/responder-safety.aspx> and <http://www.phe.gov/Preparedness/planning/cip/Pages/default.aspx>.

Box 1: PHEMCE High-Priority Threats

The PHEMCE will continue to address MCM needs to protect against high-priority threats that the Secretary of Homeland Security determines to pose a material threat sufficient to affect national security and/or that PHEMCE leadership determines to have the potential to seriously threaten national health security. The high-priority threats are unchanged from those listed in the *2015 PHEMCE SIP* and are (in alphabetical order):

Bacillus anthracis (anthrax)

Multi-drug resistant *Bacillus anthracis* (MDR anthrax)

Burkholderia mallei (glanders) and *Burkholderia pseudomallei* (melioidosis)

Clostridium botulinum toxin (botulism)

Cyanide

Emerging infectious diseases⁴

Francisella tularensis (tularemia)

Nerve agents

Nuclear agents

Pandemic influenza

Radiological agents

Rickettsia prowazekii (typhus)

Variola virus (smallpox)

Viral Hemorrhagic Fevers

Marburg

Ebola

Yersinia pestis (plague)

The PHEMCE is led by the Assistant Secretary for Preparedness and Response (ASPR).⁵ Core HHS members are the Director of the Centers for Disease Control and Prevention (CDC), the Director of the National Institute of Allergy and Infectious Diseases (NIAID) within the National Institutes of Health (NIH), and the Commissioner of the Food and Drug Administration (FDA). Key PHEMCE interagency partners include senior leadership from the Department of Veterans Affairs (VA), the Department of Defense (DoD), the Department of Homeland Security (DHS), and the Department of Agriculture (USDA). These partners work together under the PHEMCE governance structure described in [Appendix 2](#). Additionally, the PHEMCE works with HHS and U.S. Government (USG) partners, when appropriate, to consider international aspects of its mission. The PHEMCE also works closely with non-federal partners including state, local, tribal, and territorial (SLTT) governments, health systems, academia, private industry, non-governmental organizations (NGO) and ultimately the American people.

⁴ The PHEMCE has established an EID Working Group to develop a process to evaluate whether particular EIDs should be included as PHEMCE high-priority threats. The PHEMCE is already actively engaged in addressing EIDs that currently represent public health threats, such as MERS-CoV and Zika. The PHEMCE also continues to address Ebola as a naturally occurring EID; however, due to its potential use as a biological weapon, Ebola was already included as a PHEMCE high-priority threat before the 2014-15 Ebola outbreak in West Africa.

⁵ The Office of the ASPR includes component offices with key PHEMCE roles such as the Immediate Office (IO); Biomedical Advanced Research and Development Authority (BARDA); Office of Policy and Planning (OPP); Office of Acquisition Management, Contracts, and Grants (AMCG); Office of Emergency Management (OEM); and Office of Financial Planning and Analysis (OFPA).

Box 2: Responding to Zika Virus

The current Zika virus disease outbreak illustrates that communicable diseases do not recognize national borders, and that foreign disease outbreaks can directly affect Americans' safety and security. Therefore, infectious disease outbreaks are a top national security priority requiring global response and responsibility.

The Zika virus is primarily spread by infected mosquitoes, particularly *Aedes aegypti* and *A. albopictus*. In May 2015, the first local transmission of the Zika virus in the Americas was reported in Brazil. By the end of 2015, Brazilian authorities estimated a million suspected cases of Zika virus infection. Subsequently, the virus spread rapidly throughout Latin America and the Caribbean, as well as to parts of the Pacific. In February 2016, the HHS Secretary declared Zika virus posed a significant potential for public health emergency, justifying authorization of emergency use of diagnostics. In April 2016, the CDC confirmed that the Zika virus causes microcephaly and other birth defects.⁶

The U.S. response to the Zika outbreak is complex and involves many partners both within and outside of the federal government. As will be further detailed below, the PHEMCE has been actively engaged in the Zika response to develop diagnostic tests, vaccines, therapies, as well as donor screening and pathogen reduction technologies for blood products. In addition, FDA issued guidances on blood and tissues screening to secure the safety of the nation's blood supply and protect the safety of the nation's supply of human cells, tissues, and cellular and tissue-based products. The PHEMCE is also facilitating sample sharing to support development and validation of diagnostics. ASPR's Biomedical Advanced Research and Development Authority (BARDA)⁷ has modified its open solicitation to include funding opportunities for Zika diagnostics. CDC has developed several diagnostic tests to detect Zika virus including the CDC Zika IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA) and Triplex reverse transcriptase polymerase chain reaction (RT-PCR). FDA reviewed both assays and issued Emergency Use Authorizations (EUA). CDC is distributing test kits to qualified laboratories, including those in the Laboratory Response Network (LRN). The EUA mechanism enables other manufacturers to also seek EUAs for its tests for Zika virus by using the CDC tests as reference assays. CDC has also developed a new immunohistochemistry assay and PCR test for use with pathology specimens, and is using these assays on formalin-fixed tissues from placenta and autopsy specimens. In addition, the PHEMCE is supporting research to understand disease transmission and research into vector control strategies. CDC is assisting partners with investigations into the rates and risks factors for development of Guillain-Barre

⁶ Rasmussen, SA, Jamieson, DJ, Honein, MA, and Petersen, LR, Zika Virus and Birth Defects — Reviewing the Evidence for Causality, *N Engl J Med*, 2016; 374:1981-1987.

⁷ Throughout this document, activities that are led by the BARDA component of ASPR are so identified, while activities that involve BARDA in coordination with other ASPR components, or that are predominantly led by other components, are designated with an "ASPR" lead.

syndrome associated with Zika virus infection. CDC is implementing and managing vector control contracts and supporting local public health interventions. PHEMCE partners are developing a range of vaccine candidates for Zika virus prevention. For example, the NIAID's Vaccine Research Center (VRC) DNA candidate entered a Phase 1 trial on August 2, 2016, at the NIH Clinical Center. The DoD Walter Reed Army Institute of Research (WRAIR) and NIAID anticipate entering the Zika Purified Inactivated Vaccine Candidate into Phase 1 trials in the fall of 2016. BARDA is supporting development of several Zika vaccine candidates with industry partners, including Emergent BioSolutions, Moderna Therapeutics, Sanofi Pasteur, and Takeda. NIH has also partnered with Fiocruz Institute of Brazil to support the Zika in Infants and Pregnancy study, a multinational prospective cohort study of 10,000 pregnant women. The study will assess the risk of Zika virus infection with regard to pregnancy outcome and congenital manifestations in the infant. BARDA is supporting the development of two blood-screening tests for Zika virus infection; both tests have received investigational new drug (IND) status from FDA and are now in development towards a Biologics License Application (BLA). In addition, BARDA has entered into a partnership with Terumo and Cerus for the late-stage development of pathogen reduction systems for blood products that may be contaminated with Zika virus.

ACCOMPLISHMENTS IN FY 2015

Since the publication of the *2015 PHEMCE Strategy and Implementation Plan (SIP)*, the PHEMCE has made significant progress in achieving the priorities described in that document, as highlighted below. In general, the reporting period for the accomplishments in this section covers FY 2015 (from October 2014 to September 2015), except where noted. A detailed description of progress appears in [Appendix 8](#).

Medical Countermeasures Requirements

ASPR's Office of Policy and Planning (OPP), Division of Medical Countermeasure Strategy and Requirements (MCSR) streamlined the MCM requirements process to enhance decision-making and prioritization for MCM research, development, acquisition, and utilization. Additionally, by approving the development of integrated capabilities documents (ICD), the PHEMCE formally incorporated public health and medical operational capacity considerations into MCM stockpiling decision-making.⁸ Overall, this updated requirements process identifies: the critical MCMs needed to address threats; the number of people who would benefit from those MCMs; the number of MCMs that can effectively be used in an emergency; MCM product characteristics;

⁸ ICDs assess the current capacity of the medical and public health system to distribute, deliver, and effectively utilize critical MCMs; identify and quantify constraining parameters under the categories of systems, supplies, staff, and space; and project the operational quantity.

and stockpiling goals and acquisition targets⁹ for the Strategic National Stockpile (SNS)¹⁰ or alternative stockpiles. During FY 2015, the PHEMCE approved an ICD for respiratory protective devices (RPD), which identified all-hazards needs for RPDs, recommended solutions to increase the national capacity to effectively distribute and use RPDs, and set RPD and facemask stockpiling goals and acquisition targets.

Research, Development, and Procurement

The annual PHEMCE Multiyear Budget (MYB) report describes the HHS-wide coordinated five-year budget plan to research, develop, procure, and stockpile MCMs. The MYB report is required by section 2811(b) (7) of the Public Health Service (PHS) Act added by section 102 of the Pandemic and All-Hazards Preparedness Reauthorization Act (Public Law 113-5) (PAHPRA). The MYB report articulates the five-year budget plan to achieve the research, development, procurement, and stockpiling priorities described in the *PHEMCE SIP*. The PHEMCE submitted the second formal MYB report to Congress in April 2016 and will continue to meet this annual legislative requirement.

Product Approvals and Procurements

Successful development and FDA approval¹¹ of safe and effective MCMs is a critical milestone in advancing MCM preparedness. FDA approval is the culmination of many years of dedicated funding, resources, time, and effort from across the PHEMCE. In FY 2015, FDA approved the following medical products for use to prevent, treat, or diagnose diseases caused by CBRN threats and pandemic influenza:

- Anthrax Vaccine: FDA approved anthrax vaccine BioThrax[®] (anthrax vaccine adsorbed (AVA)), which was originally licensed for general use prophylaxis, for post-exposure prophylaxis (PEP) in November 2015;

⁹ Stockpiling goals are the number of MCMs (courses) in a particular class that the PHEMCE recommends stockpiling (either centrally or in alternative methods) based on comparison of policy considerations relevant to the threat, the need-based quantity, and the operational quantity. Acquisition targets are the number of a specific type of medical countermeasure that the PHEMCE recommends procuring, based on consideration of the stockpiling goal, cross-threat prioritizations, market factors, financial considerations, or other relevant programmatic decisions.

¹⁰ The Centers for Disease Control and Prevention's (CDC) SNS has large quantities of medicine and medical supplies to protect the American public if there is a public health emergency (e.g., terrorist attack, flu outbreak, earthquake) severe enough to cause local supplies to run out. Once federal and state authorities agree that the SNS is needed, medicines will be delivered to any state in the U.S. in time for them to be effective. Each state has plans to receive and distribute SNS medicine and medical supplies to local communities as quickly as possible.

¹¹ For purposes of this document, the term "approval" refers to FDA approval, licensure, or clearance under sections 505, 510(k), or 515 of the FD&C Act or section 351 of the PHS Act.

- Anthrax Treatment: FDA approved [Anthrasil™](#) (Anthrax Immune Globulin Intravenous (Human)) to treat patients with inhalational anthrax in combination with appropriate antibacterial drugs¹² in March 2015;
- Influenza Diagnosis: FDA cleared two new multiplex assays¹³ in [February](#) and [September 2015](#) and a rapid, instrument-based molecular test for the detection of influenza A and influenza B viruses from nasal swab specimens received a Clinical Laboratory Improvement Amendments (CLIA) waiver.¹⁴ This is the first molecular influenza assay to receive a CLIA waiver;
- Influenza Treatment: FDA approved the first intravenous antiviral drug for influenza, Rapivab® (peramivir injection), for the [treatment of acute uncomplicated influenza in adult outpatients in December 2014](#),¹⁵
- Pneumonic plague Treatment: FDA approved the plague treatment indication for ciprofloxacin for adults and children in February 2015 and Avelox® (moxifloxacin) for adults in May 2015;¹⁶ and,
- Radiological and Nuclear Treatment: FDA approved a new Neupogen® (filgrastim) indication to treat adult and pediatric patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome) in March 2015 and approved a new Neulasta® (Pegylated-Granulocyte-Colony Stimulating Factor, pegfilgrastim) indication to increase survival in patients acutely exposed to myelosuppressive doses of radiation in November 2015.

BARDA acquired four new products for the SNS under Project BioShield (PBS) in FY 2015. The products all address the continuum of care that is necessary for patients with burn injuries resulting from a nuclear blast or other incidents. BARDA is working closely with the American Burn Association to increase clinical use of these products so that they can be incorporated into the routine care of burn patients nationwide.

Product Advancement

NIH and BARDA are continuing to expand their broad-spectrum antimicrobial programs to address both biothreat indications and the more general public health concern of antimicrobial resistance. These efforts support Executive Order (EO) 13676, [Combating Antibiotic-Resistant](#)

¹² See: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm439752.htm>

¹³ See: http://www.accessdata.fda.gov/cdrh_docs/pdf15/k152408.pdf and http://www.accessdata.fda.gov/cdrh_docs/pdf14/k143080.pdf

¹⁴ All facilities in the United States that perform clinical laboratory testing on human specimens are regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). A CLIA-waived test is an FDA-cleared test that has been granted waived status from the CLIA requirements. These tests are typically simple to use with low risk for an incorrect result when performed by non-laboratory personnel.

¹⁵ <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm427755.htm>

¹⁶ Moxifloxacin labeling for this indication reads for “treatment of plague, including pneumonic and septicemic plague, due to susceptible isolates of *Y. pestis* and prophylaxis of plague in adult patients.”

[Bacteria \(CARB\)](#),¹⁷ which includes development of MCMs to address antibiotic-resistant bacteria. BARDA currently supports six different programs and has utilized the Other Transactional Authority (OTA) provided under Section 319L of the PHS Act to partner with two large pharmaceutical companies, GlaxoSmithKline and AstraZeneca, in the development of novel antimicrobial drugs.

Since the release of the [National Action Plan for Combating Antibiotic-Resistant Bacteria](#),¹⁸ NIAID has established contracts for *in vitro* and *in vivo* testing of new candidate therapeutics for multiple drug-resistant bacteria, including carbapenem-resistant enterobacteriaceae (CRE), *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Neisseria gonorrhoeae*, and *Clostridium difficile*. NIAID also provided preclinical services for a *Shigella* vaccine candidate, *Staphylococcus aureus* vaccine candidate, a defined product for Fecal Microbiota Transplant clinical trials, and a novel *S. aureus* therapeutic. DoD advanced a novel class of antibiotics to Phase 2 clinical testing in FY 2015.

Researchers supported by the Countermeasures Against Chemical Threats (CounterACT) program at the NIH have initiated discussions with BARDA and FDA regarding several products poised for advanced development, including products shown in animal models to improve health outcomes after exposure to nerve agents, sulfur mustard, cyanide, and chlorine. One product that has transitioned to BARDA for advanced development is the drug tissue plasminogen activator (tPA), which was shown in NIH-sponsored animal studies to reduce or eliminate blockage of the airways and reduce mortality after experimental exposure to the chemical warfare agent sulfur mustard.¹⁹ The drug tPA is already approved by the FDA to treat victims of stroke. In addition to this study, administration of the widely available nutritional supplement vitamin D reduced the injury and mortality in mice caused by the toxic chemotherapy agent nitrogen mustard,²⁰ which is very similar to sulfur mustard. For nerve agents, researchers have identified novel brain-penetrating oximes for reactivation of cholinesterase inhibited by sarin and VX surrogates.²¹ Researchers also observed that the active components of the FDA-approved intravenous cyanide antidote Nithiodote (sodium nitrite and sodium thiosulfate) also work when

¹⁷ Executive Order -- Combating Antibiotic-Resistant Bacteria is available at <https://www.whitehouse.gov/the-press-office/2014/09/18/executive-order-combating-antibiotic-resistant-bacteria>

¹⁸ The National Action Plan for Combating Antibiotic-Resistant Bacteria is available at http://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf

¹⁹ Veress LA, Anderson DR, Hendry-Hofer TB, Houin PR, Rioux JS, Garlick RB, Loader JE, Paradiso DC, Smith RW, Rancourt RC, Holmes WW, White CW. (2015) Airway tissue plasminogen activator prevents acute mortality due to lethal sulfur mustard inhalation. *Toxicol Sci.* 143:178-84.

²⁰ Au L, Meisch JP, Das LM, Binko AM, Boxer RS, Wen AM, Steinmetz NF, Lu KQ. (2015) Suppression of Hyperactive Immune Responses Protects against Nitrogen Mustard Injury. *J Invest Dermatol.* 135(12): 2971-81.

²¹ Chambers JE, Meek EC, Chambers HW. (2016) Novel brain-penetrating oximes for reactivation of cholinesterase inhibited by sarin and VX surrogates. *Ann N Y Acad Sci.* 1374: 52-58.

administered intravenously, rescuing 73-100 percent of animals when used as an antidote in three different lethal animal models (mice, rabbits, and pigs).

Product Extension

The Shelf Life Extension Program (SLEP) is a federal fee-for-service program for extending the useful shelf life of military-significant and contingency use medical products, including MCMs owned by DoD or other federal programs, such as the SNS. In FY 2015, as a result of SLEP testing that assured drug stability and quality, FDA granted shelf-life extensions for 2,000 lots (i.e., batches) of MCM drugs. FDA also issued a [memorandum to state and local public health and first responder stakeholders](#) regarding expiry date extensions of certain lots of the 100 mg capsules of the antibiotic doxycycline hyclate stockpiled for public health preparedness and response purposes.²² In addition, FDA helped to [prevent shortages of auto-injectors](#)²³ used for the treatment of nerve agent poisoning by determining, based on testing, that certain auto-injectors could be used beyond their original labeled expiration date for a period specified by FDA.

Product Enhancement

NIAID and BARDA have continued to conduct a series of clinical trials of stockpiled H5N1 and H7N9 influenza vaccines with and without MF59 and AS03 adjuvants developed, produced, and procured under contract by BARDA. While the primary focus of the NIAID clinical trials has been to assess different vaccination strategies and to advance our understanding of the breadth and duration of the immune response, the clinical study results also show that these stockpiled vaccines continue to be well tolerated and immunogenic in humans.

In collaboration with the vaccine manufacturer, NIH completed a Phase 2 trial of a next-generation adjuvanted BioThrax[®] vaccine. An addendum to the final report showing no adverse events of special interest reported was submitted to the FDA in February 2015. This improved anthrax vaccine, AV7909, produces higher antibody titers in a shorter timeframe than the licensed vaccine, BioThrax[®] and was transitioned to BARDA for advanced development in March 2015.

Effective Utilization of Medical Countermeasures

In FY 2014-15, the CDC successfully developed, piloted, and evaluated the next-generation evaluation tool for assessing state and local MCM operational readiness. The purpose of the MCM Operational Readiness Review (MCM ORR) process is to improve state and local operational capabilities, and to identify gaps in their ability to effectively distribute and dispense MCMs in a large-scale event. CDC's Office of Public Health Preparedness and Response (OPHPR), Division of State and Local Readiness (DSLRL), administers funds for preparedness

²² The memorandum is available at:
<http://www.fda.gov/downloads/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/UCM462484.pdf>

²³ See: <http://www.fda.gov/Drugs/DrugSafety/ucm376367.htm>

activities to state and local public health systems through the Public Health Emergency Preparedness (PHEP) cooperative agreements. With the cooperative agreements, CDC helps public health departments strengthen their abilities to respond to all types of public health events and build more resilient communities. In FY 2016, DSLR will collect baseline data on MCM operational readiness for all 62 PHEP awardees and all Cities Readiness Initiative (CRI) local planning jurisdictions to determine their operational readiness status. CDC's goal is for all 62 PHEP jurisdictions to have "Established" MCM programs by June 2022.

CDC/OPHPR's Division of the Strategic National Stockpile (DSNS) conducted a three-day exercise in August 2015, which was designed to evaluate the plans, policies, and procedures in place to respond to a widespread release in multiple jurisdictions of *Bacillus anthracis* spores, which can cause anthrax. The exercise tested CDC's ability to deliver the MCMs required for the full duration and scope of an anthrax response. The design of this exercise tested the assumptions and plans updated in a 2014 revision of the anthrax specific appendix to the SNS Emergency Operations Plan. The scenario tested DSNS's preparedness and team room operations, allowing participants to perform tasks, make decisions, and coordinate details inherent to an anthrax response. The exercise successfully validated the 2014 updates to the anthrax appendix and showed the value of the plan-train-exercise-assess cycle. In a separate effort, CDC led the adaptation of existing anthrax clinical guidelines to the setting of an anthrax mass casualty event. The resulting mass casualty clinical recommendations were published in *Morbidity and Mortality Weekly Report (MMWR)* in December 2015.

CDC published an updated case definition for [Middle East Respiratory Syndrome Coronavirus \(MERS-CoV\)](#) in December 2015.²⁴ CDC revised the case definition based on comments from public health partners, health care providers, professional organizations, and others. CDC will continue to update the document as necessary to incorporate new information that may become available. CDC also published updated guidance entitled "[Interim Infection Prevention and Control Recommendations for Hospitalized Patients with MERS-CoV](#)" in June 2015.²⁵ This new document supersedes the July 2014 CDC guidance and highlights the key infection control recommendations including standard, contact, and airborne precautions. In addition, it emphasizes additional elements of infection prevention and control programs that should be in place to prevent the transmission of MERS-CoV in health care settings.

Mechanical ventilators are stockpiled in the SNS and available for deployment to health care facilities, through state and local governments, to supplement local shortages of supplies during a large-scale public health emergency. CDC partnered with the American Association for Respiratory Care (AARC) to provide state respiratory therapists and other health care professionals with the information necessary to utilize SNS ventilators during a large-scale pandemic influenza emergency as well as an opportunity for hands-on experience with all three stockpiled ventilator models. Multiple live training sessions have been held across the U.S. starting in 2014 and 136 respiratory therapists and health care professionals received the

²⁴ See: <http://www.cdc.gov/coronavirus/mers/case-def.html>

²⁵ See: <http://www.cdc.gov/coronavirus/mers/infection-prevention-control.html>

training during 2014-15. The live trainings offer specific information on the SNS ventilator request process, ventilator kitting, storage and maintenance processes, how SNS ventilators will be allocated during an influenza pandemic or other public health emergency, and critical hands-on training. As a result of the positive feedback for the live training, SNS and AARC will conduct four to five live training sessions throughout the U.S. on an annual basis. In addition to the live training sessions, SNS and AARC have developed on-line trainings through the AARC website.

Regulatory Science Management

Emergency Use Authorizations (EUA) and Emergency Use Instructions (EUI)

FDA's EUA authority helps to facilitate public health or medical access to available MCMs when necessary. FDA may authorize the use of an unapproved MCM, or the unapproved use of an approved MCM, in anticipation of a potential emergency or during an actual emergency, involving a specified CBRN agent or agents if certain statutory criteria are met.²⁶ In FY 2015, FDA issued nine EUAs for diagnostic tests for Ebola virus as well as re-issued an EUA for an Ebola diagnostic test initially issued in FY 2014. FDA also issued [EUAs](#) for diagnostic tests for Enterovirus D68 (EV-D68) and the MERS-CoV.²⁷

PAHPRA amended the Federal Food, Drug and, Cosmetic Act to provide HHS the authority to facilitate the availability of streamlined information (i.e., Emergency Use Instructions (EUI)) about the use of eligible, approved MCMs needed during public health emergencies without FDA needing to issue an EUA. The HHS Secretary delegated EUI authority to the Director of CDC in 2013. CDC has developed an EUI implementation process that includes a concept of operations and framework for developing, clearing, issuing, and communicating CDC generated EUIs. In addition, CDC and FDA signed a [memorandum of understanding \(MOU\) to establish a framework for how they will coordinate in support of CDC's use of its delegated authority to develop and issue EUIs for eligible MCMs](#).²⁸ As part of the planning effort, CDC has begun assessing pandemic influenza MCMs for EUI considerations. Products being assessed include influenza antiviral drugs, stockpiled RPDs, and diagnostics. In addition, CDC issued the first EUI in April 2016 for oral doxycycline and ciprofloxacin for PEP of inhalational anthrax in coordination with FDA's issuance of emergency dispensing orders for these products; together, these actions render the need for EUAs for the emergency dispensing of doxycycline and ciprofloxacin for inhalational anthrax PEP unnecessary.²⁹

Medical Countermeasures Initiative (MCMi) Regulatory Science Program

In FY 2015, FDA continued to support the MCMi Regulatory Science Program, which was established to advance the science that supports regulatory decision making through the pursuit of data and innovative tools/technologies. This program supports intra- and extramural

²⁶ Under the Federal Food, Drug, and Cosmetic Act, as amended by the Project BioShield Act of 2004 [PL 108-276], and the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 [PL 113-5], the Secretary of HHS has the authority to authorize the "emergency use" of MCMs in emergencies under certain terms and conditions [21 U.S.C. § 360bbb-3].

²⁷ For more about EUAs see <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm>

²⁸ See: <http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm487464.htm>

²⁹ The EUI for doxycycline and ciprofloxacin is available to state and local public health officials via a password-protected CDC JOIN site. During an anthrax emergency, the EUI materials will be posted on CDC.gov for the general public.

research to develop the tools, standards, and approaches needed to both develop MCMs and assess MCM safety, efficacy, quality, and performance. This program develops tools, standards, and approaches needed to both develop MCMs and assess MCM safety, efficacy, quality, and performance. Examples of research activities supported in FY 2015 include:

- Developing models of radiation damage in lung, gut, and bone marrow [organs-on-chips](#) and using these models to test candidate MCMs to treat such damage;³⁰
- [Improving animal models](#) to evaluate serious adverse events related to use of the smallpox vaccine and therapies to counteract these complications;³¹ and,
- [Establishing a model](#) to estimate pediatric pharmacokinetics for antibacterial and antiviral MCMs.³²

Stakeholder Engagement

To foster the development and availability of safe and effective MCMs, FDA continued providing regulatory advice, guidance, and technical assistance. Collaboration of this nature occurs through a variety of mechanisms, including direct engagement with MCM sponsors and applicants, guidance documents, and advisory committee meetings and public workshops. Formal meetings between the product sponsor and FDA are held throughout the product lifecycle. During FY 2015, FDA worked to finalize and issue guidance related to MCM development or utilization including:

- [Premarket Notification Requirements Concerning Gowns Intended for Use in Health Care Settings](#) (final guidance issued in December 2015, draft issued in June 2015) – to describe FDA’s premarket regulatory requirements and the performance testing needed to support liquid barrier claims for gowns intended for use in health care settings;³³
- [Radiation Biodosimetry Devices](#) (final guidance issued in April 2016, draft issued in December 2014) – to facilitate study designs to establish the analytical and clinical performance characteristics of radiation biodosimetry MCM devices;³⁴ and,

³⁰ The project was funded under the extramural MCMi regulatory science program. For more information, see *Organs-On-Chips for Radiation Countermeasures* at: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm364491.htm>

³¹ Additional information is available in the *Journal of Virology*: <http://jvi.asm.org/content/89/6/3295.short>

³² For more information on FY 2015 activities under the MCMi Regulatory Science Program, see the MCMi Fiscal Year 2015 Program Update available at <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm490755.htm>

³³ Guidance is available at: <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM452804.pdf>

³⁴ Guidance is available at: <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM427866.pdf>

- [Product Development Under the “Animal Rule”](#)³⁵ (final guidance issued in October 2015, revised draft issued in May 2014) – to provide information and recommendations on drug and biological product development when human efficacy studies are not ethical or feasible.³⁶

FDA also held several advisory committee meetings and public workshops in FY 2015 to obtain independent input and expert advice on scientific, technical, and policy matters facilitating MCM development. Descriptions of these events can be found in [Appendix 3](#).

International Sharing of Medical Countermeasures

In 2015, ASPR/OPP’s Division of International Health Security (DIHS) continued to lead HHS, USG, and global development and implementation of policies and procedures for the international deployment of MCMs:

- ASPR/OPP/DIHS and CDC/OPHPR/DSNS continued to chair the International Sharing of MCMs Policy Group to implement and improve policies and procedures for responding to international requests for MCMs from the CDC’s SNS. The policies and research developed by this group have been used to respond to nearly 30 international requests to date, including a 2015 response to a critical Global Health Security Agenda target country.
- ASPR/OPP/DIHS also continued to chair the Global Health Security Initiative (GHSI) MCM Task Force, which consists of technical experts from the Group of Seven (G7) countries, Mexico, the World Health Organization (WHO), and the European Commission. ASPR/OPP/DIHS led efforts within the Task Force to identify and address legal, logistical, regulatory, and funding challenges associated with the rapid cross-border deployment of MCMs in response to public health emergencies. Specifically, ASPR/OPP/DIHS is leading the MCM Task Force to develop global frameworks, including checklists and other tools to guide international deployments of MCMs during emergencies, such as the checklist used to inform potential MCM deployment during the West African Ebola outbreak.
- Additionally, ASPR/OPP/DIHS continues to work with the WHO under a three-year cooperative agreement (beginning in FY 2015) to: (1) develop a process for product review of MCMs included in or pledged to the WHO stockpiles; (2) establish a process for emergency use assessment of MCMs to be deployed and used internationally during public health emergencies; and (3) support potential recipient WHO member states in building capacities for the import, registration, and emergency use of MCMs. The work

³⁵ Under certain circumstances – when it is neither ethical nor feasible to conduct human efficacy studies – FDA may grant marketing approval based on adequate and well-controlled animal efficacy studies when the results of those studies establish that the drug or biological product is reasonably likely to produce clinical benefit in humans. Demonstration of the product’s safety in humans is still necessary (21 CFR 314.600 for drugs; 21 CFR 601.90 for biological products).

³⁶ Guidance is available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM399217.pdf>

conducted under this cooperative agreement served as the basis for WHO Emergency Use Assessment and Listing procedures implemented during the Ebola outbreak and the 2015-16 Zika outbreak.

ASPR/OPP/DIHS also continues to work with North American partners, Canada and Mexico, to overcome policy and operational barriers to deploying MCMs in the region during international public health emergencies:

- In 2015, as a health security priority under the U.S.-Canada Beyond the Border Initiative (BTB), ASPR/OPP/DIHS worked with the Public Health Agency of Canada to identify and address barriers relating to the rapid deployment of MCMs from national stockpiles across the U.S.-Canada border during a public health emergency. In September 2015, ASPR/OPP/DIHS hosted a bilateral exercise with participants from across both U.S. and Canadian governments to test these capabilities and further explore identified challenges to bilateral sharing of MCMs, which include national policies and legal authorities, liabilities, regulatory processes, logistics, and funding. As a result of these efforts, the U.S. and Canada proposed a series of recommendations to facilitate the bilateral sharing of MCMs. These recommendations include the development of toolkits, frameworks, and/or processes to expedite the cross-border deployment of MCMs, for example, by establishing a commitment to share MCMs, developing model liability terms and conditions, and exercising a process for exchanging regulatory data.
- Additionally, in March 2015, ASPR/OPP/DIHS hosted a trilateral exercise under the North American Plan for Animal and Pandemic Influenza (NAPAPI). The exercise convened government representatives from the health, security, agriculture, and foreign affairs sectors of the U.S., Canada, and Mexico, to discuss plans and challenges associated with availability and access to MCMs during an influenza pandemic.
- Throughout 2015, ASPR/OPP/DIHS also hosted several technical exchanges with NAPAPI partners at both the working and senior leadership levels to share information relating to the availability of and access to pandemic influenza MCMs, including by exchanging best practices for stockpiling, deployment, and supply-chain preparedness.

By managing the acquisition of pathogen samples, ASPR/OPP continues to support the MCM research and development enterprise during public health emergencies:

- ASPR/OPP/DIHS established an HHS Sample Sharing Working Group in collaboration with CDC and other HHS stakeholders to identify and obtain viral isolates and patient samples necessary to characterize pathogens and facilitate the development of diagnostics, therapeutics, and vaccines. Under ASPR leadership, this group addresses logistical and permitting requirements as well as legal agreements needed to obtain and share such materials, and facilitates prioritization decisions between HHS and USG partners and between the USG and international partners when materials are limited.
- Within GHSI, ASPR/OPP/DIHS initiated and led the Sample Sharing Task Group (SSTG) in drafting a framework and material transfer agreement to facilitate the rapid sharing of samples among GHSI members. The framework and material transfer agreement were tested during an exercise held in May 2015, which allowed GHSI members to evaluate their policy, regulatory, and logistical protocols for responding to requests for the rapid sharing of non-influenza human samples during a public health emergency and their ability to negotiate and accept the terms of the draft material transfer agreement.

Ebola Outbreak Response

The PHEMCE continued its integrated response to the 2014-15 Ebola outbreak in West Africa throughout FY 2015 and all PHEMCE partners contributed to this response. The PHEMCE continues efforts to respond to any new cases that arise. Below are highlights of the accomplishments made by the PHEMCE in FY 2015, except where noted. For current plans regarding these activities, see the [Ebola Preparedness and Response](#) section of this report.

Vaccines and Therapeutics

The PHEMCE continued to make progress in its support of basic, preclinical, and clinical research that will lead to new approaches to prevent and treat Ebola. CDC studied the pathogenic properties of the *Zaire ebolavirus* responsible for the outbreak in West Africa. Researchers compared the new West African Ebola virus isolates to previous outbreak isolates to identify differences in their disease-causing properties. Scientists at the NIAID-funded Genomic Center for Infectious Diseases at the Broad Institute rapidly sequenced over 580 genomes isolated from Ebola virus samples received from Sierra Leone and Nigeria. These sequencing efforts resulted in over 160 assembled genomes released rapidly into the public domain including GenBank/NCBI and the NIAID Bioinformatics Resource Center to aid efforts to better understand the factors important to epidemic spread. In addition, the NIAID Genomic Center for Infectious Diseases at the Broad Institute assisted the CDC by providing sequencing and bioinformatics platforms for sequencing an additional 80 genomes isolated from Ebola virus samples from Sierra Leone. The efforts revealed insights into the epidemiology, transmission, evolution and origin of the outbreak strain and results were published. CDC also worked with the Broad Institute and U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) to obtain and complete the genomic sequencing of more than 100 Ebola specimens. BARDA, NIH, FDA, and DoD supported the development efforts for multiple potential Ebola MCMs including the therapeutic candidates ZMapp™, mAb114, BCX4430, AVI-7537 and favipiravir and multiple vaccine candidates, including chimpanzee adenovirus vector type 3 (ChAd3), ChAd26/modified vaccinia virus Ankara (MVA) vectors, several heterologous prime-boost combination vaccines using adenovirus vector platforms, and recombinant vesicular stomatitis virus (rVSV) vector. BARDA leveraged several of its core services during the Ebola response through the National Medical Countermeasure Response Infrastructure, described in greater detail below. Through NIAID's preclinical services (PCS), over 24 Ebola vaccine formulations from nine institutions have been screened for efficacy in the non-human primate (NHP) model. This effort was critical for generating data to support the selection of candidates for advanced product development and clinical development. NIH's Concept Acceleration Program (CAP) was a key element in advancing efforts on five of the nine Ebola vaccine candidates to enter human clinical testing.

CDC and partners completed vaccinating volunteers for the Sierra Leone Trial to Introduce a Vaccine against Ebola (STRIVE) in late 2015; over 8,000 health care and frontline workers were vaccinated through this program. Ongoing activities include participant follow up for adverse events and for outcomes of pregnancies, and completion of the immunogenicity sub-study with blood draws six and 12 months post-vaccination and shipment of specimens to the U.S. for testing. CDC is exploring options with the Sierra Leonean government for provision of vaccine

to high risk populations, including contacts of survivors, through non-STRIVE mechanisms such as an expanded access investigational new drug (IND) and has had preliminary discussions with the FDA regarding this.

NIAID and its partners in the Liberia-U.S. clinical research partnership known as PREVAIL (Partnership for Research on Ebola Virus in Liberia) completed vaccinating 1,500 Liberian volunteers in PREVAIL I, a Phase 2 placebo-controlled Ebola vaccine trial, in May 2015. As reported by a lead investigator in February 2016 at the Conference on Retroviruses and Opportunistic Infections, at one month, 87 percent of 500 volunteers vaccinated with the GSK cAd3-EBOZ vaccine had measurable anti-Ebola antibodies, and 94 percent of 500 vaccinated with the Merck VSV-ZEBOV had measurable anti-Ebola antibodies. Participants are currently being called back to see if they would be willing to participate in an additional four years of follow-up to determine the durability of the immune response. So far, more than 99 percent have re-consented for the extended four-year follow-up period.

In addition, NIAID and its Liberian partners completed PREVAIL II, a randomized controlled treatment trial of the experimental monoclonal antibody cocktail known as ZMapp (Mapp Biopharmaceutical), at sites in West Africa and the United States. Because of the decline in Ebola cases in West Africa, the trial was closed in January 2016 after enrolling 72 of a targeted 200 total volunteers. As initially reported in February 2016 at the Conference on Retroviruses and Opportunistic Infections, and now described in a paper published by The New England Journal of Medicine,³⁷ ZMapp was found to be well-tolerated, and the data collected, although not definitive, show a trend toward benefit, indicating it holds promise as an Ebola treatment.

Diagnostics

The PHEMCE made significant progress in the development of Ebola virus diagnostic tests in FY 2015. FDA issued an EUA to authorize the emergency use of a real-time reverse transcription polymerase chain reaction (rRT-PCR) test, developed by CDC, which detects Ebola virus within a few hours. BARDA supported the development of OraSure Technologies, Inc.'s OraQuick® Ebola Rapid Antigen Test, which is a lateral flow immunoassay that detects Ebola virus infection from a finger prick drop of whole blood or a swab of oral fluid and provides results in 15 minutes. CDC worked with industry on preclinical and field testing of the OraQuick® Ebola Rapid Antigen Test. This test was WHO listed in 2016. CDC aided industry partners in achieving FDA authorization to use under an EUA and continues to work with WHO for prequalification of the tests.

NIH supported the development of the Corgenix ReEBOV Antigen Rapid Test, an immunodiagnostic test that detects Ebola virus from a finger prick drop of blood and provides results in as little as 15 minutes. In February 2015, the WHO listed the ReEBOV Antigen Rapid Test Kit for use in outbreak countries and FDA issued an EUA for its emergency use in circumstances when use of a rapid Ebola virus test is determined to be more appropriate than

³⁷ The PREVAIL II Writing Group, for the Multi-National PREVAIL II Study Team, A Randomized, Controlled Trial of ZMapp for Ebola Virus Infection, *NEJM*, 2016; 375 (15):1448-1456.

an authorized Ebola virus nucleic acid test. A [field evaluation study performed in a high-risk population](#) demonstrated the test had 100 percent sensitivity and 92 percent specificity when compared to a PCR-based Ebola virus diagnostic test.³⁸

FDA issued 11EUAs for Ebola virus diagnostics tests. The PHEMCE continues to work with industry partners in development and evaluation of multiplex rapid diagnostic tests.

Response and Personal Protective Equipment Efforts

In FY 2015, PHEP awardees actively monitored more than 26,000 travelers returning from countries in West Africa affected with widespread Ebola. This entailed daily monitoring for a 21-day period for every at-risk traveler. CDC resources and guidance enabled the establishment of active monitoring procedures within 10 days of the decision to establish such a daily monitoring system.

CDC also worked to rapidly increase quantities of personal protective equipment (PPE) in the SNS to establish a capability to support 50 multidisciplinary health care teams providing care to Ebola patients at U.S. health care facilities until commercial product availability could meet demand. In 2015, CDC established plans to increase PPE capabilities in the SNS to protect an additional 260 health care teams, with SNS deliveries scheduled for completion in 2016. This action established a new capability for response to Ebola or other highly infectious diseases in the U.S. health care system, providing the specific types of PPE recommended in CDC guidance for the care of Ebola patients. The CDC acquired these PPE products in close coordination with commercial partners in the PPE manufacturing and distribution sectors, to ensure that deliveries to the SNS would not disrupt the high commercial demand for these same products.

CDC also engaged with partners at the federal, state, and local level and in the commercial market to monitor demand and available supplies of PPE during the most critical stages of the Ebola response. Through the onsite assessments of Rapid Ebola Preparedness teams, CDC collected urgent PPE requirements at the facilities most likely to receive an Ebola virus disease patient. CDC then worked with PPE manufacturers and distributors to prioritize order delivery to those facilities to rapidly enhance their preparedness. CDC also facilitated and encouraged sharing plans among hospitals, public health and health care coalitions in an effort to mitigate supply shortages. CDC developed an Ebola PPE calculator tool and worked with Ebola treatment centers and hospitals to help them assess their ongoing needs to meet the demands of caring for an Ebola patient.

Regulatory Science

During FY 2015, FDA continued its intense efforts to support the international response to the Ebola outbreak in West Africa. Throughout the epidemic response, FDA worked proactively with U.S. government partners, MCM developers, and international partners—including the WHO and international regulatory counterparts—to provide scientific and regulatory advice to

³⁸ The report on this study can be found at:
<http://www.sciencedirect.com/science/article/pii/S014067361561042X>

facilitate the development and availability of MCMs to respond to the epidemic. Some of FDA's many regulatory science activities included:

- Providing review and feedback on MCM development proposals including clinical trial design and data assessment;
- Maintaining regular contact with drug, vaccine, device, and diagnostic test developers, and expediting the regulatory review of data for products that are currently in the pipeline and products that are still very early in development; and,
- Enabling access to investigational MCMs—when necessary—through an appropriate mechanism such as under an EUA or under expanded access mechanisms during the period of the Ebola epidemic before clinical trials were established, when the clinical circumstances warranted.
- Supporting highly targeted regulatory science necessary to facilitate [MCM development and regulatory review including developing nucleic acid standards and regulatory-grade reference sequences to support diagnostic development](#),³⁹ [facilitating vaccine and therapeutic development through the improvement of virus neutralization assays and the identification of correlates of protection in Ebola virus disease survivors](#),⁴⁰ and informing clinical trials for Ebola MCMs through analysis of novel study designs.⁴¹

DEVELOPMENT OF THE 2016 PHEMCE SIP

Annual PHEMCE Strategy and Implementation Plan Process

The PHEMCE SIP is released annually as required by Section 2811(d) of the PHS Act,⁴² as amended by section 102 of PAHPRA. The PHEMCE adopted the following process for the SIP (also summarized in Table 2 below):

- The PHEMCE SIP will be issued annually and will address all PHS Act reporting requirements (listed in [Appendix 9](#));
- Major updates to activities will occur on even-numbered years; this entails re-evaluation of all activities in the most recent PHEMCE SIP and considers necessary revisions and addition of relevant new activities. Adjustments will be made to activities annually (as needed) when significant changes have occurred or new activities have begun; and,

³⁹ Via the FDA-ARGOS program. See: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm452650.htm>

⁴⁰ See: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm471610.htm>

⁴¹ For example, see Clinical Trials: doi: 10.1177/1740774515620145

⁴² 42 U.S.C. 300hh-10(d)

- Major re-evaluation of goals and objectives will occur in 2018 and every four years thereafter. Minor adjustments to goals and objectives (as needed) will be considered annually.

Table 2: Annual PHEMCE Strategy and Implementation Plan Process

SIP Elements	2012	2014	2015	2016	2017	2018
Major Re-Examination: Goals & Objectives	X	-	-	-	-	X
Minor Updates: Goals & Objectives	-	X	X	X	X	-
Major Re-Examination: Activities	X	X	-	X	-	X
Minor Updates: Activities	-	-	X	-	X	-
PAHPRA Reporting Requirements	N/A	X	X	X	X	X

2016 PHEMCE SIP Steering Committee

ASPR led the development of the *2016 PHEMCE SIP* through an interagency steering committee comprised of representatives from across the PHEMCE agencies. The steering committee reviewed the PHEMCE-wide strategic goals and objectives contained in the *2015 PHEMCE SIP* and saw a need to increase PHEMCE focus on addressing the operational challenges associated with effective administration of MCMs during a large-scale public health emergency. As such, the PHEMCE added two objectives to emphasize these efforts. The first new objective (Objective 2.3) addresses the need to have strategies in place to assess MCMs quickly during development and use during a public health emergency response. The second new objective (Objective 3.3) emphasizes the need for logistical and operational plans for distributing and dispensing MCMs, which was previously embedded within Objective 3.2. The PHEMCE determined that the goals and updated objectives continued to be appropriately aligned with agency-level strategies and priorities (see [Appendix 6](#)).

Based on the progress made in pursuit of these goals and objectives since 2015 (as summarized above and in [Appendix 8](#)), and in alignment with the prioritization framework developed in the *2012 PHEMCE Implementation Plan*, the steering committee identified priority activities needed to achieve the PHEMCE goals and objectives. These included activities still ongoing from the *2014/2015 PHEMCE SIPs* as well as new activities. Plans to pursue and accomplish the activities and initiatives detailed here are based on currently anticipated funding levels for PHEMCE organizations over the next five years. Following review and input from across the PHEMCE, the *2016 PHEMCE SIP* was approved by the interagency and publicly released.

As in previous iterations of the PHEMCE SIP, activities are assigned a code, which appears in gray font in front of the activity text to which it is assigned. These codes are used to facilitate tracking of activities. The activity codes used in the *2016 PHEMCE SIP* update those used in the *2014/2015 PHEMCE SIPs*. Activities that appear under the goals and objectives (Section 1)

have codes that align to the objective it supports (e.g., activity code 1.1.1 supports Objective 1.1). Activities that appear in the [threat-based](#) (Section 2) and [capabilities-based](#) (Section 3) sections of this report are coded with a T and C, respectively, and an acronym that aligns with the sub-section (e.g., activity code T.A.1 aligns to the threat-based activities under anthrax).

Consideration of Perspectives from National Advisory Committees

HHS has several national advisory committees that the PHEMCE can leverage for guidance on scientific, technical, and other matters related to MCM preparedness and response. The 2016 PHEMCE SIP was informed by previous recommendations provided to the HHS Secretary and the ASPR on PHEMCE-related issues by the National Preparedness and Response Science Board (NPRSB).⁴³ Past NPRSB engagements of particular relevance included those [conducted on the 2012 PHEMCE SIP](#);⁴⁴ the [long-term sustainability of the Strategic National Stockpile \(SNS\)](#);⁴⁵ and the [PHEMCE development of MCM preparedness goals](#).⁴⁶ At the time of writing, the NPRSB was also currently conducting a review of the [PHEMCE MCM preparedness assessment process](#), which directly informs priorities in the annual PHEMCE SIP.⁴⁷

⁴³ Previously called the National Biodefense Science Board (NBSB).

⁴⁴ NBSB Evaluation of the 2012 HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan (SIP), 2012. Available at <http://www.phe.gov/Preparedness/legal/boards/nprsb/recommendations/Documents/NBSB-letter-to-Secretary-130131.pdf>.

⁴⁵ National Biodefense Science Board and the Office of Public Health Preparedness and Response Board of Scientific Counselors, Anticipated Responsibilities of the Strategic National Stockpile (SNS) in the Year 2020: An Examination with Recommendations, 2013. Available at: <http://www.phe.gov/Preparedness/legal/boards/nprsb/recommendations/Documents/nbsb-bsc-sns-2020-final.pdf>.

⁴⁶ National Biodefense Science Board, Strategic Preparedness Goals Report, 2014. Available at: <http://www.phe.gov/Preparedness/legal/boards/nprsb/meetings/Documents/phmce-stpreport.pdf>.

⁴⁷ See: <http://www.phe.gov/Preparedness/legal/boards/nprsb/meetings/Pages/05262016-publicmtg.aspx>

SECTION 1: ACTIVITIES TO ACHIEVE STRATEGIC GOALS AND OBJECTIVES

This section identifies activities that directly support the PHEMCE goals and objectives, and which are projected for near-term (FY 2017-18), mid-term (FY 2019-20) and long-term (FY 2021 and beyond) timeframes. More detailed information on these priorities is provided in Sections 2 and 3 of this SIP, organized by specific [threat area](#) and [capabilities-based](#) approaches, respectively.

GOAL 1. Identify, create, develop, manufacture, and procure critical medical countermeasures.

Objective 1.1 Develop a strategic framework to prioritize PHEMCE resources and investments. (**Lead: ASPR; Partners: PHEMCE agencies**)

PHEMCE Prioritization Framework: Principles and Criteria

Given the range of potential threats and the resources available to address them, the availability of critical MCMs for use in a public health response depends on HHS and PHEMCE-wide resource prioritization and strategic decision-making across the PHEMCE mission space, from research and development through effective utilization. In 2012, the PHEMCE developed a coordinated, strategic framework through which to focus investments across the PHEMCE and will continue to apply this framework to inform resource allocations for research, development, manufacturing, procurement, and MCM operational planning.

The PHEMCE Prioritization Framework considers two core principles: (1) the medical and public health imperatives to limit the potential adverse health impacts posed by a variety of threats; and (2) the fiduciary responsibility to be prudent with the resources entrusted to the programs by Congress and the nation while maximizing preparedness. It then uses three primary and three moderating criteria for identifying priority investments; Box 3 lists these to the right, and the [2012 PHEMCE Implementation Plan](#)⁴⁸ describes them in more detail.

PHEMCE Prioritization Processes

We will conduct the following activities to implement the prioritization framework over the next five years:

- (1.1.1) *Portfolio Reviews (ongoing)*: ASPR leads the periodic (at least every 18 months) review of specific MCM portfolios across the PHEMCE to monitor progress in MCM preparedness, identify remaining gaps and challenges, and develop potential solutions.

Box 3: Prioritization Framework

Primary Criteria

1. Threat Priority
2. Multi-Functionality
3. Operational Capacity

Moderating Criteria

4. At Risk-Population Needs
5. Time to Product Availability
6. Life Cycle Cost

⁴⁸ See: <http://www.phe.gov/Preparedness/mcm/phemce/Pages/strategy.aspx>

These Portfolio Reviews will continue to provide venues to foster coordination among PHEMCE partner agencies in the identification of those areas requiring additional attention and resource prioritization. The 2015/2016 series reviewed Chemical threats, Antimicrobial Resistance, Anthrax, Radiological and Nuclear threats, Pandemic Influenza, and Filovirus.

- (1.1.2) *Multiyear Budget (ongoing)*: Development of the multiyear budgeting initiative, called for in the [2010 PHEMCE Review](#),⁴⁹ and subsequently required by law under the PHS Act, as amended by PAHPRA,⁵⁰ was initiated in 2011 and has continued to evolve since then, with the first PHEMCE multiyear budget report (covering FY 2014 to FY 2018) submitted to Congress in early 2015. The second annual report (covering FY 2015 to FY 2019) was submitted to Congress in April 2016. The report contains a long-term budget plan that links MCM research, development and procurement investments across NIH, ASPR, CDC, and FDA. The plan assists the Department in projecting future budget needs within and among agencies as MCM products mature and move through the development and procurement processes.
- (1.1.3) *Portfolio Tracking and Coordination Initiative (near and mid-term)*: ASPR and the DoD continue to expand the completed portfolio tracking tools to enhance portfolio management decision-making. These tools will provide a common set of business practices and harmonized performance metrics that will facilitate benchmarking and data-driven management practices to achieve shorter timelines and greater cost-efficiencies in MCM development portfolios. Efforts are specifically geared to:
 - (1.1.3a) Maintain and expand the Portfolio Tracking Tool to provide stakeholders with a real time database of MCM project and contracts. The tool will be expanded to include pandemic influenza, EID and other public health portfolios beginning in the near-term.
 - (1.1.3b) Develop the Inter-Agency Cost Model Tool to use historical, interagency cost data for the prediction, analysis, and benchmarking of PHEMCE MCM development costs. The PHEMCE has initiated collaboration with the Tufts Center for the Study of Drug Development in support of this project. This collaboration will refine and validate the planned approach, methodology, and outputs based on best practices used in industry.
 - (1.1.3c) Develop a broad-based capabilities tool to capture product development support capabilities (e.g., government facilities, infrastructure, and services) available to stakeholders.
- (1.1.4) *Portfolio Management (ongoing)*: BARDA continues to evaluate total life-cycle management costs as one aspect of product development to be considered. BARDA will continue to share this information with our PHEMCE partners, both formally and informally.

The depth, complexity, and breadth of information necessary for the PHEMCE to implement the prioritization framework also require the use of decision analysis tools. Policy-relevant considerations include, but are not limited to: the best scientific evidence; assessment of

⁴⁹ See: <http://www.phe.gov/Preparedness/mcm/phemce/Pages/review-2010.aspx>

⁵⁰ 42 U.S.C. 300hh-10(b)(7)

scientific promise; MCM needs projections; evidence-based clinical utilization protocols; an assessment of national and regional capability to effectively utilize MCMs in a public health emergency; cross-threat prioritization; and resource availability. In response, the PHEMCE and agency partners have developed several decision analysis tools to inform senior leaders at all levels.

The PHEMCE has developed and implemented a standardized process for conducting and using the results of MCM preparedness assessments that assess the current and projected national ability to: (1) develop, (2) make, (3) access, (4) plan for, and (5) effectively use MCMs. In addition, these assessments identify initiatives needed to address strategic gaps that inform future PHEMCE priorities, reflected in the annual PHEMCE SIP. (1.1.5) The PHEMCE, through its subject matter expert integrated program teams (IPT), will complete preparedness assessments for all SNS holdings in the near-term. (1.1.6) In the mid-term, the PHEMCE will use information from individual MCM preparedness assessments to evaluate overall MCM preparedness against high-priority threats. The PHEMCE will continue to refine the MCM preparedness assessment process in the near-term, based on the results of the initial pilots. (1.1.7) ASPR and CDC will seek additional mechanisms to engage with appropriate subject matter experts, both within the federal government and externally, to most accurately evaluate operational and response planning considerations of MCM use for large-scale emergencies. (1.1.8) ASPR and CDC will work to incorporate data from CDC's DSLR ORR evaluation process to inform assessment of the national operational capacity to use MCMs. (2.3.1) ASPR will work with the MCM Monitoring and Assessment IPT (MA IPT) to most effectively incorporate evaluation of MCM post-event monitoring capabilities into future assessments. (1.1.9) ASPR/OPP/MCSR is also developing approaches for incorporating [economic risk analysis](#) into PHEMCE resource decisions. This effort was initiated with the support of the HHS Ventures Fund.⁵¹

Objective 1.2 Utilize consistent approaches for medical consequence and public health response assessments and MCM requirement setting that include consideration of production, inventory management, deployment, dispensing, and administration strategies. **(Lead: ASPR; Partners: PHEMCE agencies)**

Simply stated, the PHEMCE MCM requirement process must address the questions of “Who needs what, when, and how?” The requirement process serves to improve the outcomes of public health emergencies by focusing federal investments toward an aligned research, advanced development, acquisition, deployment, and use agenda by HHS agencies. Moreover, the requirement process informs private industry and academia about civilian MCM needs and facilitates effective coordination of programs with PHEMCE interagency partners.

Working with medical, public health, technical, and scientific experts across the PHEMCE, ASPR/OPP/MCSR leads the civilian MCM requirement process and vets requirement

⁵¹ See: <http://www.hhs.gov/idealab/projects-item/building-an-economic-evaluation-model-for-emergency-preparedness/>

documents through the PHEMCE governance structure prior to finalization by the ASPR. For intentional CBRN threats, the requirement framework uses DHS Material Threat Assessments (MTA), which estimate the number of individuals exposed to each threat in a range of scenarios up to and including high-consequence scenarios. These assessments are then used as the basis for public health response and medical consequence modeling, which informs identification of a range of the number of people who would benefit from intervention with pharmaceutical or non-pharmaceutical MCMs (the need-based quantity), under various planning scenarios. The core capabilities required of the medical and public health systems to effectively utilize various types of MCMs are then analyzed, thereby allowing the PHEMCE to estimate the quantity of various MCMs that could be effectively used under the planning scenarios (the operational quantity).

The need-based and operational quantities, along with the development of product specifications, outreach to the ultimate end-users of MCMs (e.g., first responders, physicians, nurses, other allied health professionals, local and hospital laboratory directors, state and local emergency planners, and others), and other policy considerations are assessed to establish stockpiling goals. This process ensures that MCM stockpiling goals are based on sound scientific, medical, and epidemiological principles and result in a national stockpile of MCMs that can be utilized most effectively during a public health emergency.

The need-based quantities, operational quantities, desired product characteristics and stockpiling goals thus provide critical information to support PHEMCE leadership’s allocation of resources. Prior to making investment decisions and pursuing specific acquisition targets, however, the PHEMCE considers MCM needs across the entire threat portfolio, along with scientific opportunity, existing resources, and other factors, using the PHEMCE prioritization framework described previously. The figure below shows how the various pieces of the PHEMCE requirements process fit together.

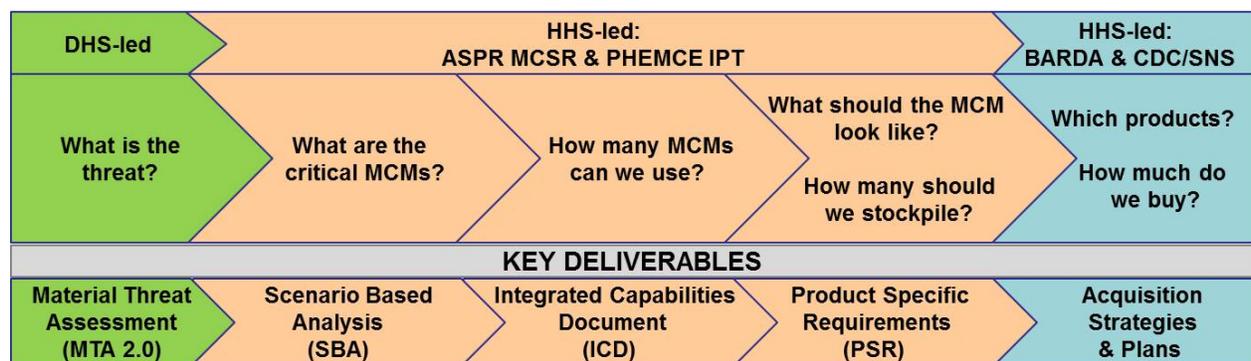


Figure 1: PHEMCE Requirements Process^{52,53,54,55}

⁵² ICDs assess the current capacity of the medical and public health system to distribute, deliver, and effectively utilize critical MCMs; identify and quantify constraining parameters under the categories of systems, supplies, staff, and space; and project the operational quantity.

Specific activities to be taken in support of developing civilian stockpiling goals include:

- *CBRN threat and risk assessments*: In 2016, DHS and HHS completed an update to the anthrax MTA using the *MTA 2.0 Strategic Implementation Plan*. (1.2.1) In the near-term, DHS and HHS will then update the *MTA 2.0 Strategic Implementation Plan*, incorporating lessons learned from the anthrax pilot and an updated DHS MTA process. (1.2.2) In the near-term, DHS and HHS will conduct MTA 2.0 assessments for smallpox, viral hemorrhagic fever viruses, botulism, radiological dispersal devices, and chemical pharmaceutical based agents to establish feasibility and scale of attack for consideration in the requirements setting process. (1.2.3) In the near-, mid-, and long-terms, DHS will continue to conduct Terrorism Risk Assessments (TRA) and update them as necessary. For example, DHS completed model updates for 10 of 11 models for which improvements were requested by stakeholders, and in reports by the National Academy of Sciences and Government Accountability Office.⁵⁶
- *Emerging infectious disease risk assessments*: As noted in the *2012 PHEMCE Implementation Plan*, there are also naturally occurring and accidental threats to national health security that are outside the realm of the DHS threat and risk assessments. EIDs, including influenza, require other methods for risk assessment. (1.2.4) In the near-term the PHEMCE, through the EID Working Group, will also complete and implement a risk assessment framework to evaluate the public health risk posed by emerging infectious diseases (other than influenza) to inform PHEMCE leadership decisions as to which pathogens, or pathogen classes, require PHEMCE response, and at what level. (1.2.5) PHEMCE leadership will determine, utilizing this framework, which emerging infectious diseases should be added to the list of PHEMCE high priority threats (see Box 1).
- *Concepts of operations (CONOPs) considerations*: BARDA has developed and maintains several modeling and decision support tools for medical and public health response assessments including Decisional Anthrax Readiness Tool (DART) 2.0 and Scenario Utilization and Medical Modeling Information Tool (known as SUMMIT) for anthrax response planning, Improvised Nuclear Device Simulator, Hospital Surge Model v. 2.0, and additional medical consequence and response models for all CBRN agents with an MTA.

⁵³ SBAs assess the scenarios, details the critical types of MCMs, and identifies the need-based quantity (i.e., the number of people who would benefit from being pretreated, diagnosed, or treated with a particular MCM class to optimally reduce morbidity and mortality).

⁵⁴ PSRs establish the desired product profiles of MCMs called for in the SBAs and identify the stockpiling goal (i.e., the number of MCMs that the PHEMCE recommends stockpiling based on consideration of policy considerations relevant to the threat, the need-based quantity, and the operational quantity).

⁵⁵ ICDs describe the core cross-threat capabilities required of the medical and public health system, prioritizes solutions to improve operational capacity, and projects the operational quantity (i.e., the number of MCMs that the medical and public health system can currently distribute, deliver, and effectively utilize during the planning scenarios)

⁵⁶ Model updates included: food, water, indoor, subway, outdoor, biological production, medical and public health response, acquisition, transport (i.e., pathway), adversary attack selection, and economic consequence (in progress). Updates included revisions to consequence assessments, incident detection, production routes, medical and public health response, adversary acquisition probabilities, interdiction probabilities, and initial and long range economic consequences.

- CDC and BARDA have also developed epidemiologic modeling tools that can be used in response to a public health emergency, such as a pandemic influenza outbreak, to inform MCM utilization policy, clinical guidance, and response strategies.⁵⁷ (1.2.6) In the near-term, CDC and BARDA will continue to enhance such modeling capabilities and collaborations. BARDA is constructing an Innovation Modeling Hub to coordinate modeling efforts across HHS and the USG with potential integration into academic modeling communities. The Innovation Modeling Hub is projected to be operational in the first quarter of 2017.

(1.2.7) In the near- and mid-terms, ASPR, working with subject matter experts from across the PHEMCE, will develop or update specific MCM requirement documents including those listed in Table 3.

Table 3: Civilian Medical Countermeasures Requirement Documents

Near-Term (FY 2017-18)
Anthrax Scenario-Based Analysis (SBA)
Vaccine for Antimicrobial Resistance Product Specific Requirement (PSR)
Point-of-care Diagnostics for Filovirus PSR
Lab-based Diagnostics for Filovirus PSR
Reusable Respiratory Protective Devices for Pandemic Influenza PSR
Filtering Facepiece Respirator for Pandemic Influenza PSR
Facemasks for Pandemic Influenza PSR
Antimicrobials for Complicated Pandemic Influenza PSR
Thermal Burn MCMs for Improvised Nuclear Device PSR
Antibacterials for Improvised Nuclear Device PSR
Antifungals for Improvised Nuclear Device PSR
Antivirals for Improvised Nuclear Device PSR
Hematopoietic-ARS for Improvised Nuclear Device PSR

⁵⁷ Examples include FluAid and FluSurge. FluAid provides a range of estimates of impact in terms of deaths, hospitalizations, and outpatient visits due to pandemic influenza, while FluSurge predicts the surge in demand for hospital-based services during an influenza pandemic, yielding estimates of the number of hospitalizations (including ICU admissions) and deaths caused by a pandemic in comparison to existing hospital capacity.

MCMs for Neurological Effects of Nerve Agent Exposure Research Requirements⁵⁸

Mid-Term (FY 2019-20)

Smallpox SBA

Radiological Dispersal Device SBA

Blood Products for Improvised Nuclear Device PSR

Rehydration Fluids for Improvised Nuclear Device PSR

Cutaneous Injury MCMs from Vesicating Agent PSR

Pulmonary Injury MCMs from Vesicating Agent PSR

Oral Delivery ICD Chapter

Intravenous Delivery ICD Chapter

Long-Term (FY 2021 and beyond)

Viral Hemorrhagic Fever SBA

Addendum to Acetylcholinesterase Reactivator PSR

Chemical Diagnostics PSR

(1.2.8) In addition, as priorities dictate and resources allow, the PHEMCE will apply the requirement process to address any new threats determined by DHS to pose a material threat to national security or those EIDs identified by PHEMCE leadership through the EID Working Group risk assessment framework.

Priority PHEMCE stockpiling goals, based on the PHEMCE requirement process (Figure 1) and prioritization framework (Box 3), are publicly communicated to stakeholders, including industry, at the time of advanced research and development (ARD) or acquisition solicitations. ASPR will create mechanisms to increase non-federal stakeholders' input during the requirement-setting process and increase visibility on the relevant outputs. In the long term, all MCM requirement-related documents will be revisited periodically to allow incorporation of new threat and risk assessments, MCM technologies, and response capabilities. DHS continues to enhance the TRAs. (1.2.9) DHS will complete an assessment of economic consequences of CBRN terrorism threats in FY 2017 and the (1.2.10) DHS developed an Adversary Decision Model, which incorporates input from the intelligence community to provide frequency estimates; it will be completed and incorporated into the final Biological Terrorism Risk Assessment (BTRA) 5.0 report.

⁵⁸ Research Requirements prioritize research goals to assist in the future advanced development or acquisition of products or services.

In addition to the threat, risk, medical consequence, and public health response assessments that estimate risk mitigation from MCMs, several analytical decision support tools are currently under development or in a pilot phase to address specific metrics identified in the prioritization framework (Box 3):

- A five-year budgeting tool was developed by ASPR as part of the SNS Annual Review that allows the PHEMCE decision-makers to see the financial impacts of changes to the SNS formulary;
- (1.1.3b) Inter-Agency Cost Model Tool which is being developed under the Portfolio Tracking and Coordination Initiative will use historical, interagency cost data for the prediction, analysis, and benchmarking of PHEMCE MCM development costs; and,
- (1.2.11) BARDA will develop end-user planning tools under the *MTA 2.0 Strategic Implementation Plan* to assist SLTT stakeholders by providing planning scenarios and rapid consequence assessments for MCM utilization—the DART, which is used to estimate the mitigated consequences of an aerosolized anthrax attack, will be available for use in the BARDA Modeling and Visualization Hub for SLTT partners through Regional Emergency Coordinators.

Objective 1.3 Ensure a robust and sustainable product pipeline for MCMs that emphasizes multi-functional capabilities rather than stand-alone applications (e.g., platform technologies, host-based innovations, broad-spectrum medical countermeasures) and includes consideration of viable commercial markets and/or routine public health applicability. **(Leads: BARDA, NIH; Partners: DoD, CDC, and USDA)**

A robust product pipeline is one in which the number of MCM candidates in the research and development process is sufficient to assure a high probability of successfully developing a candidate with sufficient safety and efficacy information to inform intended use of the product, and support FDA approval for that purpose. The PHEMCE will seek to maintain robust product pipelines where they exist and to cultivate them in areas where critical gaps still remain. The PHEMCE will take a portfolio management approach, including through the use of interagency portfolio tracking tools and multiyear budget planning across HHS agencies, to ensure that research and development activities are well coordinated across PHEMCE partners and with international partners where appropriate. Additionally, the [National Strategy for Combating Antibiotic-Resistant Bacteria](#)⁵⁹ and the [National Action Plan for Combating Antibiotic-Resistant Bacteria](#)⁶⁰ will be a high priority for the PHEMCE in the near- and mid-terms to address the ongoing public health crisis, see the [Combating Antibiotic-Resistant Bacteria \(CARB\)](#) section of this report. It is anticipated that the portfolio of MCM investments may shift over time to address

⁵⁹ The National Strategy for Combating Antibiotic-Resistant Bacteria is available at https://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf

⁶⁰ The National Action Plan for Combating Antibiotic-Resistant Bacteria is available at http://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf

unmet needs. For example, the PHEMCE considers some MCM portfolios, such as those for anthrax, botulism, and smallpox, to be significantly mature based on past successful investments and will seek to focus any future research investments in these areas primarily on improvements to the current capabilities rather than development of new capabilities.

Wherever possible, the PHEMCE will pursue MCMs that can address multiple high-priority threats and/or have routine medical applications and thus commercial viability. The PHEMCE is mindful that a “one bug, one drug” or fixed defense⁶¹ approach for MCM development is still required for some of the highest-priority threats. However, a broad-spectrum approach, when scientifically well supported, may offer more effective and efficient capabilities to address both known and unknown threats. Multi-use products, such as broad-spectrum therapeutics and multiplex diagnostic platforms, support response in a public health emergency and could also provide routine medical and public health benefits that enhance the sustainability of the MCM mission and improve daily national health security. Sustainability is also enhanced if our industry partners are able to realize commercial success for a product outside of strictly the emergency-associated medical product development required by the PHEMCE. Continued investment in current and new technologies will be based on satisfying the [prioritization criteria](#) and [requirements process](#) defined above.

The civilian MCM product pipeline predominantly consists of research and development efforts supported through the combined efforts of NIH and BARDA, in coordination with DoD and CDC, which have direct relevance to civilian national health security. The PHEMCE considers at-risk individuals’ needs throughout its efforts to ensure a robust and sustainable product pipeline; activities specifically directed at addressing at-risk individuals’ needs will be described in detail under Goal 4 of this section. We provide an overview of PHEMCE research, development, and procurement activities under this objective. More detailed information on many of these investments can be found in the [Section 2: Threat-based Approaches](#) and [Section 3: Capabilities-based Approaches](#).

NIH focuses on the basic and translational research, and the expansion of research infrastructure and research resources, that are the fundamental building blocks for developing civilian MCMs. (1.3.1) NIH will evaluate previously approved, off-patent MCMs in an effort to expand approved indications for diseases or conditions caused by other threat agents or infectious diseases as well as to increase the repertoire of MCMs with broad safety profiles to include pediatric, elderly, and immunocompromised populations. (1.3.2) In addition, NIH will continue to develop and test new products and approaches to treatment and infection control (e.g., multi-component vaccines, broad-spectrum antimicrobials, and point-of-care (POC) and broad-spectrum diagnostics), such as development of the BioFire Diagnostics platform now FDA cleared for respiratory, gastrointestinal, central nervous system, and blood infectious disease panels; support for a two dose anthrax vaccine candidate successfully developed

⁶¹ Relman DA. Bioterrorism – Preparing to Fight the Next War, *NEJM*, 2006, 354 (2): 113-115. In the context of defense against biological threats, a fixed defense is a MCM intended for use against a specific organism and not useful in scenarios that employ a different organism.

through Phase 2 (and transitioned to BARDA); and a lyophilized MVA smallpox vaccine, also transitioned to BARDA.

(1.3.3) Through FY 2020, NIH will emphasize the early-stage research programs listed in Table 4 (more details on particular programs are provided in Sections 2 and 3). Early-stage products that demonstrate promise for advanced development will be brought to the attention of BARDA through regular communications and opportunities for technology transfer.

Table 4: National Institutes of Health Near- and Mid-Term Research Priorities

Threats	Research Priorities
<p>Biological (intentional or naturally emerging diseases, including Ebola and pandemic influenza)</p>	<p>(1.3.3a) Therapeutics, including broad-spectrum antimicrobials, immunomodulators, and host-based therapeutics for bacterial and viral threats</p> <p>(1.3.3b) Vaccines with emphasis on post-exposure prophylactic potential and those that provide protection of health care workers and the local population in outbreak scenarios and enhancements to allow for more effective and efficient utilization during public health emergencies</p> <p>(1.3.3c) Development of vaccine-related technologies such as adjuvants, temperature stabilization, and alternative delivery devices to enhance the performance, life cycle costs, and utilization/operational capacity for existing biodefense vaccines, with applicability to other infectious diseases or public health situations</p> <p>(1.3.3d) Development of diagnostic assays to detect human (or pathogen) biomarkers associated with infection (preferably using existing, or mature platforms and technologies)</p> <p>(1.3.3e) Development and utilization of animal models to support FDA licensure or approval under the “Animal Rule,” as well as to inform utilization policy and optimal treatment regimens (e.g., antimicrobial course-duration shortening when combined with vaccination)</p>
<p>Radiological/nuclear (intentional or accidental)</p>	<p>(1.3.3f) Mechanisms of radiation injury at the systemic, organ, cellular, and molecular levels, with particular focus on skin and the hematopoietic, gastrointestinal, immune, pulmonary, renal, and nervous systems</p> <p>(1.3.3g) Approaches to minimize short- and long-term adverse health effects of radiation exposure, including cytokines, growth factors, anti-apoptotics, anti-inflammatory candidates, and antioxidants</p> <p>(1.3.3h) Identification and evaluation of biomarkers of radiation injury for use in biodosimetry and bioassay systems for rapid triage, radiation dose estimation, prediction of organ-specific effects and/or delayed health risk; these will be developed into high-throughput modalities for use in a mass-casualty incident</p> <p>(1.3.3i) Identification and development of decorporation and blocking agents that prevent the uptake and/or increase the elimination of radionuclides of concern. Investigation of candidate MCMs that increase mucociliary clearance of particulates in the lung</p>

Threats	Research Priorities
Chemical (intentional or accidental)	<p>(1.3.3j) Elucidation of mechanisms of chemical injury at the systemic, organ, cell, and molecular levels, with particular focus on chemicals affecting the nervous system, respiratory tract, skin, eyes, and mucous membranes, and cellular respiration</p> <p>(1.3.3k) Identification and characterization of approaches to minimize short- and long-term adverse health effects of chemical exposure</p> <p>(1.3.3l) MCMs against traditional chemical warfare agents,⁶² highly toxic industrial chemicals,⁶³ highly toxic agricultural chemicals,⁶⁴ and poisons</p>

In FY 2015, contracts were awarded for the development of antibacterial therapeutics including novel LpxC inhibitors (Achaogen, Inc.), novel quorum sensing inhibitors (Agile Sciences), second generation polymyxins (Cantab Anti-infectives Ltd.), and PoIC polymerase inhibitors (Crestone, Inc.). Contracts awarded for the development of antiviral therapeutics included host-targeting antiviral compounds for treatment of influenza (Kineta, Inc.) and Ebola and Marburg infections (Southwest Research Institute), and a contract for the development of ribonucleic acid (RNA) polymerase inhibitors for treatment of chikungunya and related viral infections (Emory University).

In 2016, NIAID initiated support for a Phase 1 clinical study of the antibacterial therapeutic TP-271 (CUBRC, Inc. and Tetrphase, Inc.), which is a novel tetracycline-based derivative.

In 2015, NIAID made 14 awards for the discovery and early stage development of new antibacterial products under Request for Assistance (RFA) -14-026, Development of Novel Therapeutics for Select Pathogens, which focused in part on new therapeutics for Gram-negative pathogens. Many of these projects are focused on novel strategies to combat antibacterial resistance, such as anti-virulence, immune-based therapies, adjunctive therapies and biofilm inhibitors.

NIAID continues to support the development of novel vaccine candidates, which target biodefense and emerging infectious disease pathogens, that include novel technologies/platforms that accelerate the immune response, improve ease of delivery, or enhance stability. These vaccine candidates also have the potential to provide protection when used for PEP in health care workers and the local population in outbreak scenarios.

Several vaccines focus on technologies that accelerate the immune response and/or improve ease of delivery. These include four anthrax vaccines, a saponin-based recombinant protective antigen (rPA) vaccine (Fraunhofer), intranasal rPA vaccine formulated in nanoemulsion adjuvant W805EC (Public Health England and NanoBio), adjuvanted rPA vaccine delivered by a Solid Dose Injection (SDI) system (Pfenex), and an oral adenovirus serotype 4 (Ad4) vaccine vector

⁶² These include the nerve agents (e.g., sarin, VX, soman), and sulfur mustard.

⁶³ Such as cyanide, chlorine, and phosgene

⁶⁴ Such as parathion, chlorpyrifos, disulfoton, and the rodenticides sodium fluoroacetate, strychnine, and tetramethylenedisulfotetramine (TETS)

expressing rPA (PaxVax). Other candidates focus on formulations that enhance stability and include two anthrax vaccines, a lyophilized formulation of AV7909 (Emergent) and a lyophilized rPA vaccine (PharmAthene). The purpose of these efforts is to evaluate the technologies (e.g., adjuvants, delivery system, and dry formulations) that may have applicability to multiple threat areas.

(1.3.4) In the near- and mid-terms, multiple candidates for next-generation anthrax vaccines or botulinum antitoxins, broad-spectrum antimicrobials, and influenza antivirals may be available for advanced development consideration.

(1.3.5) In 2015, NIH released a broad agency announcement (BAA) entitled “Development of Therapeutic Medical Countermeasures for Biodefense and Emerging Infectious Diseases” with awards scheduled for FY 2016. The disease focus for these two BAA efforts is biodefense and emerging infectious diseases with particular interest in broad-spectrum antibiotics addressing antimicrobial resistance, as well as broad-spectrum antivirals and small molecule antitoxins.

(1.3.6) NIH will continue to manage the CAP to create and coordinate teams of scientific, medical, and product development experts to guide investigators working on multi-use products for biodefense, drug resistance, and emerging disease applications. The CAP was initiated as a result of the 2010 PHEMCE Review to accelerate the development of promising, high-priority MCMs and is focused on the early phase of transitioning basic research discoveries and early phase translational concepts into promising preclinical candidates. Five of nine Ebola vaccine candidates to enter human clinical testing have been shepherded by CAP.

NIH’s long-term focus (FY 2021 and beyond) will increase the emphasis on platform technologies that either allow for the development of broad-spectrum MCMs or permit more rapid development of agent-specific MCMs. Additionally, NIH will focus on MCMs with commercial applicability for routine (non-emergency) public health diseases of both domestic and international significance.

DoD, NIH, and BARDA use [Technology Readiness Levels](#) (TRL),⁶⁵ which track product development through nine stages, to coordinate development projects, provide seamless programmatic transition, and promote continuity of funding throughout MCM development. NIH will typically carry development efforts through TRL 6 (including clinical Phase 1 studies), while BARDA picks up development of priority MCMs in TRLs 6-7 (following Phase 1). NIH will also invest in development efforts at early TRL to [address at-risk individuals’ needs](#)⁶⁶ and enhance the characteristics of current MCMs to optimize their effectiveness. BARDA will continue to support preclinical development (i.e., TRL 5) of certain MCMs to address radiological, nuclear, and chemical threats due to the lack of robust alternative funding sources.

⁶⁵ For more information, see <https://www.medicalcountermeasures.gov/federal-initiatives/guidance/about-the-trls.aspx>

⁶⁶ See Goal 4 of this document for additional information on at-risk populations and addressing their needs.

The Secretary of Defense has primary responsibility for the research, development, acquisition, and deployment of MCMs for the Armed Forces. DoD will continue to direct strategic planning for and oversight of programs to support MCM development and acquisition for Armed Forces personnel. Through their work in the PHEMCE, DoD and HHS will coordinate their efforts to promote synergy, minimize redundancy, and, to the extent feasible, harmonize MCM development efforts. DoD will continue to draw upon its longstanding investment and experience in CBRN MCM research, development, acquisition, and deployment to ensure protection of the Armed Forces, and also to accelerate and improve the overall national effort, consistent with DoD authorities and responsibilities. (1.3.7) DoD will continue to place a special focus on MCM development for CBRN threats that are of concern for the Armed Forces due to the unique facilities, testing capabilities, and trained and experienced personnel available at DoD for this purpose. (1.3.8) HHS and DoD will continue to coordinate on the research, development, and procurement of safe and effective MCMs of mutual interest. (1.3.9) DoD will continue to support PHEMCE objectives through its investments in MCMs for DoD-prioritized threat agents, including Ebola.

The BARDA CBRN MCM portfolio strategy has evolved to a multi-faceted approach that seeks to:

- Provide support to CBRN MCM developers with BARDA core assistance programs;
- Expand BARDA's broad spectrum antimicrobial and diagnostics programs in alignment with the [National Strategy for Combating Antibiotic-Resistant Bacteria](#) and the [National Action Plan for Combating Antibiotic-Resistant Bacteria](#);
- Test and evaluate products under development for CBRN indications, those approved for non-CBRN indications that could be repurposed to fulfill PHEMCE stockpiling goals, and multi-purpose product candidates that could fulfill both PHEMCE stockpiling goals and unmet everyday health care needs;
- Develop next-generation MCMs that present improvements over existing ones with regard to effectiveness, ease of administration, cost, and logistics;
- Support ARD of host-directed therapeutics;⁶⁷
- Continue establishment of public-private partnerships with industry and academia;
- Continue federal interagency alliances that enable cost-sharing in the development of key CBRN MCMs; and,
- Develop innovative technologies to address challenges encountered in CBRN MCM development.

This emphasis on cross-cutting and platform technologies will enhance the value of USG investments by stimulating a more sustainable commercial base for these products and positioning the PHEMCE to respond more effectively to the unknown threats of the future.

⁶⁷ These are therapies that reduce morbidity or mortality by targeting key host-cell molecules involved in immune-modulation, inflammation, and regulation of innate immunity.

The BARDA influenza portfolio strategy focuses on developing products with potential for increased effectiveness, greater multi-functionality, and improved operational utility. In addition to maintaining pre-pandemic influenza vaccine stockpiles and domestic influenza vaccine manufacturing infrastructure, BARDA's chief emphasis for pandemic influenza will be directed towards advanced development of more effective influenza vaccines with potential universal vaccination capability and influenza immunotherapeutics for life-threatening influenza cases. BARDA will continue to support development of non-neuraminidase inhibitor therapeutics, including host targets, immunomodulators, and drugs used in combination, with a focus on products suitable for all populations, including young children, elderly, and the severely ill. BARDA will continue to work to stimulate industry to develop improved diagnostic tests for influenza virus infection that will also inform response to pandemic influenza, focusing on moving testing closer to the point of care, improving test sensitivity and specificity, and rapid testing solutions to inform the use of antiviral drugs. Investments in next-generation ventilators that are reusable and easy to use by health care workers and the public—including children—during infectious disease outbreaks demonstrates this approach. BARDA will also invest in development of reusable, more intuitively fitting and easier to use RPDs. These and other advanced development efforts are described in more detail in [Section 3](#).

In FY 2015, BARDA continued to work closely with our NIH and DoD colleagues to monitor the progress of programs supported under research and development and transition promising candidates. In FY 2015, BARDA re-issued the three BAAs to support advanced development of CBRN and Influenza MCMs and the BAA for Innovations. They were modified to align with the *2015 PHEMCE SIP* and to address remaining gaps in preparedness as well as address new initiatives such as CARB and EID. In addition, BARDA made new awards under the Nonclinical Services Network to bring on new performers to address chemical and radiation and nuclear threats and anticipates new awards in FY 2016-17 to continue to support biothreats. BARDA is currently supporting a robust pipeline of approximately 65 candidate products under ARD. The information below highlights some of the successes in FY 2015.

- Anthrax vaccines and antitoxins: BARDA, along with our PHEMCE partners supported the approval of BioThrax[®] for the PEP indication (licensed November 2015). BARDA and NIAID completed a clinical study evaluating reduced doses of BioThrax[®] that may inform the use of this vaccine during an emergency. BARDA continues to support expansion of domestic manufacturing of the currently licensed vaccine and anticipates approval of the facility in FY 2016. BARDA continues to support development of an enhanced BioThrax[®] formulation that contains an adjuvant. BARDA has transitioned one of the rPA based anthrax vaccine candidates to clinical evaluation. Finally, BARDA is supporting the development of a transformative anthrax vaccine candidate that may provide protection in a single dose that is administered nasally. Anthrax immune globulin (manufactured by Cangene/Emergent) was licensed by the FDA in March 2015 and ETI-204 (Anthem, manufactured by Elusys) was licensed in March 2016.
- Broad Spectrum Antimicrobials and CARB: BARDA is currently supporting six programs; two of the programs are portfolios of candidates under OTAs. Two of the companies BARDA is supporting have completed their registrational Phase 3 trials and BARDA anticipates new drug application (NDA) submissions in FY 2016. BARDA is supporting one of the companies, Cempra, to conduct a pediatric trial.

- Smallpox vaccine and antivirals: BARDA continues to support one smallpox vaccine for at-risk individuals and two smallpox antiviral candidates. Bavarian Nordic (BN) continues to work toward licensure of its smallpox vaccine MVA. It has met its primary and secondary endpoints in one of its Phase 3 trials and continues to enroll in its pivotal Phase 3 trial comparing MVA to ACAM2000. BARDA and our PHEMCE partners continue to work with BN to transition the current stockpile of liquid frozen product to a lyophilized formulation. BN has shown non-inferiority in a Phase 2 clinical study and non-clinical studies comparing the liquid frozen to the lyophilized formulation. BARDA made initial procurements of bulk MVA in FY 2015 and anticipates additional procurement of bulk in FY 2016 to complete the transition to this improved formulation of the vaccine. SIGA continues to develop TPOXX (ST-246) under both PBS and ARD contracts. BARDA anticipates it moving forward with its pivotal Phase 3 study in FY 2016. Chimerix continues to develop brincidofovir and has shown efficacy in non-clinical studies and continues to pursue its commercial indications for cytomegalovirus (CMV) and adenovirus infections.
- Burn Programs: BARDA continues to support a portfolio of programs to address the continuum of care for burn patients: both field applications and definitive care. BARDA added one new program, PolyNovo, to the portfolio in FY 2015. In addition, four programs were transitioned or added under PBS. These include: a silver impregnated field dressing, an enzymatic debridement technology, a cell-based skin substitute, and donor tissue sparing technology. The products can be used in concert to improve the care and outcome of individuals with burn injuries.
- Radiation and Nuclear: BARDA continues to support multiple candidates to address the various subsyndromes resulting from exposure to ionizing radiation or radiological dispersal. In March of 2015, based in part on NIAID-funded preclinical studies, FDA approved a new indication for Neupogen[®], to increase survival in adult and pediatric patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome, H-ARS). This program has been supported by the PHEMCE partners and has been purchased under PBS since 2013 and maintained under vendor managed inventory. In November of 2015, FDA approved Neulasta[®] for H-ARS, based in part on preclinical studies funded by the NIAID. BARDA is working with our colleagues at the FDA to develop models for hematopoietic and gastro-intestinal injury using the minipig. Together, the goal is to establish models that will stand up to regulatory rigor and support the approval of candidate products. BARDA is also reaching out to large pharmaceutical companies to evaluate already approved products or those under development to determine their potential efficacy to address the various sub-syndromes resulting from acute radiation exposure. One example is that BARDA is working with Johnson & Johnson under a material transfer agreement to evaluate its thrombopoietin mimetic to address vascular injury that results from acute exposure to ionizing radiation. NIAID is also working with several companies on the development of thrombopoietin mimetics.
- Chemical: BARDA continues to support the University of Hertfordshire to develop improved decontamination guidance for first responders. BARDA has held multiple end user engagements and field exercises with state and local officials to develop this improved guidance. The initial guidance was released, [Primary Response Incident](#)

[Scene Management](#) (PRISM) series,⁶⁸ and BARDA will continue to refine this guidance. BARDA made a new award to the University of Colorado, which is working with Genentech to evaluate its product, tPA, for lung injury resulting from exposure to chlorine. BARDA is reaching out to large pharmaceutical companies to evaluate already approved products or those under development to determine their potential to address injuries resulting from exposure to chemical agents.

- Biodosimetry and biodiagnostics: BARDA continues to support a portfolio of diagnostic tests both for point-of-care and automated laboratory settings to determine the absorbed dose of ionizing radiation an individual may have received. BARDA anticipates successful programs to transition to PBS in FY 2016-17. BARDA has also made awards to support platform technologies for biodiagnostics to address multiple bacterial pathogens.
- Ebola Response: BARDA went from supporting a single Ebola therapeutic in FY 2014 to supporting several therapeutic candidates in FY 2015. BARDA's current plans to develop MCMs to address Ebola are addressed in greater detail in the [Ebola Preparedness and Response](#) section of this report. These include continued support of Mapp Bio (ZMapp), BioCryst (BCX4430), and Regeneron (REGN3479-70-71); support for non-clinical, manufacturing, and clinical studies; under the Centers for Innovation in Advanced Development and Manufacturing (CIADM), a partnership with Genentech to evaluate their humanized versions of ZMapp; and efforts with Medicago and Fraunhofer to evaluate expression of ZMapp in other tobacco based plant systems. In addition, BARDA supported and continues to support four Ebola vaccine candidates; Protectus, NewLink /Merck, Glaxo Smith Kline (GSK), and Janssen/Bavarian Nordic. BARDA is also supporting a point-of-care, rapid diagnostic antigen test with OraSure Technologies, Inc. Finally, BARDA employed the National Medical Countermeasures Response Infrastructure (core services) to: support fill/finish and manufacturing of Ebola therapeutics; evaluate therapeutics under the Nonclinical Development Network; assist companies by providing regulatory support when filing INDs; support the clinical research organization to support the CDC sponsored STRIVE study in Sierra Leone under the Clinical Studies Network; use of the CIADMs to manufacture an Ebola therapeutic; and lead efforts for modeling of the Ebola outbreak through BARDA's Analytic Decision Support Division.

(1.3.10) The projected advanced development and acquisition priorities through FY 2020, as determined by the PHEMCE prioritization framework, are shown in Table 5. More details on particular programs and timelines are provided in Sections 2 and 3. BARDA is able to both support the advanced development of products through annual appropriations, and acquire products for the SNS using funds appropriated to the Special Reserve Fund (SRF), as authorized under section 319F-2 of the PHS Act, as amended by the Pandemic and All-Hazards Preparedness Act (PAHPA) and PAHPRA.⁶⁹ BARDA may acquire products for the SNS when the product has sufficient safety and efficacy information to permit use under an EUA or may reasonably be concluded to qualify for FDA approval within 10 years of the decision to procure.

⁶⁸ See: <https://www.medicalcountermeasures.gov/barda/cbrn/decontamination-guidance-for-chemical-incidents/>

⁶⁹ 42 U.S.C. 247d-6b – additional detail provided in Section 3

MCMs currently FDA-approved for the desired indication are available for direct purchase by the CDC for the SNS.

Table 5: Advanced Development (AD) and Procurement Priorities

Medical Countermeasure Category	(1.3.10a) AD Priorities Through FY 2020 ⁷⁰	Current HHS Holdings ⁷¹	(1.3.10b) Procurements Programmed Through FY 2016 ⁷²	(1.3.10c) Additional Procurements Projected Through FY 2020 ⁷³
Anthrax Antitoxin	X	X	SRF ⁷⁴	DSNS, SRF ⁷⁵
Anthrax Vaccine	X	X	DSNS ⁷⁶	DSNS, SRF
Botulism Antitoxin	X	X	--	DSNS, SRF ⁷⁷
Broad Spectrum Antimicrobials ⁷⁸	X	X ⁷⁹	DSNS	DSNS, SRF
Cyanide Antidote	X	--	--	--
Diagnostics – Biodosimetry	X	--	--	SRF
Diagnostics – Biological Threats	X	--	--	SRF
Diagnostics – Pandemic Influenza	X	--	--	--
Diagnostics – Antimicrobial Resistance	X	--	--	--
Diagnostics – EID	X	--	--	--
Diagnostics – Volatile Nerve Agents	X	--	--	--
Nerve Agent Antidote	X	X	DSNS	DSNS, SRF
Nuclear Agents – ARS – Gastrointestinal, Skin, and/or Lung Therapeutics	X	--	--	SRF
Nuclear Agents – ARS – Hematopoietic Therapeutics	X	X	SRF	--

⁷⁰ These priorities include new products coming through the research and development pipelines, as well as enhancements to current products in the SNS.

⁷¹ Includes inventory held in both the SNS and alternative stockpiles

⁷² Contingent upon existing resources

⁷³ Assuming appropriations are available to maintain currently stockpiled and programmed levels

⁷⁴ Solicitations are ongoing to maintain existing preparedness levels and manufacturing capacity established under previous contracts.

⁷⁵ Purchase of MCMs using the SRF between FY 2017 and FY 2020 are planned pending annual appropriations.

⁷⁶ DSNS refers to the Division of Strategic National Stockpile, the CDC division responsible for managing the SNS, whose mission is to deliver critical medical assets to the site of a national emergency.

⁷⁷ Projected investments are not for new procurements. Instead projected costs are associated with conversion of the stored plasma; however, plasma has already been purchased. These investments are anticipated to transition from SRF to DSNS during this timeframe.

⁷⁸ Antimicrobials include antibiotics, antifungals, and antivirals.

⁷⁹ This includes antimicrobials for the following threat agents: anthrax, plague, tularemia, typhus, and secondary infections resulting from radiological and nuclear agents or pandemic influenza.

Medical Countermeasure Category	(1.3.10a) AD Priorities Through FY 2020 ⁷⁰	Current HHS Holdings ⁷¹	(1.3.10b) Procurements Programmed Through FY 2016 ⁷²	(1.3.10c) Additional Procurements Projected Through FY 2020 ⁷³
Nuclear Agents – Anti-emetics	--	X	DSNS	DSNS
Nuclear Agents – Thermal Burn Therapeutics	X	X	--	DSNS, SRF
Pandemic Influenza Antivirals	X	X	DSNS	DSNS
Pandemic and Pre-Pandemic Influenza Vaccines	X	X	BARDA	BARDA
Patient (Chemical) Decontamination	X	--	--	--
Personal Protective Equipment (PPE)	--	X	--	--
Radiological Agents – Decorporation/ Blocking Agents	X	X	DSNS	SRF, DSNS
Respiratory Protective Devices	X	X	--	DSNS
Smallpox Antivirals	X	X	--	SRF
Smallpox Vaccine	X	X	DSNS, SRF	DSNS
Ventilators	X	X	--	DSNS
Viral Hemorrhagic Fever (Marburg and Ebola) Antivirals and Therapeutics	X	--	--	SRF
Viral Hemorrhagic Fever (Marburg and Ebola) Vaccine	X	--	--	SRF

USDA leads USG efforts to protect against any agent that poses a threat to plant or animal⁸⁰ health. These efforts protect public health as it relates to the adulteration of food and other products regulated by the Secretary of Agriculture. These efforts also address the environment as it relates to agriculture facilities, farmland, and air and water within the immediate vicinity of an agricultural disease or outbreak. More broadly, USDA leads in the research, development, and licensure of products, practices, technologies, or other agricultural countermeasures (i.e., those not used solely in response to a human medical incident or in a non- agriculture-related public health emergency) necessary to enhance or maintain the agricultural biosecurity of the U.S. In particular, USDA has research activities specifically focused on veterinary MCMs, and maintains veterinary MCM stockpiles. (1.3.11) Also, USDA coordinates with HHS, through the FDA Commissioner and the CDC Director, on the surveillance of zoonotic diseases. USDA helped establish the [One Health Initiative](#)⁸¹ that provides a focal point to comprehensively consider and address zoonotic threats.

⁸⁰ The Animal Health Protection Act of 2002 defines the term “animal” as any member of the animal kingdom (except a human).

⁸¹ See <http://www.onehealthinitiative.com/>

Objective 1.4 Promote effective domestic and international partnerships with MCM developers and manufacturers, and support core services. **(Leads: ASPR, NIH; Partners: DoD, CDC, FDA, and HHS OGA)**

Developers and manufacturers of MCMs for the public health emergency threats described in this SIP face technical, regulatory, manufacturing, testing, commercialization, and other business challenges that can exceed the resources of private entities. Financial and technical partnerships among government, developers, and manufacturers can help foster business sustainability and diversify business risk for private companies and non-profit organizations. USG scientists from within HHS and its interagency partners will continue to work with developers, beginning at the early stages of development, to anticipate and resolve problems that could create delays in the process.

The USG is focused on maintaining adequate domestic manufacturing capacity for key MCMs. (1.4.1) BARDA will continue to support public-private partnerships with manufacturers to maintain MCM production facilities within the U.S. to increase domestic vaccine and biological therapeutics manufacturing capacity.

To secure a willing and capable partnership with the commercial sector for these unique products, the USG helps to ensure that these innovators and manufacturers have access to core manufacturing and downstream services to promote the availability of critical MCMs needed to meet civilian goals. NIH, BARDA, and DoD maintain a wide array of product development and support services that provide infrastructure capabilities for MCM development.⁸² The NIH core services cover the spectrum of capabilities that are required for early stages of product development and include animal model development support, research facilities, manufacturing support, and advice on working with other federal agencies, such as BARDA, DoD, and FDA. (1.4.2) In particular, NIH, in conjunction with BARDA, CDC, and DoD partners, works closely with the FDA to develop animal models and consider submissions to the FDA's [Animal Model Qualification Program](#).⁸³ Efficacy evaluations of CBRN MCMs will be performed in adequate animal models in compliance with data quality and integrity procedures (e.g., Good Laboratory Practices (GLP)). Additionally, the DoD supports a facility that enables testing and evaluation of MCM against agents requiring biosafety level (BSL)-4 containment. (1.4.3) Efforts are ongoing to standardize the reagents, protocols, and assays used within the facility to provide a GLP testing service for the government and industry partners.

BARDA is now positioned to provide a range of core services to assist MCM developers in various aspects of product testing, development, validation, and production. BARDA now refers

⁸² The PHEMCE will also work with other federal partners with resources in this area, including the [Advanced Manufacturing Partnership National Program](#) Office recently established by the National Institute of Standards and Technology (NIST). More information is available at <http://www.manufacturing.gov/welcome.html>.

⁸³ See: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284078.htm>

to the suite of core services as the National Medical Countermeasure Response Infrastructure. BARDA has established:

- The Nonclinical Development Network (in 2010) to provide core services (e.g., product testing, animal model qualification for testing of products developed under the “Animal Rule,” assay development, and reagent qualification) to product developers to ensure that scientific and regulatory requirements for approval and utilization of MCMs can be met; more than 40 MCM testing projects in animal models have been initiated since its inception.
- The CIADMs (in 2012) (additional information provided in Section 3) have provided manufacturing support to product developers. Increasingly, the CIADMs are being incorporated into BARDA’s strategy for effectively responding to emerging infectious disease outbreaks, like Ebola and Zika virus.
- A domestic Fill-Finish Manufacturing Network (in 2013) to supplement manufacturing of pandemic influenza vaccines and other sterile injectable products needed in an emergency or during shortages.
- A Clinical Studies Network (CSN) (in 2014) to allow BARDA to conduct clinical trials with investigational or approved MCMs. This network consists of several Clinical Research Organizations (CRO) that are capable of conducting Phase 1-4 clinical trials and of expediting clinical trials in the event of a public health emergency. The CSN supported the CDC’s STRIVE study in West Africa, evaluating the safety and immunogenicity of a candidate Ebola vaccine.
- The Division of Regulatory and Quality Affairs (RQA) to help to minimize inherent risks within the regulatory review and approval process for medical countermeasures. RQA develops strategies to facilitate the regulatory development pathway and to anticipate product lifecycle issues. It applies quality and regulatory best practices to the life cycle management of MCMs ultimately needed for stockpiling, delivery, and use.

Notably, all four of BARDA’s core service capabilities have been engaged to support MCM development during the response to the Ebola and Zika virus outbreaks.

(1.4.4) PHEMCE partners will also enter into strategic bilateral and multilateral engagements with international partners to identify joint opportunities for product development, including efforts to support the establishment of sustainable international pandemic influenza vaccine production capacity. BARDA is collaborating with AstraZeneca and Innovative Medicines Initiative to conduct the clinical studies supporting antimicrobial drug development. Innovative Medicines Initiative will support sites in Europe and BARDA will support sites within the U.S. BARDA also entered negotiations with the Ministry of Health in the Kingdom of Saudi Arabia to establish a clinical study infrastructure there to evaluate MERS-CoV therapeutic candidates.

(1.4.5) In 2015, BARDA continued to provide support towards collaborations with the WHO and 11 resource-limited countries to establish manufacturing infrastructure for pandemic influenza vaccines. The overall collective vaccine manufacturing capacity goal of 500 million doses was reached in December 2015. BARDA will maintain its financial and technical support of the WHO Global Action Plan, working in concert with the Developing Countries Vaccine Manufacturers Network and other partners to expand sustainable influenza vaccine manufacturing capacity in developing countries.

HHS participates in the Medical Countermeasures Consortium (MCMC) under the auspices of the Chemical, Biological, and Radiological (CBR) MOU. The CBR MOU is an agreement among the defense agencies of Australia, Canada, the United Kingdom, and the U.S. The aim of the MOU is to achieve greater cooperation in research, development, production and procurement in the field of CBRN Defense. The MCMC under the MOU supports the effective fielding of MCM systems and components against CBRN threat agents to support military and civilian health protection. Examples of such cooperation include:

- **Mathematical Modeling and Systems Biology:** The United Kingdom's Defence Science and Technology Laboratory (Dstl), Public Health England (PHE), Australia's Defence Science and Technology Organisation (DSTO), and the U.S. DoD are collaborating to identify antimicrobial targets and conduct mathematical modeling of pathways. A data sharing exercise between Dstl and PHE is underway to combine systems biology data for select agents and ESKAPE pathogens,⁸⁴ such as *Acinetobacter baumannii*, to identify potential novel, conserved drug targets.
- **Diagnostics:** MCMC initiated a task for antimicrobial resistant (AMR) diagnostics in September 2014 between Defence Research and Development Canada (DRDC), Dstl, USAMRIID, DSTO, and the Australian Department of Health. A bioinformatics preliminary target search is currently underway and a survey of phenotypic methods will be completed mid-2016. All CBR MOU partner nations are exploring potential collaborative areas to advance the development of POC diagnostics for AMR strains.
- **Therapeutics:** DoD's Defense Threat Reduction Agency (DTRA) invested in the ciprofloxacin for inhalation (Lipoquin® and Pulmaquin®) program. Canada's DRDC and the Dstl have an ongoing collaboration related to pre-clinical research on the efficacy of inhaled liposomal ciprofloxacin (Lipoquin®) for bacterial agents of biowarfare concern. Additionally, DRDC is also engaged in the advanced development of Lipoquin® for clinical bacterial infections.

GOAL 2. Establish and communicate clear regulatory pathways to facilitate medical countermeasure development and use.

Reducing regulatory uncertainties is critical for fostering both MCM development and availability. Regulatory oversight of medical product development for high-consequence but low-frequency events includes both the stewardship that the USG exercises to assure products are safe and effective, as well as the regulatory oversight of MCM utilization. The PHEMCE will continue support for regulatory science to develop new tools, standards, and approaches to accelerate the development, approval, and effective utilization of a wide range of MCMs for both emergency response and daily health needs, while maintaining the high standards for safety and efficacy that the American people expect.

⁸⁴ ESKAPE pathogens encompass the following six pathogens with growing multidrug resistance: *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter spp.*

Objective 2.1 Identify scientific and regulatory issues that challenge MCM development or use during public health emergencies and coordinate activities among PHEMCE partners to address those challenges. **(Lead: FDA; Partners: PHEMCE agencies)**

The regulatory assessment of MCMs by FDA for approval is data-driven.⁸⁵ However, there are often gaps in scientific knowledge that may impede or prevent a thorough assessment. These gaps in knowledge arise from multiple sources, including intrinsic uncertainties about the effects of threat agents in potential public health emergencies, as well as from insufficient product development tools, such as animal models, for generating the necessary data to support regulatory decision-making. Discrepancies in available scientific information and tools result in regulatory uncertainties that many developers perceive as contributing to a higher-than-typical risk environment for engaging in MCM development.

(2.1.1) The FDA, through MCMi,⁸⁶ engages with PHEMCE partners in identifying and resolving the regulatory and scientific challenges to MCM development and use, based on near-, mid-, and long-term PHEMCE priorities and requirements. The [MCMi addresses key challenges](#) in three areas: (1) enhancing FDA's product review and approval processes for the highest-priority MCMs and related technologies; (2) advancing regulatory science to create the tools necessary to support MCM development and regulatory review; and (3) modernizing the legal, regulatory, and policy framework to facilitate MCM development and availability.⁸⁷

(2.1.2) To enhance the MCM review and approval processes, FDA has established multidisciplinary [Public Health and Security Action Teams](#) (Action Teams) to identify and help resolve regulatory and scientific challenges for high-priority MCMs and related technologies.⁸⁸

⁸⁵ In situations where potentially useful MCMs are available but not yet FDA-approved for the particular use contemplated, FDA has a variety of regulatory mechanisms that can allow for the use of these products, including as part of a clinical trial or as part of an expanded access program or under an emergency use authorization. For additional information on [expanded access to investigational drugs](#), see <http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/AccessToInvestigationalDrugs/default.htm>. For additional information on [emergency use authorization](#), see <http://www.fda.gov/emergencypreparedness/counterterrorism/ucm182568.htm>.

⁸⁶ FDA launched the MCMi in August 2010 in response to the *2010 PHEMCE Review* and to build on the substantive MCM work ongoing at FDA. The [MCMi mission](#) is to promote the development of MCMs by enhancing FDA's regulatory processes and fostering the establishment of clear regulatory pathways for MCMs, and to facilitate timely access to available MCMs by establishing effective regulatory policies and mechanisms. For more information, see <http://www.fda.gov/EmergencyPreparedness/MedicalCountermeasures/default.htm>.

⁸⁷ FDA accomplishments under the MCMi are detailed in the MCMi annual status reports available at <http://www.fda.gov/emergencypreparedness/counterterrorism/medicalcountermeasures/aboutmcmi/ucm270744.htm>

⁸⁸ More information on FDA's Action Teams can be found at <http://www.fda.gov/emergencypreparedness/counterterrorism/medicalcountermeasures/ucm389898.htm>

Since 2011, FDA has established five Action Teams with the following three teams active during FY 2015:

- *(2.1.2a) Multiplex and Microbial Sequencing In Vitro Diagnostics Action Team:* This Action Team is working to facilitate the development of multiplex and microbial deoxyribonucleic acid (DNA) sequencing-based *in vitro* diagnostic tests. Such diagnostics could be used to test for multiple pathogens simultaneously from a single clinical specimen, providing valuable information when responding to a public health emergency. The Action Team is continuing collaboration with the National Center for Biotechnology Information (NCBI), the Lawrence Livermore National Laboratory (LLNL), and the Institute for Genome Sciences at the University of Maryland to establish quality criteria for microbial reference databases that will be critical to developers seeking to validate their candidate multiplex *in vitro* diagnostic tests. The Action Team is also continuing to facilitate the population of a publicly available and accessible database for regulatory-grade microbial genomic reference sequences ([FDA-ARGOS](#)), established in FY 2014, through NCBI. The sequencing contract was awarded to the Institute for Genomic Sciences at the University of Maryland to sequence and deposit additional genus-diverse and public health need isolates. Around 2,000 isolates will be sequenced with the FDA-ARGOS project.⁸⁹
- *(2.1.2b) ARS/Biodosimetry Action Team:* This Action Team is working to facilitate the development and regulatory review of MCMs for acute radiation syndrome (ARS) indications. FDA's Division of Medical Imaging Products completed the first draft of, and members of the Action Team provided feedback on, guidance to help sponsors develop drugs under the "Animal Rule" for treatment of ARS. *(2.1.2b1)* In addition, this Action Team will work to facilitate the development and regulatory review of biodosimetry devices and will continue to provide regulatory support on establishing the performance of radiation biodosimetry devices.
- *(2.1.2c) Warfighter-Trauma Action Team:* This Action Team is working to facilitate the development and evaluation of MCMs and related technologies to support the warfighter and trauma victims. This Action Team is collaborating with DoD to identify programs, products, and technologies of high-priority for the DoD and is providing assistance on selected regulatory and policy issues. Focus areas include traumatic brain injury, hemorrhage, nerve agents, and research that involve minimal risk to human subjects.

(2.1.3) FDA will also continue to build the science base necessary to support MCM development and regulatory assessment through its [MCMi Regulatory Science Program](#).⁹⁰ The goal of this program is to develop the tools, standards, and approaches to assess MCM safety, efficacy, quality, and performance and to help translate cutting-edge science and technology into innovative, safe, and effective MCMs, including for at-risk populations. The MCMi Regulatory Science Program includes both intramural and [extramural research efforts](#) and emphasizes

⁸⁹ The FDA-ARGOS database is available at <http://www.ncbi.nlm.nih.gov/bioproject/231221>

⁹⁰ More information on FDA's MCM Regulatory Science Program is available at <http://www.fda.gov/emergencypreparedness/counterterrorism/medicalcountermeasures/mcmregulatoryscience/ucm263071.htm>

collaborations that focus on partnerships between USG agencies, academia, NGO, and industry.⁹¹

To ensure that the MCMi Regulatory Science Program is appropriately targeted and coordinated with USG MCM priorities, FDA engages representatives from the NIH, CDC, BARDA, and DoD to evaluate MCMi Regulatory Science Program research proposals for scientific and technical merit and feasibility as well as for alignment with PHEMCE priorities; reviewers are encouraged to flag any projects that may duplicate other efforts in other agencies. Priority research areas supported under the MCMi Regulatory Science Program include: developing animal models and tools to evaluate safety and efficacy; identifying and qualifying biomarkers for safety and efficacy; using protein engineering to stabilize vaccine proteins; developing methods to assess MCM product quality and related product release assays; validating next-generation *in vitro* diagnostics platforms; assessing the performance of emergency medical equipment and enhancing emergency preparedness and response capabilities, including risk communication; and tracking and evaluating the safety and clinical benefit of MCMs used during public health emergencies. FDA has established a flexible, broad, and robust intra- and extramural research portfolio under the MCMi Regulatory Science Program to meet its goals in these priority research areas as well as responding to new regulatory science challenges identified during public health emergencies as exemplified by the recent Ebola and Zika outbreaks.

Other PHEMCE partners also fund regulatory science projects and work closely to identify and fill priority data gaps related to stockpiled MCMs and other needs, fostering rapid response and maximizing preparedness. For example, both the NIH and BARDA met regularly in 2015 with the FDA Action Teams to discuss development of animal models for ARS. Having these regular interactions informed development of the most appropriate animal models. DoD continues exploring opportunities for "pre-EUA" or other interim fielding capability filings for therapeutics.

(2.1.4) PHEMCE partners will work with the FDA's [Drug Development Tool \(DDT\) Qualification Program](#)⁹² to develop tools – such as animal models for use under the “Animal Rule” and biomarkers – to facilitate MCM development by identifying and filling priority data gaps.

Qualified animal models are considered product-independent, which allows for a qualified model to be used to test the efficacy of multiple investigational products for the qualified context of use when those products are being developed for approval under the “Animal Rule.”

⁹¹ Extramural MCM regulatory science is primarily funded through a BAA, which accepted responses until May 22, 2014, available at https://www.fbo.gov/?s=opportunity&mode=form&id=862c0ec16447bad7c7196f5d451ec601&tab=core&_cview=0

⁹² A qualified DDT can be included in an IND or a NDA/Biologics License Application (BLA) submission without the need for FDA to reconsider and reconfirm the suitability of the DDT as long as there are (1) no serious study flaws; (2) no attempts to apply the DDT outside the qualified context of use; and (3) no new and conflicting scientific facts not known at the time the qualification was determined. For more information, see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/default.htm>

(2.1.5) FDA works closely with other partners (e.g., PHEMCE, state and local public health agencies) to ensure that U.S. laws, regulations, and policies enable the application of advances in regulatory science to the regulatory review process and adequately support preparedness for and response to CBRN and emerging infectious disease threats by facilitating the availability of MCMs (e.g., through efforts related to development, distribution, and administration and use (including monitoring and assessment)). When changes are needed to better protect public health, FDA works with appropriate partners to develop and propose new approaches. For example, PAHPRA, which was enacted in March 2013, includes a number of important provisions that amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to clarify FDA's EUA authority and to establish new emergency use authorities to allow for certain preparedness activities and rapid deployment of certain FDA-approved MCMs without FDA having to issue an EUA (e.g., through emergency dispensing orders, expiration dating extensions). (2.1.6) Working closely with partners such as CDC and ASPR, FDA has implemented and proactively used these amended and new authorities for preparedness purposes and in response to emerging threats, including Ebola virus, H7N9 influenza, Zika virus, and EV-D68. To facilitate stakeholder understanding of these authorities, FDA also published *Emergency Use Authorization of Medical Products and Related Authorities*, a draft guidance for industry and public health stakeholders that details [FDA's recommendations and procedures for issuance of EUAs](#), to reflect PAHPRA's amendments to the EUA authority and additional MCM emergency use authorities.⁹³ This draft guidance updated the 2007 guidance *Emergency Use Authorization of Medical Products*.

PAHPRA also amended the FD&C Act to codify many of the activities already ongoing at FDA under the MCMi to foster the development of MCMs, including the provision of technical assistance on animal model development activities, maintaining action teams, and training for FDA reviewers. It also included provisions for a formal Regulatory Management Plan (RMP) process for regulatory engagements for certain eligible, prioritized MCMs. (2.1.7) In addition, FDA continues to provide policy assistance for relevant partners as necessary on issues including public health stakeholders' and first responders' ready access to and use of MCMs; MCM development challenges that are unique to the warfighter; extending the useful life of stockpiled MCMs through expiration dating extensions based on scientific data (e.g., through stakeholder guidance and memos); MCM monitoring and assessment during a public health emergency; guidance development; and MCM import and export during emergency responses.

Objective 2.2 Assist MCM developers in working interactively with FDA during product development and regulatory review. **(Lead: FDA; Partners: NIH, ASPR, BARDA, and DoD)**

Many of the developers engaged in MCM development are small biotechnology companies that bring a nimble and innovative approach to the development of new products. However, a challenge these companies often face is limited experience in taking a product through advanced development to FDA approval. For example, these companies often lack experience

⁹³ See: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm>

with animal testing, assay development, product manufacturing, clinical trials, and navigating the regulatory process. For companies without existing infrastructure in these areas, accessing specialized services is difficult and expensive.

The PHEMCE is committed to assisting MCM developers in navigating the USG MCM regulatory assessment and review processes. (2.2.1) FDA will continue to assist in the clarification of regulatory pathways and reduction of regulatory challenges using the following methods:

- Meetings with product sponsors or applicants seeking technical assistance related to the development, regulatory assessment, and manufacturing of MCMs;
- Enhanced inspection, including pre-approval and compliance activities, to support early identification of problems that might impede MCM development;
- Issuance of rules and regulations, based on laws enforced by FDA, and guidance documents that represent FDA's current thinking on a topic to help foster MCM development and availability;
- Stakeholder engagements, including meetings, conferences, and workshops, to educate the public on both FDA regulatory processes and its current thinking on regulatory issues, and to garner input from interested parties on regulatory issues; and,
- Public Advisory Committee meetings to obtain independent expert advice on scientific, technical, and policy matters on specific topics.

(2.2.2) BARDA regulatory and quality affairs subject matter experts will assist private-sector partners in the development of regulatory strategies, including the design and execution of pivotal animal studies and clinical studies, preparation of regulatory documentation, and strategic communication on regulatory issues.

Objective 2.3 Establish and implement strategies to expedite the development and evaluation of MCMs during a public health emergency. **(Lead: FDA; Partners: CDC, ASPR, BARDA, and NIH)**

Ideally, all MCMs used in a public health emergency response should be approved for their intended use. However, responding to potential or declared public health emergencies may require use of MCMs unapproved for any indication or approved products being used for an unapproved indication, including MCMs with limited nonclinical data and/or human data or MCMs that are still in the early phases of development. There are several recent examples of this, such as the H1N1 pandemic, the Ebola outbreak in West Africa, the Zika outbreak in the Americas, and MERS-CoV in Saudi Arabia. Under these circumstances, the opportunity to assess their safety, efficacy, effectiveness, and recipient compliance with the appropriate dosage will only occur as the MCM is deployed as part of the event response. Unfortunately, these same experiences have also shown that there are limitations in the current MCM assessment capabilities that hinder our ability to obtain timely and necessary MCM information. Therefore, it is critical to augment current MCM assessment capabilities and infrastructures to adequately assess MCMs in the setting of a public health emergency response. The PHEMCE has added this new objective to address these challenges.

(2.3.1) The MA IPT will evaluate current MCM preparedness assessment capabilities and develop a strategy for a PHEMCE-wide comprehensive capability to facilitate a timely and appropriate assessment of MCMs during a public health emergency. The IPT acknowledges that in the setting of a public health emergency, traditional data collection and rapidly conducting controlled clinical trials to enable advanced product development may not be feasible and is developing a multi-pronged strategy that will facilitate new or streamline existing MCM assessment in this setting.

(2.3.2) The MA IPT will identify enhancements to current drug and vaccine safety monitoring systems and determine the feasibility of leveraging clinical information from electronic health records that could help to assess MCMs deployed in a public health emergency. In addition, the PHEMCE is exploring the feasibility of developing a new capability by linking existing clinical trials networks through a PHEMCE-led central coordination hub to establish a public health emergency “network-of-networks.” This system would be used for conducting advanced product development clinical trials and enable enhanced data collection and analysis of MCMs used during potential and declared public health emergencies. (2.3.3) If this approach is determined to be feasible, the initial pilot stage of the project will use a common protocol to link up to eight clinical sites from four different clinical trial networks through a PHEMCE-led centralized coordinating center to pre-position select public health emergency MCM studies.

(2.3.4) The outputs of planning and, if funded, executing the pilot project will be used by the MA IPT to inform the development of a USG strategy for enhanced assessment of public health emergency MCMs.

Development and validation of MCMs and other response measures during a potential or actual public health emergency often require access to samples related to the pathogen causing the emergency. (2.3.5) Since public health emergencies often cross international borders, ASPR/OPP/DIHS will lead an HHS Sample Sharing Working Group, which will coordinate the identification and acquisition of necessary samples from international partners and prioritize their distribution domestically and internationally. (2.3.6) USDA, with support from NIAID, will look into and address specific import issues and delays related to influenza virus specimens used by the research community.

GOAL 3. Develop logistics and operational plans for optimized use of medical countermeasures at all levels of response.

The nation must be prepared to use MCMs appropriately in an emergency. This requires robust relationships among federal planners and the regional and SLTT stakeholders who would ultimately be at the operational edge of a public health emergency response. Activities required to support this goal include development of optimal approaches for MCM inventory management and for plans, policies, procedures, and guidance to ensure timely, safe, and effective MCM distribution and utilization. Preparedness will also require ensuring that fiscal and administrative authorities and practices that govern the funding, procurement, contracting, hiring, and legal capabilities necessary to mitigate, respond to, and recover from public health threats and emergencies can be accelerated, streamlined, and accountably managed at all levels of government. Achieving these objectives will require communications, training, and

education with response stakeholders and ultimately with the American people. In addition, the infrastructure and strategies must be developed to evaluate and monitor the use, safety, and performance of MCMs during a response to allow adjustment of operations in real-time as needed.

Objective 3.1 Promote innovative approaches to inventory management to enable a sustainable preparedness infrastructure. **(Lead: CDC; Partners: ASPR, DHS)**

The PHEMCE will focus on issues of long-term sustainability and enhanced flexibility to ensure cost-effectiveness of federal MCM stockpiles while maintaining readiness. This will be accomplished through optimizing the SNS formulary and ensuring cost-effective formulary management. ASPR and CDC will ensure that the SNS and BARDA inventory management and sustainable preparedness infrastructures are aligned with the ASPR response logistics and DSNS distribution mechanisms. These activities are coordinated with those of regional partners to achieve the best allocation of resources during a response and to provide a consistent national framework for the regional coordination of prevention, mitigation, preparedness, response, and recovery activities.

Optimization of the SNS Formulary

(3.1.1) The PHEMCE SNS Annual Review represents a continual process for optimizing the contents of the SNS. The Review, required by both statute⁹⁴ and Presidential Directive,⁹⁵ comprehensively examines the SNS formulary each year, including non-pharmaceutical MCMs and ancillary supplies; identifies and prioritizes formulary gaps; and recommends additions or modifications to the contents of the SNS, in alignment with the PHEMCE prioritization framework. For example, based on a recent reassessment of the Federal Medical Stations (FMS) held in the SNS, CDC will maintain 32 of the large, 250-bed capacity FMSs, create 10 more nimble, 50-bed capacity FMSs, and develop stand-alone bariatric modules for deployment with FMS assets as needed. DoD participates throughout the PHEMCE SNS Annual Review process to ensure consideration of DoD equities during the development of stockpiling recommendations. (3.1.2) In the near-term, the PHEMCE will also be re-visiting the appropriate roles and responsibilities of the SNS, based on progress made to date, future opportunities, and in consideration of the need for long-term sustainability of this critical national asset.

Cost-Effective Management of SNS Assets

CDC will effectively and efficiently maintain, replace, and manage assets in the SNS across their life cycles to ensure they can be accessed and provided when and where needed, within operational and logistical constraints. This is an important component to promote a sustainable MCM preparedness infrastructure. To accomplish these functions, the CDC will utilize a robust inventory management system, including state-of-the-art monitoring systems, Quality Control Unit evaluation of storage facilities, and comprehensive annual inventories and inventory tracking mechanisms. CDC/DSNS continues to utilize commercial medical supply chain

⁹⁴ 42 U.S.C. 247d-6b(a)

⁹⁵ Homeland Security Presidential Directive-21

partners and best practices to maintain SNS held MCMs in cost effective third party logistics arrangements which support the flexibility and surge capabilities necessary to meet MCM response requirements. Additionally, through direct engagement with the commercial medical supply chain and industry partners, DSNS is employing new models to improve access to MCMs not held in the SNS and support response to diseases without available MCMs. During the Ebola response, DSNS relied on relationships with commercial supply chain partners to coordinate and prioritize PPE shipments directly from manufacturers and distributors to health care facilities with urgent requirements without federal procurement, receiving or deployment. In response to the ongoing spread of Zika, for which there are no available MCMs, DSNS is implementing and managing vector control contracts and supporting local public health interventions to limit transmission of the disease through known avenues and protect the most vulnerable populations with the resources available. (3.1.3) The VA will continue to provide contracting services for the SNS. CDC will ensure MCMs requiring rapid administration for clinically effective use will be held, as appropriate, in forward-placed or prepackaged storage for ready access.⁹⁶

(3.1.4) CDC will also continue to participate in the FDA/DoD SLEP⁹⁷ to extend the useful life of appropriate stockpiled products when it is cost-effective, to improve efficiency, and to maximize existing investments. (3.1.5) Finally, CDC will continue to examine ways to reduce the time required to deploy assets at the federal level, and better understand the costs at the federal and SLTT levels.

Objective 3.2 Develop and communicate medical countermeasure utilization policy, guidance, and response strategies, which take into account FDA regulatory frameworks and are responsive to end-user needs. **(Leads: ASPR, CDC; Partners: PHEMCE agencies)**

The success of the PHEMCE will be measured by the ability to quickly, safely, and effectively utilize MCMs and to effectively develop, communicate, and provide guidance and education on the role of MCMs in a public health emergency response. To accomplish this, the federal PHEMCE agencies must work closely with non-federal partners at all levels.

Linking Bench to Community (Leads: BARDA, NIH)

End-user needs are key drivers in MCM development. For example, NIH early research into vaccine adjuvants is aimed not only at increasing vaccine efficacy, but also at developing a faster onset of protection with fewer vaccine doses, resulting in decreased stockpiling costs and

⁹⁶ Examples include the CHEMPACK program of more than 1,900 forward-placed caches of nerve agent antidotes held in local custody throughout the nation, and the SNS 12-Hour Push Packages, which are poised to support arrival anywhere in the nation within 12 hours of the federal decision to deploy SNS assets.

⁹⁷ The DoD/FDA SLEP is a fee-for-service program used to defer drug replacement costs for large stockpiles of date-sensitive pharmaceuticals held in environmentally controlled locations by extending their shelf life beyond the manufacturer's original expiration date. The program is limited to DoD and selected federal agencies.

improved response logistics. Similarly, NIH research into temperature stabilization for critical MCMs may decrease or eliminate the need for cold chain storage, thereby decreasing stockpiling costs and allowing for a more rapid delivery and faster administration in the event of an emergency. The PHEMCE requirements process has been updated to include analyses of end-user needs to provide interagency programmatic coordination towards these considerations. The PHEMCE-approved requirements process has added research requirements for MCMs that are currently in TRL of three or less. Research requirements provide agencies that fund early-stage research with requirements that prioritize research goals that promote desired characteristics for advanced research and development, stockpiling, and ultimately the end-users' needs. The addition of the integrated capabilities documents within the requirements process ensures that product specific requirements, which define product characteristics and stockpiling goals, are informed by the public health and medical systems capabilities. The threshold and objective characteristics identified in the product specific requirements are used to set research priorities for MCMs in advanced research and development. To assist with these process improvements, the PHEMCE is currently developing strategies to increase non-federal stakeholder engagement with the requirements process.

(3.2.1) In the advanced development of priority MCMs, BARDA will work with developers and end-users through external outreach to ensure that MCM development plans take into account the most up-to-date utilization policies, response strategies, evolving regulatory guidance for use, and other relevant factors. Strengthening this feedback loop between the end-users and the developers of MCMs will result in products that can be most effectively used in public health emergencies.

Federal Response Planning and Guidance (Leads: ASPR, CDC, DHS Partners: PHEMCE Agencies)

Over the next five years, the PHEMCE, through the leadership of the CDC and ASPR, and as supported by other USG partners and external experts,⁹⁸ will leverage the lessons learned at all levels from previous incident responses to develop and share MCM response strategies, clinical utilization guidelines, and MCM CONOPs with end-users as appropriate. In December 2015, CDC published "[Clinical Framework and Medical Countermeasure Use During an Anthrax Mass-Casualty Incident](#)" in the *MMWR*.⁹⁹ The PHEMCE will coordinate to ensure MCM operational and response strategies as well as clinical guidelines are appropriately captured in the federal all-hazards emergency response planning process as well as the ASPR all-hazards and regional emergency response planning processes.

(3.2.2) ASPR's Office of Emergency Management (OEM) and DSNS will evaluate whether FMS or other temporary beds could be used in response to a CBRN incident to expand operational capacity. OEM will lead an evaluation which will include a capabilities evaluation, determination and subsequent development of required resources. (3.2.3) ASPR and CDC will lead PHEMCE

⁹⁸ Including clinical experts and state and local health officials

⁹⁹ See: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6404a1.htm>

evaluation of cross-threat constraints on emergency preparedness posed by intravenous (IV) MCM formulations and identify initiatives to address these gaps.

First responders are critical in supporting communities as they recover from the impacts of public health and medical incidents. (3.2.4) The PHEMCE will assess the need and availability of MCMs for federal first responders, which will be included in MCM response strategies. Depending upon the outcome, an overarching policy for federal first responders with regards to the acquisition and distribution may be developed. Planning for the protection of non-federal first responders is primarily a state and local activity, but PHEMCE agencies will continue to provide general recommendations, modeling projections, and other supporting information to guide such planning efforts. The PHEMCE will assess the need and availability of MCMs for federal personnel support response efforts and will include policies for addressing federal response staff in MCM response strategies. HHS and DHS have also collaborated on how to ensure non-federal first responders receive MCMs to ensure they are able to rapidly respond as required during a biological incident. HHS and DHS jointly released [guidance for occupational health directors and equivalent professionals concerning increasing the first responder community's preparedness](#).¹⁰⁰ This guidance addresses actions to help enable non-federal first responders to immediately support the public during an anthrax attack and to augment current state and local plans for MCM distribution. Specifically, the guidance informs occupational health directors of options available, including:

- Providing first responders with prescriptions for an initial (10 day) supply of suitable antibacterial drugs at home to prevent the development of anthrax infection and disease in the event of an anthrax attack to ensure they are fully able to devote immediate attention to the needs of the community.
- Informing first responders about the appropriate instructions for storage and use of these medicines, including specific instructions (provided by the guidance) for the prescription of doxycycline.
- Communicating to first responders that the costs of the medicines will need to be voluntarily borne by the first responder, unless the jurisdictions choose to absorb those costs.

The PHEMCE will develop the following deliverables to facilitate national public health emergency response for high-priority threats:

- (3.2.5) A national response strategy for smallpox vaccines was completed in FY 2016. Additional MCM response strategies for anthrax, botulism, glanders and melioidosis, and radiocesium exposure will be prioritized for completion in appropriate timeframes based on available resources;
- (3.2.6) Clinical practice guidelines for MCMs to address botulism (FY 2017), ARS-associated neutropenia¹⁰¹ (FY 2018), and chemical agents (FY 2019);

¹⁰⁰ See: <https://www.dhs.gov/publication/letter-occupational-health-professionals-first-responder-anthrax-preparedness>

¹⁰¹ As may occur following, for example, use of an improvised nuclear device

- (3.2.7) CDC will update websites and communication materials to reflect the most recent planning and guidance, including training for practitioners;
- (3.2.8) CONOPs for MCMs to address neutropenia (mid-term), glanders and melioidosis (mid-term), and botulism (long-term);
- (3.2.9) The PHEMCE is developing guidance to address pediatric patient decontamination needs;
- (3.2.10) The PHEMCE, through the Medical Countermeasure Operational Planning Work Group, will develop a lexicon and planning alignment tool to enable a common operating picture; and,
- (3.2.11) The Medical Countermeasure Operational Planning Work Group will standardize templates and a framework for development and approval for MCM operational planning documents: response strategies, CONOPs, clinical guidance, and messages and educational materials.

Adding to Key Federal Policy and Response Capabilities (Lead: ASPR)

ASPR and CDC are leading several initiatives to ensure preparedness in key functional areas critical for an effective national response:

- (3.2.12) *Emergency Policy Coordination*: ASPR has established the Disaster Leadership Group (DLG) as the mechanism to ensure a coordinated, department-wide, strategic approach to HHS emergency response and recovery efforts among the HHS executive leadership. As the Secretary's principal advisor on all matters related to public health and medical emergency preparedness and response, the ASPR will chair and convene the DLG as needed to discuss, coordinate, and promote approaches to address the policy, budget, legislative, and external communication strategies and needs associated with the response. The DLG will identify and resolve policy issues and potential barriers, including those related to MCM production, distribution, dispensing, administration, and use, which may directly impact effective response operations during specific emergency events.
- (3.2.13) *Fiscal and Administrative Preparedness*: Recent public health emergencies, such as the 2009 H1N1 pandemic influenza, the 2010 Deepwater Horizon oil spill, and the 2014-15 Ebola outbreak highlighted the need for a much more responsive fiscal and administrative framework to most effectively utilize resources during an emergency. In support of the MCM-related aspects of this larger effort, ASPR will ensure that the fiscal and administrative practices to rapidly produce and effectively distribute MCMs are incorporated into pre-event planning activities. HHS hosted an administrative preparedness table top exercise, which identified improved mechanisms. (3.2.13a) The Health Resources Priorities and Allocation System (HRPAS) interim final rule was released for public comment in July 2015 and the final rule is anticipated for publication by 2017.
- (3.2.14) *Science Preparedness*: ASPR will lead an initiative to coordinate science preparedness and response efforts across the diverse span of interagency emergency preparedness efforts, including those related to MCMs. Research before, during, and after an emergency is critical to our future capacity to better prevent injury, illness, disability, and death, while supporting recovery. This effort can also ensure that the appropriate subject matter experts from government, academic institutions, NGO, and the private sector can be used to assist in response to a public health emergency. In the

near- and mid-terms, ASPR will focus on areas such as clinical protocols and datasets, specimens, workforce, policies, rapid funding mechanisms for research, and surveys.

- (3.2.15) *MCM Resource Allocation*: CDC has already developed, in collaboration with other PHEMCE partners, guidance on the allocation of anthrax vaccines in the event current stockpiles were inadequate to meet the need in a large-scale event. (3.2.15a) ASPR, with the support of CDC, will work with partners to identify other current efforts by states, academia, health care experts, biomedical ethicists, medico-legal experts, behavioral health experts, and others to address MCM resource allocation in public health emergencies in which these critical assets may be in short supply.

International Efforts (Lead: ASPR; Partners: DoD, FDA, CDC, HHS OGA, USDA)

While the PHEMCE focus is predominantly on meeting U.S. domestic MCM needs, the need for capacity to distribute and utilize MCMs is also a challenge to the global community. U.S. utilization policies, clinical guidance, and response strategies should be integrated with those of our international partners where appropriate. Building on the lessons learned during the 2009 H1N1 influenza pandemic and the nuclear power plant incident in Fukushima in 2011, the PHEMCE will identify and address barriers to building a sustainable global infrastructure for MCMs. (3.2.16) Relevant HHS agencies and PHEMCE partners will continue to engage international partners to identify joint opportunities for product development. (3.2.17) For example, DoD is currently working with the United Kingdom's Ministry of Defence to develop animal models for the testing and evaluation of MCMs against bacterial and filovirus threats. (3.2.18) PHEMCE partners will collaborate with WHO and the [GHSI](#) partners¹⁰² to overcome barriers and develop protocols to facilitate the international deployment and distribution of MCMs during public health emergencies. (3.2.19) Additionally, ASPR will lead U.S. efforts under Objective 9 of the recently launched [Global Health Security Agenda](#) to engage with international partners to "improve global access to medical and non-medical countermeasures during health emergencies."¹⁰³ (3.2.20) Regionally, ASPR will work with Canada and Mexico in the near- and mid-terms to overcome barriers to providing mutual assistance and to harmonize utilization policies for MCMs during international public health emergencies under the framework of the [BTB](#),¹⁰⁴ and as called for in [NAPAPI](#).¹⁰⁵

Objective 3.3 Develop logistics and operational plans that promote innovative approaches to distribution and dispensing/administration to ensure timely, efficient access to MCMs. (Leads: ASPR and CDC; Partners: PHEMCE agencies)

Operational plans, including logistical considerations, are critical to effectively distribute, dispense, and administer MCMs in a timely manner during a public health emergency or other situation in which deployment of MCMs is necessary to protect public health and safety. These

¹⁰² See <http://www.ghsi.ca/english/index.asp>

¹⁰³ See <https://www.ghsagenda.org/>

¹⁰⁴ See <http://www.dhs.gov/beyond-border-shared-vision-perimeter-security-and-economic-competitiveness>

¹⁰⁵ See <http://www.phe.gov/Preparedness/international/Documents/napapi.pdf>

functions were previously embedded by the PHEMCE in Objective 3.2. However, given the importance of these efforts, we added this new objective to identify activities for these functions.

In 2014, DSLR released *Receiving, Distributing, and Dispensing Strategic National Stockpile Assets: A Guide for Preparedness Version 11*, which provides detailed MCM planning guidance for SLTT preparedness programs. DSLR currently provides SLTT planning guidance and conducts annual reviews with state and local MCM stakeholders using the MCM ORR. (3.3.1) CDC will obtain initial data for nearly 500 state and local jurisdictions by June 2016, and will complete an analysis of the significant trends nationally within the data and expects to report in late 2016. The goal of the MCM ORR process is to identify planning and operational gaps and provide targeted technical assistance so jurisdictions can build program capacity to meet their preparedness goals. CDC's goal is for all 62 PHEP jurisdictions to have "Established" operational readiness levels by June 2022. (3.3.2) In 2016-17, DSLR will provide targeted technical assistance to address operational gaps identified during the MCM ORR site visits in 2015-16.

(3.3.3) DSLR and DSNS are working together to identify minimum competencies for state and local MCM planners and developing training programs to address training needs. In April 2016, during the 2016 Preparedness Summit, DSLR and DSNS collaborated to conduct an MCM Link training workshop targeting state and local preparedness directors and MCM planners.

Workshop topics included:

- Updates on the MCM ORR Implementation Strategy for 2016-2017
- SNS Formulary Updates
- MCM Supply Chain and Inventory Management
- Federal Updates Regarding the Emergency Use of MCMs
- Informing Federal MCM Stockpiling Decisions
- CDC Training Offerings and Competency Assessments
- National Association of County and City Health Officials (NACCHO) MCM Resources

In addition, DSLR is developing a Medical Countermeasure Operational Resource Guide to accompany CDC's *Receiving, Distributing, and Dispensing Strategic National Stockpile Assets: A Guide for Preparedness Version 11*. The guide is designed to be a tool that all health sectors can use to more easily access information regarding the MCM deployment and administration process, including the roles certain sectors play in the process and the operational aspects of dispensing and administering MCMs.

Consideration of the current and anticipated CONOPs and public health response capabilities at the federal and SLTT levels is critical to ensuring that stockpiled MCMs can be safely and effectively used in a public health emergency. CDC and BARDA have developed several modeling tools that facilitate planning at the federal and SLTT levels, providing officials with ways to evaluate plans without resource-intensive drills or exercises. For example, DSNS

supports the [RealOpt®](#)¹⁰⁶ and [TourSolver®](#)¹⁰⁷ modeling suites, used for point-of-dispensing (POD) planning and optimization and MCM distribution and routing planning and analysis, respectively. These suites are available to SLTT partners free of charge through support contracts held by CDC to fund the providers. Through the use of these systems, existing plans can be evaluated and improved through realistic modeling and optimization, without the costly expense of iterative drills and exercises to test alternative plans.

(3.3.4) Through ongoing collaborative efforts with PHEMCE partners and external stakeholders, the FDA will work to modernize the legal, regulatory, and policy frameworks to facilitate the development and availability of MCMs; enhance pre-event planning; and foster rapid MCM deployment and use in public health emergencies. (3.3.5) ASPR will assess, streamline, and enhance deployment and sustainment protocols and tracking processes. (3.3.6) The VA's Office of Public Health will lead an effort to study and streamline closed PODs as a means to distribute MCMs during a public health emergency.

Support for State, Local, Tribal, and Territorial Response Efforts (Leads: CDC, ASPR; Partners: FDA, DHS)

Some SLTT public health and health care systems face reduced funding and greater demands in general and for public health preparedness activities. The PHEMCE will seek to support SLTT authorities by ensuring that federal MCM emergency response plans are flexible enough to fit into SLTT and private response partners' activities.

ASPR will continue to develop, refine, and sustain health care coalitions consisting of a collaborative network of hospitals, health care organizations, public health, emergency medical service, and other public and private sector health care partners within a defined region to ensure the delivery of medical care, including MCMs, during emergencies that exceed the limits of conventional medical capabilities within a community. (3.3.7) The CDC, in collaboration with ASPR, will continue to provide guidance to SLTT partners on receiving and effectively utilizing (i.e., deploying, distributing, and dispensing) MCMs provided by the SNS. (3.3.8) CDC will also work with PHEMCE partners to promote exercises of these capabilities at the SLTT and federal levels. (3.3.9) ASPR and DHS will encourage regional emergency planning alliance participation in these exercises, while ASPR and CDC will work to include health care coalitions as well. (3.3.10) ASPR, CDC, and DHS will work to continue to conduct regular call-down/notification and assembly drills to test staff and volunteer mobilization. (3.3.11) The DHS Office of Health Affairs is coordinating the First Responder Vaccine Initiative to develop the infrastructure for an anthrax vaccination pilot to evaluate the feasibility of a voluntary pre-event anthrax vaccination program among first responders using anthrax vaccine scheduled to rotate out of the SNS. This is being piloted in two states with DHS facilitating transfer of the vaccine from the SNS to the states. (3.3.12) Additionally, CDC, in coordination with ASPR, will determine whether PHEP grants or other mechanisms can be enhanced to provide increased collaborative planning with state and local colleagues for chemical threats.

¹⁰⁶ See: <http://www2.isye.gatech.edu/medicalor/realopt/research.php>

¹⁰⁷ See: <https://snstoursolver.c2routeapp.com/about.html>

(3.3.13) ASPR will also enhance coordination on preparedness among regional HHS partners by developing a consistent national framework for the regional coordination of prevention, mitigation, preparedness, response, and recovery activities, including those required for effective MCM utilization by doing the following:

- (3.3.13a) ASPR will collaborate broadly with PHEMCE and non-federal partners, to include regional health care coalitions and state authorities, to develop resilient systems of care that will be able to optimally respond to and recover from public health emergencies. Such efforts will include direct funding support, as well as initiatives aimed at building MCM delivery and utilization capabilities at the regional level, including the [Hospital Preparedness Program](#).¹⁰⁸
- (3.3.13b) ASPR, in conjunction with the Federal Emergency Management Agency (FEMA) continues to conduct regional MCM planning, with a target of completing this planning activity and developing FEMA response plans that include MCM capabilities (e.g., staffing, logistical support), within the top 10 Urban Area Security Initiative areas under the CRI program by the end of FY 2017. These regional MCM annexes to the FEMA regional all hazards plan will describe the federal support to be provided to supplement CRI plans for MCM dispensing following an aerosolized anthrax attack. These efforts implement a key provision of the EO #13527 (December 2009), "Establishing a Federal Capability for the Timely Provision of Medical Countermeasures Following a Biological Attack."

(3.3.14) ASPR will further seek to complement and supplement MCM efforts by hosting a number of workshops across the USG to address dispensing gaps and (3.3.15) hosting a national level tabletop exercise as well as collecting and developing performance metrics.

(3.3.16) Additional planning for MCM issues continues with the FEMA-led development of the Biological Incident Annex. Regional planning efforts in this area will begin in each of the 10 regions beginning in FY 2016-17. This initiative will further highlight MCM dispensing and distribution planning efforts.

(3.3.17) An MCM Incident Annex will be developed for MCMs that identifies Federal, SLTT roles and responsibilities with regard to MCM distribution. FEMA, ASPR, and CDC will collaborate on the development of a National MCM response plan Incident Annex that captures the MCM response framework that clarifies roles and responsibilities between SLTT.

Objective 3.4 Develop and provide MCM communications, training, and education to inform all stakeholders. **(Leads: CDC, ASPR; Partners: FDA, USDA)**

The PHEMCE will continue to focus attention on providing accurate evidence, science-based information, and training on the use of MCMs during a public health emergency. The PHEMCE will ensure effective communications with both responders and the public through the timely release of credible, understandable, and actionable information both prior to and during public health emergencies. The PHEMCE will work with partners to deliver messages to audiences and make national health security messages available in multiple formats and languages and covering such topics as preparedness, response, and recovery.

¹⁰⁸ See <http://www.phe.gov/preparedness/planning/hpp/Pages/default.aspx>

(3.4.1) The CDC, in coordination with FDA and ASPR, will conduct ongoing education and communication activities aimed at clinicians and the public to support the appropriate use of MCMs as they pertain to influenza prevention and control. CDC developed and tested anthrax communication messages that can be found on CDC's website. (3.4.2) CDC also will work with 70 partners to ensure that SLTT public health officials and designated hospital authorities have sufficient knowledge of the contents and dispensing policies associated with the materiel from the SNS. In FY 2015, SNS trained 1,661 individuals at the federal, state, and local level through 66 training opportunities. Additionally, self-paced online courses provided CDC training for another 1,776 federal, state and local planning and response personnel in FY 2015. (3.4.3) CDC will continue to implement and maintain training programs in risk communication to train government leaders and partners in risk communications through its Crisis and Emergency Risk Communication (CERC) program. CERC offers in-person training, online training, and resource materials for risk communication training. CDC's FY 2016 activities include updating the CERC manual and materials as needed, coordinating sponsored training for government leaders and partners, and maintaining a trained cadre of people able to give CERC trainings.

(3.4.4) In addition, ASPR will develop and implement a plan to disseminate best practices for establishing and maintaining regional coordination for public health emergencies. Specifically, the PHEMCE will promote partnerships among emergency management, health care, behavioral health care, and human services stakeholders by providing technical assistance and education to SLTT and non-governmental partners in a sustainable, scheduled forum.

Objective 3.5 Develop and implement strategies to assess, evaluate, monitor, and communicate MCM safety, performance, and patient adherence during and after a public health emergency response. **(Leads: FDA, CDC, ASPR)**

Optimal use of MCMs in an emergency response situation requires rapid feedback on how well these interventions are working to protect individuals and their families. This information may be used to inform timely refinements of clinical utilization policies during the response. The availability of this information can also allow public health officials and medical professionals to adjust their medical response strategies as needed. (3.5.1) CDC, FDA, and BARDA will continue to assist drug manufacturers in creating registries to capture information during events as part of specific post-marketing requirements for recently approved MCMs.

The PHEMCE plans to conduct the following activities, the results of which would subsequently be leveraged by the MA IPT to develop a strategy for enhanced assessment of MCMs during a public health emergency:

- (3.5.2) Explore opportunities for collaborations with the FDA's [Sentinel Initiative](#) to assess the utility and timeliness of claims-based data for use in the assessment of public health emergency MCM use for safety and effectiveness.¹⁰⁹

¹⁰⁹ See: <http://www.fda.gov/Safety/FDAsSentinelInitiative/ucm2007250.htm>

- (3.5.3) Build public health emergency MCM safety, efficacy, and effectiveness assessment capabilities and exercise such capabilities in an upcoming anthrax exercise to further assess current capabilities and identify gaps in a simulated scenario.
- (3.5.4) Explore the feasibility of extracting certain MCM data from the DoD and VA electronic health records (EHR) systems. The MA IPT EHR workgroup has developed a minimum data set to assess the feasibility of capturing meaningful data through a pilot study to test the DoD and VA EHR systems using seasonal influenza vaccine safety and effectiveness as the case study. Collaboration partners at DoD and VA have indicated that this also meets each department’s internal objectives and are exploring funding options to execute the proposed pilot study.
- (3.5.5) Define “big data” in the context of MCM monitoring and assessment and assess the landscape for crowd-sourcing information to provide meaningful MCM use and performance information. The MA IPT Big Data workgroup is in discussions with the ASPR [TRACIE](#)¹¹⁰ capability to determine potential opportunities for collaboration. (3.5.6) ASPR will incorporate information gained in this way into the lessons learned and corrective action process, thus allowing for feedback into FEMA-led interagency MCM federal and regional planning. (3.5.7) During public health emergency responses, CDC will use media monitoring services, as well as work with response partners, to monitor public reaction to the distribution of MCMs, including rumors and misperceptions. CDC may refine its messages or develop new content based on the findings from these services.
- (3.5.8) Develop a concept of operations to execute the pediatric anthrax vaccine study that is part of the anthrax vaccine response plan.

GOAL 4. Address medical countermeasure gaps for all sectors of the American civilian population.

[At-risk individuals](#),¹¹¹ who make up a significant proportion of the American civilian population, may have diverse and unique vulnerabilities and MCM needs. The PHEMCE remains fully committed to working toward the goal of protecting the entire U.S. population, including at-risk individuals, from intentional threats, pandemic influenza, and other EIDs posing a threat to national health security. Significant progress has been made in this area since the release of the 2012 *PHEMCE Strategy* and subsequent *Implementation Plan*, as summarized in [Appendix 3](#). While the PHEMCE considers the needs of at-risk individuals throughout all of the activities described in Goals 1-3 above, the following objectives describe the specific activities directed at

¹¹⁰ More information on ASPR’s Technical Resources, Assistance Center, and Information Exchange (TRACIE) can be found at: <https://asprtracie.hhs.gov/>

¹¹¹ At-risk individuals have needs in one or more of the following access or functional areas: communication, maintaining health, independence, services/support/self-determination, and transportation. At-risk individuals may include children, older adults, and pregnant women as well as people who have disabilities, live in institutionalized settings, are from diverse cultures, have limited English proficiency or are non-English speaking, are transportation disadvantaged, have chronic medical disorders, or have pharmacological dependency.
<http://www.phe.gov/preparedness/planning/abc/pages/default.aspx>

at-risk individuals' needs that the PHEMCE will pursue, with the ultimate goal of protecting the whole spectrum of the American population in the event of a public health emergency.

Objective 4.1 Develop medical consequence and public health response assessments and requirements for at-risk individuals. **(Lead: ASPR; Partners: PHEMCE agencies)**

The PHEMCE requirement framework, as detailed in Objective 1.2 above, includes consideration of at-risk individuals' needs at every stage of the process. This includes examining age, sex, racial, and ethnic influences in health and disease to inform MCM formulation and dosage requirements when data is available and appropriate. (4.1.1) The PHEMCE Pediatric and Obstetric (PedsOB) IPT actively monitors PHEMCE activities to ensure the needs of pediatric and obstetric populations are considered. They will continue to provide subject matter expertise for assisting in development and vetting the MCM requirements framework, MCM strategies, and for promotion of the availability of pediatric¹¹² and obstetric MCMs in public health emergencies.

Notably, dosage forms suitable for pediatric populations may also benefit other at-risk groups. For example, in parallel with its evaluation of the minimum practical age for using crushed tablets instead of more expensive antimicrobial suspensions in pediatric populations, the PedsOB IPT also considered use of these suspension dosage forms for geriatric populations and people who have difficulty swallowing.

Medical interventions do not have uniform effects for all at-risk populations represented in the U.S. Therefore, it is critical to ensure sex, racial, and ethnic diversity at the enrollment phase of clinical research, in clinical trials, and in the design of nonclinical cellular research. Ensuring for diversity in clinical research, as appropriate with respect to the health of human subjects, and nonclinical research expands our understanding of how diverse populations respond to medical products and ensures that MCMs are safer and more effective for everyone.¹¹³

Additionally, BARDA and CDC have collated the existing, albeit limited, clinical and scientific literature on agent susceptibility and MCM utility in these populations. At-risk populations, such as children, pregnant women, older adults, and those with underlying medical conditions, potentially have differences in susceptibility to CBRN agents and/or altered disease severity following exposure. In many cases, the first-line treatments for CBRN agents have not been tested or are not recommended for use in at-risk populations. (4.1.2) Important gaps exist in the scientific knowledge regarding the use of MCMs in these at-risk groups, and BARDA will support research efforts to close these gaps, in alignment with the prioritization criteria detailed

¹¹² Pediatric populations refer to individuals under the age of 21 years.

¹¹³ Development of MCMs that address needs of at-risk populations is supported by the NIH and FDA. For more information on the [NIH Revitalization Act of 1993](#), see https://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. For more information on [Section 907 of the FDA Safety and Innovation Act](#), see <http://www.fda.gov/RegulatoryInformation/Legislation/SignificantAmendmentstotheFDCAAct/FDASIA/ucm389100.htm>.

previously, and as ethically feasible. This data collection will inform utilization of current MCMs and the desired characteristics of future products. (4.1.3) The PedsOB IPT and other PHEMCE partners will assist in the development of scenarios and validate assumptions for specific at-risk populations in public health and medical consequence assessments.

Objective 4.2 Support MCM advanced development and procurement for at-risk individuals.
(Leads: BARDA, NIH, and FDA; Partner: CDC and DoD)

The needs of at-risk individuals pose challenges to the development and acquisition of MCMs specifically formulated for these groups. The PHEMCE will continue to support evaluation of those MCMs currently held in the SNS for use among at-risk individuals, as well as development of additional dosage forms where needed,¹¹⁴ including maximizing use of MCM dosage forms that are suitable for use in multiple populations.

While HHS currently stockpiles MCMs for potential use by at-risk individuals, such usage is restricted in some cases under regulatory mechanisms including IND protocols or EUAs. Box 4 lists the currently stockpiled MCMs for potential use in pediatric populations, along with the associated threats addressed by those MCMs.

**Box 4: Stockpiled Medical Countermeasures
Potentially Available for Use in Pediatric Populations**

- Oral Solid and Liquid Antimicrobials* – *Anthrax, Plague, Tularemia, Typhus*
- IV Antimicrobials* – *Anthrax, Pandemic Influenza[^], Plague, Radiological and Nuclear Threats[^], Tularemia, Typhus*
- Vaccines – *Anthrax, Pandemic Influenza, Smallpox*
- Antitoxins or Immunoglobulins – *Anthrax, Botulism, Smallpox[±]*
- Oral and IV Chelators – *Radiological Threats*
- Hematopoietic Agents – *Radiological and Nuclear Threats*
- Thermal Burn Supplies – *Radiological and Nuclear Threats*
- Nerve Agent Antidotes – *Chemical Threats*
- Oral Solid Antivirals – *Pandemic Influenza, Smallpox[±]*
- Inhaled and Oral Liquid Antivirals – *Pandemic Influenza*
- IV Antivirals – *Pandemic Influenza, Radiological and Nuclear Threats[^], Smallpox[±]*
- Ventilators – *All Hazards*

[^] for secondary infections

[±] includes potential treatments (including investigational) for vaccine complications

*oral solid and IV antimicrobials will be added for Burkholderia in the FY 2016-17 time frame

¹¹⁴ The SNS authority specifically requires that the emergency health security of children and other at-risk individuals be taken into account in determining which MCMs and supplies are needed for the SNS (Section 319F-2 of the PHS Act (42 U.S.C. 247d-6b)).

The PHEMCE will support MCM development and FDA approval to address the needs of at-risk individuals, including expansion of label indications and/or development of new dosage forms as needed. Specifically, the PHEMCE will pursue the following activities:

- (4.2.1) NIAID, in collaboration with BARDA and DoD's Armed Forces Radiobiology Research Institute (AFRRI), will continue to support the development of rodent and porcine juvenile models of ARS. The radiation dose responses of the Sinclair and Gottingen strains of mini-pig will be evaluated and compared to the known pathogenesis of humans. An animal model of pediatric ARS is important to ascertain safety and efficacy of candidate MCMs. (ongoing)
- (4.2.2) NIH established the Pediatric Trials Network in 2010 to create an infrastructure to study critical drugs and diagnostic devices in children with the goal of improving their labeling for pediatric use. (ongoing)
- (4.2.3) BARDA will support studies to develop pediatric and geriatric indications and dosage forms as needed in all MCM late-stage development and procurement projects. BARDA contracts for product development also include considerations of safety in pregnant women and immunocompromised individuals. (ongoing)
- (4.2.4) The SNS Annual Review process explicitly takes into account the needs of at-risk individuals. SNS Annual Review decisions will advance appropriate products or dosage forms for these groups, and/or suitable operational alternatives when available and as resources allow. (ongoing)
- (4.2.5) BARDA, working with CDC, will support efforts to achieve FDA licensure (in healthy populations) for a smallpox vaccine, which is ultimately intended for use in immunocompromised individuals and those with atopic dermatitis in an emergency. (near-term)

Objective 4.3 Develop and implement strategies, policies, and guidance to support the appropriate use of MCMs in all civilian populations during an emergency.
(Leads: ASPR, CDC; Partner: FDA)

At-risk individuals must have coordinated and equitable access to MCMs during public health emergencies. To support the use of stockpiled MCMs in at-risk individuals, in the near- and mid-terms, the PHEMCE will pursue policies and programs related to regulatory challenges associated with products intended for at-risk individuals, including filling priority data gaps associated with developing pre-EUA packages to support the use of stockpiled MCMs in these populations.

(4.3.1) CDC guidance provided to federal and SLTT partners on MCM distribution and dispensing/administration, as described under Objective 3.2, will likewise include consideration of at-risk individuals' needs. (4.3.2) The PHEMCE will use its established relationships with the American Academy of Pediatrics and other clinical organizations serving the needs of at-risk individuals to help inform MCM strategies and policies.

ASPR and the Administration for Children and Families established the Children's HHS Interagency Leadership on Disasters (CHILD) Working Group in 2010 to identify and comprehensively integrate departmental activities related to the needs of children across all HHS inter- and intra-governmental disaster planning initiatives and operations. The CHILD Working Group, which includes representatives from ASPR, CDC, FDA, and NIH, coordinates

the collection of information for the biennial Report of the CHILD Working Group. This report is a compilation of HHS activities addressing the needs of children across disaster preparedness, response, and recovery.

The CHILD Working Group developed six recommendations specific to pediatric MCM needs in its 2011 report, several of which have already been implemented. In the 2012-13 Report, the CHILD Working Group prioritized three new areas of focus for future efforts and recommendations: (1) neonates and pregnant women; (2) children at heightened risk; and (3) interdepartmental and non-governmental collaboration. Currently, efforts are underway to develop the 2014-2015 Report.

ASPR will also focus resources toward anticipating and addressing the needs of at-risk individuals during a disaster as follows:

- (4.3.3) During an emergency, OEM will assist and supplement state and local MCM distribution and dispensing efforts as needed, including those aimed at pediatric and other at-risk individuals;
- (4.3.4) ASPR's Division of Health System Policy will continue to facilitate connecting federal capabilities to existing private sector distribution centers (e.g., emergency management systems, hospitals, pharmacies) including at public and critical access hospitals serving at-risk individuals; and,
- (4.3.5) ASPR, through its engagement and support of the Federal Education and Training Interagency Group and the National Center for Disaster Medicine and Public Health, will support the development of training curriculum guidance for managing at-risk population needs in times of disasters. (ongoing)

SECTION 2: THREAT-BASED APPROACHES

The PHEMCE recognizes the need to address the high-priority threats identified in this document. While the PHEMCE is evolving toward capability-based approaches, it will maintain key threat-based approaches needed to address these threats to national health security. This section describes in detail the threat-based activities and programs based on the PHEMCE prioritization framework to support the approaches described in [Section 1](#) of this document.

ANTHRAX

The HHS PHEMCE anthrax activities include:

- Pursuing dose- and antigen-sparing approaches for the currently approved vaccine
- Reducing vaccine life cycle costs
- Developing enhanced and next-generation anthrax vaccine candidates
- Providing and maintaining enough vaccine regimens for the SNS to meet the established PHEMCE goal
- Enhancing the sustainability of anthrax vaccines by lowering cost per dose
- Encouraging competition among product sponsors
- Investing in novel expression and manufacturing platform technologies that are readily transferrable before or after a public health emergency to increase production capacity for anthrax vaccine
- Conducting animal model efficacy studies to support approval under the “Animal Rule” of antimicrobials currently approved for other indications for use against inhalation anthrax
- Development of anthrax diagnostic tools appropriate for use in a large scale incident.

Near-term (FY 2017-18)

Anthrax Vaccine

(T.A.1) NIAID continues to support the development of early-stage research and next-generation anthrax vaccine candidates that include novel technologies/platforms that accelerate the immune response, improve ease of delivery, and/or enhance stability. NIH supports these vaccine candidates under product development contracts:

- A lyophilized rPA vaccine (PharmAthene). This vaccine candidate is currently under formulation development and preclinical testing.
- A plant-based rPA vaccine with a saponin-based adjuvant (Fraunhofer). This is currently under preclinical testing.
- A subcutaneous pellet vaccine composed of rPA expressed from *Pseudomonas fluorescens* to be delivered via a Glide SDI system with or without an adjuvant (Pfenex). Several stable formulations have been selected for evaluation in preclinical studies.

- An intranasal anthrax vaccine based on the Public Health England, Health Protection Agency's proprietary *Escherichia coli*-based rPA vaccine component combined with NanoBio's novel nanoemulsion adjuvant W805EC technology component, to be administered using the Pfeiffer Bidose nasal sprayer. Engineering lots of adjuvant and rPA bulk drug substance have been manufactured and pre-clinical studies are underway.
- A replication competent, oral Ad4 vaccine vectors expressing rPA (PaxVax). Different regimens of rPA-Ad4 vaccines, with or without the licensed AVA, were evaluated in a Phase 1 clinical trial.

In collaboration with the vaccine manufacturer, NIH completed a Phase 2 trial of a next generation adjuvanted AVA vaccine. An addendum to the final report showing no adverse events of special interest reported was submitted to the FDA in February 2015. This improved anthrax vaccine, NuThrax™ (AV7909), produces higher antibody titers in a shorter timeframe than the licensed AVA vaccine. (T.A.2) NIH transitioned funding of NuThrax™ to BARDA for advanced development in March 2015.

(T.A.3) Furthermore, BARDA will continue development of existing rPA vaccine candidates in its pipeline and longer-term approaches supporting novel, viral-vectored, vaccine platforms.

(T.A.4) In addition, BARDA will provide vaccine candidates with advanced development and manufacturing assistance from the CIADMs as appropriate.

(T.A.5) BARDA will support expansion of domestic manufacturing capacity for the currently approved anthrax vaccine, including validating new manufacturing processes, conducting additional non-clinical and clinical studies, and pursuing licensure of a new facility. BARDA continued to support product testing and optimization/validation of vaccine manufacturing processes for BioThrax® in a new manufacturing facility. A Supplemental Biologics License Application (sBLA) was submitted to FDA in April 2016 for production of BioThrax® in the new manufacturing facility.

(T.A.6) Concurrently, BARDA will continue the development of the existing rPA vaccine candidates in its pipeline, and build on NIH investments to advance a next-generation anthrax vaccine toward licensure through validating manufacturing processes and conducting non-clinical and clinical studies. BARDA has advanced one of the rPA candidates into a clinical trial to evaluate safety and immunogenicity. It is anticipated that as a result of these activities, a next-generation anthrax vaccine may be available for procurement for the SNS by FY 2017.

(T.A.7) DoD will work with PHEMCE partners to identify how to address the long-term, pre-exposure vaccine needs of DoD. DoD will continue to invest in prophylaxis efforts to address *B. anthracis* strains that are resistant to the licensed anthrax vaccine as well as next-generation PA-based vaccines. Such vaccine-resistant *B. anthracis* strains, either naturally occurring or genetically engineered, would leave the forces more vulnerable to a bioweapon attack. The DoD strategy is to develop broad-specificity vaccines that are effective pre- and post-exposure to aerosolized *B. anthracis*-derived threat agents. To counter this threat, the DoD is taking a two-pronged approach:

- Leverage the existing anthrax vaccine – blend *B. anthracis* capsule with PA-based vaccine to bolster anthrax vaccine. As the capsule is essential for *B. anthracis* pathogenesis in animals and humans, this blended vaccine will significantly deter efforts to engineer around this MCM.
- Develop a live-attenuated anthrax vaccine – the advantage of such a vaccine is the broader coverage afforded against unknown genetically-engineered *B. anthracis* threat agents, which will greatly reduce the probability of technical surprise. To create a similar but safer live attenuated anthrax vaccine, the DoD is engaged in an international project agreement with the Israel Ministry of Defense to co-develop a next-generation live-attenuated anthrax vaccine. The DoD intends to defer further development of this vaccine once it reaches an interim fielding capability after FY 2017 in readiness for rapid deployment should an emergency requirement arise.

Anthrax Antitoxins and Antimicrobials

(T.A.8) BARDA will support late-stage development of an additional antitoxin with greater effectiveness and thermostability, specifically monoclonal anthrax antitoxins including lyophilized formulations. (3.5.1) CDC and BARDA are supporting drug manufacturers in fulfilling their post-marketing requirements for approved products. (T.A.9) CDC is sharing information with the drug manufacturer regarding patients treated with the investigational antitoxin to date.

(T.A.10) Using antimicrobials that are currently approved for other indications, NIH has completed animal efficacy studies to support approval of these antimicrobials under the “Animal Rule” for use against inhalational anthrax. Submission of data to FDA is anticipated in FY 2016. Additional antimicrobial development efforts are also underway at NIH, discussed below as part of the broad-spectrum antimicrobial program. All such anthrax antimicrobial programs are intended to expand our repertoire of antibiotics that are effective against anthrax. NIAID has demonstrated amoxicillin and amoxicillin/clavulanate activity in an animal model of prophylaxis of inhalational anthrax, and is currently working with FDA and drug sponsors to seek a label indication to serve the general population as well as children and pregnant women. (T.A.11) Additionally, NIH will support studies to inform utilization policy and response planning for these products.

(T.A.12) ASPR and CDC will lead analysis of the optimal ratios of products for oral antimicrobial PEP, considering resistance, tolerability, cost, and fluctuations in market availability. (T.A.13) CDC will support the evaluation of *B. anthracis* to establish breakpoints for additional antimicrobial agents to inform MCM usage.

(1.1.8) As a result of the MCM preparedness assessment for anthrax PEP oral solid antibiotics, ASPR and CDC will co-lead determining whether additional data from DSLR’s ORR evaluation process would change assessment of operational capacity.

Non-pharmaceutical Anthrax MCMs

(T.A.14) CDC will conduct a market analysis of the availability of the quantity of chest tubes needed during an anthrax public health emergency.

Mid-Term (FY 2019-20)

Anthrax Antitoxins and Diagnostics

(T.A. 15) BARDA anticipates product licensure of one or more additional anthrax antitoxins in this timeframe. Anthrax immune globulin (AIG) was licensed by the FDA in March 2015 and Anthim (obitoxaximab, manufactured by Elusys) was licensed in March 2016. (T.A. 16) The DoD has initiated the construction of a program to discover and develop non-traditional therapeutic candidates with broad spectrum activity to include anthrax.

BARDA anticipates FDA clearance of two anthrax diagnostic tools, one laboratory and one point of care.

Long-Term (FY 2021 and beyond)

Anthrax MCM Response Strategy

(3.2.5) ASPR will develop a response strategy for the utilization of pharmaceutical anthrax MCMs including vaccines, antimicrobials, antitoxins, and non-pharmaceutical MCMs such as chest tubes and ventilators.

Anthrax Vaccine

NIH long-term research in this area will pursue the development of anthrax vaccines with PEP potential that provide enhancements to the currently available vaccine for more effective utilization in public health emergencies. Ultimately, the objective is an anthrax vaccine for PEP that is effective in one dose and produces a rapid onset of immunity, resulting in a substantially reduced duration of required antimicrobial PEP therapy.

BARDA will continue to support advanced development of next-generation anthrax vaccines. BARDA will also continue to support studies to evaluate vaccines with various adjuvants and altered delivery mechanisms with the goal of reducing the number of doses necessary to obtain protective immunity. Finally, BARDA will continue to provide vaccine candidates with advanced development and manufacturing assistance from the CIADMs.

Anthrax Antitoxins, Antimicrobials, and Diagnostics

Research activities related to novel forms of antitoxins are underway at NIH and are expected to yield results in the long-term. BARDA will support the advanced development of next-generation, small molecule antitoxins for treatment of antimicrobial-resistant strains of anthrax as they become available. This will include efforts to ensure that appropriate animal models are available for advanced development.

NIH will support research into diagnostic platforms and the identification of biomarkers indicative of anthrax exposure to inform clinical decisions relative to antibiotic PEP administration. Additionally, NIH will support research into a more detailed characterization of symptomatic anthrax disease in order to guide clinical decisions regarding optimal antimicrobial therapy, as well as the need for additional antitoxin therapy. The PHEMCE will continue to support efforts to develop more rapid drug susceptibility assays for anthrax under the leadership of CDC.

OTHER BACTERIAL THREATS

PHEMCE activities for other bacterial threats include:

- Providing additional MCMs for the treatment and/or PEP of diseases caused by biological threat agents through discovery of novel compounds that have the potential to be effective against drug-resistant variants and address bacterial agents for which a material threat determination has been made;
- Revitalizing the pipeline of antimicrobial drugs to treat hospital- and community-acquired multi-drug resistant (MDR) bacterial infections for use in routine public health applications to advance the [National Action Plan for Combating Antibiotic-Resistant Bacteria](#) to address the on-going antimicrobial drug-resistance crisis; and
- Establishing public-private partnerships to incentivize companies developing antimicrobials to both continue their commercial development and initiate development for biodefense indications.

Near-Term (FY 2017-18)

(*T.OB.1*) NIH maintains *in vitro* and animal model testing services for the infectious disease community, especially for those bacterial threats for which special handling is required (e.g., due to Select Agent status or BSL-3 containment requirements). In FY 2017, NIAID plans to award indefinite delivery/indefinite quantity service contracts to expand existing pre-clinical capabilities to include non-traditional therapeutics development for bacterial pathogens and continuation of biopharmaceutical support for therapeutic development including reagent development for diagnostic platforms. NIAID also made product development contract awards in September 2016 to support preclinical and Phase 1 development of promising therapeutics that demonstrate broad-spectrum therapeutic activity against viral and bacterial pathogens.

(*T.OB.2*) In addition, to support product development under the “Animal Rule,” NIH and BARDA will seek qualification of animal models of anthrax, plague, and tularemia for PEP and treatment indications, through the FDA’s [Animal Model Qualification Program](#).¹¹⁵ These efforts will follow the successful precedent set when NIH, BARDA, and DoD collaborated to co-develop the animal models that helped support the licensure of BioThrax[®] anthrax vaccine for a PEP indication in November 2015.

(*T.OB.3*) DoD will invest in the development of MCMs against multi-drug resistant MDR bacteria that are of interest to the DoD. These efforts will involve leveraging investments in new antibiotics across the government as well as investing in partnerships with industry to repurpose or re-target their existing candidates. DoD will invest in prophylactic MCMs that rapidly and durably protect against bacterial threat pathogens with minimal doses. (*T.OB.4*) Near-term efforts focus on FDA licensure of vaccines capable of protecting against pneumonic disease

¹¹⁵ See:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284078.htm>

resulting from *Yersinia pestis*. (T.OB.5) Efforts to develop prophylaxis against *Francisella tularensis*, *C. burnetii* and *Burkholderia pseudomallei* will be in the discovery and initial development stages during the near-term. A number of candidates for *F. tularensis* are under initial development and include live attenuated, bacterial vectored and novel subunit-based candidates. Vaccines strategies for *B. pseudomallei* include novel subunit, polysaccharide and outer membrane vesicle-based candidates.

(T.OB.6) NIH will augment antimicrobial efficacy datasets in support of approval of clinical indications for anthrax, plague, and tularemia for off-patent antimicrobials in the SNS and/or in routine use. NIAID evaluated the treatment efficacy of doxycycline against inhalational tularemia in cynomolgus macaques and found that it was effective. NIAID is working with the drug sponsor to submit data to the FDA to support refinement of the label. (T.OB.7) NIAID plans to test the efficacy of ciprofloxacin in 2016. Ciprofloxacin is not labeled for a tularemia indication. (T.OB.8) Additionally, NIH is working with FDA to evaluate the efficacy of doxycycline for pneumonic plague based upon animal efficacy studies.

(T.OB.9) BARDA will support the advanced research and development of novel antimicrobials for PEP and diagnostics for treatment and diagnosis of biological threat agents while addressing the threat of antimicrobial resistance in routine public health settings as part of the CARB initiative. (T.OB.10) BARDA, under the animal model network, is establishing key reagents and animal models for testing MCMs against *Burkholderia pseudomallei* and *B. mallei*. (T.OB.11) BARDA will continue testing of candidate products against *B. pseudomallei* and *B. mallei*.

(T.OB.12) CDC will develop, and FDA will provide feedback on, pre-EUA packages for meropenem, trimethoprim/sulfamethoxazole, and amoxicillin/clavulanate for the treatment of melioidosis and glanders.

Mid-Term (FY 2019-20)

(T.OB.13) NIH will maintain antibiotic efficacy datasets for off-patent antimicrobials within the SNS, as well as for antimicrobials in common routine use. (T.OB.14) BARDA will continue advanced development of antimicrobial and diagnostic candidates; pending results of clinical trials, BARDA may procure several of these candidates under PBS. DoD will continue to support the development of new MCMs against MDR bacteria and continue to look for opportunities to leverage existing investments by the USG. (T.OB.15) DoD intends to file an Investigational New Drug (IND) application by FY 2018 in support of an indication against MDR bacterial agents of interest to the DoD. BARDA will develop laboratory and Point of Care diagnostics for several additional biothreats.

(T.OB.16) DoD will continue to invest in prophylactic medical countermeasures against bacterial threat pathogens. Mid-Term efforts will focus on advanced development toward FDA licensure of current candidates in initial development for *F. tularensis*, *C. burnetii*, and *B. pseudomallei*. Discovery and development efforts for advanced vaccines against novel targets for *Y. pestis*, *F. tularensis*, *C. burnetii*, *B. pseudomallei*, and emerging biological warfare threats will continue. Strategies will include discovery and advancement of products that target naturally mutating and

genetically engineered biological threats with an emphasis on products that offer broad protection against multiple strains or species.

Long-Term (FY 2021 and beyond)

BARDA will support late-stage development activities in support of PEP and treatment of *Burkholderia* infections.

DoD will continue to support the development of new MCMs against MDR bacteria through the conduct of adequate and well-controlled animal efficacy studies submitted under Special Protocol Assessments with the FDA and continue to look for opportunities to leverage existing investments by the USG. DoD will continue to support the development of prophylactic MCMs against known and emerging bacterial threat pathogens. Approaches that target nontraditional approaches including specific countermeasures (vaccines, immunoglobulins) and non-specific countermeasures that effectively activate the immune system will be expanded.

SMALLPOX

The PHEMCE smallpox activities include:

- Maintaining an adequate stockpile of vaccines and Vaccinia Immune Globulin Intravenous (VIGIV)
- FDA approval of MVA vaccine, intended for use in at-risk populations
- Approval of two smallpox antivirals with different mechanisms of action

Near-Term (FY 2017-18)

Smallpox Vaccine

Existing smallpox vaccines are mature. In 2016, the PHEMCE approved the Smallpox Vaccine Response Strategy, which provides information to support decisions regarding the effective use of smallpox vaccines in the SNS after the detection of smallpox disease. *(T.S.1)* In the near-term, the PHEMCE will maintain sufficient quantities of smallpox vaccines in the SNS to provide a response capability to vaccinate every American during a smallpox emergency, if appropriate, including use of a vaccine for at-risk populations.

(4.2.5) BARDA, working with CDC, will support activities to achieve FDA approval for the MVA smallpox vaccine, which is intended for use in at-risk populations. *(T.S.2)* BARDA will continue to provide technical support for the manufacture and acquisition of the MVA vaccine for at-risk populations. *(T.S.3)* BARDA will also continue development of a lyophilized formulation of MVA to allow a longer shelf life and storage at higher temperatures in order to reduce life cycle management costs.

Smallpox Antivirals and Diagnostics

(T.S.4) Antivirals, SIGA's tecovirimat and Chimerix's CMX001, for the treatment of smallpox are in advanced development. *(T.S.5)* The PHEMCE will assess policy implications of antivirals and their use. *(T.S.6)* BARDA-supported deliveries of tecovirimat to the SNS are ongoing. *(T.S.7)*

CDC submitted the 510(k) to FDA for the variola virus specific assays in April 2016 and is now developing a strategy to deploy to Laboratory Response Network (LRN) labs. CDC continues to compile data on an Orthopoxvirus generic assay for future FDA submission. In addition, the PHEMCE, through coordination with the MA IPT, will identify monitoring and assessment needs and approaches for tecovirimat.

Mid-Term (FY 2019-20)

Smallpox Vaccine

In the mid-term, the PHEMCE will continue to maintain smallpox vaccines and VIGIV (as needed) in the SNS. *(T.S.8)* The PHEMCE will also develop appropriate animal model(s) to evaluate VIGIV or other therapeutic candidates in treating adverse events associated with the current vaccine. Data reported in Spring 2015 showed that monoclonal antibody (mAb) therapeutics are more effective than VIGIV in curing vaccine-related adverse events (AE) in a mouse model.

(T.S.9) BARDA will manage the transition from the present liquid-frozen form of the MVA smallpox vaccine to a freeze-dried formulation with superior life cycle management properties.

Smallpox Antivirals

(T.S.10) NIH efforts focused on next-generation smallpox antivirals will support those products that emerge from the broad-spectrum antiviral program. Once those candidates have obtained FDA approval for other viral indications, most likely via traditional regulatory pathways, NIH will pursue an orthopoxvirus clinical indication under the “Animal Rule.” *(T.S.11)* BARDA will continue to support approval of one or more antiviral products. *(T.S.12)* CDC will also conduct studies to inform the clinical use of these MCMs.

PANDEMIC INFLUENZA

The HHS PHEMCE pandemic influenza activities include:

- Maintain the established comprehensive portfolio approach to develop, acquire, and build an infrastructure for a broad array of MCMs to respond to pandemic influenza, including vaccines, therapeutics, diagnostics, and non-pharmaceutical MCMs.
- Sustain a robust domestic pandemic influenza vaccine manufacturing capacity.
- Address various aspects of MCM utilization for pandemic influenza, and develop and distribute communication and educational materials before and during an influenza pandemic.
- Develop a more effective/universal influenza vaccine with the potential to stimulate broader, more durable immunity that may eliminate the need for annual modifications to the influenza vaccine or annual boosters and serve as priming doses for future pandemic influenza vaccines.

Near-term (FY 2017-18)¹¹⁶

Communications and Response Planning

(*T.PI.1*) As called for in the [H1N1 Improvement Plan](#),¹¹⁷ HHS will continue to ensure that operational plans for pandemic influenza communication are updated, exercised, evaluated, and improved to facilitate effective communication strategies. (*T.PI.2*) CDC will continue to expand its capacity to provide translated and culturally appropriate materials for non-English-speaking communities across the U.S., as well as the capacity to develop plain language (easily understood) materials for public audiences. For example, CDC will: (*T.PI.3*) (1) develop procedures to ensure that information in future pandemics is provided in accessible and alternative formats; (*T.PI.4*) (2) refine and implement partnership strategies to improve communication with hard-to-reach and at-risk populations; (*T.PI.5*) (3) use partnerships and other information dissemination channels to effectively reach and inform clinicians regarding CDC's policies, guidelines, and recommendations related to pandemic influenza MCMs; and (*T.PI.6*) (4) develop an approach, definitions, tools, and models for a risk communication response plan.

(*T.PI.7*) ASPR will maintain and continue to promote the use of the Interim [Healthcare Coalition Checklist for Pandemic Planning](#) (HCCPP).¹¹⁸ In conjunction with other tools, the HCCPP can help health care coalitions expand their pandemic influenza emergency response plans to include a diverse mix of partners, including schools, businesses, community organizations, and government agencies. The HCCPP tool outlines recommended actions based on each of the eight preparedness capabilities in ASPR's [Healthcare Preparedness Capabilities: National Guidance for Healthcare System Preparedness](#).¹¹⁹

Influenza Vaccine Stockpiles

BARDA collaborates closely with PHEMCE partners, including CDC, NIH, and FDA, to make decisions regarding influenza vaccines suitable for the pre-pandemic vaccine stockpile. The CDC [Influenza Risk Assessment Tool](#) (IRAT), which assesses the potential pandemic risk posed by novel influenza A viruses and other data streams, informs decisions regarding the composition of the pre-pandemic vaccine stockpile.¹²⁰ In 2015, the Influenza (Flu) Risk Management Meeting (FRMM) reviewed the quantity, composition, and status of A (H5N1) and A(H7N9) vaccine antigens, and AS03 and MF59 adjuvants in the national pre-pandemic influenza vaccine stockpile. This resulted in the development and manufacture of A (H5N8)

¹¹⁶ Information regarding respiratory protective devices for influenza needs is addressed in the capabilities-based approaches section.

¹¹⁷ Available at: <http://www.phe.gov/Preparedness/mcm/h1n1-retrospective/Documents/2009-h1n1-improvementplan.pdf>

¹¹⁸ Available at: <http://www.phe.gov/Preparedness/planning/hpp/reports/Documents/pandemic-checklist.pdf>

¹¹⁹ Found at: <http://www.phe.gov/Preparedness/planning/hpp/reports/Documents/capabilities.pdf>

¹²⁰ See: <http://www.cdc.gov/flu/pandemic-resources/tools/risk-assessment.htm>

avian influenza vaccines for further study and to mitigate potential gaps in the previously stockpiled A(H5N1) vaccine. The contracts also allow HHS to purchase cell-based and recombinant vaccine in addition to conventional egg-based vaccine during a pandemic.

(T.PI.8) BARDA will maintain and update the existing stockpile of novel influenza vaccine viruses and pre-pandemic vaccines and adjuvants as needed. BARDA will work in collaboration with FDA to identify any additional testing to assess the stability and usability as well as confirm immunogenicity of long-term stored vaccines and adjuvants. In 2015, BARDA sponsored its first IND with a vaccine product: the BARDA Ready in Times of Emergency study will evaluate the safety and immunogenicity of inactivated influenza A/Vietnam (H5N1) vaccine, stored for a prolonged period of time formulated as antigen-alone or with MF59 adjuvant.

(T.PI.9) CDC, working with BARDA and FDA, will develop rapid methods and biosynthetic technologies to produce candidate vaccine viruses that allow accelerated production of vaccine lots for eventual fill and finish by manufacturers. NIH also produces candidate vaccine viruses through a contract with St. Jude Children's Research Hospital in collaboration with WHO.

(T.PI.10) In addition, in collaboration with BARDA and FDA, CDC will complete work on the development of rapid laboratory methods to expedite testing to determine the antigen content of influenza vaccine bulk material and enable vaccine formulation prior to product fill and finish.

Influenza Antigen-Sparing Technology

(T.PI.11) NIH through NIAID has continued to conduct a series of clinical trials of stockpiled A(H5N1) and A(H7N9) vaccines with and without MF59 and AS03 adjuvants. While the primary focus of the NIAID clinical trials has been to assess different vaccination strategies and to advance our understanding of the breadth and duration of the immune response, the clinical study results also show that these stockpiled vaccines continue to be well tolerated and immunogenic in humans.

NIH maintains an active grant portfolio supporting basic research into novel adjuvants. *(T.PI.12)* NIH and BARDA will continue to collaborate in the clinical evaluation of adjuvants coupled with a variety of influenza vaccines. The goal is to provide antigen-sparing benefits (i.e., decreased amount of viral hemagglutinin antigen needed to provide immunity), broad heterosubtypic immunity (i.e., protection against multiple virus variants), and prime-boost effects (i.e., one dose may be sufficient instead of two or more) for influenza vaccines.

Influenza Vaccine Development

(T.PI.13) NIH and BARDA continue to collaborate on the clinical evaluation of adjuvants coupled with a variety of influenza vaccines. NIH continues to maintain an active grant portfolio supporting basic and preclinical research into novel vaccine adjuvants, including understanding their mechanism of action. BARDA and NIH continue to work closely together on clinical trials to test the antigen sparing effect of stockpiled adjuvants in combination with stockpiled avian influenza vaccines.

(T.PI.14) NIAID will continue to support the development of a chimeric hemagglutinin (HA) universal influenza vaccine candidate that generates an immune response against the stem part of the influenza HA protein and may elicit broad protective immunity against multiple influenza strains. *(T.PI.15)* NIH and CDC continue to deposit reagents useful for the scientific and

research and development (R&D) communities to support universal influenza vaccine research and development into NIAID's Biodefense and Emerging Infections Research Resources Repository and the Influenza Reagent Resource, respectively.

Cell- and recombinant-based influenza vaccine development is a key element in the PHEMCE intermediate and long-term pandemic influenza preparedness strategy in order to provide adequate domestic vaccine manufacturing surge capacity. The U.S. cell-based influenza vaccine was approved in November 2012, and a U.S. cell-based manufacturing facility was approved in June 2014. The first U.S. recombinant influenza vaccine was approved in January 2013 and a U.S.-based manufacturing facility was approved in May 2015. These developments were supported by BARDA. *(T.PI.16)* The more effective/universal influenza vaccine development program launched at BARDA in 2015 with awards to Cambridge University to develop broadly cross-reactive A(H5N1) influenza vaccines and to Vaxart for Phase 2 clinical evaluation of an oral influenza vaccine tablet that stimulates cellular immunity and longer lasting humoral immunity. BARDA, working with HHS colleagues, has developed a plan to produce high yielding / immunogenic influenza vaccine viruses for distribution to manufacturers. BARDA and other HHS partners also have developed improved assays to replace the current calibration technique for the single radial immunodiffusion assay used to determine vaccine potency.

(T.PI.17) BARDA is coordinating with the CDC, FDA, and U.S. influenza vaccine manufacturers and regulatory stakeholders (HHS, International Federation of Pharmaceutical Manufacturers & Associations, and WHO) to assess and implement alternative potency assays that will improve vaccine development and manufacturing of seasonal and pandemic influenza.

As part of an HHS effort to mitigate seasonal influenza vaccine mismatches, BARDA convened a stakeholder's workshop/exercise on November 10, 2015, comprising participants from NIH, CDC, and FDA, as well as WHO Collaborating Centers and Essential Regulatory Laboratories, and representatives from U.S. licensed influenza vaccine manufacturers, for improving influenza vaccine virus selection.

Influenza Antivirals

BARDA completed support during 2015 for a pivotal Phase 3 clinical study of a host-targeted influenza antiviral drug candidate (developed by Romark) that showed no increased efficacy over oseltamivir for the treatment of acute, uncomplicated influenza patients. BARDA began support for the development of a novel antiviral drug targeting the influenza viral RNA polymerase (developed by Janssen) and a novel monoclonal antibody (developed by Visterra), both for the treatment of patients hospitalized with influenza. *(T.PI.18)* NIH will continue to support the development of an influenza broad-spectrum therapeutic (Autoimmune Technologies, LLC) with multi-functional potential, which entered Phase 2 clinical trials in 2015. *(T.PI.19)* NIH will develop both small-molecule drugs and monoclonal antibodies as broad-spectrum influenza therapeutics. NIH will develop these MCMs initially as treatments, with the potential for prophylactic use in the future, especially in those individuals who respond poorly to vaccines. NIH continues to maintain an active grant portfolio supporting basic and preclinical research into novel influenza antivirals, including investigation into novel targets.

(T.PI.20) BARDA will support development of host-targeted antiviral drug candidates, as well as new combination therapies, monoclonal antibody therapies, and new classes of influenza

antiviral drugs. (T.PI.21) BARDA will support advanced development of at least two drugs with novel mechanism(s) of action through Phase 3 clinical studies. (T.PI.22) BARDA continues to seek opportunities to develop new antiviral treatments through the Influenza BAA, with a focus on products with novel mechanisms of actions, and those effective in severely ill, hospitalized patients and suitable for at-risk populations, including pediatrics.

(T.PI.23) CDC will develop new plans for influenza antiviral distribution and dispensing.

(T.PI.24) ASPR and CDC will determine the roles IV antivirals could have in responding to a pandemic influenza public health emergency.

Influenza Diagnostics

In 2015, the Influenza Genome Sequencing Project (IGSP) at the NIAID-funded Genome Sequencing Center at the J. Craig Venter Institute sequenced and released into the public domain GenBank, over 17,500 complete genomes of influenza. The IGSP continues to provide the scientific community with complete genome sequence data for human and animal influenza viruses. (T.PI.25) NIH will continue to sequence and provide genomic data for influenza viral isolates to support current and future diagnostic efforts.

(T.PI.26) BARDA will continue supporting development of diagnostics to inform seasonal and pandemic influenza treatment with an emphasis on higher quality and faster testing at the point of care. Of particular importance are testing strategies and tools, which quickly inform the use of antiviral drugs and systems that assist in differentiating seasonal influenza and pandemic influenza.

Mid-Term (FY 2019-20)

Communications and Response Planning

(T.PI.27) CDC will refine and expand the use of immunization information systems among all providers, including non-traditional providers. (T.PI.28) CDC will continue work to increase the percentage of [persons receiving annual influenza vaccinations](#).¹²¹ (T.PI.29) CDC also will work with federal and SLTT partners to implement guidance developed by the USG for situations during which limited vaccine availability requires prioritization of vaccination.

Influenza Vaccine Stockpiles

(T.PI.30) BARDA will continue to maintain and adjust novel influenza vaccine virus and pre-pandemic influenza vaccine stockpiles, as warranted, in collaboration with PHEMCE partners and through utilization of the IRAT-derived information as described above.

¹²¹ The target for adults over 18 is 70 percent with completion projected in 2020. For more information, see <http://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives>

Influenza Vaccine Development

(*T.PI.31*) BARDA will support at least two more effective/universal vaccine candidates expected to be evaluated in Phase 2 clinical studies in the mid-term. BARDA will also initiate the evaluation of heterologous prime-boost strategies to inform pre-pandemic influenza preparedness.

BARDA will coordinate efforts to improve seasonal influenza vaccine development and manufacturing to mitigate the risk of influenza vaccine virus mismatched through an interagency program focused on influenza virus characterization and manufacturing technologies that will improve vaccine composition decisions and decrease production timeline variability and duration.

Influenza Antivirals

(*T.PI.32*) BARDA will continue support for the advanced development of novel (non-neuraminidase inhibitor) influenza therapeutics, including promising new viral and host-targeting candidates and monoclonal antibody treatments.

Influenza Diagnostics

(*T.PI.33*) CDC will ensure the implementation of laboratory reference diagnostics for influenza at public health laboratories and refine the methods by which specimens are tested for surveillance purposes. CDC plans to expand the capacity to rapidly detect novel influenza A virus and emerging antiviral resistance. In addition, CDC will improve the timeliness and accuracy of laboratory assays for measuring influenza immunity. (*T.PI.34*) Finally, CDC and BARDA will continue support of the development of sequencing-based diagnostic assays and prototype device development for diagnosis of influenza viruses and other respiratory pathogens.

(*T.PI.35*) BARDA will support development efforts for FDA approval of a rapid molecular point of care influenza diagnostic that will inform seasonal and pandemic influenza care.

Long-term (FY 2021 and beyond)

Influenza Vaccine Stockpiles and Response Planning

BARDA will maintain and update the pre-pandemic stockpile as needed to maintain preparedness, as determined in collaboration with PHEMCE partners. When improved influenza vaccines with universal potential are available, the PHEMCE will reexamine the utility of existing pre-pandemic stockpiles.

CDC will work to refine policies and plans related to pre-pandemic vaccine distribution modalities (e.g., pre-pandemic vaccine allocation guidance, utilization strategies, stockpiling goals, and communications plans). This effort will focus on the refinement of the pandemic vaccine prioritization strategy and implementation plans as necessary, including communication plans. In coordination with FDA, CDC will also conduct influenza vaccine safety studies in at-risk populations (e.g., pregnant women) and explore opportunities to improve awareness of

vaccine adverse events and increase reporting to the Vaccine Adverse Event Reporting System (VAERS) by clinicians and other vaccine providers.

Influenza Vaccine Development

NIH is focusing on a wide array of universal influenza vaccine concepts, with several candidates entering preclinical development over the next several years. NIH is also developing a repository of required influenza-related reagents to support universal influenza vaccine development. In addition, NIH is working closely with the FDA to develop and refine additional assays, including sterility and potency testing, to support future vaccine development efforts.

In close coordination with NIH, CDC, and FDA, BARDA will support the advanced development and licensure of new influenza vaccines with improved effectiveness. These vaccines will use recombinant and antigen sparing/immunomodulatory approaches to create better vaccines that provide greater protection against seasonal and pandemic influenza viruses.

Influenza Antivirals

In this time frame, it is anticipated that at least four additional influenza therapeutics supported by BARDA may be approved for use in the U.S., if data demonstrate safety and efficacy.

EMERGING INFECTIOUS DISEASES

For EIDs, viral agents remain a dominant source of likely novel outbreaks. PHEMCE activities for other viral threats include:

- Addressing existing viral threats
- Strengthening the capability to respond to emerging viral threats through a broad-spectrum antiviral program
- Improve HHS's ability to rapidly develop and deploy diagnostics for emerging threats

The threat of re-emerging and emerging infectious diseases poses a challenge to public health and national security and is being assessed by the PHEMCE. *(T.EID.1)* The PHEMCE has established an EID Working Group charged with identifying which potential EID threats should be included as PHEMCE high-priority threats to inform EID MCM development and utilization investments. The PHEMCE is already actively engaged in addressing EID that currently represent public health threats as highlighted below.

(T.EID.2) NIAID will continue pre-clinical and early clinical development of therapeutics and vaccines to establish a pipeline of potential medical countermeasures for established or emerging viral disease threats. *(T.EID.3)* NIH will undertake animal efficacy studies to evaluate these agents' broad-spectrum activity and examine their potential to replace existing stockpiled MCMs once they gain approval. *(T.EID.4)* BARDA will expand platform programs with the potential to address more threats, such as the filoviruses, with vaccines and monoclonal antibodies platform technologies for rapid MCM responses to EIDs.

Zika Virus Preparedness and Response¹²²

Zika is an emerging health threat, a flavivirus closely related to dengue, yellow fever and West Nile viruses. Zika virus is primarily spread by infected mosquitoes, particularly *Aedes aegypti* and *A. albopictus*. In May 2015, the first local transmission of Zika in the Americas was reported in Brazil. By the end of 2015, Brazilian authorities estimated a million suspected cases of Zika virus infection. Subsequently, the virus spread rapidly throughout Latin America and the Caribbean, as well as to parts of the Pacific. In February 2016, the WHO declared the recent cluster of microcephaly cases and Guillain-Barré, which had been temporally associated with Zika virus transmission, a public health emergency of international concern, and the HHS Secretary declared Zika virus to pose a significant potential of a public health emergency justifying authorization of emergency use of diagnostics. In April 2016, the CDC confirmed that the Zika virus causes microcephaly and other birth defects. The U.S. response to the Zika outbreak is complex and involves many partners both within and outside of the federal government. Within HHS, ASPR convened the DLG to regularly discuss, coordinate, and promote approaches to address the policy, budget, legislative, and external communication strategies and needs associated with the response. The DLG is working to identify and resolve policy issues and potential barriers, including those related to MCM production, distribution, dispensing/administration, and use, which may directly impact effective response operations during the Zika virus outbreak.

CDC has developed, and received FDA Emergency Use Authorization for two diagnostic tests to detect Zika virus including: the Trioplex reverse transcriptase polymerase chain reaction (RT-PCR) and the CDC Zika IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA). The Trioplex RT-PCR assay is designed to detect Zika virus, dengue virus and chikungunya virus RNA, which can sometimes be detected early in the course of illness. A positive test result indicates a high likelihood of recent Zika virus infection. The MAC-ELISA is an antibody test used for qualitative detection of Zika virus IgM antibodies, which typically develop toward the end of the first week of illness and may indicate previous infection of Zika virus. ASPR is leading the HHS Sample Sharing Working Group to identify domestic and international sources of Zika positive clinical specimens and viral isolates to support development and validation of these diagnostics and other MCM.

FDA reviewed both assays and issued EUAs to authorize their emergency use. CDC is distributing test kits to qualified laboratories including those in the LRN. As of September 2016, the FDA has also issued [EUAs for 10 Zika diagnostic tests developed by commercial manufacturers](#).¹²³ FDA is actively engaged with product developers, CDC, NIH, and BARDA to advance the development of diagnostic tests, vaccines, therapies, and donor screening and pathogen reduction technologies for blood products to help mitigate the Zika virus outbreak. (T.Z.1) BARDA is supporting the development of two blood-screening tests for Zika virus

¹²² This section describes planned activities as of spring 2016. Due to the evolving nature of the Zika virus outbreak response at the time of this writing, priorities may shift in order to best meet newly identified preparedness and response needs.

¹²³ See: <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#h7n9>

infection, one an RT-PCR-based screening test and the other a transcription-mediated amplification (TMA)-based test. Both tests have received IND status from FDA and are now in development towards a BLA.

To ensure the safety of the nation's blood supply, FDA issued guidance in February 2016 recommending deferrals of individuals from donating blood if they have been to areas with active Zika transmission. This guidance was revised in August 2016 to recommend universal testing of donated whole blood and blood components for Zika virus in the U.S. and U.S. territories. As an additional safety measure, FDA issued a new guidance in March 2016 providing recommendations to reduce the potential transmission risk of Zika virus from human cells, tissues, and cellular and tissue-based products.

CDC also provides financial and technical resources to states and territories through our Epidemiology and Laboratory Capacity and PHEP cooperative agreements to strengthen their capacity to prepare for and respond to emerging threats like Zika virus. These resources may be used to help health departments expand their capacity to test for local and travel-associated cases of Zika virus infection, prepare for cases of local Zika virus transmission, and to implement community education and prevention programs to reduce human-mosquito contact and therefore reduce the risk of Zika transmission. These resources may also be used to implement vector control strategies to prevent further spread of Zika virus, for example to support the implementation of vector epidemiology, surveillance, and educational campaigns.

In April 2016, CDC hosted a Zika Action Plan summit for state, territorial and local officials and public health partners. Attendees were given information and tools needed to improve Zika preparedness and response within their states and jurisdictions, including the latest scientific knowledge about Zika, implications for pregnant women, best communications practices and strategies for mosquito control. The summit offered an opportunity to identify gaps in preparedness and response and begin development of comprehensive Zika Readiness Action Plans for jurisdictions. Additionally, CDC issued approximately 10 clinical guidances and will continue to update these guidances as new information becomes available.

In March 2016, CDC's DSNS assembled and delivered 5,000 Zika Prevention Kits to Puerto Rico, the U.S. Virgin Islands, and American Samoa. CDC is now into the next phase of the response, which includes building over 26,000 more kits, leading the procurement effort for purchasing the contents of the kits and collaborating with the CDC Foundation for donations, and facilitating arrangements for vector control in the affected territories. CDC awarded a number of vector control and community outreach contracts.

NIAID will continue leveraging existing resources and funding mechanisms to support research into diagnostics, therapeutics, vaccines, and vector control to combat Zika virus. NIAID maintains a program that provides preclinical research resources for the use of scientists worldwide to advance translational research against infectious diseases. These resources are designed to bridge gaps in the product development pipeline and lower the scientific, technical, and financial risks incurred by industry. Additionally, NIAID will continue facilitating the collection of clinical isolates for authentication, characterization, and production of viral stocks for use by the research community; the development of small animal and non-human primate models to screen therapeutics and vaccines; the development of Zika specific monoclonal

antibodies; and the development of formalin inactivated whole virus vaccine for evaluation. Furthermore, NIAID also continues to support the sequencing of both Zika virus and vector genomes, as well as provide systems biology analyses and bioinformatics resources to the research community.

NIAID will continue to support the evaluation and validation of diagnostics including multiplex assays for the rapid detection of strains of dengue, chikungunya, and Zika viruses as well as a method that shows promise as a tool to track virus evolution and its susceptibility to vaccine and drug interventions. In addition, NIAID support of metabolomics studies to identify biosignatures of Zika infection will continue.

(T.Z.2) NIAID, in conjunction with several Institutes and centers, will continue to support both in vitro and in vivo screening of therapeutic candidate compounds, antibodies, and peptides to identify those with antiviral activity against Zika.

(T.Z.3) NIAID will continue to support the development of multiple candidate vaccines including live-attenuated chimeras, combining the Zika virus with a flavivirus (e.g., dengue), a vesicular stomatitis virus (VSV) vectored vaccine expressing the Zika E protein, and mRNA and DNA vaccines that would encode for Zika membrane and/or E protein(s). (T.Z.4) WRAIR is working with BARDA and NIAID on an inactivated Zika vaccine. The vaccine, developed by the WRAIR, demonstrated proof of concept with dengue (GSK and FioCruz collaboration, Phase 1) and Japanese encephalitis (Ixiaro, licensed). NIAID and WRAIR are planning to support the evaluation of several candidate Zika vaccines in Phase I clinical trials.

Targeting *A. aegypti* mosquitoes, the vector responsible for transmission of Zika virus, presents another opportunity to impact the public health response. NIAID will continue to support research to understand disease transmission, including the monitoring and surveillance of *A. aegypti* mosquitoes, as well as research into vector control strategies such as larvicides and the use of the bacteria *Wolbachia* as a biocontrol.

NIH will also continue its support of the *Zika in Infants and Pregnancy*, a prospective natural history study focusing on the course of Zika virus and its effects on pregnant women and their infants. NIAID is also supporting additional natural history studies in the U.S. and abroad to study clinical, virological, and immunological outcomes in children and adults following Zika virus infection.

To understand more about Zika virus infection, CDC, in collaboration with state, local and territorial health departments, the Puerto Rico Department of Health, and Colombia's Instituto Nacional de Salud, established registries (U.S. Zika Public Health Registry), Puerto Rico (Zika Active Pregnancy Surveillance System), and Colombia (SIVIGILA/Proyecto Vez). The data collected through these registries will provide information about the timing, absolute risk, and spectrum of outcomes associated with Zika virus infection during pregnancy is needed to direct public health action related to Zika virus and guide testing, evaluation, and management. In addition to estimating the risk of complications, CDC is also conducting studies to answer additional questions such as the impact of viral persistence in bodily fluids, and early childhood developmental issues that may be associated with maternal Zika infection during pregnancy or infant Zika infection.

(T.Z.5) ASPR/BARDA is collaborating with the Butantan Institute in Sao Paulo, Brazil, to assist them in developing their own inactivated virus Zika vaccine. ASPR/BARDA will send technical subject matter experts in mid-April to review Butantan's development plans and timeline. BARDA is working closely with the WHO to make funds available to Butantan to accelerate this effort to be able to respond locally to the current Zika virus outbreak.

(T.Z.6) There is collaboration between HHS (ASPR/BARDA, NIH/NIAID) and DoD (WRAIR) to make an inactivated whole virion vaccine in Vero cells. This effort involves BARDA CIADMs for process optimization and larger scale manufacturing. Preclinical testing is expected to start in summer with human clinical studies to start in the fall.

BARDA is continuously assessing the vaccine landscape efforts by large pharma and small biotech companies of which there are over 25 developing vaccine candidates for Zika virus. Many products are in the early discovery stage of development. BARDA is supporting development of several Zika vaccine candidates with industry partners, including Emergent BioSolutions, Moderna Therapeutics, Sanofi Pasteur, and Takeda. BARDA is in communication with many vaccine developers, informing them of the Tech Watch program under medicalcountermeasures.gov and funding opportunities through BARDA's BAAs and NIAID announcements.

ASPR, in collaboration with CDC and other interagency partners, continues to lead efforts to obtain acute and convalescent serum samples from affected countries, affected U.S. territories, and U.S. travelers that can be shared across agencies and with commercial test developers to support Zika virus diagnostic development. Further, BARDA and CDC have evaluated two Zika-specific serological tests that are currently available outside the U.S. Neither of these tests were sufficiently sensitive to approach the sensitivity of the CDC Mac-ELISA.

BARDA has modified its open solicitation to include funding opportunities for Zika diagnostics and are reviewing development projects submitted in response. The amendment includes development of point-of-care and laboratory-based serologic assays for Zika virus, and multi-analyte assays to discriminate Zika, dengue, and chikungunya virus infections.

BARDA has entered into a partnership with Terumo and Cerus for the late-stage development of pathogen reduction systems for blood products that may be contaminated with Zika virus. As a by-product of the development of this latter system, a better and safer supply of platelets may be afforded in the U.S. to treat thrombocytopenia in individuals exposed to ionizing radiation after a nuclear incident.

(T.Z.7) BARDA is supporting Roche Molecular Systems to conduct a clinical study to evaluate the sensitivity and specificity of the blood donation screening test in its actual use. (T.Z.8) BARDA also anticipates supporting at least one industry partner in the development of a high through-put screening system for detection of Zika virus in blood using existing molecular technologies.

(T.Z.9) ASPR/BARDA will support the development, EUA submission, clinical evaluation, and filing of an application for clearance with FDA for serologic tests for Zika infection. Both laboratory tests and point of care tests will be supported.

Ebola Preparedness and Response¹²⁴

Near-term (FY 2017-18)

(T.E.1) The PHEMCE continues to support basic, preclinical, clinical and regulatory science research that will lead to new approaches to prevent and treat Ebola. BARDA, NIH, FDA, and DoD support the development of multiple potential Ebola MCMs including the therapeutic candidates ZMapp™, mAb114, BCX4430, AVI-7537 and favipiravir; and multiple vaccine candidates, including chimpanzee adenovirus vector type 3 (ChAd3), ChAd26/MVA vectors and rVSV vector. The FDA issued draft guidance to describe the Agency's [premarket regulatory requirements and the performance testing needed](#) to support liquid barrier claims for gowns intended for use in health care settings.¹²⁵

(T.E.2) BARDA will continue advanced development of existing and new Ebola vaccine and therapeutic candidates that meet PHEMCE product specific requirements towards FDA licensure and approval. Provided sufficient maturity of Ebola vaccine and therapeutic candidates is reached, BARDA may procure initial products utilizing the SRF for stockpiling. In 2015, BARDA supported the development of 12 MCMs for Ebola. These candidates will be evaluated for potential transition to PBS in 2017 based on performance, alignment with PHEMCE requirements, available funding and data to support potential procurement and FDA approval.

(T.E.3) NIAID will continue to be active in the Filovirus Animal Nonclinical Group (FANG) which is an interagency and interdepartmental group to support the advanced development of Filovirus MCMs, both vaccines and therapeutics. The FANG, co-chaired by NIAID and DoD, continues to focus on the product development tools and other interagency product development issues relevant to the FDA approval of Filovirus MCM. Other participating members include BARDA, CDC, and FDA. Currently, a filovirus MCM portfolio review is ongoing. Working groups meet monthly and also include BSL-4 facilities and contract research organizations. Efforts focus on developing well characterized challenge materials (WCCM), animal models, and standardized assays and understanding human disease.

DoD will continue in activities to enable MCM development, including in aerosolized and parenteral models of Ebola and Marburg infection in rhesus macaques and cynomolgus macaques. The Ebola and Marburg FilmArray diagnostic device will go through 510K clearance. These tools will allow for comparison across platforms, specifically the validation of Ebola enzyme-linked immunosorbent assay (ELISA). The DoD is establishing mechanisms to preposition drugs and diagnostics via pre-EUA.

¹²⁴ This section describes planned activities as of spring 2016. Due to the evolving nature of the Ebola outbreak response at the time of this writing, priorities may shift in order to best meet newly identified preparedness and response needs.

¹²⁵ See

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM452804.pdf>

NIAID prepared a searchable database of unpublished results from *in vitro* and *in vivo* testing of approved drugs against Ebola. This database was posted on the website of the WHO so that researchers could avoid running duplicative experiments, (T.E.4) and will be expanded to include all published data on approved drugs in a searchable format.

Ebola Therapeutics

NIH/NIAID supported the preclinical and clinical evaluation of ZMapp, a monoclonal antibody cocktail (Mapp Biopharmaceutical) for treatment of Ebola. (T.E.5) NIAID supported a multi-center Phase 1/2 trial evaluating the safety and efficacy of ZMapp in Ebola-infected patients in West Africa and the United States. DoD/DTRA supported NHP studies to assist with design of the Phase 2 clinical trial, while BARDA supported manufacture of ZMapp for the Phase 1/2 trial. BARDA is also working to optimize and accelerate ZMapp manufacturing and support regulatory and nonclinical activities.

BARDA worked with NIAID and DoD to support the development of ZMapp and assumed the lead role in supporting the manufacturing of product to make it available for clinical trials in West Africa and the U.S. BARDA continues to provide support for manufacturing of additional treatment courses of ZMapp and supports regulatory and nonclinical activities. BARDA also employed the Fill/Finish and Manufacturing Network, one of the core services offered by BARDA to fill the ZMapp product.

NIAID is supporting preclinical and clinical evaluation of antibody mAb114, isolated from a human Ebola survivor. Antibody mAb114 is unique in that as a single agent it provides 100 percent protection against NHP challenge when administered five days after infection. NIAID has accelerated development through a relationship with MedImmune and Defense Advanced Research Projects Agency (DARPA). MedImmune is conducting process development, initiated from NIAID's mAb114 Chinese hamster ovary (CHO) cell line clones, and will ultimately provide 1,000 doses of vial product. Release of the current good manufacturing practice (cGMP) manufactured material is projected for first quarter of 2017 with a Phase 1 study to be conducted by NIAID thereafter. NIAID and DARPA are actively pursuing avenues for advanced development of mAb114, including with MedImmune and other government agencies.

(T.E.6) NIAID is supporting the preclinical and clinical development of BCX4430, an RNA-dependent RNA polymerase inhibitor (BioCryst) for treatment of Ebola and Marburg. BCX4430 has shown efficacy in NHP Ebola infection models. BCX4430 is currently being evaluated in Phase 1 safety and pharmacokinetics trial in healthy human subjects. BARDA continues to work collaboratively with NIAID supporting manufacturing activities for BCX4430.

For therapeutics, NIAID support includes determination of pharmacokinetic (PK) data with existing drugs being considered for 'repurposing' as Ebola therapy, and to assist with prioritization for accelerated clinical testing. NIAID preclinical services (PCS) is also supporting PK studies of novel therapeutics candidates with promising *in vitro* activity against Ebola in order to inform future rodent and NHP efficacy studies through NIAID contracts or in collaboration with other facilities. Clinical evaluation services are offered through Vaccine and Therapeutics Evaluation Units (VTEUs), which are capable of performing Phase 1 through

Phase 4 studies in diverse populations, and Phase 1 Evaluation Units, which offer services for evaluation of safety and pharmacokinetics for therapeutics in development.

BARDA has formed a partnership with Regeneron to support development of their cocktail of human monoclonal antibodies (REGN3479-70-71) generated against the current outbreak strain of Ebola. Unlike the ZMapp product, the Regeneron product is manufactured in CHO cells and has been manufactured under cGMP at commercial scale. BARDA has supported the non-clinical evaluation, manufacturing and is supporting the Phase I study to start in FY 2016. Regeneron offers a rapid platform for developing human antibodies against emerging infectious disease pathogens.

BARDA utilized the CIADM in a partnership with Genentech to support manufacturing activities of their humanized versions of the antibodies that comprise ZMapp. Under this partnership, BARDA worked with Genentech to transfer the cell clones to the CIADM for further characterization and large scale manufacturing of material. The product will be evaluated in non-clinical studies using another of BARDA's core services: the Nonclinical Development Network.

BARDA is supporting two additional companies that produce products in tobacco plants. BARDA is supporting Medicago and Fraunhofer to express ZMapp clones in their proprietary expression systems and plants. BARDA, Medicago, Fraunhofer and Mapp Bio have worked in a collaborative effort to evaluate manufacturing in other tobacco based plant systems. Small scale quantities of product will be made and evaluated under the BARDA Nonclinical Development Network.

(T.E.7) DoD will continue testing and evaluating broad-spectrum anti-virals against additional members of the Filovirus (Ebola, Marburg, etc.) and Alphavirus (Venezuelan equine encephalitis (VEE), Western equine encephalitis (WEE), etc.) families.

Ebola Vaccines

(T.E.8) NIAID is supporting development of multiple vaccines, therapeutics and diagnostics through PCS and Clinical Evaluation network. PCS evaluate therapeutics and vaccines efficacy and PK data.

Through NIAID's PCS, over 24 Ebola vaccine formulations from nine institutions have been screened for efficacy in the NHP model. This effort was critical for generating data to support the selection of candidates for advanced product development and clinical development. This led to a partnership between Crucell/Janssen/Johnson & Johnson (J&J) and BN for the development of the Ad26/ MVA-BN Filo prime-boost combination. The Ebola virus glycoprotein recombinant (rGP) nanoparticle vaccine candidate adjuvanted with Matrix-M is currently under development by Novavax. Novavax has sponsored a Phase 1 trial in Australia and NIAID subsequently evaluated this vaccine in NIAID's Preclinical Services. NIAID continues to support evaluation of the monovalent rGP/Matrix-M in the NHP model.

NIAID is supporting, through targeted product development projects and previously existing preclinical resources, preclinical services, and clinical testing of monovalent Ebola vaccine and multivalent vaccines against Zaire and Sudan strains of Ebola and Marburg, including:

- (T.E.9) NIAID/GSK's chimp adenovirus (cAd3) vectored Ebola vaccine cAD-EBOZ - Phase 1 trials of ChAd3 vectored vaccine began in 2014 at the NIH. Phase 2/3 trial began in Liberia in February 2015.
- (T.E.10) VSV vectored Ebola vaccine VSV-ZEBOV (NewLink Genetics/Merck) - Phase 1 trials began in October 2014. Phase 2/3 trial began in Liberia in February 2015.
- (T.E.11) A heterologous prime-boost combination of adenovirus 26-vectored vaccine Ad26.ZEBOV (Crucell/Janssen/J&J) and a MVA-vectored vaccine (MVA-BN Filo, BN). NIAID continues to support preclinical, manufacturing and Phase 1 clinical trials in the United States. Other Phase 1 clinical trials are ongoing in the U.K., and Africa. Phase 2 clinical trial is ongoing in Africa, the U.K., and France.
- (T.E.12) A heterologous prime-boost combination using two adenovirus vector platforms, Ad26 and Ad35, against Sudan and Zaire strains of Ebola and Marburg (Crucell/Janssen/J&J). NIAID currently supports the Ad26/Ad35 preclinical development and manufacturing.

(T.E.13) NIAID is supporting the development of other Ebola and Marburg vaccine candidates currently in Phase 1, including MVA-BN Filo in combination with GSK's ChAd3 vectored Ebola vaccine (BN), a nanoparticle based Ebola vaccine (Novavax), a VSV-based Ebola vaccine (Profectus Biosciences) and a parainfluenza type-3 based Ebola vaccine (NIAID/University of Texas).

(T.E.14) NIAID is also supporting development of a number of preclinical vaccine candidates including an adenovirus 5 (Ad5)-based intranasal vaccine, a Virus-like Particles (VLP)/DNA combination Ebola vaccine to be administered via a microneedle patch; an Ebola/Marburg DNA vaccine; a MVA-based Ebola vaccine that generates VLPs with Ebola glycoprotein on their surfaces; and a prime-boost combination of MVA-BN Filo and Fowlpox multivalent vaccine against Marburg, Ebola and Sudan viruses. NIAID, in collaboration with investigators at Thomas Jefferson University, created a dual-purpose candidate vaccine to simultaneously protect against both rabies and Ebola viruses. The vaccine candidate is being further developed through a partnership with IDT Biologika and has been licensed to Excell BIO of Saint Paul, Minnesota, for clinical testing and commercialization. NIAID and DoD are partnering with Thomas Jefferson University researchers to support production of sufficient quantities of the candidate to begin clinical testing.

(T.E.15) NIAID continues to support development of challenge materials and reagents, animal model development, assay development and standardization, screen novel vaccine platforms for efficacy, and coordinate BSL-4 efforts. NIAID's Preclinical Services support five task orders to advance filovirus vaccines. These include 1) Efficacy Testing of Filovirus Vaccines in Non-Human Primates, 2) Development of Standardized Filovirus Immune Assays and Reagents, 3) In vitro prediction of filovirus vaccine immunogenicity (Ad26/MVA) and efficacy in humans, 4) Evaluation of Filovirus Vaccines in a General Use Prophylaxis (GUP) Immunogenicity and Ebolavirus Challenge Studies to Identify Potential Correlates of Protection, and 5) Evaluation of Ebolavirus and Other Filovirus Vaccines in a Novel Ferret Model.

BARDA is currently supporting four Ebola vaccine candidates.

- BARDA is supporting GSK's chimp adenovirus vectored Ebola virus vaccine (cAD-EBOZ). BARDA is supporting manufacturing activities to increase and validate the commercial manufacturing process and make sure that vaccine doses are available for clinical trials.
- BARDA is supporting NewLink Genetics/Merck's VSV vectored Ebola vaccine VSV-ZEBOV. BARDA has provided support for manufacturing, scale up, and multiple clinical trials including a recent Phase 3 lot-to-lot consistency trial to support potential licensure of the vaccine. BARDA also provided support under the Clinical Studies Network, another of BARDA's core services, to support the CDC sponsored STRIVE study in Sierra Leone. BARDA supported the clinical research organization that managed the trial and also provided logistics and cold chain support on the ground in West Africa for shipment and storage of vaccines.
- BARDA is currently supporting the prime/boost vaccine manufactured by Crucell/Janssen/J&J and BN (highlighted above under NIAID efforts). BARDA is complementing the work supported by NIAID and focusing on manufacturing scale-up and validation of the manufacturing process.

BARDA has worked collaboratively with DoD to support Profectus in the development of its Ebola vaccine candidate. BARDA has provided funds to support manufacturing activities and will transfer product to the DoD for use in clinical studies.

The rVSVΔG vaccine for Ebola Virus has proven safety and efficacy in human clinical trials and is on track to be submitted for FDA licensure. A rVSVΔG multivalent Filovirus vaccine (Ebola virus, Sudan virus, and Marburg virus) will be pursued via the following critical milestones: 1) a pre-Investigational New Drug (IND) submission in late 2016; 2) complete current Good Manufacturing Practice (cGMP) toxicity studies to support a Phase 1 trial in late CY 2017; and 3) initiate Phase 1 clinical trials in 2018.

Ebola Diagnostics

In collaboration with other PHEMCE partners, FDA continues to support diagnostic development and the availability of diagnostics for Ebola virus under EUA. BARDA is supporting OraSure Technologies, Inc. for the development of a rapid, point-of-care (POC) diagnostic test for Ebola (the OraQuick® Ebola Rapid Antigen Test). In July 2015, FDA issued an EUA for OraSure, a [whole blood POC diagnostic](#) being field-tested in West Africa.¹²⁶ In March 2016, FDA issued an EUA for the emergency use of this assay with [oral fluid swabs](#) for cadaver management.¹²⁷ CDC worked with industry on preclinical and field testing of the OraQuick® Ebola Rapid Antigen Test. BARDA continues to support development of the diagnostic to expand the performance and ability to test other bodily fluids.

(T.E. 16) CDC and NIAID will continue to study the pathogenic properties of the new West African Ebola virus isolates compared with previous outbreak isolates and to support rapid

¹²⁶ See: <http://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM456909.pdf>

¹²⁷ See: <http://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM489304.pdf>

assessment of promising antiviral therapeutics. CDC and NIAID will also work on (T.E.17) development and validation of rapid (i.e., POC) Ebola diagnostic assays and multiplex assays for differential diagnosis and to guide patient care in Africa; (T.E.18) deep sequencing analysis of Ebola virus isolates and clinical material for microvariant genotypes of virus isolates from the West African outbreak; (T.E.19) and the development of experimental animal models (including ferrets, guinea pigs, and other rodent models) to analyze transmission, pathogenesis, and MCM effectiveness against West African Ebola viruses compared to previous outbreak isolates. CDC sequenced 200 Ebola genomes in FY 2015.

Lassa virus assay will be developed as a research use only assay on the FilmArray for the U.S. Army Medical Materiel Development Activity fever panel. (C.D.8) DoD is coordinating with NIAID to include Ebola virus, Marburg virus, *B. anthracis*, and other biological warfare agents on the same fever panel.

Mid-term (FY 2019-20)

Vaccines and Therapeutics

(T.E.20) DoD will continue to invest in prophylactic MCMs against the Filovirus family and other emerging viral threats. Efforts will focus on discovery and development of a new generation of novel prophylaxes against pan-viral biological warfare threats (e.g., filovirus, alphavirus and emerging viruses). Nontraditional approaches to antiviral protectants using both specific countermeasures (vaccines, immunoglobulins) and non-specific countermeasures that effectively activate the immune system will be pursued with an emphasis on production of mosaic antigenic proteins for use in broad spectrum vaccines for viruses.

Ebola Personal Protective Equipment

(T.E.21) The CDC National Institute for Occupational Safety and Health (NIOSH) and DSNS are refining the NIOSH [PPE-Info database](#)¹²⁸ to provide a tool by 2016 for end-users to quickly identify gowns and coveralls on the market that meet CDC PPE guidance for handling Ebola patients or patients under investigation.

Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

MERS-CoV was first identified in Saudi Arabia in 2012, and HHS declared that MERS-CoV posed significant potential for a public health emergency that justified authorization of emergency use of diagnostics in 2013.¹²⁹ As such, the PHEMCE has supported efforts to address MERS-CoV as a potential emerging threat. Human-to-human transmission of this virus is not fully understood, but some MERS-CoV cases appear to potentially have resulted from contact with infected animals (e.g., camels); when human-to-human transmission has occurred,

¹²⁸ A compendium of federal regulations and consensus standards for Personal Protective Equipment (PPE), is available at: <http://www.cdc.gov/ppepros>

¹²⁹ The HHS declaration of [MERS-CoV as a public health threat](#) available at: <http://www.phe.gov/emergency/news/healthactions/phe/Pages/MERS-CoV.aspx>

it has tended to be through close contact, such as caring for or living with an infected person. Infected people have spread MERS-CoV to others in health care settings, such as hospitals. Researchers studying MERS have not seen any ongoing spreading of MERS-CoV in the community. So far, all cases of MERS have been linked through travel to or residence in countries in and near the Arabian Peninsula. The largest known outbreak of MERS outside the Arabian Peninsula occurred in the Republic of Korea in 2015 and was associated with a traveler returning from the Arabian Peninsula. As of this writing there have been only two imported cases in the U.S. (i.e., in Indiana and Florida in 2014) with no further transmission.

(T.MC.1) DoD's WRAIR, in a collaboration developed through the International Vaccine Institute, Korea, is working with Inovio and GeneOne Life Sciences to execute the first in human Phase 1 study of a DNA MERS-CoV vaccine. The study is enrolling and will continue at WRAIR's Clinical Trials Center.

NIAID will continue to support activities to address MERS-CoV as a public health threat:

(T.MC.2) maintenance of an active grant portfolio supporting basic research into MERS-CoV natural history, virology, and pathogenesis; *(T.MC.3)* and basic and preclinical research into the development of novel vaccines and therapeutics for MERS. NIAID supported preclinical safety studies for a polyclonal antibody therapeutic (Sanford Applied Biosciences). A Phase 1 clinical trial (Safety, Tolerability, and Pharmacokinetics of SAB-301 in Healthy Adults) conducted by NIAID at the National Institutes of Health Clinical Center started in May 2016 with an estimated completion date of April 2017. Sanford Applied Biosciences submitted an IND package to FDA in March 2016 in support of the clinical trial. *(T.MC.4)* NIAID will continue to support development of transgenic mouse and other relevant animal models for MERS-CoV infection. NIAID supported the development of two new mouse models and two nonhuman primate models. These models will be used to perform exploratory activity studies for novel vaccines and therapeutics. *(T.MC.5)* NIAID will continue awarding contracts for screening MCMs against MERS-CoV *in vitro* and *in vivo*.

(T.MC.6) CDC conducts domestic surveillance and will continue to be engaged with countries in or near the Arabian Peninsula, including deploying teams to assist as requested in MERS-CoV outbreak investigation and control and to continue ongoing epidemiology studies.

(T.MC.7) Reinforcing awareness of the MERS-CoV potential threat, CDC will continue measures for border screening and travel notices including:

- Reinforcing guidance for CDC Quarantine Station staff to assess ill travelers for MERS-CoV, provide them with informational cards if case definitions are met, and coordinate with health departments if emergency medical transport is needed;
- Reminding airlines of the need for vigilance for recognizing ill travelers on flights from the Arabian Peninsula and to report to CDC under existing procedures;

- Continuing the travel notice to practice enhanced precautions (i.e., Level 2: Alert) currently on the CDC [Travelers Health website](#);¹³⁰ and,
- In an effort to continue reinforcing awareness of the MERS-CoV potential threat, DHS Customs and Border Protection, using just-in-time training (called “musters”), developed in coordination with CDC, should enhance vigilance for travelers with overt signs of illness at U.S. international airports.

BOTULISM

PHEMCE botulism activities include:

- Establishing and maintaining a long-term supply of heptavalent botulism antitoxin (BAT)
- Developing next-generation botulism therapeutics that offer reduced manufacturing and storage costs

Near-Term (FY 2017-18)

(T.B.1) NIH continues to support development of next-generation botulism antitoxin mAb. A botulism serotype A anti-toxin mAb cocktail has completed Phase 1 trials with NIH support, while botulism serotype B&E anti-toxin mAb cocktails are expected to enter Phase 1 trials in 2016. A serotypes C&D anti-toxin mAb cocktail is nearing completion of IND-enabling activities. Serotype F&G anti-toxin mAb candidates are undergoing final selection.

CDC has determined that BAT completely eliminates the toxic effect of botulinum toxin A/F (previously identified by California Department of Public Health (CDPH) as serotype H) in mice.

(T.B.2) NIH will continue to support the manufacture of a newly identified botulinum toxin, Bot A/F, to enable PHEMCE partners to test efficacy of licensed BAT therapeutic, and candidate anti-Botulism mAbs that are currently in development.

(3.2.6) CDC will develop clinical guidelines for clinicians to assist with the identification and treatment of botulism. *(T.B.3)* DTRA JSTO and NIH will continue R&D for novel next-generation therapeutics. *(T.B.4)* DoD will invest in prophylactic MCMs that rapidly and durably protect against Botulinum neurotoxin with minimal doses. Near-term efforts focus on FDA licensure of vaccines capable of protecting against inhalational disease resulting from exposure to Botulinum neurotoxin A and B. Additional investments include development of vaccines against additional botulinum toxin serotypes other than A/B and mAb-based antitoxins against multiple serotypes of botulinum neurotoxin. *(T.B.5)* ASPR will evaluate the potential for transferring skilled staff (e.g., respiratory therapists) from other jurisdictions to supplement areas where there is not adequate staffing to improve treatment capabilities in a botulism public health response.

¹³⁰ More information on travel notice definitions is available at <http://wwwnc.cdc.gov/travel/notices#travel-notice-definitions>

Mid-Term (FY 2019-20)

(T.B.6) BARDA will support the advanced development of the next-generation monoclonal antibody product(s) as they become eligible for transition from NIH to ensure that the MCM meets the PHEMCE requirement for a large-scale foodborne scenario. (T.B.7) DoD will continue to invest in prophylactic MCMs against Botulinum neurotoxin exposure. Efforts will focus on continued development of pretreatment strategies for small molecule inhibitors of multiple serotypes of botulinum neurotoxin intoxication by targeting the host's critical signaling pathways.

(T.B.8) Based on the results of the botulism MTA 2.0 assessment, the PHEMCE will examine monitoring and assessment capabilities for various scales of incident. (T.B.9) In addition, ASPR will lead an economic analysis of the potential benefits of next-generation MCMs based on the MTA 2.0 assessment.

RADIOLOGICAL AND NUCLEAR THREATS

PHEMCE activities for radiological and nuclear threats include:

- Elucidating mechanisms of radiation injury at the system, organ, cell, and molecular levels, with special focus on the hematopoietic, gastrointestinal, immune, pulmonary, renal, skin, neurological, and vascular systems;
- Identifying and characterizing MCM approaches to minimize the short- and long-term adverse health effects of radiation exposure, including cytokines, growth factors, anti-apoptotics, anti-inflammatory agents, and antioxidant candidates, as well as products with other novel mechanisms of action;
- Emphasizing candidates that have routine medical/clinical indications and can be administered effectively under current or anticipated CONOPs;
- Developing definitive-care treatments for thermal burns, as well as providing incentives, through public-private partnerships, for companies developing thermal burn and other nuclear and radiological exposure treatments to continue commercial development while meeting civilian emergency preparedness requirements.

Near-Term (FY 2017-18)

(1.3.3f) NIAID's Radiation Nuclear Countermeasures Program (RNCP) will continue funding research to elucidate mechanisms of radiation damage; identify and characterize new MCMs to increase survival and mitigate radiation injuries; and advance promising MCM candidates towards FDA licensure. (1.3.3h) In addition, RNCP will continue to explore new biomarkers and biodosimetry approaches that are predictive of organ and tissue damage from acute radiation exposure. The activities of the recently re-competed NIAID Centers for Medical Countermeasures against Radiation Consortium and Product Development Support Services contract will be integral in this effort. The RNCP will employ broad-based product development capabilities to continue the evaluation and development of more than 17 promising MCM candidates for mitigation of hematopoietic, gastrointestinal and lung radiation injuries, for

anticipated transition to BARDA between 2017 and 2020. In addition, approximately 150 MCMs continue to be pursued within the RNCP portfolio for early research and development.

(T.RN.1) NIAID will develop and release new initiatives for FY 2017 awards that include a BAA to support IND-enabling studies for promising MCMs and biodosimetry approaches, as well as a grants solicitation to support the characterization and mitigation of radiation-induced endothelial cell and vascular injuries. FY 2018 initiatives are also planned for studies related to the use of cell therapies to treat radiation injuries.

(T.RN.2) NIAID will organize conferences and workshops to enhance communications of the state of science, identify research gaps, and to discuss topics/issues important to MCM and biodosimetry research and development. Results of workshops will be submitted to peer-reviewed journals for publications. A workshop on program-wide Standardization of Radiation Dosimetry will be held to establish capabilities to guide and monitor radiation exposure and dosimetry in NIAID-funded research and development facilities. NIAID and Radiation Injury Treatment Network are co-sponsoring two symposia in 2016: Radiation Medical Management as a Function of Concept of Operations (July 2016) and Late Effects of Acute Radiation Exposure (November 2016).

(T.RN.3) The PHEMCE will conduct market analyses on antimicrobials and other products needed to respond to the public health and medical consequences of radiological or nuclear threats. These analyses will include gap analyses and determination of market capacities to inform strategic national stockpiling.

Medical Countermeasures for ARS and the Delayed Effects of Acute Radiation Exposure (DEARE)

NIAID-supported preclinical studies led to successful IND submission for clinical development of a novel decorporation agent (Hydroxypyridinone, HOPO) as well as for a cellular product (PLX-R18) to address incomplete bone marrow recovery following hematopoietic cell transplant. The first-in-human Phase 1 studies for these two agents will proceed in near future.

NIH has identified more than 75 candidate MCMs in the early discovery phase for hematopoietic ARS. NIH has also identified more than 15 candidates in the early discovery phase for gastrointestinal ARS and more than five candidates in the early discovery phase for the treatment of pulmonary radiation injuries. *(T.RN.4)* NIH will continue to evaluate and develop these candidates toward IND submission. Successful candidates will be identified that can move forward to BARDA for potential advanced development. Beginning in 2018, DoD will consider new research, development, test, and evaluation investments to address priority gaps in MCMs and monitoring/surveillance, leveraging investments by HHS towards developing MCMs against the sub-syndromes of ARS.

BARDA continued market research and end-user engagements on drugs that may be available to treat conditions that may result from exposure to ionizing radiation or chemical agents. In addition, when promising candidates were identified, BARDA met with these companies to determine their level of interest in working together. *(T.RN.5)* BARDA will support evaluation of a number of commercial drugs for repurposing to enable use in the treatment of exposure to radiological and nuclear agents, ensuring that at-risk population needs are considered.

(T.RN.6) BARDA will also support the advanced research and development (ARD) of novel compounds for PEP and treatment of blood, gastrointestinal, lung, and skin exposures from radiological and nuclear insults.

DoD's Joint Requirements Office actively participates on the Radiation and Nuclear (Rad-Nuc) IPT and coordinates with other parts of DoD, specifically, the AFRRRI, JSTO and the Joint Program Executive Office for Chemical and Biological Defense. HHS and DoD monitor candidate identification and tracking development efforts as products mature.

Thermal Burn Therapeutics

(T.RN.7) BARDA will assess results from the current proof-of-concept studies for promising candidates for thermal burn injuries and continue to support the development of thermal burn definitive care products. BARDA transitioned for ARD or engaged with developers to support four new MCMs under PBS in FY 2015. These included: a silver impregnated field dressing, enzymatic debridement technologies, cell-based skin substitute, and donor tissue sparing technologies to address the continuum of care that is necessary for individuals with burn injuries. The goal of the suite of products is to improve the care and potential outcome of patients with burn injuries. BARDA is also working closely with the American Burn Association to increase clinical use of these, and other, products where appropriate in the every day care of burn patients to increase the commercial viability of the products and companies.

Decorporation and Blocking Agents

(T.RN.8) NIH will explore new decorporation agents for radionuclides of current interest and explore candidate MCMs that increase the mucociliary clearance of particulates from the lung.

(T.RN.9) BARDA will continue to support ARD of Prussian blue dosage forms appropriate for children under the age of two years. (T.RN.10) The PHEMCE will also biannually re-evaluate the prioritization, with the PHEMCE Prioritization Framework, of resources to support additional national radiobioassay capabilities that would be critical to informing the appropriate use of decorporation agents following a radiological incident. (T.RN.11) CDC, with ASPR support, is working to develop CONOPs for use of MCMs following a radiological dispersal device (RDD). Once this is completed, it will be incorporated into a public health response model.

(1.2.2) DHS and HHS will conduct an MTA 2.0 assessment for RDD.

Mid-Term (FY 2019-20)

Medical Countermeasures for ARS and DEARE

(T.RN.12) NIH will continue to evaluate additional candidates for hematopoietic ARS, gastrointestinal ARS, and pulmonary and cutaneous radiation injuries in rodent, swine, canine and non-human primate animal models, and in IND-enabling studies. Successful candidates will be identified that can move forward to BARDA for potential advanced development.

(T.RN.13) Rodent and NHP animal models are being further developed and will be submitted to the FDA for qualification, for use under the "Animal Rule," to be used when appropriate as available models for the adequate and well-controlled animal efficacy studies.

Decorporation and Blocking Agents

(1.2.7) The PHEMCE will use the results of the RDD MTA 2.0 to establish need-based quantity and operational capacity, stockpiling goal, and assess market capabilities to ensure sufficient quantity of Prussian blue would be available. (T.RN.14) ASPR/CDC/NIH will develop additional public messages (e.g., risk of exposure, candidacy for Prussian blue) and post on Radiation Emergency Medical Management and CDC websites. (T.RN.15) In addition, CDC will develop an exercise and training package for RDD scenarios, including operational capacity considerations.

Long-Term (FY 2021 and beyond)

In the long term, BARDA will emphasize achieving regulatory approval of MCMs for use in treating injuries from radiation exposure.

Medical Countermeasures for ARS and DEARE

BARDA will work to maintain the current inventory of anti-neutropenic products for the SNS and work toward procurement of additional products as they mature to address other sub-syndromes of DEARE. Using appropriate animal models, BARDA will support studies to obtain additional data to support pre-EUA applications and ultimately regulatory approval for these products.

Decorporation and Blocking Agents

ASPR and CDC will develop a tiered response strategy that includes how assay (detection and diagnosis tools) would be used (including risk factors such as likely exposure to agent and onset of potential symptoms) for various scales of emergencies. ASPR and CDC will investigate options to increase capacity to determine the best way to assess level of internal contamination, and candidacy and duration for Prussian blue intervention. BARDA will monitor programs under development at NIH to determine if and when they may be eligible for transition to BARDA.

CHEMICAL THREATS

The HHS PHEMCE chemical activities include:

- Developing in vitro and animal models for efficacy screening of novel therapeutics
- Developing MCMs for the treatment of injuries caused by exposure to chemical threats, with an emphasis on products that can be administered effectively under current or anticipated CONOPs
- Maintaining public-private partnerships with companies developing chemical agent treatments
- Developing improved decontamination guidance for first responders

Near-Term (FY 2017-18)

(T.C.1) NIH will support investments against classical chemical agents (e.g., nerve agents and vesicants) and toxic industrial chemicals (TICs). Included are compounds that can damage the

nervous system, respiratory tract, skin, mucous membranes, and other organs. Research on classical chemical agents is being supported by the NIH grant and contract programs, as well as the extensive Interagency Agreement (IAA) with the U.S. Army Medical Research Institute of Chemical Defense. In 2015, new NIH CounterACT publications covered brodifacoum, chlorine, cyanide, hydrogen sulfide, organophosphate pesticides, sarin, and soman agents.

In 2015, the NIH CounterACT program made several new discoveries about important chemical agents. Based on similarities between the mechanisms that underlie the toxicity of cyanide and hydrogen sulfide, work on antidotes that are effective for both of these chemical threats is underway. Mechanistic research was shared at the NIH CounterACT annual meeting at Rutgers University & New York Academy of Science in June 2015. (1.3.3j) NIH is now supporting investigation of blocking arsenicals-induced cutaneous injury, development of the vitamin B12 analog cobinamide as a hydrogen sulfide antidote, mechanisms and treatment strategies for bromine inhalation-induced lung injury, molecular imaging of chemical threats and countermeasures, and mechanisms and countermeasures of halogen-induced injury to pregnant mice.

Researchers within the NIH CounterACT network have advanced translational research based on a solid foundation of basic knowledge on chemical threats. (1.3.3k) The program will continue to support research on target identification for new therapeutics, safety, and efficacy re-purposing studies of FDA-approved drugs, and developing large and small animal models on the pathophysiology of new and emerging chemical threat agents. Animal models include short-term toxicity, as well as long-term non-lethal effects of chemical agents. A systematic review of the long-term effects of sarin nerve agent in humans and animal models was initiated by NIH in 2015 and will be incorporated in a White Paper on the long-term effects of nerve agents. NIH is supporting the investigation of treatments of soman toxicity, therapies for ocular mustard gas exposure and other chemical injuries, and use of atropine for chlorine inhalation toxicity.

A current FDA-approved cyanide antidote is called Nithiodote. It includes sodium thiosulfate and sodium nitrite, which are given intravenously after cyanide poisoning. In 2015, NIH investigators discovered that these active components of Nithiodote can be just as effective in pigs, rabbits, and mice when administered by a much more rapid intramuscular injection. The NIH CounterACT program includes small and large grants focused on cyanide, and a Research Center of Excellence at Harvard University. (T.C.2) The NIH will continue its support of research on cyanide antidotes, including those that are more effective and easily administered.

(T.C.3) BARDA and DoD are supporting advanced development of promising anticonvulsants, such as midazolam, as potential replacements or supplements for diazepam for the treatment of nerve agent-induced seizures.

(T.C.4) BARDA will continue to support the ARD of novel compounds for treatment or PEP following exposure to chemical agents. (T.C.5) BARDA will also evaluate commercially available drugs using animal models to determine if their approved use can be expanded to the treatment of chemical exposures.

(T.C.6) In addition, BARDA will continue to support the development of MCMs to treat injuries due to exposure to chemical agents. (T.C.7) The DoD will conduct clinical trials to evaluate the effectiveness of its Improved Nerve Agent Treatment System (INATS). INATS is intended to

replace the current Antidote Treatment – Nerve Agent, Auto-Injector (ATNAA), consisting of atropine and pralidoxime. The design of the new system will be more efficacious, requiring fewer treatments than ATNAA, and to be effective against a broader range of nerve agent threats. The DoD is developing a centrally acting anti-muscarinic adjunct to the nerve agent treatment regimen. *(T.C.8)* The DoD will also continue advanced development of its Bioscavenger, a novel prophylactic treatment against the effects of nerve agents. *(T.C.9)* BARDA, DoD, and CDC will continue to plan and coordinate mitigation options to address potential auto-injector shortages. DoD will conduct threat agent science studies and complete initial risk assessment for pharmaceutical-based agents to inform future investments.

(T.C.10) ASPR will develop, with PHEMCE partners, recommendations for patient decontamination research to be undertaken and publish the results in a journal to inform researchers and clinicians.¹³¹ BARDA supported the University of Hertfordshire to develop improved decontamination procedures for first responders. The initial guidance was made available to first responders. *(T.C.11)* BARDA is working with the University of Hertfordshire on a subsequent project to extend the earlier research and in turn revise the initial guidance for first responders.

(T.C.12) ASPR and CDC will develop a stockpiling and deployment strategy for cyanide antidotes.

Mid- and Long-Term (FY 2019 and beyond)

NIH will focus research efforts on highly toxic chemicals of greatest public health concern. This will include an emphasis on TIC exposures, such as industrial chemicals and pesticides. Planned activities include: (1) integrating research of potential products into evolving standards of emergency care; (2) assessing products already approved for use in the U.S. for applicability to chemical casualty care; (3) assessing products from military applications for civilian use; and (4) developing and/or improving medical diagnostic tests and assays to detect the presence of specific chemicals or their metabolites in bodily fluids.

BARDA will support the ARD of novel compounds for PEP and treatment following exposure to chemical agents—placing emphasis on achieving regulatory approval of products for use in treating injuries due to chemical agent exposures. BARDA will also support the repurposing of commercial products approved for other uses for potential use as treatments for exposure to chemical agents.

DoD continues to support the development of improved treatments to chemical threats of concern for the Armed Forces, to include the discovery and development of new countermeasures for emerging threats. DoD will continue to evaluate MCM against chemical threats other than nerve agents, and aims to field medical solutions towards novel threats.

¹³¹ More information on patient decontamination efforts is described in the Capabilities-Based Approaches section below as a non-pharmaceutical MCM.

SECTION 3: CAPABILITIES-BASED APPROACHES

The PHEMCE continues to emphasize programs that will provide more flexible and sustainable capabilities over the long term. The promotion of technologies that have more than one application, and/or of infrastructures that can rapidly adjust to new demands and respond to new threats best reflects this approach. This evolution is highly dependent on early-stage research and early identification of biotechnologies that may already be applied in routine product development. NIH, DoD, and BARDA programs on platform technologies and broad-spectrum approaches are thus key to fueling this early pipeline. Similarly, efforts underway at BARDA and DoD are critical in advancing the nation's capability to build and sustain a flexible manufacturing and development infrastructure, as well as in identifying products that may be repurposed or altered to meet PHEMCE needs. In addition to the many cross-cutting capabilities described in Section 1 with respect to the strategic goals and objectives they address, this section highlights several specific examples of these capabilities-based approaches.

COMBATING ANTIBIOTIC-RESISTANT BACTERIA (CARB)

In September 2014, President Obama issued EO 13676, [Combating Antibiotic-Resistant Bacteria](#), which, among other activities, directed the PHEMCE to develop new and next-generation countermeasures that target antibiotic-resistant bacteria that present a serious or urgent threat to public health.¹³² This EO resulted in the [National Strategy for Combating Antibiotic-Resistant Bacteria](#)¹³³ and the [National Action Plan for Combating Antibiotic-Resistant Bacteria](#).¹³⁴ The PHEMCE agencies are heavily engaged in these activities.

(C.AR.1) NIH and BARDA will continue to expand their broad-spectrum antimicrobial programs to address both biothreat indications and the more general public health concern of antimicrobial resistance. BARDA currently supports six different programs and has utilized the OTA authority provided under the PHS Act to partner with two large pharmaceutical companies in the development of novel antimicrobial drugs, and anticipates submission of two NDAs to FDA in 2016. *(C.AR.2)* BARDA is specifically called upon by the EO, in addition to targeting biodefense threats, to develop new and next-generation countermeasures that target antibiotic-resistant bacteria that present a serious or urgent threat to public health.

BARDA has initiated its AMR diagnostics program and supports development of multiple new AMR diagnostic tools in the near term, including point-of-care viral and bacterial diagnostics,

¹³² Combating Antibiotic Resistant Bacteria is available at <https://www.whitehouse.gov/the-press-office/2014/09/18/executive-order-combating-antibiotic-resistant-bacteria>

¹³³ The National Strategy for Combating Antibiotic-Resistant Bacteria is available at https://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf

¹³⁴ The National Action Plan for Combating Antibiotic-Resistant Bacteria is available at http://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf

rapid phenotypic AMR diagnostics, rapid molecular AMR diagnostics, and sequencing-based platforms that are simplified for ease of use in clinical settings.

NIAID's goals of advancing basic, translational and clinical research to develop better ways to prevent, diagnose, and treat antibiotic-resistant bacteria are furthered by the objectives and milestones within the National Action Plan for Combating Antibiotic-Resistant Bacteria.

(C.AR.3) NIH is working with CDC and FDA to develop a National Sequence Database of Resistant Pathogens and to sequence additional reference strains of resistant bacteria.

(C.AR.4) NIAID issued an RFA to solicit research programs that use systems biology to identify new drug targets that can be used to develop antibiotics with modes of action that make the development of resistance less likely.

(C.AR.5) In June 2015, [NIH issued a Request for Information \(NOT-OD-15-104\)](#)¹³⁵ to obtain comments to inform development of a prize competition for AMR rapid, POC diagnostic test(s).

In October, 2015, [NIH and BARDA convened a public consultation to seek comments regarding the technical criteria and performance characteristics of the diagnostic\(s\) for which the prize\(s\) will be offered](#),¹³⁶ NIH and BARDA discussed the need for rapid AMR diagnostics with the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria Working Group #3 – Diagnostics Innovations.

The Challenge Competition Announcement has been developed taking into consideration the stakeholder input and was released in September 2016. In addition, BARDA re-issued BAAs, which included emphasis on CARB.

BARDA will continue to stimulate the antibacterial pipeline by forming public-private partnerships with companies engaged in the research and development of novel antibacterials. BARDA will explore collaborations with the New Drugs 4 Bad Bugs programs of the Innovative Medicines Initiative. Currently, BARDA has six partnerships through which it has funded development of eight candidate antibacterials; four are in Phase 3 clinical development.

(C.AR.6) In the near term, BARDA intends to diversify its portfolio by making initial investments in nontraditional antibacterial therapies (e.g., antibody or microbiome approaches) and products that can prevent infection upon entry into a hospital setting or reduce the length of a hospital stay.

DoD, HHS, and USDA co-chair a CARB task force that is in the process of developing policy and implementation guidance to support all aspects of the [National Strategy for Combating Antibiotic-Resistant Bacteria](#). (C.AR.7) The Task Force provided its initial 180-day update on time and will make any necessary updates in the fall of 2016.

WRAIR maintains a repository of more than 30,000 well-characterized multidrug resistant organism isolates to support countermeasure R&D. (C.AR.8) A novel topoisomerase small molecule broad-spectrum therapeutic against a panel of MDR clinical pathogens, including demonstrated efficacy against *Burkholderia pseudomallei* and MDR *Yersinia pestis*, will be

¹³⁵ See: <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-104.html>

¹³⁶ See: <https://dpcpsi.nih.gov/sites/default/files/AMR%20Public%20Consultation%20Meeting%20Summary%20FINAL.pdf>

submitted to FDA by FY 2017. A NDA is anticipated in approximately FY 2021. Preclinical evaluation for proof of concept efficacy against anthrax and tularemia small animal models of infection was completed in the first quarter of 2016. Proof of concept efficacy was demonstrated for both pathogens. Pivotal NHP studies for tularemia will be initiated in the first quarter of 2017 and anthrax studies will be initiated in the second quarter of 2017. Advanced pre-clinical testing, to include manufacturing, safety, and additional *in vivo* activity studies, is underway. A thorough QT evaluation trial in humans was conducted in the fourth quarter FY 2015 and evaluated by a QT review committee and the QT Interdisciplinary Review Team at the FDA. Appropriate correction methods were used to compensate for changes in heart rate and (corrected) results were within the FDA limits for chronic use in humans.

To support the development of diagnostics to improve treatment of antibiotic-resistant bacteria, enhance infection control, and facilitate outbreak detection as described in the National Action Plan for CARB, the CDC, in collaboration with FDA will use its expertise and core strengths to (C.AR.9) expand the Resistant Bacteria Bank and provide well-characterized and curated bacterial isolates to aid development of antibiotics and diagnostics; (C.AR.10) contribute data to the National Sequence Database of Resistant Pathogens; and (C.AR.11) advance development and use of rapid and innovative diagnostic tests in collaboration with DoD. The Antimicrobial Resistance Isolate Bank will be a unique centralized, curated collection of samples that are available to pharmaceutical companies, biotech and diagnostic companies, and researchers. (C.AR.12) JSTO will conduct a study on the feasibility of integrating identification of antimicrobial resistance into future diagnostic systems. Results will include data from CDC efforts.

(C.AR.13) BARDA and NIAID work with a consortium of industry partners to establish and operationalize the Antibiotic Resistance Biopharmaceutical Incubator (Accelerator) to accelerate drug development. BARDA and NIAID will develop mechanisms for improving options to clinical testing for antimicrobial therapeutics that currently are disadvantaged by limited access to small sample sizes, urgent need for patient treatment, and diagnostic uncertainty of causative agent (e.g., new clinical trials network). (C.AR.14) NIAID will also improve or expand opportunities in the pre-competitive space for industry and others to increase options for new antimicrobial compounds.

CHEMICAL, BIOLOGICAL, RADIOLOGICAL, AND NUCLEAR DIAGNOSTICS

PHEMCE activities for CBRN diagnostics include:

- Developing both high-throughput and POC diagnostics that will inform the use of MCMs for the treatment of conditions or diseases caused by radiological/nuclear threats, biological pathogens, or chemical agents/toxins;
- Developing platform technologies that offer the capacity for a multiplexed capability, so that as additional threats are encountered, they can be seamlessly integrated into existing systems;

- Developing and advancing diagnostic policies to prevent, detect, and control public health security threats from CBRN agents; and,
- Diagnostics for [pandemic influenza](#) and for [emerging infectious diseases](#) are addressed in the sections of this report addressing those threats.

Near-Term (FY17-18)

(C.D.1) BARDA initiated its Biodosimetry portfolio development, transitioning 11 promising candidates from NIH and other sources in 2009. BARDA is supporting the development of both laboratory and POC systems. Commercial off-the-shelf (COTS) diagnostic instrumentation has been utilized in the development of the high-throughput biodosimetry diagnostic systems. The portfolio has matured well and the remaining candidates are approaching product verification stage. BARDA plans to transition 2-3 successful candidates from this portfolio into acquisition programs, completing FDA filings and initiating product acquisition for the SNS.

The programs to date have moved from proof-of-concept to system verification and some have developed prototype devices. (C.D.2) BARDA will continue working with the developers to ensure they partner, where possible, with manufacturers of existing platforms.

(C.D.3) BARDA will continue the development of POC diagnostic devices for detection of biological threat agents.

(C.D.4) CDC with support from other agencies (e.g., FDA and DHS) will help to coordinate the development of highly sensitive, specific, and robust assays for high-priority biological threat agents (i.e., bacterial, viral, and toxins) in accordance with the LRN Design Control Process. Select assays will be evaluated for deployment and employment through the CDC LRN to support rapid detection, diagnosis, event characterization, and epidemiological investigations. These assays can be used as presumptive or confirmatory assays for public health actions and decisions.

DoD will continue support for two diagnostics programs in the near term; the Joint Biological Agent Identification and Diagnostic System (JBAIDS) and the Next Generation Diagnostics System (NGDS) Increment 1. The JBAIDS program has eight pre-EUA data packages for *in vitro* diagnostic (IVD) assays that can be quickly deployed in the event of a health emergency for the identification of low probability, high consequence pathogens in clinical samples. (C.D.5) Additionally, JBAIDS development of pre-EUA assays studies for Pan-Burkholderia and Ebola Bundibugyo is ongoing. The JBAIDS also has surveillance kits to detect anthrax and smallpox in the environment as well as an FDA-approved IVD anthrax kit.

The NGDS is meant to provide chemical and biological diagnostic capabilities that are suitable for use as far forward as possible, dependent upon the availability of medical manpower and treatments, to maximize patient outcomes and inform the use of force health protection countermeasures. The portfolio tracking tool was updated with NGDS Increment 1 information and is continually monitored/edited as needed. (C.D.6) DoD will develop FDA-approved IVD capabilities for anthrax and smallpox as part of the diagnostic FilmArray® NGDS Warrior Panel. The DoD will be taking tests for *Bacillus anthracis*, *Coxiella burnetii*, *Francisella tularensis*, and *Yersinia pestis*, along with Ebola/Marburg to 510(k) clearance in the near term under the

Warrior Panel for the FilmArray. (C.D.7) NGDS Increment 1 will replace the JBAIDS diagnostic platform starting in FY 2017. NGDS Increment 1 improvements over JBAIDS include: 1) availability of FDA-approved COTS assays with military utility (e.g., Respiratory and Blood Culture Identification panels), the screening capability to simultaneously interrogate one specimen for multiple different analytical targets (i.e., up to 30 targets) in one run, and a robust COTS IVD Assay Pipeline (Gastrointestinal, Meningococcal, Sexually Transmitted Infections, and Tropical Disease panels).

(C.D.8) NIH, with the DoD, will support the development of a multiplex diagnostic to detect infectious disease pathogens associated with acute fevers. This panel will be developed to detect eight viruses (Ebola, Marburg, Lassa Fever, Crimean-Congo Hemorrhagic Fever, Chikungunya, Dengue, West Nile, and Zika), five bacteria (*Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis*, *Salmonella typhi*, *Leptospira* spp.), and two parasites (*Plasmodium* spp., *Leishmania donovani*).

Mid-Term (FY 2019-20)

(C.D.9) In the mid-term, DoD will also develop an environmental assay for smallpox as part of the NGDS Increment 1 Sentinel Panel.

(C.D.10) CDC will develop and validate additional radionuclide bioassay diagnostic tests to allow rapid detection and measurement of radionuclides in clinical specimens. The goal is to develop a suite of assays capable of rapidly detecting the radionuclides identified by an HHS-led interagency workgroup as most likely to be used in radiological terrorism. These assays can be used to identify who was internally contaminated in an incident, and to assess the need for, and efficacy of, decorporation therapies.

(C.D.11) NIH, with the DoD, will continue to support activities directed towards 510(k) clearance of a multiplex diagnostic to detect infectious disease pathogens associated with acute fevers. This panel is being designed to detect eight viruses (Ebola, Marburg, Lassa Fever, Crimean-Congo Hemorrhagic Fever, Chikungunya, Dengue, West Nile, and Zika), five bacteria (*Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis*, *Salmonella typhi*, *Leptospira* spp.), and two parasites (*Plasmodium* spp., *Leishmania donovani*).

Long-Term (FY 2021 and beyond)

In the long term, BARDA will support activities that include development, implementation, FDA approval, manufacturing preparation, and appropriate stockpiling for CBRN diagnostic systems, including both assays and instrumentation, for identifying and characterizing unknown threats in both high-throughput and POC systems.

DoD is developing the NGDS Increment 2 to expand the breadth of chemical and biological (including infectious and emerging disease) agent diagnostics to support those diseases/toxins that the NGDS Increment 1 cannot detect. It will provide potential far-forward capability to rapidly process and analyze remotely collected human clinical samples with FDA-approved immunoassay diagnostic systems and qualified assays for diagnostic and surveillance applications.

CDC will develop highly sensitive, specific and robust assays in accordance with the LRN Design Control Process for moderate to high-priority biological threat agents (i.e., bacterial, viral (including Ebola Virus Disease), and toxins) for deployment and employment through the CDC LRN.

NON-PHARMACEUTICAL MEDICAL COUNTERMEASURES

MCMs include non-pharmaceutical medical devices (e.g., mechanical ventilators and respiratory protective devices) and approaches (e.g., patient decontamination). Other non-pharmaceutical interventions that refer to community mitigation strategies (e.g., hand hygiene, social distancing) used to prevent the spread of disease, contamination, or other adverse effects related to an incident are not addressed directly by the PHEMCE. These are addressed in the [National Health Security Strategy](#).¹³⁷

Near-Term (FY 2017-18)

Respiratory Protective Devices (RPDs)

(C.NP.1) CDC certifies RPDs and maintains a “[Trusted Sources Webpage](#)” so that informed RPD selection decisions can be made.¹³⁸ (C.NP.2) To shepherd new respirators to market that meet the standards of both FDA and NIOSH, VA will continue to chair and complete an interagency effort known as Project BREATHE (Better Respiratory Equipment using Advanced Technologies for Healthcare Employees). (C.NP.3) In addition, CDC will strengthen RPD design, use, testing, and certification for the occupational setting. (C.NP.4) In addition, beginning in the near-term and extending beyond 2018, CDC will conduct research to better understand influenza transmission and determine when the use of N95 respirators or other devices may be more appropriate. (C.NP.5) In the near term, the PHEMCE will stand up a RPD IPT to create recommendations for increasing supply/decreasing demands of RPDs for a future pandemic.

BARDA will support development of novel RPD devices and new RPD manufacturing technologies to reduce the cost of RPD preparedness, investigating both reduction in the quantity of RPDs needed to achieve the required level of preparedness as well as technologies to manufacture needed RPDs on demand.

Mechanical Ventilators

(C.NP.6) BARDA will identify opportunities to promote ventilator standardization and interchangeable components. BARDA initiated a new project with Philips Resprionic S.A. to develop a novel next-generation portable stockpile ventilator. This new ventilator will be

¹³⁷ 2015-2018 National Health Security Strategy, available at: <http://www.phe.gov/Preparedness/planning/authority/nhss/Pages/default.aspx>

¹³⁸ See http://www.cdc.gov/niosh/npptl/topics/respirators/disp_part/RespSource.html

compatible with multiple patient circuit designs manufactured by multiple suppliers and has greatly reduced maintenance requirements.

Patient Decontamination

In December 2014, the PHEMCE published the guidance document Patient Decontamination in a Mass Chemical Exposure Incident: National Planning Guidance for Communities. This guidance was subsequently integrated into emergency response training curricula. (3.2.9) The PHEMCE is now developing guidance to address pediatric patient decontamination needs.

Mid-Term (FY 2019-20)

Respiratory Protective Devices

(C.NP.7) CDC will work with standard-setting organizations to incorporate health care worker RPDs research project findings on improving respirator compliance, comfort, and tolerability into industry and consensus standards, and selection and use guidance documents. (C.NP.8) HHS will develop systems to monitor the safety, effectiveness, and shortages of RPDs after deployment.

Mechanical Ventilators

(C.NP.9) CDC will reassess strategies for distributing SNS ventilators to the states to help ensure federal assets will be used equitably.

Long-Term (FY 2021 and beyond)

Respiratory Protective Devices

CDC will fund research to better understand benefits of using re-usable respirators in the health care setting. CDC will continue to update and improve its RPD approval program and will continue to maintain and update a “Trusted Sources Webpage” so that informed RPD selection decisions can be made. The FDA and NIOSH are working towards a framework for coordination and collaborative efforts. Specifically, this framework (1) describes the mechanism by which specific information pertaining to medical devices, surgical N95 respirators and/or NIOSH-approved N95 filtering facepiece respirators (FFRs) used in a health care setting may be exchanged between the two agencies based on aspects of the NIOSH approval mechanisms for FFRs, and (2) provides for efficient and coordinated regulatory oversight of these RPDs.

CENTERS FOR INNOVATION IN ADVANCED DEVELOPMENT AND MANUFACTURING (CIADM)

PHEMCE activities for the [CIADMs](#) include:

- Expanding the nation’s domestic ability to respond rapidly and nimbly to bioterrorism threats, pandemic influenza, and other emerging infectious disease threats;
- Providing experienced biopharmaceutical developers to aid CBRN MCM developers, resulting in a more robust, timely, and successful product development pipeline and stockpile;

- Incorporating innovative technologies that will provide a more efficient model for MCM product development relative to cost and time; and,
- Providing [domestic manufacturing surge capacity for pandemic influenza vaccine](#).¹³⁹

Near-Term (FY 2017-18)

(*C.CIADM.1*) BARDA will support completion of the construction of critical infrastructure within the CIADMs. It is anticipated that some of these centers may have limited capability to provide certain advanced development and manufacturing core services during this time frame, if required by the USG. The Centers will provide MCM development and manufacturing capabilities to address public health threats as needed. (*C.CIADM.2*) The Centers will also be initiating the activities required for the licensing of pandemic influenza vaccine candidates, including in-licensing as needed, and process development related to the eventual technology transfer of the candidate into the facility. (*C.CIADM.3*) BARDA will also support, through the CIADM governance board, the issuance, evaluation, and task orders for advanced development and manufacturing core services as programs flow from HHS and DoD. (*C.CIADM.4*) BARDA will support activities towards licensure of pandemic influenza vaccine candidates in the CIADMs and will provide for the appropriate framework to maintain a state of readiness in the event of a pandemic or other national public health emergency. (*C.CIADM.5*) Center academic partners will offer advanced training for the next generation of biotechnology workers.

Mid-Term (FY 2019-20)

BARDA will continue to provide assistance to CBRN MCM developers through the CIADM governance board.

Long-Term (FY 2021 and beyond)

The CIADMs will continue to support advanced development of CBRN MCM candidates, as needed from HHS and DoD development programs.

CROSS-CUTTING CAPABILITIES

The PHEMCE has developed a range of capabilities that could address multiple potential national health security threats, as well as the multiple PHEMCE goals and objectives. This subsection summarizes some of these cross-cutting capabilities; Section 1 describes many of these in greater detail with respect to the strategic goals and objectives they address.

Core Services

PHEMCE activities for Product Development Core Services include:

¹³⁹ For more information, see <https://www.medicalcountermeasures.gov/barดา/core-services/ciadm.aspx>

- Developing a suite of preclinical and advanced development core service capabilities to improve the efficiency of public-private partnerships in delivering needed MCMs;
- Qualifying an array of animal models to support product development under the “Animal Rule”; and,
- Building and maintaining a world-class workforce of subject matter experts in the management of clinical trials, clinical medicine, regulatory and quality affairs, pharmacology and toxicology, manufacturing and bioprocessing, analytic decision support, and modeling.

As described in greater detail in previous sections, NIH and BARDA provide a range of core services in support of MCM development and manufacturing. (C.CC.1) As part of these core services, NIH will continue to maintain its Preclinical services and VTEUs for vaccine and therapeutics testing capacity during clinical trials in support of public health emergencies. (1.3.6) NIH will also continue to manage the CAP, which is designed to accelerate development of promising MCMs.

BARDA, in conjunction with NIH, will support the development of new animal models of melioidosis, tularemia, ARS, and other diseases or conditions caused by threat agents as needed.

(C.CC.2) BARDA will also establish an Innovation Modeling Hub, which will provide analytic decision support and access to real-time modeling capabilities to senior decision-makers within ASPR and the PHEMCE. BARDA has already established core services for non-clinical evaluation, CIADMs, a Fill-Finish network, and a Clinical Studies network that are complementary to the core services established at the NIH. BARDA will continue to adapt its business model and its provision of core services to complement the capabilities and strengths of its private sector partners, reducing redundant efforts and streamlining the product development pathway.

In the mid-term, NIH and BARDA will seek qualification of animal models through the FDA Animal Model Qualification Program, focusing on models for the highest-priority threats and those needed for maturing product development initiatives. BARDA will fully integrate the provision of core services into its public-private partnerships, adapting increasingly flexible models of partnership to expedite product development and facilitate long-term strategic relationships. NIH’s infrastructure services will continue to provide appropriate *in vitro* and *in vivo* testing for candidate MCMs, especially those requiring adequate biocontainment facilities, as well as product-specific services, in support of overall anti-infective development capabilities.

FDA plays a critical role in supporting the MCM mission from discovery through development to deployment and use. As described under Goal 2, FDA works with PHEMCE partners to identify and resolve regulatory and scientific challenges that impede MCM development and use across all PHEMCE priorities. Through its MCMi, FDA has established multidisciplinary Public Health and Security Action Teams to identify and help resolve regulatory and scientific challenges for high-priority MCMs and related technologies; an MCM Regulatory Science Program to build the science base necessary to support MCM development and regulatory assessment; and a policy team that works to ensure that FDA laws, regulations, and policies adequately support MCM development, distribution, and use. FDA also works directly with both individual product

developers and the MCM development community to clarify regulatory requirements and provide scientific and technical expert review of MCM product applications, with the ultimate goal of approving safe and effective MCMs. In addition, FDA fosters preparedness and effective, timely responses to public health emergencies with MCMs that are available but not yet FDA-approved for the intended use through a variety of regulatory mechanisms that allow for emergency use of such products. (C.CC.3) BARDA is working on developing a matrix to determine high-priority programs for inclusion in the Regulatory Management Plan mandated under the FD&C Act, as amended by PAHPRA.¹⁴⁰

The DoD's crosscutting initiatives that support the PHEMCE include laboratory facilities located both within and outside the contiguous U.S. (C.CC.4) and a soon-to-be-established advanced development and manufacturing (ADM) facility. The ADM facility, when fully established, will support the manufacture, advanced testing, and evaluation of MCMs against agents of interest. The capability will be able to work cooperatively with analogous facilities established by HHS. Current DoD laboratory capabilities include dedicated space to conduct studies at all biological safety levels; facilitate the discovery, early development, and testing of vaccines, therapeutics, and diagnostics and the associated relevant animal models for the evaluation of new MCMs; and provide the infrastructure and personnel to characterize emerging chemical and biological threats.

(C.CC.5) The DoD has embarked on a long-term stewardship effort to maintain its MCM capabilities and is currently refurbishing its chemical and biological flagship laboratories. These efforts, critical to DoD, are also integral to the nation by providing a sustained set of assets and scientific expertise necessary for MCM development. Specifically, the DoD is establishing a dedicated BSL-4 laboratory capable of conducting tests that meet GLP requirements and evaluation of MCMs, and is also investing in state-of-the-art laboratory facilities. The overall cooperative efforts between HHS and DoD with regard to advanced development and manufacturing provide an agile and responsive capacity for the nation to manufacture MCMs. (C.CC.6) In addition, the WRAIR has operated a cGMP vaccine and other biologics manufacturing facility for over 50 years producing 10-20 new products a year (2,000 doses per manufacturing run) for human testing. The facility will close its doors in July 2016 for an 18-month major renovation into a flexible manufacturing facility. Capabilities and capacity will substantially increase following the renovation.

Surveillance and MCM Utilization

CDC maintains several cross-cutting capabilities that can be drawn upon to help guide the best use of MCMs, provide MCMs in a timely manner and reduce the adverse health impacts during an emergency. CDC's scientific expertise and core laboratory science, epidemiology, and surveillance functions provide public health authorities with timely, accurate, and interpretable information that enables health officials to make informed decisions – such as placement and use of MCMs, and social distancing measures – needed for saving lives and protecting the public.

¹⁴⁰ 21 U.S.C. 360bbb-4.

(C.CC.7) Within CDC there is a core laboratory capacity to detect, identify, confirm, and quantify the vast majority of the high-priority biological, chemical, and radiological threat agents.

(C.CC.8) In addition, CDC manages the LRN, a group of local, state, federal, and international laboratories with unique testing capabilities for detecting high-priority biological and chemical threat agents. LRN labs play a critical role in our nation's ability to detect, characterize, and communicate information on confirmed threat agents.

(C.CC.9) CDC also supports some 280 surveillance-related activities to monitor and assess the population's health, including ILINet, and PulseNet, which may help authorities detect and characterize or confirm an attack. In addition, CDC supports the development, evaluation, and improvement of state and local capabilities for MCM distribution and dispensing through programs providing guidance, training, exercise, and evaluation for MCM preparedness and response functions.

Finally, the DSNS maintains partnerships for priority access to ground and air transportation to deliver medicines and supplies for state and local emergency response. Similarly, CDC's Vaccines for Children infrastructure offers a mechanism for ordering and shipping routine childhood vaccines as well as pandemic influenza vaccine to health departments and other vaccine providers in the event of a disease outbreak.

(C.CC.10) DoD will continue to develop programs such as biosurveillance and support of diagnostics to aid the interagency in the use of MCMs to protect the population. (C.CC.11) MCS Diagnostics is developing the framework for a FilmArray User community of interest website/portal. DoD may incorporate this portal into the Biosurveillance Portal (BSP) that already exists within the DoD through JPM Information Systems. This FilmArray user portal will contain troubleshooting information, FAQs, training guides, points of contact, and other resources for FilmArray users.

CONCLUSION

This 2016 PHEMCE SIP records progress made by the PHEMCE in the past year and updates the priorities included in the 2015 PHEMCE SIP for federal MCM research, development, acquisition, stockpiling, distribution, dispensing, and monitoring programs. ASPR will continue to track execution of these priorities. Periodic updates will continue to be provided through the PHEMCE governance structure and included in future iterations of the PHEMCE SIP. Through this process the PHEMCE will facilitate accountability, foster coordination, and identify and address potential challenges in pursuit of these important goals and objectives. The PHEMCE will publish a 2017 PHEMCE SIP to report on progress and provide other updates as needed to this report.

APPENDIX 1: ACRONYMS

AAP	American Academy of Pediatrics
AARC	American Association for Respiratory Care
ABC	Division for At-Risk, Behavioral Health and Community Resilience
AD	Advanced Development
Ad4	Adenovirus Serotype 4
ADS	Analytical Decision Support
AE	Adverse Event
AFRRI	Armed Forces Radiobiology Research Institute
AIG	Anthrax immune globulin
AMR	Antimicrobial Resistant
ARD	Advanced Research and Development
ARS	Acute Radiation Syndrome
ASPR	Assistant Secretary for Preparedness and Response
ATNAA	Antidote Treatment-Nerve Agent Auto-Injector
AVA	Anthrax Vaccine Adsorbed
BAA	Broad Agency Announcements
BARDA	Biomedical Advanced Research and Development Authority
BAT	Botulism antitoxin
BLA	Biologics License Application
BN	Bavarian Nordic
BSL	Biosafety Level
BTB	U.S.-Canada Beyond the Border Initiative
BTRA	Biological Terrorism Risk Assessment
cAd	Chimp adenovirus
CAP	Concept Acceleration Program
CARB	Combating Antibiotic-Resistant Bacteria
CBR	Chemical, Biological, and Radiological
CBRN	Chemical, Biological, Radiological, and Nuclear
CDC	Centers for Disease Control and Prevention
CDPH	California Department of Public Health

CERC	Crisis and Emergency Risk Communication
cGMP	Current Good Manufacturing Practice
chA	Chimeric Hemagglutinin
ChAd3	Chimpanzee Adenovirus Vector Type 3
CHILD	Children's HHS Interagency Leadership on Disasters
CHO	Chinese Hamster Ovary
CIADM	Centers for Innovation in Advanced Development and Manufacturing
CLIA	Clinical Laboratory Improvement Amendments of 1988
CMV	Cytomegalovirus
CONOPs	Concepts of Operations
COTS	Commercial Off-the-Shelf
CounterACT	Countermeasures Against Chemical Threats
CRE	Carbapenem-Resistant <i>Enterobacteriaceae</i>
CRI	Cities Readiness Initiative
CRO	Contract Research Organization
CSN	Clinical Studies Network
DARPA	Defense Advanced Research Projects Agency
DART	Decisional Anthrax Readiness Tool
DDT	Drug Development Tool
DEARE	Delayed Effects of Acute Radiation Exposure
DHS	U.S. Department of Homeland Security
DIHS	Division of International Health Security
DLG	Disaster Leadership Group
DNA	Deoxyribonucleic Acid
DoD	U.S. Department of Defense
DRDC	Defence Research and Development Canada
DSLRL	Division of State and Local Readiness
DSNS	Division of the Strategic National Stockpile (at CDC)
Dstl	Defence Science and Technology Laboratory
DSTO	Defence Science and Technology Organisation
DTRA	Defense Threat Reduction Agency

EBOV	Ebola Virus
EEC	Enterprise Executive Committee
EHR	Electronic Health Records
EID	Emerging Infectious Diseases
ELISA	Enzyme-Linked Immunosorbent Assay
EO	Executive Order
ESC	Enterprise Senior Council
EUA	Emergency Use Authorization
EUI	Emergency Use Instructions
EV-D68	Enterovirus D68
FANG	Filovirus Animal Nonclinical Group
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDA	Food and Drug Administration
FDA-ARGOS	Database for Regulatory Grade Microbial Sequences
FEMA	Federal Emergency Management Agency
FFR	Filtering Facepiece Respirators
FMS	Federal Medical Station
FRMM	Influenza (Flu) Risk Management Meeting
FY	Fiscal Year
G7	Group of Seven
GHSI	Global Health Security Initiative
GLP	Good Laboratory Practices
GSK	Glaxo Smith Kline
HA	Hemagglutinin
HCCPP	Interim Healthcare Coalition Checklist for Pandemic Planning
HCPWG	Pediatric Health Care Preparedness Working Group
HHS	U.S. Department of Health and Human Services
HIV	Human Immunodeficiency Virus
HPAI	Highly Pathogenic Avian Influenza
HRPAS	Health Resources Priorities and Allocation System
IAA	Interagency Agreement

ICD	Integrated Capabilities Document
IGSP	Influenza Genome Sequencing Project
INATS	Improved Nerve Agent Treatment System
IND	Investigational New Drug
IOM	Institute of Medicine
IPT	Integrated Program Team
IRAT	Influenza Risk Assessment Tool
IV	Intravenous
IVD	<i>In vitro</i> diagnostic
J&J	Johnson & Johnson
JBAIDS	Joint Biological Agent Identification and Diagnostic System
JSTO	Joint Science and Technology Office (at DoD)
LLNL	Lawrence Livermore National Laboratory
LRN	Laboratory Response Network
mAb	Monoclonal Antibody
MAC-ELISA	IgM Antibody Capture Enzyme-Linked Immunosorbent Assay
MA IPT	MCM Monitoring and Assessment IPT
MCM	Medical Countermeasures
MCMC	Medical Countermeasures Consortium
MCMi	Medical Countermeasures Initiative
MCSR	Medical Countermeasures Strategy and Requirements
MDR	Multi-Drug Resistant
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
MMWR	Morbidity and Mortality Weekly Report
MOU	Memorandum of Understanding
MTA	Material Threat Assessment
MVA	Modified Vaccinia Ankara (smallpox vaccine)
MYB	Multiyear Budget
NACCD	National Advisory Committee on Children and Disasters
NACCHO	National Association of County and City Health Officials
NAPAPI	North American Plan for Animal and Pandemic Influenza

NBSB	National Biodefense Science Board
NCBI	National Center for Biotechnology Information
NDA	New Drug Application
NGDS	Next Generation Diagnostics System
NGO	Non-Governmental Organizations
NHP	Non-Human Primate
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NIOSH	National Institute for Occupational Safety and Health
NIVDP	National Influenza Vaccination Disparities Partnership
NPRSB	National Preparedness and Response Science Board
OEM	Office of Emergency Management
OPHPR	Office of Public Health Preparedness and Response
OPP	Office of Policy and Planning (at HHS/ASPR)
OPT	Office of Pediatric Therapeutics (at FDA)
ORR	Operational Readiness Review
OTA	Other Transactional Authority
PAC	Portfolio Advisory Committee
PAHPA	Pandemic and All-Hazards Preparedness Act
PAHPRA	Pandemic and All-Hazards Preparedness Reauthorization Act (Public Law 113-5)
PAPR	Powered Air Purifying Respirator
PBS	Project BioShield
PCR	Polymerase Chain Reaction
PCS	Preclinical Services
PCT	Project Coordination Team
PedsOB IPT	Pediatrics and Obstetrics Integrated Program Team
PEP	Post-Exposure Prophylaxis
PHAA	Public Health Actionable Assays
PHE	Public Health England
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHEP	Public Health Emergency Preparedness

PHS Act	Public Health Service Act
PK	Pharmacokinetic
POC	Point-of-Care
POD	Point-of-Dispensing
PPE	Personal Protective Equipment
PRISM	Primary Response Incident Scene Management
PREP	Public Readiness and Emergency Preparedness
PSR	Product Specific Requirement
R&D	Research and Development
Rad-Nuc	Radiation and Nuclear
RCT	Randomized Controlled Trial
RDD	Radiological Dispersal Device
RFA	Request for Assistance
rGP	Glycoprotein Recombinant
RMP	Regulatory Management Plan
RNA	Ribonucleic Acid
RNCP	Radiation Nuclear Countermeasures Program
rPA	Recombinant (anthrax) Protective Antigen
RPD	Respiratory Protective Devices
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
rVSV	Recombinant Vesicular Stomatitis Virus
sBLA	Supplemental Biologics License Application
SBA	Scenario-Based Analysis
SDI	Solid Dose Injection
SIP	Strategy and Implementation Plan
SLEP	Shelf-Life Extension Program
SLTT	State, Local, Tribal, and Territorial
SNS	Strategic National Stockpile (at CDC)
SRF	Special Reserve Fund
SSTG	Sample Sharing Task Group
STRIVE	Sierra Leone Trial to Introduce a Vaccine against Ebola

SUMMIT	Scenario Utilization and Medical Modeling Information Tool
TIC	Toxic Industrial Chemical
TMA	Transcription-Mediated Amplification
tPA	Tissue Plasminogen Activator
TRA	Terrorism Risk Assessment
TRACIE	Technical Resources, Assistance Center and Information Exchange
TRL	Technology Readiness Level
U.S.	United States
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
USDA	U.S. Department of Agriculture
USG	U.S. Government
VA	U.S. Department of Veterans Affairs
VAERS	Vaccine Adverse Event Reporting System
VEE	Venezuelan Equine Encephalitis
VIGIV	Vaccinia Immune Globulin Intravenous
VLP	Virus-Like Particles
VSV	Vesicular Stomatitis Virus
VTEU	Vaccine and Therapeutics Evaluation Units
WCCM	Well Characterized Challenge Materials
WEE	Western Equine Encephalitis
WG	Working Group
WRAIR	Walter Reed Army Institute of Research
WHO	World Health Organization

APPENDIX 2: PHEMCE ORGANIZATIONAL STRUCTURE

July 2006, HHS established the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE or Enterprise). The PHEMCE’s mission is to advance national preparedness against CBRN and EID threats, including pandemic influenza, by coordinating MCM-related efforts within HHS and in cooperation with interagency PHEMCE partners. The forum for cooperation and overall mission fulfillment is the Enterprise Senior Council (ESC) and its supporting infrastructure (Figure 2). Structurally, the ASPR leads the ESC, which is comprised of the senior leadership of NIAID, CDC, and FDA with comparable senior level representatives from DoD, DHS, VA, and USDA. Additional HHS components participate in a non-voting capacity, including the Office of the General Counsel, Office of the Assistant Secretary for Health, Office of the Assistant Secretary for Legislation, and the Office of the Assistant Secretary for Planning and Evaluation. The PHEMCE activities are organized and governed using the hierarchy shown in Figure 2.

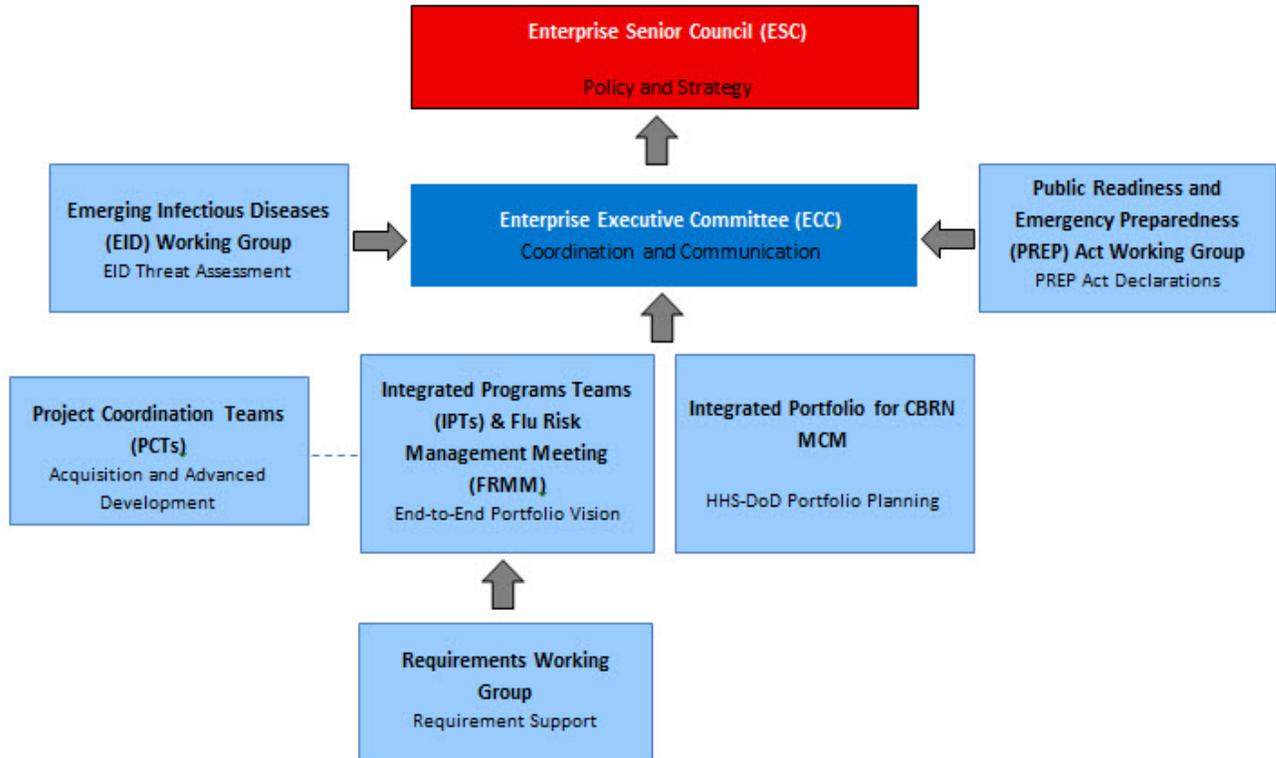


Figure 2: PHEMCE Governance Structure

Enterprise Senior Council (ESC) – It is the mission of the ESC to provide, on behalf of the HHS Secretary, coordinated, strategic direction and policy oversight for HHS “end-to-end” MCM preparedness activities, defined as: requirements generation, research, early- and late-stage product development, procurement and stockpiling, utilization planning, and monitoring, evaluation, and assessment activities for all threats, including CBRN, pandemic influenza, and

other EID. As the most senior level in the PHEMCE structure, the ESC will address strategic issues related to the prioritization of resources and the development of policies in accordance with national needs for MCMs. It will coordinate HHS efforts with the MCM-related activities of other departments/agencies.

The ESC is a consensus interagency body chaired by the HHS ASPR, as the HHS Secretary's principal advisor on federal public health and medical preparedness and response for public health emergencies. The HHS principal members are the Director of the CDC, the Director of the NIAID within the NIH, and the Commissioner of the FDA. The principal interagency members are the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs, Office of the Under Secretary of Defense for Acquisition, Technology, and Logistics from DoD; the Assistant Secretary for Health Affairs and Chief Medical Officer from DHS; the Assistant Secretary for Operations, Security, and Preparedness from VA; and the Undersecretary for Food Safety from USDA.

Enterprise Executive Committee (EEC) – The EEC of the PHEMCE is the operational-level decision and coordination body for all of its policy and product-level issues. It provides the critical interface and organizing capability between the strategic focus of the ESC and the tactical-level efforts conducted within the subordinate IPT and Working Group (WG) levels (Figure 2). The EEC reports directly to, and receives guidance from, the ESC. The EEC will coordinate, and approve as delegated, end-to-end PHEMCE MCM activities related to requirement analyses, research, early- and late-stage product development, stockpiling, utilization planning, and monitoring, assessment and evaluation in support of MCM policy and strategy established and approved by the ESC. The EEC is responsible for vetting important programmatic, procurement, requirements, and portfolio actions and identifying solutions and recommended actions requiring approval at higher levels. Additionally, the EEC manages the work at the lower IPT and subgroup levels, directly manages the annual assessment of the SNS, and composes PHEMCE-level documents, such as the annual PHEMCE SIP and PHEMCE MYB.

Integrated Program Teams (IPT) – The IPTs are established by the PHEMCE EEC to provide a complete, end-to-end vision of MCMs for any of a variety of needs, such as against a well-defined threat type (e.g., anthrax, radiological/nuclear, etc.), a potential future threat (e.g., novel antimicrobial resistant organisms), for commodity areas that span a range of threats (e.g., diagnostics) or for major cross-cutting issues related to unaddressed population needs (e.g., at-risk populations). The IPT areas of consideration range from requirement-analysis to development and production, to stockpiling, delivery and dispensing to the end user, adverse event monitoring, communications, guidance and policy development, and evaluating MCM effectiveness and replacement needs. They report to the EEC.

Requirements Working Groups (WG) – The Requirements WGs are established by the EEC to assist the IPTs in determining which types of MCMs are needed for response to public health emergencies and other threats to national health security. The WGs provide their products to the appropriate IPT(s) for further development and/or passing along to the EEC.

Project Coordination Teams (PCT) – PCTs are established by the BARDA Director to support the development and administration of each MCM acquisition or advanced development program managed by BARDA.

Emerging Infectious Disease (EID) Working Group – The EID WG was established by the EEC to evaluate the public health risk posed by EIDs, excluding influenza, as charged by the EEC or ESC and to provide recommendations to the EEC regarding which pathogens, or pathogen classes, require PHEMCE response, and at what level.

Public Readiness and Emergency Preparedness (PREP) Act Working Group (WG) – The PREP Act WG was established by the ESC in 2012 to ensure that recommendation to the Secretary regarding PREP Act liability protections and declarations are conducted with a consistent, transparent, and reproducible process. Representation includes ASPR, OGC, ASFR, ASPE, ASL, CDC, FDA, HRSA and NIH.

Integrated Portfolio for CBRN Medical Countermeasures/Portfolio Advisory Committee (PAC) – The PAC seeks to maximize national preparedness to respond to CBRN threats by aligning HHS and DoD MCM development and related infrastructure resources. The PAC reports to the EEC. The activities of the PAC enhance intra- and inter-departmental collaboration in CBRN MCM development, establish a shared understanding of each agency's programmatic requirements, and develop an integrated set of goals. The PAC is co-chaired by the BARDA and the Office of the Deputy Assistant Secretary of Defense for Chemical and Biological Defense.

Figure 3 depicts specific PHEMCE mission components, organizations with lead responsibilities and capabilities in these areas, and shows the complex interconnectedness of the PHEMCE organizations and mission space.

APPENDIX 3: PHEMCE COORDINATION WITH NON-FEDERAL STAKEHOLDERS

The PHEMCE coordinates and collaborates with non-federal stakeholders through a variety of venues. This appendix highlights recent activities with SLTT, regional, international, industrial, and professional society stakeholders. These interactions shape federal MCM planning and identify new ways to address national MCM needs. In January 2016, the PHEMCE hosted a two-day [PHEMCE Stakeholders Workshop](#), which highlighted past progress and future directions in developing, stockpiling and effectively utilizing MCMs.¹⁴¹

ASPR and its partner agencies have led broad engagements with SLTT stakeholders through NACCHO to provide an overview of the PHEMCE and federal plans for ensuring MCM preparedness. NACCHO and ASPR hosted a webinar in March 2015 for SLTT partners to learn about the purpose and priorities of the PHEMCE. In addition, ASPR hosted a PHEMCE Town Hall session at the 2015 Public Health Preparedness Summit in April 2015 in Atlanta, Georgia. ASPR also hosted a learning session at the Summit focused on the requirements process and MCM medical utilization and response integration. This session stimulated valuable dialogue that identified gaps and potential solutions between federal and SLTT preparedness planning. These engagements highlighted the areas where federal plans may intersect with and impact state and local health department planning and encouraged increased connectivity at all levels of government.

ASPR/OPP, Division for At-Risk, Behavioral Health & Community Resilience (ABC) contributed to the [Caring for Older Adults in Disasters: A Curriculum for Health Professionals](#), a competency-based disaster health curriculum focused on the care of older adults.¹⁴² The National Center for Disaster Medicine and Public Health published this resource in September 2015. The purpose of the curriculum is to enable educators to teach health professionals about caring for older adults in disasters, and covers a wide array of modules—including lessons on medication, pharmacy, access and functional needs, and public health considerations. In 2015, ABC coordinated two HHS-wide data calls in preparation for the 2014-2015 Report of the CHILD Working Group. This biennial report is a compilation of HHS activities addressing the needs of children across disaster preparedness, response, and recovery. The expected draft date is mid-2016.

NIAID supported the following workshops that were held to share information with the filovirus research community:

- WCCM workshop in May 2015 by the FANG to provide update WCCM status and characterization of virus outbreak strains.
- A joint workshop in October 2015 by the FANG and WHO to discuss how to bridge the nonclinical data to the human data, analysis of vaccine endpoints to support establishing

¹⁴¹ See: <http://www.phe.gov/Preparedness/mcm/phemce/PHEMCEworkshop/Pages/default.aspx>

¹⁴² See: <http://ncdmph.usuhs.edu/KnowledgeLearning/2015-OAC.htm>

a correlate of protection, and difference between in vitro and in vivo models to test therapeutics.

Under the MCMi program, FDA established multidisciplinary Public Health and Security Action Teams (Action Teams) as necessary to advance priority MCMs by working with internal and external entities—as appropriate—to identify and catalyze the resolution of regulatory and scientific challenges to MCM development. Some of the notable MCMi Action Team activities in FY2015 included:

Multiplex and Microbial Sequencing *In Vitro* Diagnostics Action Team –

- Continuing to facilitate the population of the publicly available and accessible [FDA-ARGOS](#), established in FY 2014, through NCBI. The sequencing contract was awarded to the Institute of Genomic Sciences at the University of Maryland to sequence and deposit additional genus-diverse and public health need isolates. Approximately 2,000 isolates will be sequenced as part of the FDA-ARGOS project.¹⁴³
- Continuing to collaborate with the CDC [LRN](#) to develop high confidence assays to detect biothreat agents.¹⁴⁴

ARS Action Team –

- Supporting the development of a draft guidance to help sponsors develop drugs under the “Animal Rule” for treatment of ARS;
- Supporting the issuance of draft and final guidance for [Radiation Biodosimetry Medical Countermeasure Devices](#).¹⁴⁵

FDA holds Advisory Committee Meetings and public workshops as part of its usual efforts to obtain independent input and expert advice on scientific, technical, and policy matters to facilitate MCM development. Key meetings and public workshops held during FY 2015 include:

- October 21-22, 2014 – [Collaborative Approaches for Medical Device and Healthcare Cybersecurity](#) – A workshop to identify cybersecurity challenges to medical devices and strategies to address those challenges to strengthen medical device cybersecurity (co-hosted by HHS and DHS);¹⁴⁶
- December 12, 2014 – [Immunology of Protection from Ebola Virus Infection](#) – A workshop to discuss important aspects of Ebola virus and vaccine immunology to inform

¹⁴³ As part of this project, FDA set up collaborations to acquire the following prospective samples: 1) clinical isolates from Children’s Hospital and George Washington University in Washington, D.C., to enhance diversity of GenBank; 2) biothreat and near-neighbor isolates/gDNA from USAMRIID/CRP; 3) Ebola isolates/gDNA from Public Health Canada/NIAID collaboration and USAMRIID/CRP; 4) AMR isolates from Children’s Hospital; and 5) difficult-to-acquire isolates from the American Type Culture Collection. The FDA-ARGOS is available at <http://www.ncbi.nlm.nih.gov/bioproject/231221>

¹⁴⁴ For more information on the LRN, see <http://emergency.cdc.gov/lrn/index.asp>

¹⁴⁵ Guidance available at (final guidance issued in April 2016, draft issued in December 2014): <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM427866.pdf>

¹⁴⁶ See: <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm412979.htm>

future clinical, scientific, and regulatory decision-making related to vaccines against Ebola (co-sponsored by FDA, NIH, DoD, CDC, and BARDA);¹⁴⁷

- February 20, 2015 – [Optimizing FDA's Regulatory Oversight of Next-Generation Sequencing Diagnostic Tests](#) – A workshop to discuss and receive feedback on FDA's regulatory approach to diagnostic tests for human genetics or genomics using next-generation sequencing technology;¹⁴⁸
- May 12, 2015 – The FDA [Vaccines and Related Biological Products Advisory Committee](#) met to discuss the development and licensure of Ebola vaccines;¹⁴⁹
- May 27-28, 2015 – The [FDA Science Forum](#) highlighted the cutting-edge science conducted at FDA, including MCM-related regulatory science topics;¹⁵⁰
- August 21, 2015 – [M-CERSI Symposium on Biomarkers in Drug Development](#) – A one-day symposium for scientists and researchers from industry, academia, and FDA to gain perspective on biomarker development and application of biomarkers in preclinical and clinical research, including evidentiary considerations for biomarker use in drug development, hosted by the University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI);¹⁵¹
- September 28, 2015 – [Promoting Semantic Interoperability of Laboratory Data](#) – A workshop to receive and discuss input from stakeholders regarding proposed approaches to promoting the semantic interoperability of laboratory data between in vitro diagnostic devices and database systems, including laboratory information systems and electronic health records (co-hosted by CDC and the National Library of Medicine (NLM)).¹⁵²

In FY 2014, CDC awarded a contract to the Institutes of Medicine (IOM), now part of the National Academies of Sciences, Engineering, and Medicine, to establish a standing committee of experts to evaluate CDC's supply chain management for MCMs and to help inform CDC's decision-making. The committee includes experts in state and local public health, medical countermeasure production, warehouse and product distribution, logistics management, emergency medical services, emergency medicine, risk communications, and FDA regulatory issues. The work of the committee concluded after five meetings and one workshop with a final meeting in July 2016, where the committee identified several high level opportunities for CDC to address, including:

- Necessity for aligned requirements, mission and funding to ensure that required SNS capabilities can be achieved and maintained within a stable and reliable funding level.

¹⁴⁷ See:

<http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm424037.htm>

¹⁴⁸ See: <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm427296.htm>

¹⁴⁹ See: <http://www.fda.gov/AdvisoryCommittees/Calendar/ucm438627.htm>

¹⁵⁰ See: <http://www.fda.gov/ScienceResearch/AboutScienceResearchatFDA/ucm429403.htm>

¹⁵¹ See: <http://www.pharmacy.umaryland.edu/centers/cersievents/biomarkers/>

¹⁵² See: <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm453897.htm>

- Improvement of the PHEMCE process through more collaborative and open processes to decrease siloed decision making, and increase the role of state and local representatives to influence.
- Improvement of technical assistance and communication to state and local partners, which can be addressed to ensure that the right training, information and guidance is available before a response, and timely information and support is available during a response.

The progress, content, and outcomes of each meeting and workshop are documented and publically available on the [National Academies website](#).¹⁵³

In August 2014, the National Academies, at the request of NIOSH, convened a workshop, “The Use and Effectiveness of Powered Air Purifying Respirators in Health Care,” to help prioritize and accelerate NIOSH activities to update certification requirements for powered air purifying respirators (PAPR). Research focus included efficacy, current training, maintenance, supplies, and possible enhancements and barriers to use. Settings will include inpatient, clinic, nursing home, and community (home) settings. The report (*The Use and Effectiveness of Powered Air Purifying Respirators in Health Care: Workshop Summary Released: January 6, 2015*) discussed ways to improve PAPR design and standards (assess the risks and protective factors, identify design attributes, and drive the market to meet health care needs); increase education and training; and strengthen implementation and use of PAPRs in health care.

NIH accelerated scientific research on Zika and issued notices to researchers highlighting high-priority research areas. Areas of high priority include animal models of Zika virus infection; the development of sensitive diagnostics and effective drugs and vaccines; studies on alternative routes of transmission; and studies to understand the mechanisms by which Zika affects the nervous system and pregnancy outcome in women. Additionally, NIH issued funding opportunity announcements for research on Zika virus and its complications as well as candidate therapeutics, vaccines, and diagnostics.

NIAID organized an international conference, *Zika Virus in the Americas: An HHS Expert Consultation to Accelerate the Development of Countermeasures*, in Bethesda, Maryland, on March 28-29, 2016. Topics of discussion included Zika pathogenesis, epidemiology, and natural history; discussions on development of vaccines, diagnostics and therapeutics; mosquito transmission and vector control strategies; and general discussions on future strategies for acceleration of the research and development of countermeasures.

¹⁵³ See: <http://www.nationalacademies.org/hmd/Activities/PublicHealth/Stockpile.aspx>

APPENDIX 4: PROGRESS IN ADDRESSING AT-RISK POPULATION MEDICAL COUNTERMEASURE NEEDS

Since the release of the 2015 PHEMCE SIP, significant progress has been made in addressing the MCM needs of [at-risk](#)¹⁵⁴ populations. As required by section 2811(d) of the PHS Act¹⁵⁵ selected highlights of this progress are listed below.

Table 6: Progress in Addressing At-Risk MCM Needs

PHEMCE Mission Component ¹⁵⁶	Progress
Requirements Setting	<ul style="list-style-type: none"> • The PHEMCE approved requirement templates that included at-risk populations. • The PedsOB IPT has been and will continue to be consulted by BARDA's Division of Analytic Decision Support (ADS) when modeling scenarios are being developed and applied that involve medical countermeasure scenarios for the pediatric and obstetric populations. For example, ADS came to the PedsOB IPT to validate its modeling parameters for the pediatric and obstetric populations for purposes of the anthrax Material Threat Assessment 2.0 and the Anthrax Scenario-based Analysis.
Advanced Development/ Manufacturing	<ul style="list-style-type: none"> • Through the PHEMCE, Neupogen[®] and Neulasta[®] were FDA-approved in 2015 for hematopoietic ARS indications with pediatric dosing. • BARDA continued development of vaccine and therapeutic candidates to address at-risk population needs. These included Prussian blue (radiocesium decorporation), smallpox and influenza vaccines, influenza antiviral drugs, and novel antibiotics (solithromycin) for special populations (pediatric, human immunodeficiency virus (HIV)+, pregnant women, and seniors). • CDC and BARDA published a journal article evaluating the safety of BioThrax[®] anthrax vaccine in 18-20 year old individuals, as a first step towards evaluating the safety of this vaccine in pediatric populations. • Models have been developed for both mice and minipigs through the NIAID-funded, 2010-2015 product development support services contract (mice) and through an IAA with AFRRRI.
Regulatory Science Management	<ul style="list-style-type: none"> • FDA has sponsored research in developing a mouse model to assess treatments for progressive vaccinia. Progressive vaccinia is a life threatening complication that can occur when and immunocompromised individual is exposure to a certain type of smallpox vaccine. • FDA has sponsored research to develop mathematical models that would help guide appropriate dosing of antibacterials and antivirals in pediatric populations.

¹⁵⁴ At-risk individuals have needs in one or more of the following access or functional areas: communication, maintaining health, independence, services and support, and transportation. At-risk individuals may include children, older adults, and pregnant women as well those with disabilities, live in institutionalized settings, are from diverse cultures, have limited English proficiency or are non-English speaking, are transportation disadvantaged, have chronic medical disorders, or have pharmacological dependency. More information is available at: <http://www.phe.gov/Preparedness/planning/abc/Pages/at-risk.aspx>

¹⁵⁵ 42 U.S.C. 300hh-10(d)

¹⁵⁶ As listed in the 2012 PHEMCE Strategy

PHEMCE Mission Component ¹⁵⁶	Progress
Procurement / Inventory Management / Stockpiling	<ul style="list-style-type: none"> • Addition of ondansetron 4mg oral dissolvable tablets for pediatrics; addition of 65mg potassium iodide tablets for pediatrics; recommendation to increase holdings of amoxicillin for PEP for anthrax to cover children age 18 and under as per CDC recommendations • 2015 delivery of oseltamivir to the SNS for replenishment to address pediatric needs • PedsOB IPT actively participates in the SNS Annual Review to identify and prioritize pediatric and obstetric MCM gaps. • The SNS holds more than enough smallpox vaccines for the entire U.S. population, including millions of regimens of the unlicensed MVA vaccine that has the potential to be used in an emergency under an EUA in individuals of all ages with HIV or atopic dermatitis, including nursing and pregnant women. • In 2015 BARDA purchased bulk smallpox MVA vaccine that was stored for formulation as a lyophilized product later. BARDA continued support of the on-going pivotal Phase 3 safety study comparing smallpox MVA and ACAM2000 vaccines.
Deployment / Distribution / Dispensing / Administration	<ul style="list-style-type: none"> • CDC developed, piloted, and evaluated the next generation medical countermeasure evaluation tool for assessing state and local operational readiness. The medical countermeasure ORR tool is designed to improve state and local operational capabilities, and identify gaps in their ability to effectively distribute and dispense medical countermeasures in a large-scale event. The MCM ORR tool included provisions for mapping locations of at-risk populations according to jurisdictional risk assessments; providing training for community partners representing at-risk populations; and translation of MCM information for at-risk populations. • As a result of the continued Regional MCM planning, OEM continues to assist in the development of plans to supplement state and local plans as the result of EO #13527. This planning effort is all-encompassing and will support efforts of the state and locals as they seek to enhance public health preparedness to affect all populations including pediatric and other at-risk populations. Current areas for consideration include addressing the MCM resource allocation needs of at-risk populations including developing models and formulations that account for the particular needs of children, pregnant women, older adults, and individuals with immunocompromised conditions.

Additionally, the PHEMCE has coordinated with the FDA's Office of Pediatric Therapeutics (OPT), to identify and address the needs of pediatric and maternal populations. OPT works closely with the FDA review divisions to facilitate the development and availability of MCMs for children. For example, OPT works with FDA scientists and reviewers to provide regulatory advice and guidance to product developers and PHEMCE partners to assure enrollment of children only in clinical studies that are scientifically necessary and ethically appropriate. It also works to ensure that any pediatric studies conducted for MCMs are rigorously designed and conducted in accord with scientific understanding of issues such as exposure-response and extrapolation.

OPT also serves as a member of the National Advisory Committee on Children and Disasters (NACCD). The panel was established in 2014 under Section 2811A of the PHS Act, as amended by PAHPRA, to provide expert consultation to the Secretary of HHS and the ASPR on the medical and public health needs of children before, during, and after a disaster or public health emergency. In FY 2015, FDA's Office of Counterterrorism and Emerging Threats worked

closely with OPT and the National Institute of Child Health and Human Development to present to the ASPR's NACCD the [activities of FDA in promoting development of MCM's for pediatrics](#).¹⁵⁷

In addition, the NACCD established several working groups and OPT chairs the HCPWG. The HCPWG will address health care preparedness for public health threats, medical disasters, or mass trauma/casualty emergencies for the pediatric population. The working group plans to examine the state of facility preparedness, quality control programs, and MCMs (i.e., drugs, devices, and PPE) in relation to the pediatric population, as well as to assess granting structures, develop mitigation strategies for identified gaps, and identify best practices and tools for increasing health care readiness involving children during health care emergencies.

¹⁵⁷ See: <http://www.phe.gov/Preparedness/legal/boards/naccd/Documents/healthcare-prep-wg-20151311.pdf>

APPENDIX 5: ADVANCED RESEARCH AND DEVELOPMENT AND PROCUREMENT

Project BioShield Authorities and Reporting Requirements

The PBS Act of 2004 amended the PHS Act and the FD&C Act to provide additional and more flexible authorities and funding to support the development and procurement of MCMs against CBRN threat agents. It was also designed to give the government the authority to quickly authorize such MCM use during emergencies. These authorities were further delineated, clarified, expanded, and extended PAHPA and PAHPRA. Section 5 of the PBS Act (42 U.S.C. 247d-6c) required the Secretary of 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, as enacted Section 319F-1 of the PHS Act (42 U.S.C. 247d-6a) and amended by PAHPA, 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 the use of limited competition, expedited peer review, and increased simplified acquisition thresholds.
- Security Countermeasure Procurements and SRF – 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 SRF for the procurement of security countermeasures that may be placed in the SNS. Furthermore, Section 3 of the PBS Act as enacted section 319F-2 of the PHS Act (42 U.S.C. 247d-6b), and amended by PAHPA and PAHPRA, 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.
- EUA for Medical Countermeasures – Section 4 of the PBS Act, as enacted under Section 564 of the FD&C Act (21 U.S.C. 360bbb-3), and amended by PAHPRA, enables the FDA Commissioner¹⁵⁸ to issue an EUA to authorize the use of certain unapproved medical products, or to authorize certain unapproved uses of approved medical products,¹⁵⁹ following a declaration by the Secretary of HHS that circumstances exist to justify the authorization based on one of four determinations by the Secretary of Defense, Secretary of Homeland Security, or Secretary of HHS. Before an EUA may be issued, FDA must conclude that certain criteria for issuance of the authorization (e.g., the agent referred to in the HHS declaration can cause a serious or life-threatening disease or condition; the product may be effective in diagnosing, treating or preventing the disease or condition the known and potential benefits of the product outweigh its known and potential risks; and no adequate, approved, available alternatives) are met.

¹⁵⁸ The HHS Secretary delegated the authority to issue an EUA to the FDA Commissioner.

¹⁵⁹ This authority is limited to products to respond to emergencies that involve biological, chemical, radiological, or nuclear agents.

Reporting is required on emergency uses of certain biologicals, drugs and devices, emergency declarations, and conditions of authorization.

In 2013, under PAHPRA, 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 annual PHEMCE SIP, enacted by PAHPRA as Section 2811(d) of the PHS Act. This information is therefore provided here and is also described in the [Project BioShield Annual Reports](#).¹⁶⁰

Authority Usage

In FY 2015, 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 practices were deemed adequate for acquisition activity in 2015.

HHS did not use authority for personal services contracts under PHS Section 319F-1(d) to hire experts or consultants for the purpose of performing, administering, or supporting qualified countermeasure research and development activities.

Advanced Research and Development (ARD) and Procurements

BARDA will continue to provide monthly reports to the authorizing and appropriating committees detailing expenditures. These procurements are vetted through the PHEMCE leadership and are consistent with the annual PHEMCE SIP goals and objectives.

¹⁶⁰ The Project BioShield Annual Reports are available at <https://www.medicalcountermeasures.gov/barda/cbrn/project-bioshield-overview/project-bioshield-annual-report.aspx>.

Table 7a: FY 2015 Advanced Research and Development Contracts

Threat Area	Time from Submission to Award	FY15 Award Amount	Benchmarks / Milestones
Broad-Spectrum Antimicrobials	Portfolio Partnership of Innovative Treatments for Multidrug Resistant Infections (AstraZeneca) – 78 days	\$50M	Clinical supplies for Aztreonam and AVI lyophile packed, labelled and available for distribution ahead of FSI
Diagnostics	Anthrax Detection and MDR Anthrax Instrument and Assays (First Light BioSciences) – 26 days	\$5.5M	The lab analyzers' electrical, mechanical and imaging operations perform according to specifications
	Biomarker Characterization and Confirmation for Rapid Clinical Diagnosis of the Select BioThreat Agents: Burkholderia pseudomallei, Burkholderia mallei, and Yersinia pestis (SRI International) – 73 days	\$2.5M	Generation of Protocols for sample prep and handling of BM infected samples Proposed biomarker set for BM
Innovation	N/A	N/A	N/A
Ventilators	N/A	N/A	N/A

Threat Area	Time from Submission to Award	FY15 Award Amount	Benchmarks / Milestones
Influenza	Advanced Development of Cell-Based Influenza Vaccines (GlaxoSmithKline) – 50 days	\$80M	Scale-up and qualification of an EB66 cell-based manufacturing process and associated lot release analytical assays
	Continuous Manufacturing Supporting Immunotherapeutics (Janssen) – 101 days	\$102.5M	
	Influenza Sequencing Platform(InDevR) – 4 days	\$6.8M	Assay Performance Benchmark: performance within + 5% of relevant metrics for open platform FC8G assay (assay performed manually)
	Advanced Development of VIS410(Visterra) – 53 days	\$29M	Clinical assay development & validation; Validation report
	Shelf Life Extension Study of AS03 Stored in Bags (GlaxoSmithKline) - 12 days	\$400K	Monthly reports, shelf-life extension study
	Advanced Development of a Room Temperature, Stable, Oral Recombinant Influenza Vaccine (Vaxart) – 34 days	\$14M	Complete the Drug Product Manufacturing (VXA-A1.1 Tablets)
	Optimization of Pre-Pandemic H5N1 Vaccine Stockpile (University of Cambridge)– 137 days	\$8M	Data on protective efficacy of antigenically advanced H5 influenza viruses in ferrets

Threat Area	Time from Submission to Award	FY15 Award Amount	Benchmarks / Milestones
Viral Hemorrhagic Fever	GMP Manufacturing of Vecteded Ebola-Zaire Vaccine (Profectus BioSciences) – 5 days	\$6.5M	Finished dossier: Vector that will support practical vaccine manufacture
	ChAd3 Commercial Manufacturing Scale-up and Development (GlaxoSmithKline) – 36 days	\$13M	Production of quantities of virus particles that is 5X greater than basal process
	rVSV-G Production Formulation Lyophilization (BioProtection Systems/ NewLink) – 32 days	\$53M	Stability Testing of Drug Product; Qualification of Potency Assay to Support Product Release
	Nicotiana Benthamiana Expression System (Medicago USA) – 38 days	\$2M	Ability to notify of significant incidents within 24 hours. Draft report within 48 hours of incident.
	Tobacco-based mAb Production and Testing (Fraunhofer USA, Inc.) – 38 days	\$2M	Ability to notify of significant incidents within 24 hours. Draft report within 48 hours of incident.
	Development of Ebola Therapeutic Candidate BCX-4430 (BioCryst) – 32 days	\$18M	Manufacture cGMP BCX4340 (10kg campaign DS Batch 4); Prepare a Campaign Summary Report
	OraQuick Ebola Rapid Antigen Test (OraSure Technologies) – 139 days	\$9M	Ability of the OraQuick® Ebola Rapid Antigen Test to detect Ebola virus/antigen in FS/WB and achieve EUA approval.
	Development of Prophylactic Monovalent Ebola Vaccine (Crucell Holland B.V.) – 44 days	\$29M	Development and optimization of the glycerol process at pilotscale, scale up to commercial batch size and validation
Manufacturing of Novel Ebola Therapeutics and IND Enabling Studies (Regeneron) – 139 days	\$17M	Rat 3-week toxicology study and initiation of the Tissue Cross Reactivity Study with no findings to date of clinical significance	
Total	--	\$447.9M	--

Table 7b: FY 2015 Project BioShield Procurement Contracts

Threat Area	Time from Submission to Award	FY15 Award Amount	Benchmarks / Milestones
Anthrax	N/A	N/A	N/A
Botulism	Maintenance of Hyper-Immune Horse Herd (Auburn University) – 187 days	\$7M	The Contractor shall be responsible for the re-immunization of the horses with botulinum toxins, toxoids, and/or adjuvants as necessary and for monitoring the levels of anti-toxin antibodies at which time the Contractor shall initiate plasmapheresis under appropriate cGMP conditions. The Contractor shall include in its monthly report to the CO and COR a summary of anti-toxin titers.
Broad-Spectrum Antimicrobials	N/A	N/A	N/A
Chemical	Evaluation of PA for Lung Injury Associated with Chemical Exposure (University of Colorado) – 68 days	\$5M	Well validated swine sulfur mustard exposed animal model
	GO-AHEAD: Guidance on All-Hazards Enhanced Action Decontamination (University of Hertfordshire) – 64 days	\$7M	Detailed analysis on the relationship between volatility and contamination density for clothed (M01) and unclothed (M02).
Diagnostics	N/A	N/A	N/A
Plague	N/A	N/A	N/A

Threat Area	Time from Submission to Award	FY15 Award Amount	Benchmarks / Milestones
Radiological/Nuclear	Rad/Nuc Animal Model IDIQ (University of Illinois at Chicago) – 177 days	\$50K	Pertains to All: Porcine Model Development of Cutaneous Radiation Injury
	Chem Animal Model IDIQ (MRIGlobal) – 177 days	\$50K	
	Chem Animal Model IDIQ (Battelle Memorial Institute) – 177 days	\$50K	
	Chem Animal Model IDIQ (Lovelace Biomedical and Environmental Research Institute) – 177 days	\$50K	
	Rad/Nuc Animal Model IDIQ (SNLB) – 177 days	\$50K	
	Rad/Nuc Animal Model IDIQ (SRI International) – 177 days	\$50K	
	Chem Animal Model IDIQ (Netherlands Organisation for Applied Scientific Research) – 177 days	\$50K	
	Rad/Nuc Animal Model IDIQ (Lovelace Biomedical and Environmental Research Institute) – 177 days	\$50K	
	Rad/Nuc Animal Model IDIQ (University of Maryland-Baltimore)-177 days	\$50K	
Smallpox	N/A	N/A	N/A
Total	--	\$87.5M	--

Table 7c: FY 2015 Strategic National Stockpile (SNS) Procurement / Replenishment Contracts¹⁶¹

Threat Area	Actual FY 2015
Anthrax	\$133M
Botulism	\$0M
Burkholderia	\$0M
Chemical	\$48M
Influenza	\$67M
Plague	\$3M
Radiological/Nuclear	\$0M
Smallpox	\$84M
Tularemia	\$2M
Federal Medical Station (FMS)	\$1M
Medical Supplies and Ancillary Items (MS&AI) and non-MS&AI ¹⁶²	\$16M
Total	\$355M

Projected PHEMCE Funding by Threat Area

Five-year cost projections associated with the research, development, procurement, and stockpiling of MCMs for use against CBRN threats and emerging infectious diseases are captured in the PHEMCE MYB Report. The PHEMCE MYB Fiscal Years 2015-19 report was delivered to Congress in April 2016.

¹⁶¹ SNS requirements for the stockpile are based on factors that vary from year to year. These include PHEMCE recommendations, expiring product, replenishment decisions, procurement costs and availability, shelf life extension, and funding considerations.

¹⁶² Medical Supplies and Ancillary Items (e.g., sutures, catheters, gloves, and syringes) and non-MS&AI (e.g., gelpacks, temperature monitoring devices, and shipping containers) include a wide variety of items which support multiple threat categories.

APPENDIX 6: STRATEGIC ALIGNMENT

The 2016 PHEMCE SIP aligns with agency-level strategic plans. The table below summarizes how the 2016 PHEMCE SIP aligns with the [HHS Strategic Plan](#) and the [National Health Security Strategy](#).

Table 8: Strategic Alignment with Other Strategic Documents

PHEMCE Goals	HHS Strategic Plan ¹⁶³	National Health Security Strategy
Goal 1: Identify, create develop, manufacture, and procure critical medical countermeasures	Goal 2: Advance Scientific Knowledge and Innovation, Objective A: Accelerate the process of scientific discovery to improve health; Goal 3: Advance the Health, Safety, and Well-being of the American People, Objective F: Protect Americans' health and safety during emergencies, and foster resilience to withstand and respond to emergencies	Strategic Objective 2: Enhance the National Capability to Produce and Effectively Use Both Medical Countermeasures and Non-Pharmaceutical Interventions.
Goal 2: Establish and communicate clear regulatory pathways to facilitate medical countermeasure development and use.	Goal 2: Advance Scientific Knowledge and Innovation, Objective C: Advance the regulatory sciences to enhance food safety, improve medical product development, and support tobacco regulation; Goal 3: Advance the Health, Safety, and Well-being of the American People, Objective F: Protect Americans' health and safety during emergencies, and foster resilience to withstand and respond to emergencies	Strategic Objective 2: Enhance the National Capability to Produce and Effectively Use Both Medical Countermeasures and Non-Pharmaceutical Interventions
Goal 3: Develop logistics and operational plans for optimized use of medical countermeasures at all	Goal 3: Advance the Health, Safety, and Well-being of the American People, Objective F: Protect Americans' health and safety during emergencies, and foster resilience to withstand and respond to emergencies	Strategic Objective 2: Enhance the National Capability to Produce and Effectively Use Both Medical Countermeasures and Non-Pharmaceutical Interventions, Strategic Objective 4: Enhance the Integration and Effectiveness of the Public Health, Healthcare, and Emergency Management Systems, Strategic Objective 5:

¹⁶³ HHS Strategic Plan FY 2014 – 2018; available at <http://www.hhs.gov/strategic-plan/priorities.html>

levels of response	respond to emergencies	Strengthen Global Health Security
<p>Goal 4: Address medical countermeasure gaps for all sectors of the American population</p>	<p>Goal 1: Strengthen Health Care, Objective E: Ensure access to quality, culturally competent care, including long-term services and supports, for vulnerable populations; Goal 2: Advance Scientific Knowledge and Innovation, Objective A: Accelerate the process of scientific discovery to improve health and Objective C: Advance the regulatory sciences to enhance food safety, improve medical product development, and support tobacco regulation; Goal 3: Advance the Health, Safety, and Well-Being of the American People, Objective F: Protect Americans' health and safety during emergencies, and foster resilience to withstand and respond to emergencies.</p>	<p>Strategic Objective 2: Enhance the National Capability to Produce and Effectively Use Both Medical Countermeasures and Non-Pharmaceutical Interventions, Strategic Objective 4: Enhance the Integration and Effectiveness of the Public Health, Healthcare, and Emergency Management Systems.</p>

APPENDIX 7: NEAR-TERM DELIVERABLES

This table summarizes activities with near-term deliverables, identified in this Strategy and Implementation Plan, which are projected at the time of this writing for completion by the end of FY 2018. The 2017 PHEMCE SIP will report on the progress made toward achieving these deliverables.

Table 9: Near-Term Deliverables

2016 Activity Number	Milestone Description	Lead Agency	Projected Completion Date
1.1.2	Submit the annual MYB report to Congress.	ASPR	FY 2016-18
1.1.5	PHEMCE IPTs will complete preparedness assessments for all SNS holdings in the near-term.	ASPR	FY 2018
1.1.7	Engage with appropriate subject matter experts, both within the federal government and externally, to most accurately evaluate operational and response planning for MCM preparedness assessments.	ASPR / CDC	FY 2018
1.1.8	ASPR and CDC will work to incorporate data from CDC's DSLR ORR evaluation process to inform assessment of the national operational capacity to use MCMs.	ASPR / CDC	FY 2018
1.2.1	Update the MTA 2.0 SIP, incorporating lessons learned from the anthrax pilot and an updated DHS MTA process.	DHS	FY 2018
1.2.2	Conduct MTA 2.0 assessments for smallpox, viral hemorrhagic fever viruses, botulism, radiological dispersal devices, and chemical pharmaceutical based agents.	DHS	FY 2018
1.2.4	Develop and implement a risk assessment methodology and process through which the PHEMCE will determine which EID threats require PHEMCE response.	ASPR	2016
1.2.5	PHEMCE leadership will determine, utilizing this framework, which emerging infectious diseases to add to the list of PHEMCE high priority threats (see Box 1).	ASPR	FY 2018
1.2.7	Develop or update MCM requirement documents for CBRN threats, as well as requirements that address multiple threats, as detailed in Objective 1.2, Table 3.	ASPR	FY 2018
1.2.9	Complete an assessment of economic consequences of terrorism threats.	DHS	FY 2017

2016 Activity Number	Milestone Description	Lead Agency	Projected Completion Date
1.2.10	Complete an Adversary Decision Model, which incorporates input from the intelligence community to provide frequency probabilities, and incorporate it into the final BTRA 5.0 report.	DHS	FY 2018
1.3.5	In 2015 NIH released a BAA entitled "Development of Therapeutic Products for Biodefense and Emerging Infectious Diseases" with awards to be made in FY 2016.	NIH	FY 2016
2.3.1	The MA IPT will evaluate current MCM preparedness assessment capabilities and develop a strategy for a PHEMCE-wide comprehensive capability to facilitate a timely and appropriate assessment of MCMs during a public health emergency.	FDA	FY 2018
2.3.2	The MA IPT will identify enhancements to current drug and vaccine safety monitoring systems and the potential to leverage clinical information from electronic health records that could help to assess MCMs deployed in a public health emergency.	FDA	FY 2018
3.1.1	Submit to Congress the SNS Annual Review report.	HHS	FY 2016-18
3.1.2	The PHEMCE will re-visit the appropriate roles and responsibilities of the SNS, based on progress made to date, future opportunities, and in consideration of the need for long-term sustainability of this critical national asset.	ASPR / CDC	FY 2018
3.2.2	OEM and DSNS will evaluate whether FMS or other temporary beds could be used in response to a CBRN incident to expand operational capacity. The evaluation will include needs and requirements for staff and supplies.	ASPR / CDC	FY 2018
3.2.3	ASPR and CDC will lead PHEMCE evaluation of cross-threat constraints on emergency preparedness posed by IV MCM formulations and identify initiatives to address these gaps, leveraging existing efforts by CDC to evaluate ancillary supplies.	ASPR / CDC	FY 2018
3.2.6	Develop clinical practice guidelines for MCMs to address botulism (FY 2017) and ARS-associated neutropenia (FY 2018).	ASPR / CDC	FY 2017-18
3.2.13	The PHEMCE, through collaboration with finance, budget, and contract management partners, will identify strategies to accelerate the MCM-related administrative decision-making processes.	ASPR	2017
3.2.20	Work with Canada and Mexico to address barriers to providing mutual assistance and harmonizing utilization policies for MCMs during international public health emergencies under the framework of the BTB, and as called for in NAPAPI.	ASPR	FY 2018

2016 Activity Number	Milestone Description	Lead Agency	Projected Completion Date
3.3.1	In 2016-17, DSLR will provide targeted technical assistance to address operational gaps identified during the MCM ORR site visits in 2015-16.	CDC	FY 2018
3.4.3	Update CERC manual and materials as needed, coordinate sponsored training for government leaders and partners, and maintain a trained cadre of people able to give CERC trainings.	CDC	FY 2018
4.2.5	Support efforts to achieve FDA approval (in healthy populations) for a smallpox vaccine that is ultimately intended for use in immunocompromised individuals in an emergency.	BARDA / CDC	FY 2018
T.A.1	Obtain results from preliminary studies into various technologies for temperature stabilization and alternative routes of delivery for next-generation anthrax vaccines.	NIH	FY 2018
T.A.10	Submission for FDA review of animal model studies to support approval under the "Animal Rule" for use against inhalation anthrax of antimicrobials currently approved for other indications.	NIH	FY 2016
T.A.12	ASPR and CDC will lead analysis of the optimal ratios of products for oral antimicrobial PEP, considering resistance, tolerability, cost, and fluctuations in market availability.	ASPR / CDC	FY 2018
T.OB.2	Qualify animal models for anthrax, plague, and tularemia in support of PEP and treatment indications, through the FDA's Animal Model Qualification Program.	NIH / BARDA	FY 2018
T.OB.10	Continue testing of candidate products against <i>Burkholderia pseudomallei</i> and <i>Burkholderia mallei</i> .	BARDA	FY 2018
T.OB.12	CDC and FDA will develop a pre-EUA package for meropenem, trimethoprim/sulfamethoxazole, and amoxicillin/clavulanate for the treatment of melioidosis and glanders.	CDC / FDA	FY 2018
T.S.5	The PHEMCE will assess policy implications of antivirals and their use.	ASPR / CDC	FY 2018
T.S.6	Complete delivery to the SNS of the required treatment courses of the smallpox antivirals currently under contract.	BARDA	FY 2018
T.PI.3	Develop procedures to ensure that public information in future pandemics is provided in accessible and alternative formats.	CDC	FY 2018

2016 Activity Number	Milestone Description	Lead Agency	Projected Completion Date
T.PI.4	Refine and implement partnership strategies to improve communication with hard-to-reach and at-risk populations.	CDC	FY 2018
T.PI.6	Develop an approach, definitions, tools, and models for a risk communication response plan.	CDC	FY 2018
T.PI.8	Maintain and update the existing stockpile of novel influenza viruses and pre-pandemic vaccines and adjuvants as needed.	BARDA	FY 2018
T.PI.9	Develop rapid methods and biosynthetic technologies to produce candidate vaccine viruses that allow accelerated production of vaccine lots for eventual fill and finish by manufacturers.	CDC / BARDA / FDA	FY 2018
T.PI.10	Develop rapid laboratory methods to expedite testing to determine the antigen content of influenza vaccine bulk material and enable vaccine formulation prior to product fill and finish.	CDC/ FDA / BARDA	FY 2018
T.PI.14	Initiate preclinical development of novel viral antigen and universal influenza vaccine concepts.	NIH	FY 2018
T.PI.17	Implement plan for production of high yielding/immunogenic influenza vaccine strains for distribution to manufacturers and use of the improved potency assays to assist in vaccine development for seasonal and pandemic influenza.	BARDA	FY 2018
T.PI.21	BARDA will support advanced development of at least two drugs with novel mechanism(s) of action through Phase 3 clinical studies; two drugs could be approved for use in the U.S. in this time frame.	BARDA	FY 2018
T.PI.23	Develop new plans for antiviral distribution and dispensing.	CDC	FY 2018
T.PI.26	Continue supporting development of diagnostics to inform seasonal and pandemic influenza treatment with an emphasis on higher quality and faster testing at the point of care.	BARDA	FY 2018
T.B.1	NIH will continue to evaluate a collection of next-generation botulism antitoxin mAbs. Botulism serotype B&E cocktails will be in Phase 1 trials in 2016. Serotypes C&D cocktail is nearing completion of IND-enabling activities. Serotype F&G candidates are undergoing final selection.	NIH	FY 2018
T.B.2	NIH will continue to support the manufacture of a newly identified botulinum toxin, Bot A/F, to enable PHEMCE partners to test efficacy of licensed BAT therapeutic, and candidate anti-Botulism monoclonal antibodies that are currently in development.	NIH	FY 2018

2016 Activity Number	Milestone Description	Lead Agency	Projected Completion Date
T.RN.3	Conduct market analyses on antimicrobials and other products needed to respond to the public health and medical consequences of radiological or nuclear threats.	HHS	FY 2018
T.RN.10	Re-evaluate (annually) the prioritization, with the PHEMCE Prioritization Framework, of resources to support additional national radiobioassay capabilities that would be critical to informing the appropriate use of decorporation agents following a radiological incident.	CDC	FY 2018
C.D.4	CDC with support from other agencies (e.g., FDA and DHS) will help to coordinate the development of highly sensitive, specific, and robust assays for high-priority biological threat agents (i.e., bacterial, viral, and toxins) in accordance with the LRN Design Control Process.	DHS / CDC	FY 2018
C.D.5	Develop additional pre-EUA assays for Joint Biological Agent Identification and Diagnostic System (JBAIDS) for Pan-Burkholderia and Ebola Bundibugyo.	DoD	FY 2018
C.D.6	Develop FDA-approved IVD capabilities for anthrax and smallpox as part of the NGDS Increment 1 platform.	DoD	FY 2018
C.CIADM.1	BARDA will support completion of the construction of critical infrastructure within the CIADMs. The Centers will provide MCM development and manufacturing capabilities to address public health threats as needed.	BARDA	FY 2018
C.CIADM.2	Centers will initiate the activities required for the licensing of pandemic influenza vaccine candidates, including in-licensing as needed, and process development related to the eventual technology transfer of the candidate into the facility.	BARDA	FY 2018
C.CC.2	Establish an Innovation Modeling Hub to provide analytic decision support and access to real-time modeling capabilities to senior decision-makers within ASPR and the PHEMCE.	BARDA	FY 2017
C.CC.3	BARDA is working on developing a matrix to determine high-priority programs for inclusion in the Regulatory Management Plan mandated under the FD&C Act, as amended by PAHPRA.	FDA / BARDA	FY 2018
C.CC.4	Establish an MCM advanced development and manufacturing facility.	DoD	FY 2018

**APPENDIX 8: PROGRESS TOWARDS NEAR-TERM 2014/2015 PHEMCE SIP MILESTONES
(as of FY 2015 unless otherwise noted)**

Table 10: Progress Towards Near-Term 2014/2015 PHEMCE SIP Activities¹⁶⁴

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
1.1.2	Submit the annual MYB report to Congress.	ASPR	FY 2015-16	The PHEMCE MYB Fiscal Years 2015-2019 report was delivered to Congress in April 2016. This report was based on enacted funding levels in FY 2015 and FY 2016, and the FY 2017 President's Budget. The agencies' professional judgments projected the out year estimates for FY 2018 and FY 2019. The first MYB Plan offered an in-depth look at the budgets across agencies related to the medical countermeasure enterprise. These efforts continue to be robust and efficient. We restructured the 2015 report to include budget offerings by threat or portfolio. In addition, this report includes pandemic influenza activities at ASPR, a more comprehensive estimate of the MCM activities at FDA, and a case study examining the PHEMCE's role in the Department's response to the Ebola outbreak in West Africa.
1.1.7	Interagency IPTs will implement the framework and associated metrics to assess current and target levels of MCM preparedness against five preparedness determinants.	ASPR	FY 2016	The PHEMCE has developed a standardized process for conducting and using the results of the preparedness assessments. In addition, PHEMCE IPTs have conducted four pilot studies to apply the process and metrics. Initiatives to address gaps identified will be included in the annual PHEMCE SIP. IPTs are engaged in conducted further MCM preparedness assessments. In addition, the NPRSB is evaluating the PHEMCE's implementation of the process.

¹⁶⁴ Any items that were marked "Complete" in the 2014 PHEMCE SIP are not repeated in this table.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
1.2.1	Update initial anthrax MTA.	DHS	FY 2015	COMPLETED – DHS and HHS completed the MTA 2.0 for anthrax in March 2016.
1.2.3	Coordinate modeling efforts to ensure that the models and parameters are consistent to bring the TRAs and MTAs into alignment in support of MCM planning.	BARDA / DHS	FY 2016	COMPLETED – The public health response model comparison was finalized in quarter two of FY 2016.
1.2.4	Update the TRA development process in accordance with the <i>TRA Stakeholder Engagement Strategy</i> .	DHS	FY 2015	CLOSED – A TRA implementation plan will not be developed.
1.2.5	Produce a TRA program implementation plan.	DHS	FY 2016	CLOSED – A TRA implementation plan will not be developed.
1.2.9	Lead development of a risk assessment methodology and process through which the PHEMCE will determine which EID threats require PHEMCE response.	ASPR	FY 2016	The EID WG anticipates completion of this risk assessment in 2016.
1.2.11	Develop or update MCM requirement documents for CBRN threats, as well as requirements that address multiple threats, as detailed in Objective 1.2, Table 2 of <i>2014 PHEMCE SIP</i> .	ASPR	FY 2016	The PHEMCE streamlined the MCM requirements process to enhance decision-making and prioritization for MCM research, development, acquisition, and management plans. Information in requirements documents has been aligned to this process and standardized. During FY 2015, the PHEMCE approved a civilian MCM requirements document that evaluated the appropriateness of stockpiling RPDs, identifying all-hazards needs for RPDs, and setting RPD stockpiling goals and acquisition targets. The PHEMCE approved the Improvised Nuclear Device SBA in FY 2016. Progress continues to be made developing requirements listed as near-term in Table 2.
1.3.6	In 2015 NIH plans to release a BAA entitled “Development of Therapeutic Products for Biodefense and Emerging Infectious Diseases” with awards to be made in FY 2016.	NIH	FY 2016	Solicitation was released; awards are anticipated to be made in FY 2016.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
2.1.7	Update the 2007 <i>Guidance on the Emergency Use Authorization of Medical Products</i> to be consistent with the amendments to FDA's EUA authorities under PAHPRA.	FDA	FY 2016	COMPLETED – Updated draft guidance was released in April 2016. ¹⁶⁵
3.1.1	Submit to Congress the SNS Annual Review report.	HHS	FY 2014-16	The 2014 SNS Annual Review, which provided recommendations for FY 2017, was completed in September 2015. The 2015 SNS Annual Review (FY 2018 Plan) was completed in August 2016. The 2016 SNS Annual Review (FY2019 Plan) is on track for on time completion.
3.1.2	Develop a risk-based analysis of investment needs by using perspectives from the intelligence community and DHS risk assessment processes.	CDC / DHS	FY 2015	CLOSED – Recommendations from the Risk Formulary Study supported several formulary decisions taken by the PHEMCE affecting the SNS. They determined that the study had fulfilled its original purpose of assessing the trajectory of the SNS and continued integration of the study in the SNS Annual Review was not necessary.
3.2.9	Develop national response strategies for anthrax (FY 2015), botulism, glanders and melioidosis, and smallpox.	ASPR / CDC	FY 2016	In 2016, the PHEMCE approved the Smallpox Vaccine Response Strategy, which provides information to support decisions regarding the effective use of smallpox vaccines in the SNS after the detection of smallpox disease. The Medical Countermeasure Operational Planning Work Group will prioritize future response strategies for development.

¹⁶⁵ See: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm>

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
3.2.10	Develop clinical practice guidelines for MCMs to address chemical agents, smallpox, anthrax, and botulism.	ASPR / CDC	FY 2016	CDC's National Center for Emerging and Zoonotic Infectious Diseases is leading the effort to develop clinical guidelines for botulism for adults, children and pregnant women. A scientific meeting of experts is scheduled for June 2016. Clinical guidance for an anthrax mass casualty event was published by CDC. ¹⁶⁶
3.2.11	Develop an assessment of state and local capacity to utilize cytokines for ARS-associated neutropenia following use of an improvised nuclear device.	ASPR	FY 2015	COMPLETED – Assessment of state and local capacity to utilize cytokines for ARS-associated neutropenia has been completed.
3.2.15b	The PHEMCE, through collaboration with finance, budget, and contract management partners, will identify strategies to accelerate the MCM-related administrative decision-making processes.	ASPR	FY 2016	An Administrative Preparedness Anniversary meeting was held in May of 2015. TTX participants came together in this meeting to consider next steps, share lessons learned, and provide progress updates. Discussion covered potential methods to enhance funding capabilities during non-Stafford events and single-source administrative preparedness tools for response. Priority areas were identified and responsibilities were assigned for follow-on work. ASPR will hold progress meeting to capture any advancements. Also use of HRPAS to rate contracts as they are being issued, will allow for accelerated decisions and fulfillment during emergency responses. It is anticipated that HRPAS will be published as a final rule by 2017.

¹⁶⁶ See: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6404a1.htm>

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
3.2.29	Work with Canada and Mexico to address barriers to providing mutual assistance and harmonizing utilization policies for MCMs during international public health emergencies under the framework of the BTB, and as called for in NAPAPI.	ASPR	FY 2016	<p>In 2015, as a health security priority under the BTB, OPP's Division of International Health Security (DIHS) worked the Public Health Agency of Canada to conduct and document extensive research on the legal, regulatory, and logistical capabilities and barriers for the rapid deployment of MCMs from national stockpiles across the U.S.-Canada border during a public health emergency. In September 2015, DIHS hosted a bilateral exercise with participants from across both U.S. and Canadian governments to test these capabilities and further explore identified legal, regulatory, and logistical challenges to the international deployment of MCMs. As a result of these efforts, the U.S. and Canada identified 22 working-level recommendations to address these challenges which will be implemented through the development of a bilateral toolkit to facilitate the rapid cross-border deployment of medical countermeasures.</p> <p>Additionally, in March 2015, DIHS hosted a trilateral NAPAPI exercise with government representatives from the health, security, agriculture, and foreign affairs sectors of the United States, Canada and Mexico to discuss plans and challenges associated with availability and access to MCMs during an influenza pandemic. Throughout 2015, DIHS also hosted several technical exchanges with NAPAPI partners at both the working and senior leadership levels to share information on policies related to MCMs for pandemic influenza. Over the long term, these efforts will contribute to the development of a trilateral toolkit to facilitate the rapid cross-border deployment of pandemic influenza MCMs, similar to the tool that is currently being developed for BTB.</p>

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
3.3.3	Update the CERC manual and materials as needed, coordinate sponsored training for government leaders and partners, and maintain a trained cadre of people able to give CERC trainings.	CDC	FY 2015	The Division of Emergency Operations is responsible for the management of the CERC training program. During 2015, CERC training was provided to 254 individuals via seven in-person training sessions through CDC University and 721 individuals via other venues. Approximately 24 presentations about CERC were given to UNICEF, Emory University, FEMA, VA, IOM, WorldCom, Rockefeller Foundation, and the Department of the Interior; 27 individuals participated in the first CERC train-the-trainer, including participants from Puerto Rico, American Samoa, and South Korea; More than 575 continuing education units were awarded to 863 individuals who completed CERC online training, with 752 completing the pandemic influenza online training module; A total of 91,868 CERC website page views were generated during 2015.
4.2.1	Develop rodent and porcine juvenile models of ARS.	NIH / BARDA / DoD	FY 2016	Models have been developed for both mice and minipigs through the NIAID-funded, 2010-15 product development support services contract (mice) and through an IAA with AFRRRI. BARDA continued collaborations with PHEMCE partners to develop these animal models.
4.2.6	Support efforts to achieve FDA approval (in healthy populations) for a smallpox vaccine that is ultimately intended for use in immunocompromised individuals in an emergency.	BARDA / CDC	FY 2016	BARDA continued support of the on-going pivotal Phase 3 safety study comparing smallpox MVA and ACAM2000 vaccines. BARDA continued under Project BioShield to stockpile IMVAMUNE a smallpox vaccine for immunocompromised persons. Bavarian Nordic is performing a Phase 2 clinical trial to demonstrate comparability of the current liquid-frozen vaccine to a lyophilized formulation . ¹⁶⁷

¹⁶⁷ See: <https://globenewswire.com/news-release/2015/05/13/735318/10134192/en/Bavarian-Nordic-Announces-Positive-Results-from-Two-Pivotal-Clinical-Studies-of-IMVAMUNE-r-Smallpox-Vaccine.html>

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.A.1	Publish anthrax clinical guidance for use in the general population during a mass casualty event.	CDC	FY 2016	COMPLETED – Clinical guidance was published in December 2015. ¹⁶⁸
T.A.2	Complete human clinical Phase 2 testing of adjuvants that could enhance performance of the approved anthrax vaccine and reduce the doses necessary to achieve full immunity in a post-exposure setting.	NIH	FY 2015	COMPLETED – Phase 2 testing was completed in FY 2015.
T.A.4	Work with the anthrax vaccine manufacturer to support research into dose-sparing strategies for PEP vaccine use.	NIH / CDC / FDA / BARDA	FY 2015	COMPLETED – Two manuscripts, one for the NHP immunogenicity and efficacy study the other for the crosswalk of the NHP to human data have been submitted for publication.
T.A.7	Obtain results from preliminary studies into various technologies for temperature stabilization and alternative routes of delivery for next-generation anthrax vaccines.	NIH	FY 2015	NIAID continues to support the development of early-stage research and next-generation anthrax vaccine candidates that include novel technologies/platforms that accelerate the immune response, improve ease of delivery, and/or enhance stability. Six vaccine products are currently undergoing formulation development and/or preclinical testing. A replication competent, oral Ad4 vaccine vectors expressing rPA (PaxVax). Different regimens of rPA-Ad4 vaccines, with or without the licensed AVA, were evaluated in a Phase 1 clinical trial.
T.A.12	Submission for FDA review of animal model studies to support approval under the “Animal Rule” for use against inhalation anthrax of antimicrobials currently approved for other indications.	NIH	FY 2015	Amoxicillin and amoxicillin-clavulanate (Augmentin) have both been tested and found to be efficacious in PEP of inhalational anthrax.

¹⁶⁸ Bower, WA, Hendricks, K, Pillai, S, Guarnizo, J, and Meaney-Delman, D, Clinical Framework and Medical Countermeasure Use During an Anthrax Mass-Casualty Incident, Morbidity and Mortality Weekly Report, December 2015.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.OB.2	Qualify animal models for anthrax, plague, and tularemia in support of PEP and treatment indications, through the FDA's Animal Model Qualification Program.	NIH / BARDA	FY 2016	<p>Anthrax: Efforts on the anthrax animal model qualification have been decelerated as the therapeutic candidate that would benefit from a qualified animal model proceeded with BLA submission. NIAID has supported FDA's review of the assay component of the BLA submission, which is also part of the animal model qualification.</p> <p>Plague: NIAID is performing statistical meta-analyses of all the completed studies for the NHP model qualification.</p> <p>Tularemia: NIAID submitted a second briefing package to FDA that includes all of the study reports and summaries, along with statistical meta-analyses of data. Analysis of human clinical data is ongoing. NIAID anticipates submitting another briefing package to FDA in 2016. This is anticipated to complete the tularemia NHP model qualification submissions and move to the final qualification review.</p>
T.OB.8	Initiate the testing of candidate products against <i>Burkholderia pseudomallei</i> and <i>Burkholderia mallei</i> .	BARDA	FY 2016	Testing continues with promising results.
T.S.2	Publish the National Smallpox Vaccine Response Strategy that will offer guidance on domestic vaccination strategies, as well as vaccine selection and prioritization for select subgroups, in an emergency triggered by a confirmed clinical case of smallpox.	CDC / ASPR	FY 2016	COMPLETED – The PHEMCE completed the Smallpox Vaccine Response Strategy.
T.S.3	Develop contingency activities to ensure stockpile maintenance for ACAM2000 and VIGIV.	CDC / ASPR	FY 2016	COMPLETED – As of FY 2016, CDC DSNS has warm base contracts in place for ACAM2000 vaccine and VIG to maintain these SNS held products.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.S.6	Complete delivery to the SNS of the required treatment courses of the smallpox antivirals currently under contract.	BARDA	2014	Deliveries of tecovirimat are ongoing.
T.PI.3	Develop mechanisms to further integrate social media and other communication tools into preparedness activities.	CDC	FY 2016	<p>COMPLETED – CDC use of social media for efficient dissemination of key communication messages continues to expand, as new social media platforms arise and as new partners are identified. CDC uses a variety of social media channels to deliver messages to the public and to convene partners via @CDCFlu, @CDCgov, @DrFriedenCDC Twitter, CDC's Facebook, Google+ and Instagram profiles. When appropriate, communication messages are coordinated with @CDCemergency, @CDCtravel, CDC Emergency on Facebook, and CDC Travelers Health on Facebook.</p> <p>During the 2014-15 season, CDC: 1) partnered with 13 Flu Vaccination Digital Ambassadors to promote flu vaccination on their websites, blogs, and social media channels at least four times throughout the season; 2) hosted/participated in six Twitter chats with multi-sector partners, 3) held three Facebook Forums generating 270 questions and comments, 1,540 likes, and 528 shares; 4) conducted a countdown to National Influenza Vaccination Week Blog Relay; and 5) leveraged the #VaxWithMe Selfie campaign and interactive timeline to drive visibility of flu vaccination and spark public engagement with over 522 participants generating more than 18 million impressions.</p>

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.PI.5	Develop procedures to ensure that public information in future pandemics is provided in accessible and alternative formats.	CDC	FY 2016	<p>CDC continues to use multiple platforms for including traditional media, web, social media and mobile messaging for the delivery of public health messages to the public. The National Center for Immunization and Respiratory Diseases' Influenza Division and OPHPR's Emergency Risk Communications Branch develops strategies for communicating to the general public in advance of and during pandemics. Currently all pages of cdc.gov/flu are managed through a web content syndication system and are mobile friendly.</p> <p>During the 2014-15 season, using digital and traditional media generated over 385 million impressions, of which 294 million were earned through partner/Digital Ambassador posts, 58 million through a six week media buy, and 33 million impressions through one radio media tour and two earned print advertorials. In addition, CDC piloted a pandemic influenza vaccine 2-dose text reminder system.</p> <p>CDC is currently working with HHS to expand http://www.cdc.gov/flu/pandemic-resources/ to incorporate unique pandemic influenza content from www.flu.gov, including planning and preparedness and historical information to ensure that the delivery of flu-related information is comprehensive, while maintaining timeliness, accuracy, and credibility of messages.</p>

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.PI.6	Refine and implement partnership strategies to improve communication with hard-to-reach and at-risk populations.	CDC	FY 2016	<p>The CDC continues to support the National Influenza Vaccination Disparities Partnership (NIVDP) as the national multi-sector campaign, spearheaded by local influential partners who commit to promote the importance of flu vaccination among underserved populations. Through the NIVDP, CDC regularly convenes community-based listening sessions where partners help to inform the development of messages, materials and best practices. During the 2014-15 flu season, the NIVDP recruited 171 new community partners and collaborated with Walgreens, Safeway, CVS, the Ventanillas de Salud program, and local health departments to organize 216 flu vaccination promotion events in 95 cities, including rural communities with limited access to influenza vaccination.</p> <p>CDC has maintained the ability to efficiently communicate and disseminate seasonal influenza messages to hard-to-reach and at-risk populations through the NIVDP monthly partners conference calls, partner planning meetings, webinars, recognition events, Facebook, and the online InFLUential Newsletter (approximately 1,000 views/mo). The NIVDP Facebook account allows CDC to quickly inform/mobilize grassroots partners in order to reach disparate populations.</p> <p>During the 2014-15 flu season, CDC partnered with the American Academy of Pediatrics (AAP) to increase pediatrician awareness of influenza prevention and treatment strategies through monthly newsletters, key messages, and webinars; updated the AAP National Preparedness Month web page to share strategies for ensuring children at highest risk of developing flu complications receive flu vaccine and early treatment; and to increase Head Start staff/child care provider awareness of influenza prevention and control strategies through the AAP PediaLink online training course.</p>

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.PI.8	Develop an approach, definitions, tools, and models for a risk communication response plan.	CDC	FY 2016	Continuing to develop a communication strategy and implementation plan for outreach to external partners and internal stakeholders, especially as it relates to public health preparedness and response activities. Continuing to review and refine the database of CDC's Division of Emergency Operations' and Emergency Risk Communication Branch's internal stakeholders and external partners. Development of a needs assessment survey for external partners and internal stakeholders is in process. Updated JIC 101 training slides to reflect cooperative partnership between lead CIO communicators and Emergency Risk Communications Branch staff for communication activities during emergency responses.
T.PI.10	Assess the current policy for the pre-pandemic influenza vaccine stockpiles, including the adjuvant stockpile, and guidance for their use.	CDC / BARDA	FY 2016	COMPLETED – The FRMM reviewed in 2015 the quantity, composition, and status of H5N1 and H7N9 vaccine antigens and AS03 and MF59 adjuvants in the national pre-pandemic stockpile resulting in the development and manufacturing of H5N8 avian influenza vaccines for further study and to mitigate potential gaps in previously stockpiled H5N1 vaccine.
T.PI.11	Maintain and update the existing stockpile of novel influenza viruses and pre-pandemic vaccines and adjuvants as needed.	BARDA	FY 2016	BARDA with PHEMCE partners, including CDC, NIH, and FDA, deliberated on the pre-pandemic influenza vaccine stockpile composition using the IRAT leading to the decision that there were no changes needed in the stockpile composition at this time.
T.PI.12	Develop rapid methods and biosynthetic technologies to produce candidate vaccine viruses that allow accelerated production of vaccine lots for eventual fill and finish by manufacturers.	CDC / BARDA / FDA	FY 2016	CDC developed recombinant candidate vaccine viruses specific to the North American A(H5N8) highly pathogenic avian influenza (HPAI) viruses that emerged in late 2014 and the A(H5N2) HPAI viruses that caused widespread poultry outbreaks in spring and summer 2015.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.PI.13	Develop rapid laboratory methods to expedite testing to determine the antigen content of influenza vaccine bulk material and enable vaccine formulation prior to product fill and finish.	CDC/ FDA/BARDA	FY 2016	In 2014-15 CDC tested ELISA based potency assay for H7 influenza, and supported FDA's work of validation of this platform for seasonal influenza.
T.PI.15	Initiate preclinical development of novel viral antigen and universal influenza vaccine concepts.	NIH	FY 2016	In 2015 and 2016, the VTEUs have continued to conduct clinical trials testing the safety and immunogenicity of an inactivated H7N9 vaccine with and without AS03 or MF59 adjuvants in healthy adults and the elderly. ^{169, 170} VTEUs have also began implementation of a clinical trial to evaluate an H5N8 vaccine with and without AS03 and MF59 adjuvant in healthy adults. BARDA and NIAID's Division of Microbiology and Infectious Diseases collaborated on clinical trials to test the antigen sparing effect of stockpiled oil-in-water adjuvants in combination with stockpiled H5N1 and H7N9 avian influenza vaccines. Results from these studies showed that H7N9 inactivated vaccines were immunogenic when adjuvanted with MF59 or AS03 but not immunogenic as antigen-alone vaccine formulations. Also BARDA and NIAID/Laboratory of Infectious Diseases collaborated to conduct prime/boost clinical studies that revealed the capacity of live attenuated H7N9 influenza vaccines to prime for inactivated H7N9 vaccines.

¹⁶⁹ Jackson LA, Campbell JD, Frey SE, et.al., Effect of Varying Doses of a Monovalent H7N9 Influenza Vaccine With and Without AS03 and MF59 Adjuvants on Immune Response: A Randomized Clinical Trial, JAMA. 2015 Jul 21;314(3):237-46.

¹⁷⁰ Mulligan MJ, Bernstein DI, Winokur P, et. al., Serological responses to an avian influenza A/H7N9 vaccine mixed at the point-of-use with MF59 adjuvant: a randomized clinical trial, JAMA. 2014 Oct 8;312(14):1409-19.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.PI.16	Move at least one universal influenza vaccine candidate into Phase 1 clinical trials.	NIH / BARDA	FY 2016	<p>In 2015 NIAID supported the chimeric HA vaccine candidate with an IND enabling animal toxicology study and the development of clinical and potency assays. In coordination with BARDA, NIAID also supported studies into improving the stability of chimeric HA vaccine candidates. Additionally, NIAID began implementation of a clinical trial through the NIAID VTEUs in collaboration with Biondavax Pharmaceuticals to investigate a universal influenza vaccine candidate that stimulates a T-cell and B-cell responses against seasonal and pandemic influenza strains. BARDA and NIH collaborated to transition a novel chimeric HA (cHA) vaccine candidate from pre-clinical to clinical stage development. BARDA contracted with bioCSL to produce and release clinical investigations lots of two cHA vaccine candidates - cHA5/1 and cHA8/1. NIH supported on-going toxicology studies but is not conducting a clinical study due to loss of stability of chimeric vaccines.</p> <p>BARDA also began support of an adenovirus-vector HA universal influenza vaccine candidate.</p>
T.PI.19	Initiate support of one or two promising influenza vaccines through the BAA funding mechanism.	BARDA	FY 2016	<p>COMPLETED – BARDA began support for development of an adenovirus-vector HA universal influenza vaccine candidate and renewed the development of cell-based influenza vaccine candidates.</p>
T.PI.22	Implement plan for production of high yielding/immunogenic influenza vaccine strains for distribution to manufacturers and use of the improved potency assays to assist in vaccine development for seasonal and pandemic influenza.	BARDA	FY 2016	<p>BARDA continued support for the development of new flu vaccine potency assays in collaboration with FDA, National Institute for Biological Standards and Control, and industry partners.</p>

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.PI.26	BARDA will support advanced development of at least two drugs with novel mechanism(s) of action through Phase 3 clinical studies; two drugs could be approved for use in the U.S. in this time frame.	BARDA	FY 2016	BARDA continued support in 2015 for a pivotal Phase 3 clinical study of a host-targeted flu antiviral drug candidate that showed no increased efficacy over oseltamivir in the treatment of hospitalized flu patients and began support for development of novel flu antiviral drug targeted to the viral RNA polymerase.
T.PI.27	NDA filing for a small molecule, broad-spectrum anti-viral targeting pandemic and seasonal influenza.	DoD	FY 2016	CLOSED – This product is being phase out. All advanced development efforts are being consolidated into a single anti-viral program as of June 2016.
T.PI.28	Develop new plans for antiviral distribution and dispensing.	CDC	FY 2016	Plans to leverage pharmaceutical supply chain are under development. Plans are being reassessed to consider impact of generic drugs options set to come to market in 2017.
T.PI.31	Commence development of new sequencing-based diagnostic assays and prototype device development for detection of influenza viruses and other respiratory pathogens.	BARDA	FY 2016	COMPLETED – BARDA began support in 2015 for the development of a flu diagnostic candidate using new nucleotide sequencing technology.
T.OV.1	Move broad-spectrum antiviral candidates into clinical testing.	NIH	FY 2016	COMPLETED – Phase 1 study is ongoing for antivirals against dengue and flu and as well as Phase 2 challenge study for influenza therapeutic.
T.OV.5	Make additional awards for vaccine candidates based on supplemental funding.	BARDA	FY 2016	COMPLETED – We supported in 2015 the development of four Ebola vaccine candidates (Profectus, GSK, NewLink/Merck and Crucell/Bavarian Nordic) using FY 2015 CR and Ebola Supplemental Appropriations.
T.OV.10	The pivotal ZMapp™ preclinical safety data supported by NIAID will be available in February 2015 to allow for a NIAID-supported Phase 1 trial to begin in the first quarter of 2015.	NIH	FY 2015	COMPLETED –Final report on safety data was sent to Mapp Biopharmaceutical, Inc. in 2015. Phase 1 launch is anticipated in FY 2016.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.OV.11	ZMapp™ is expected to be included in the master randomized control trial (RCT) protocol expected to begin in the U.S. and West Africa in early 2015.	NIH / BARDA	FY 2015	COMPLETED – RCT is closed due to reduced number of subjects to enroll in study.
T.OV.13	NIH is partnering with DoD to conduct trials of an additional vaccine candidate, an rVSV-vectored EBOV in development by NewLink Genetics Corp with funding from the DoD.	NIH / DoD	FY 2016	COMPLETED – Phase 1 trials were completed Fall 2015 at WRAIR and at the NIH Clinical Center. A Phase 3 vaccine trial and a Phase 3 ring vaccination trial (as opposed to large-scale mass vaccination) were conducted in Guinea. Interim analysis published in The Lancet in July 2015 indicated that the rVSV-ZEBOV was highly efficacious and safe. ¹⁷¹
T.OV.14	Advance Ebola candidate vaccines to Phase 2/3 efficacy testing.	NIH / DoD	FY 2016	COMPLETED – DoD is assisting with closing out these advanced clinical studies by validating a key ELISA (expected by July 2016) ICW FDA. Also, DoD is working with several vaccine developers other than Newlink (Merck, Janssen, Bavarian Nordic et.al) to advance prospective Ebola vaccine candidates through the regulatory process.
T.OV.21	Favipiravir, and another potential therapeutic, TKM-Ebola, may undergo Phase 2 trials in West Africa in early 2015.	DoD	FY 2016	CLOSED – TKM-Ebola is no longer under development by the DoD.

¹⁷¹ Henao-Restrepo, AM, Longini, IM, Egger, M, et al., Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial, The Lancet, Vol. 386, No. 9996, p. 857–866, 29 August 2015.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.B.1	NIH will continue to evaluate a collection of next-generation botulism antitoxin monoclonal antibodies. Botulism serotype B&E cocktails will be in Phase 1 trials during this period. Serotypes C&D may also advance to clinical testing during this period. Serotype F&G candidates are undergoing final selection.	NIH	FY 2016	A botulism serotype A anti-toxin mAb cocktail has completed Phase 1 trials with NIH support, while NIH anticipates botulism serotype B&E anti-toxin mAb cocktails to enter Phase 1 trials in 2016. A serotypes C&D anti-toxin mAb cocktail is nearing completion of IND-enabling activities.
T.B.2	Evaluate botulism type "H"(Bot H) strain for sensitivity to the approved BAT as well as appropriate candidate monoclonal antibodies.	NIH	FY 2016	CDC has determined that BAT completely eliminates the toxic effect of botulinum toxin FA (previously identified by CDPH as serotype H) in mice. NIH is supporting efforts to manufacture sufficient quantities of pure serotype "H" botulinum toxin to enable PHEMCE partners to do a full characterization.
T.RN.1	Conduct market analyses on antimicrobials and other products needed to respond to the public health and medical consequences of radiological or nuclear threats.	HHS	FY 2016	We continued market research and end-user engagements on drugs that may be available to treat conditions that may result from exposure to ionizing radiation or chemical agents.
T.RN.5	Conduct exercises to pilot different cytokine distribution and dispensing models to address ARS-associated neutropenia.	ASPR / VA	FY 2016	CLOSED – This activity was closed due to budget constraints.
T.RN.6	Conduct user engagements to determine the needs of the end-users and their ability to administer products after an incident.	ASPR	FY 2016	CLOSED – This activity was closed due to budget constraints.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
T.RN.11	Re-evaluate (annually) the prioritization, with the PHEMCE Prioritization Framework, of resources to support additional national radiobioassay capabilities that would be critical to informing the appropriate use of decontamination agents following a radiological incident.	CDC	FY 2015-16	CDC, with MCSR support, is working to develop CONOPS for an RDD. Once this is completed, it will be incorporated into the economic risk assessment model.
C.D.2	Define alternative methodologies for the generation of requisite datasets for specific threat agents for which traditional clinical specimens are insufficient to support approval.	NIH	FY 2016	COMPLETED – NIH and FDA collaborated to develop methods to generate mock (spiked) clinical samples for use to conduct clinical sensitivity studies required for FDA clearance for low prevalence pathogens. ¹⁷²
C.D.6	Develop highly sensitive, specific, and robust Public Health Actionable Assays (PHAA) for high-priority biological threat agents (i.e., bacterial, viral, and toxins) for deployment and employment through the CDC Laboratory Response Network (LRN).	DHS / CDC	FY 2016	DHS has transitioned the following PHAA assays to CDC for evaluation and consideration for deployment to the LRN: <i>Francisella tularensis</i> , <i>Yersinia pestis</i> , <i>Rickettsia prowazekii</i> , <i>Rickettsia rickettsii</i> , Variola virus, Ricin, Ebola, and Marburg viruses. Real-time PCR assays for <i>Francisella tularensis</i> and <i>Yersinia pestis</i> are in phase 2 of design control for development. DHS is currently working on developing assays for <i>Clostridium botulinum</i> , <i>Burkholderia mallei</i> , <i>Burkholderia pseudomallei</i> , <i>Coxiella burnetii</i> and Lassa PHAA. Future plans include <i>Bacillus anthracis</i> , <i>Brucella spp.</i> , VEE, eastern equine encephalitis, Junin, Crimean-Congo hemorrhagic fever, staphylococcal enterotoxin B, and a multiplex antigen assay for <i>Bacillus anthracis</i> , <i>Yersinia pestis</i> , <i>Francisella tularensis</i> , <i>Burkholderia mallei</i> and <i>Burkholderia pseudomallei</i> .

¹⁷² Dong M, Fisher C, German A, Rios M, Nakhasi H, Hobson J, Beanan M, Hockman D, Grigorenko E, Duncan R (2016) Standardized Method to Generate Mock (Spiked) Clinical Specimens by Spiking Blood or Plasma with Culture Pathogens. J Applied Microbiology, 120:1119-1129. <http://www.ncbi.nlm.nih.gov/pubmed/26835651>

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
C.D.7	Develop additional pre-EUA assays for JBAIDS for Pan-Burkholderia and Ebola Bundibugyo.	DoD	FY 2016	The pre-EUA assay studies for pan-burk and Ebola Bundibugyo are ongoing.
C.D.8	Develop FDA-approved IVD capabilities for anthrax and smallpox as part of the NGDS Increment 1 platform.	DoD	FY 2016	Ongoing. Both anthrax and smallpox will be included in the diagnostic Warrior Panel.
C.D.9	Develop an environmental assay for smallpox as part of the NGDS Increment 1 platform.	DoD	FY 2016	Ongoing. Smallpox environmental assay will be part of the NGDS Inc 1 Sentinel Panel.
C.NP.4	Reassess the quantity and composition of RPD stockpiles for pandemic influenza and other threats, taking fiscal constraints into account, to determine whether the stockpiling of RPDs in the SNS should be continued.	CDC / ASPR	FY 2016	COMPLETED – In February 2015, the PHEMCE approved the ICD: RPDs and Facemask Chapter which identified the need for RPDs and facemasks during a pandemic influenza response and determined preliminary stockpiling goals for those products.
C.NP.7	Begin work with appropriate organizations to integrate the patient decontamination planning guidance into emergency response training curricula.	HHS / DHS	FY 2016	COMPLETED – DHS Office of Health Affairs is participating, and representing the patient decontamination planning guidance, on the curriculum committee for FEMA's Center for Domestic Preparedness, which trains large numbers of emergency responders on patient decontamination. Principals from the planning guidance have been incorporated into the Chemical Hazards Emergency Medical Management website, run by HHS' National Library of Medicine and ASPR.
C.CIADM.1	BARDA will support completion of the critical infrastructure within the CIADMs. It is anticipated that these centers will have limited capability to provide certain advanced development and manufacturing core services during this time frame, if required by the USG.	BARDA	FY 2016	Construction of BARDA CIADM continued on-track for full operation by 2017. Construction of the pilot manufacturing facilities at the Novartis CIADM and the influenza vaccine manufacturing facility at the TAMUS CIADM were completed in 2015. Two Ebola monoclonal antibody development and manufacturing projects were initiated in 2015 at the Emergent CIADM.

2014/2015 Activity Number	Description	Lead Agency	2014/2015 SIP Target Date	Progress
C.CIADM.2	Centers will initiate the activities required for the licensing of pandemic influenza vaccine candidates, including in-licensing as needed, and process development related to the eventual technology transfer of the candidate into the facility.	BARDA	FY 2016	Novation of the BARDA contracts including the cell-based influenza vaccines and the CIADM from Novartis to CSL (Seqiris) started in 2015. GSK and the TAMUS CIADM continue development of cell-based influenza vaccines. Technology transfer of the recombinant influenza vaccines from VaxInnate to the Emergent CIADM continued.
C.CC.2	Establish an Innovation Hub to provide analytic decision support and access to real-time modeling capabilities to senior decision-makers within ASPR and the PHEMCE.	BARDA	FY 2016	We started in 2015 the construction of our Visualization Hub for mathematical modeling and development of software and modeling content for its IT system.
C.CC.3	Develop a matrix to determine high-priority programs for inclusion in the Regulatory Management Plan mandated under PAHPRA.	FDA / BARDA	FY 2016	There are currently no MCMs in development that have been deemed in need of a Regulatory Management Plan.
C.CC.7	Establish an MCM advanced development and manufacturing facility.	DoD	FY 2016	The development of the Nanotherapeutics facility in Alachua, Florida, is ongoing and will contain pilot and cGMP production suites with facility now anticipated to be operational in the first quarter of FY 2017.

APPENDIX 9: PUBLIC HEALTH SERVICE ACT REQUIREMENTS

Table 11: Public Health Service Act Requirements

PHS Act Information Requirements	Location in <i>PHEMCE SIP</i>
Description of the CBRN agents that may present a threat to the U.S. and corresponding efforts to develop medical/security countermeasures and pandemic/epidemic products.	Introduction – Box 1 Section 1: Activities to Achieve Strategic Goals and Objectives Section 2: Threat-based Approaches Section 3: Capabilities-based Approaches
Progress evaluation of all activities related to countermeasures/products, including research, advanced research, development, procurement, stockpiling, deployment, distribution, and utilization.	Accomplishments in FY 2015 Appendix 4: Progress In Addressing At-Risk Population Medical Countermeasure Needs Appendix 5: Progress Towards Near-term 2014/2015 PHEMCE SIP Milestones
Identify and prioritize near-, mid-, and long-term needs with respect to such countermeasures or products to address a CBRN threat(s).	Section 1: Activities to Achieve Strategic Goals and Objectives Section 2: Threat-based Approaches Section 3: Capabilities-based Approaches
Summarize advanced development and procurement awards with respect to each category of CBRN threat: <ul style="list-style-type: none"> – Time elapsed since the issuance of the initial solicitation/request to adjudication; – Projected timelines, anticipated funding allocations, benchmarks, and milestones for each MCM priority and evaluation of progress in meeting these timelines, allocations, benchmarks and milestones; – Projected needs with regard to replenishment of the SNS. 	Appendix 5: Advanced Research and Development and Procurement
Be informed by recommendations from NBSB (now called the National Preparedness and Response Science Board (NPRSB)).	Development of the 2016 PHEMCE SIP – Consideration of Perspectives from National Advisory Committees
Report on the amount of funds available for procurement in the PBS SRF and the impact this funding will have on meeting the requirements.	Appendix 5: Advanced Research and Development and Procurement
Incorporate input from federal, state, local, and tribal stakeholders.	Appendix 3: PHEMCE Coordination with Non-Federal Stakeholders

PHS Act Information Requirements	Location in <i>PHEMCE SIP</i>
<p>Identify progress made in meeting the MCM priorities for at-risk individuals:</p> <ul style="list-style-type: none"> – Stockpiling and replenishment of the SNS – Addressing the needs of pediatric populations with respect to MCM and products in SNS: <ul style="list-style-type: none"> ▪ A list of MCMs needed for pediatric populations; ▪ Description of measures taken to coordinate with the Office of Pediatric Therapeutics (FDA); ▪ Description of existing gaps in the SNS and the development of such MCMs to address the needs of pediatric populations; ▪ Evaluation of the progress made in addressing pediatric populations needs; 	<p>Appendix 4: Progress In Addressing At-Risk Population Medical Countermeasure Needs</p> <p>Section 1: Activities to Achieve Strategic Goals and Objectives, Goal 4</p>
<p>Identify the use of certain authorities and activities added to the PHS Act by the PBS Act:</p> <ul style="list-style-type: none"> – The actions taken under the authority, including, the identification of the threat agent, emergency, MCM, etc. with respect to the use of such authority; – The reasons underlying the decision to use such authority, including, the options that were considered and rejected with respect to the use authority; – The number of, nature of, and other information concerning the persons and entities that received a grant, cooperative agreement, or contract pursuant to the use of such authorities, and the persons and entities that were considered and rejected for such a grant, cooperative agreement, or contract; – Whether a contract was entered into within a year for procurements approved by the President (delegated to OMB); – The number of persons paid \$50,000 and the number of persons paid \$100,000 under personal services contracts. 	<p>Accomplishments in FY 2015, Regulatory Science Management</p> <p>Appendix 5: Advanced Research and Development and Procurement</p>

PHS Act Information Requirements	Location in <i>PHEMCE SIP</i>
<p>In the first <i>PHEMCE SIP</i> released following PAHPRA, description of the manner in which HHS is coordinating with DoD regarding countermeasure activities to address chemical, biological, radiological, and nuclear threats. Such report shall include information with respect to:</p> <ul style="list-style-type: none"> – Research, advanced research, development, procurement, stockpiling, and distribution of countermeasures to meet identified needs; – HHS-DoD coordination to address MCM needs for various segments of the population. 	<p>Fulfilled in the <i>2014 PHEMCE SIP</i>, Section 2: Interagency Partner Roles and Collaborations in Supporting Strategic Goals and Objectives; not required for subsequent <i>PHEMCE SIP</i> versions. DoD (and other interagency) coordination is highlighted throughout this document.</p>