



U.S. Department of Health and Human Services

**2012 Public Health Emergency
Medical Countermeasures
Enterprise (PHEMCE) Strategy**

TABLE OF CONTENTS

EXECUTIVE SUMMARY	2
OVERVIEW OF PHEMCE STRATEGIC GOALS AND OBJECTIVES	3
INTRODUCTION	5
ACCOMPLISHMENTS SINCE 2007	8
CHANGES TO THE MEDICAL COUNTERMEASURE LANDSCAPE	9
DEVELOPMENT OF THE 2012 PHEMCE STRATEGY	11
STRATEGIC PRIORITIZATION FRAMEWORK	12
PHEMCE STRATEGIC GOALS AND OBJECTIVES.....	14
GOAL 1. Identify, create, develop, manufacture and procure critical medical countermeasures.	14
Objective 1.1	14
Objective 1.2.....	14
Objective 1.3.....	15
Objective 1.4.....	15
GOAL 2. Establish and communicate clear pathways to facilitate medical countermeasure development and use.....	16
Objective 2.1	16
Objective 2.2.....	17
GOAL 3. Develop logistics and operational plans for optimized use of medical countermeasures at all levels of response.....	17
Objective 3.1	18
Objective 3.2.....	18
Objective 3.3.....	19
Objective 3.4.....	20
GOAL 4. Address medical countermeasure gaps for all sectors of the American civilian population.	20
Objective 4.1	21
Objective 4.2.....	21
Objective 4.3.....	21
IMPLEMENTATION OF THE STRATEGY	22
APPENDIX 1 – GLOSSARY.....	23
APPENDIX 2 - ACRONYMS	27
APPENDIX 3 – PHEMCE ORGANIZATIONAL STRUCTURE	28
APPENDIX 4 – PROGRESS REPORT	32
APPENDIX 5 – STRATEGIC ALIGNMENT.....	37

EXECUTIVE SUMMARY

The U.S. Government has a responsibility to protect the health and safety of its citizens. The American people continue to face a host of national health security threats from chemical, biological, radiological, and nuclear (CBRN) agents (e.g., weapons that could be used to kill or injure a large number of people) and emerging infectious diseases (EID) (e.g., 1918-19 influenza pandemic outbreak). Under the leadership of the Department of Health and Human Services (HHS) the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) is the coordinating body for the federal agencies in charge of protecting the civilian population from potential adverse health impacts through the use of medical countermeasures, which are medicines, devices, or other medical interventions that can lessen the harmful effects of these threats.

Since the first PHEMCE Strategy and Implementation Plan were released in 2007, critical medical countermeasures have been developed, acquired, and stockpiled for emergency use. Plans have been made across all levels of government to ensure these critical assets can be used effectively in an emergency. Additionally, experiences ranging from real public health emergencies to national-level exercises have presented opportunities for the PHEMCE to assess medical countermeasure preparedness planning and to reallocate resources based on lessons learned.

Above all, the PHEMCE mission and outputs must preserve and protect people's lives against a wide range of dangerous threats and do so as good stewards of the taxpayer's dollars. These are two core principles of the PHEMCE Strategy. Standing on past progress and seeking to make the best use of available resources, the *2012 PHEMCE Strategy* establishes these strategic goals for the PHEMCE over the next five years:

- Identify, create, develop, manufacture, and procure critical medical countermeasures.
- Establish and communicate clear regulatory pathways to facilitate medical countermeasure development and use.
- Develop logistics and operational plans for optimized use of medical countermeasures at all levels of response.
- Address medical countermeasure gaps for all sectors of the American civilian population.

PHEMCE Leadership has identified a set of criteria against which all investments must be prioritized. These include (1) addressing the most significant threats, (2) fostering approaches with the potential to provide protection against multiple important threats, and (3) maintaining the capability to effectively use the assets developed in the envisioned operational setting. The *2012 PHEMCE Implementation Plan*, to be released in summer 2012, will further describe the prioritization of programs based on these criteria. This Strategy and the Implementation Plan together provide the blueprints the PHEMCE will follow in the near, mid-, and long-terms to make the best use of available resources to enhance national health security.

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 medical countermeasure requirement setting that include consideration of effective production, storage, deployment and administration strategies.

Objective 1.3: Ensure a robust and sustainable product pipeline for medical countermeasures 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.

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 MCM development and use.

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

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

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 medical countermeasure utilization policy, guidance and response strategies, including FDA regulatory frameworks, that are responsive to end-user needs, that are integrated with State, local, tribal and territorial (SLTT) and private sector response plans, and when possible international partners, and that ensure timely, safe, and effective medical countermeasure distribution and utilization.

Objective 3.3: Develop and provide medical countermeasure communications, training, and education information to inform all stakeholders.

Objective 3.4: Develop and implement strategies to assess, evaluate, and monitor medical countermeasure safety, performance, and patient compliance 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.¹

Objective 4.2: Support medical countermeasure advanced development and procurement for at-risk individuals.

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

¹ At- risk individuals have needs in one or more of the following functional areas: communication, medical care, maintaining independence, supervision, and transportation. At-risk groups may include children, senior citizens, 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>

INTRODUCTION

The United States 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, including pandemic influenza. A failure to anticipate these threats – or the lack of a capacity to effectively respond to them – could leave an untold number of Americans dead or permanently disabled. The United States must therefore have the nimble, flexible capability to produce and effectively utilize medical countermeasures²³ in the face of any attack or threat whether known or unknown – novel or reemerging – natural or intentional. In addition, these capabilities must be communicated to the American public both before and during an emergency.

The Secretary of Health and Human Services (HHS) leads all Federal public health and medical response to public health and medical emergencies covered by the National Response Framework.⁴ A number of National Strategies and Presidential Directives establish HHS as the lead Federal department responsible for the protection of the health of the civilian population against both intentional and accidental or naturally occurring threats.⁵ Additionally, the HHS Strategic Plan 2010-2015 calls for reducing the occurrence of infectious diseases, protecting Americans' health and safety during emergencies, and fostering resilience in response to emergencies; these goals are also reflected in particular strategic initiatives set by the Secretary.⁶ Effectively fulfilling this responsibility and accomplishing these goals necessitates coordination of medical countermeasure-related activities occurring across multiple Federal departments. To provide this coordination, HHS established the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE)⁷ in July 2006 to coordinate Federal efforts to enhance civilian preparedness⁸ from a medical countermeasure perspective. The PHEMCE is

² Medical countermeasures include both pharmaceutical interventions, such as vaccines, antimicrobials, antidotes, and antitoxins, and non-pharmaceutical interventions, such as ventilators, diagnostics, personal protective equipment (PPE), 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.

³ Medical countermeasures 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)).

⁴ See section 2801 of the Public Health Services Act (42 U.S.C. 300hh)

⁵ These include but are not limited to the National Strategy for Public Health and Medical Preparedness (Homeland Security Presidential Directive-21, October 2007); the National Response Framework (January 2008); the National Health Security Strategy (December 2009); and the National Preparedness Goal (Presidential Policy Directive – 8, March 2011).

⁶ Available at <http://www.hhs.gov/secretary/about/priorities/priorities.html>

⁷ Available at <http://www.gpo.gov/fdsys/pkg/FR-2006-07-06/pdf/06-6004.pdf>

⁸ This mandate includes consideration of the particular needs of first responder populations who are placed at 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 the support they need, including medical countermeasures, is described elsewhere and not detailed here: <http://www.phe.gov/Preparedness/planning/cip/Pages/default.aspx>

charged with addressing the needs to produce and make medical countermeasures available to limit potential adverse health impacts on the large and diverse U.S. civilian population. The PHEMCE is working to meet the public health emergency needs of the entire civilian population, including groups that require special medical considerations, such as children and the elderly, as well as for first responders, health personnel, and other critical infrastructure personnel, by taking a “whole of community” approach in planning, response, and recovery efforts.

This is a complex mission space and many Federal agencies have responsibilities that are critical to its success. The PHEMCE is led by the Assistant Secretary for Preparedness and Response (ASPR).⁹ Core HHS members are the Director for 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 U.S. Department of Agriculture (USDA). Additionally the PHEMCE works with appropriate HHS and U.S. Government partners to consider international aspects of its mission when appropriate. The PHEMCE also works closely with a variety of non-Federal partners including State, local, tribal and territorial governments, public health systems, academia, private industry, and ultimately the American people.

The PHEMCE mission is to advance national preparedness for natural, accidental, and intentional threats by coordinating medical countermeasure-related efforts within HHS and in cooperation with PHEMCE interagency partners. The PHEMCE provides a governance structure to achieve this coordination (described in Appendix 3).

The PHEMCE mission components include:

- **Requirements Setting:** The PHEMCE is responsible for establishing requirements for civilian medical countermeasures based on many factors, including threat and risk assessments. DHS is the lead in conducting the threat and risk assessments that are leveraged in PHEMCE requirements setting. ASPR leads the requirements-setting process with engagement from all PHEMCE partners and expert inputs, including medical consequence and public health response assessments.
- **Early Stage Research:** NIH conducts and supports basic research to better understand threats of civilian public health concern. This research provides the foundation for developing medical products and strategies to diagnose, treat, and prevent a wide range of threats. DoD and USDA also conduct early stage research that is pertinent to the PHEMCE mission.

<http://www.phe.gov/about/OPP/DHSHCP/Pages/default.aspx>

<http://www.phe.gov/preparedness/planning/postal/Pages/default.aspx>

⁹ The Office of the ASPR includes component offices with key PHEMCE roles such as the Biomedical Advanced Research and Development Authority (BARDA), Office of Policy and Planning (OPP), and Office of Preparedness and Emergency Operations (OPEO).

- Advanced Development/Manufacturing: ASPR/BARDA is the lead PHEMCE partner supporting advanced development and scale up of manufacturing capacity for medical countermeasures, including promoting partnerships with developers and manufacturers. DoD and USDA also conduct advanced development that is coordinated and leveraged through the PHEMCE.
- Regulatory Science Management: The PHEMCE conducts regulatory science¹⁰ to facilitate medical countermeasure development, regulatory assessment, and use. The FDA is the lead agency charged with ensuring medical countermeasures are safe and effective. Activities conducted in support of this mission component intersect with many other mission components in product development and utilization.
- Procurement / Inventory Management / Stockpiling: The PHEMCE oversees the procurement of medical countermeasures and their associated inventory management, including stockpiling. Both the CDC and ASPR/BARDA have lead roles in procuring medical countermeasures for stockpiling. The CDC leads the procurement and maintenance of commercially available medical countermeasures for stockpiling in the Strategic National Stockpile (SNS). BARDA procures certain medical countermeasures for the SNS using the Special Reserve Fund (SRF) authorized under the Project BioShield Act of 2004. DoD and the Department of Veterans' Affairs may also serve as needed in planning or executing stockpiling options.
- Response Planning, Policy, Guidance and Communication: The CDC and ASPR coordinate the development of Federal response plans, policy, guidance, and communication, and develop clinical utilization and allocation strategies as appropriate for medical countermeasures and assets. DoD, DHS, and VA are key PHEMCE partners in this mission component.
- Deployment / Distribution / Dispensing / Administration: The CDC and ASPR coordinate interactions with State, local, tribal, territorial (SLTT), and private entities to provide timely and effective deployment, distribution, dispensing, and administration of medical countermeasures in an emergency. The VA is a key PHEMCE partner in this mission component.
- Monitoring / Evaluation / Assessment: The CDC and FDA lead efforts to monitor safety and performance of deployed medical countermeasures during and after an emergency response. Other PHEMCE partners such as NIH can provide additional capability for

¹⁰ Regulatory Science is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products.
[http://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/default.htm?utm_campaign=Goo&utm_source=fdaSearch&utm_medium=website&utm_term=regulatory science&utm_content=1](http://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/default.htm?utm_campaign=Goo&utm_source=fdaSearch&utm_medium=website&utm_term=regulatory%20science&utm_content=1).

clinical trials management or other support roles in evaluation of safety and performance.

A periodic assessment of strategy and capabilities in light of changing scientific and fiscal circumstances is appropriate. Difficult choices must be made to manage risk in ways that favor success in meeting a public health emergency. To this end, HHS updates PHEMCE Strategy and Implementation Plans every five years or more often if needed. The 2007 *PHEMCE Strategy and Implementation Plan for Chemical, Biological, Radiological, and Nuclear (CBRN) Threats*, while acknowledging the complete PHEMCE mission space, predominantly focused on advanced development and acquisition priorities for medical countermeasures using funds available in the Special Reserve Fund authorized under the Project BioShield Act of 2004.¹¹ The 2012 *PHEMCE Strategy* and its related *Implementation Plan* (to be released in summer 2012) are broader in scope, establishing priorities throughout the PHEMCE mission space. Moreover, they address medical countermeasure planning and policies for pandemic influenza and other emerging infectious diseases (in addition to the intentional CBRN threats previously covered in the 2007 effort). The 2012 *PHEMCE Strategy* is intended to guide PHEMCE activities for the next five years.

Fulfilling the PHEMCE mission will also require balanced investments in consideration of the long-term sustainability of the Enterprise. Toward this end, the HHS Secretary is also implementing a five year budget planning process across the HHS components of the PHEMCE in order to achieve closer coordination and prioritization of investments in public health emergency preparedness that will be tied to the framework provided by this Strategy. In general this Strategy provides a framework for clarifying priorities, improving decision analysis, and enhancing planning, budgeting, and evaluation activities throughout the PHEMCE.

ACCOMPLISHMENTS SINCE 2007

The 2007 *PHEMCE Strategy and Implementation Plan for CBRN Threats* described advanced development and acquisition priorities for CBRN medical countermeasures. Consonant with these plans, seven new critical medical countermeasures have been delivered to the Strategic National Stockpile (SNS) or are in the process of delivery. These medical countermeasures address threats including anthrax, smallpox, botulism toxin, and radiological and nuclear agents. They will allow HHS to better respond to public health emergencies caused by intentional threats or natural events, ultimately saving lives and reducing illness. A brief summary of the key CBRN advanced development and acquisition accomplishments since 2007 with respect to these priorities is shown in Appendix 4. In addition to these accomplishments other notable examples of medical countermeasure advancements include:

¹¹ P.L. 108-276; available at <http://www.hsdl.org/?view&did=449237>

- National preparedness levels for botulism were greatly enhanced through completion of stockpile delivery of a new botulinum antitoxin. This new antitoxin is currently used for treatment of sporadic, naturally occurring cases of botulism in the U.S.
- The clinical trial infrastructure developed for biodefense applications was used to support essential clinical studies required for licensure of the 2009 H1N1 vaccines.
- State and local preparedness activities have improved, including laboratory capabilities and response readiness planning for medical countermeasures distribution.¹² For example, CDC has assisted planning by Cities Readiness Initiative (CRI) participants which has evolved from single hazard, agency-centric plans to all-hazards multi-agency and private partnership plans.
- FDA has issued critical guidance documents that have helped clarify certain pathways to medical countermeasure regulatory approval¹³.

In the aggregate, these PHEMCE accomplishments have greatly enhanced our public health emergency preparedness for a wide range of threats and scenarios, and have informed the future directions of the PHEMCE.

CHANGES TO THE MEDICAL COUNTERMEASURE LANDSCAPE

Since the initial *PHEMCE Strategy and Implementation Plan* documents were published in 2007, there have been many changes to the medical countermeasure landscape, including the advancements summarized above. Experiences ranging from real public health emergencies to national-level exercises have presented opportunities for the PHEMCE to assess medical countermeasure preparedness planning and to reallocate resources based on lessons learned. For example:

- A recent national-level tabletop exercise of an anthrax attack on a major American city highlighted the need for increased planning to address pediatric prophylaxis needs following an anthrax incident and to better develop and articulate anthrax vaccine allocation guidelines.
- The March 2011 Fukushima–Dai’ichi nuclear power plant incident highlighted that ready access to available medical countermeasures is a major component of public health and safety responses to address such incidents, as well as the importance of international

¹² *Public Health Preparedness: 2011 State-by-State Update on Laboratory Capabilities and Response Readiness Planning.*

¹³ Including but not limited to: *The FDA Emergency Use Authorization Final Guidance (July 2007); Guidance for Industry Animal Models – Essential Elements to Address Efficacy under the Animal Rule Draft Guidance (January 2009); Guidance for Industry Qualification Process for Drug Development Tools (October 2010).*

considerations for medical countermeasure utilization policies. This incident additionally emphasized the importance of appropriate and accurate risk messaging to the surrounding populations following catastrophic events as well as the connectivity of the global community in the face of disaster.

- The 2009 H1N1 influenza pandemic demonstrated that, while current medical countermeasure capabilities enabled a robust national response, there remain continuing needs to accelerate and improve disease detection capabilities, medical countermeasure development production, and distribution capabilities, and the process by which limited medical countermeasures are allocated. Additionally, the pandemic response exposed world-wide gaps in detection and response capabilities and tested the ability of the World Health Organization (WHO) in collaboration with developed countries, including the U.S., to respond to international requests for antivirals and vaccine. Together these highlighted the importance of U.S. Government support for building global capacity for medical countermeasure development and use, including U.S. deployment of medical countermeasures internationally during emergencies, where appropriate.

New national strategic plans have greatly influenced the PHEMCE and our understanding of what it means to be prepared with regard to medical countermeasures. The 2009 release of a quadrennial National Health Security Strategy and the later released Implementation Plan by HHS addresses many aspects of public health emergency preparedness, including the important role of medical countermeasures, and the PHEMCE is aligning its efforts moving forward with the goals articulated here. Also, Presidential Policy Directive 8 on national preparedness, released in 2011, provided further direction aimed at strengthening the security and resilience of the United States by preparing for threats that pose the greatest risk to the security of the Nation, including acts of terrorism, pandemics, and catastrophic natural disasters.¹⁴

Our medical countermeasures development capability was called out for review by the HHS Secretary in response to the 2009 H1N1 influenza pandemic and other response and planning efforts. Her charge to identify needed improvements resulted in a series of new infrastructure initiatives and enhancements to expand our nation's capacity to respond quickly and effectively to CBRN and emerging infectious disease threats and to support regulatory innovation, domestic manufacturing capacity, and PHEMCE-wide management and effectiveness.¹⁵ President Obama in his 2010 State of the Union message also called for "launching a new initiative that will give [the United States] the capacity to respond faster and more effectively to bioterrorism or an infectious disease—a plan that will counter threats at home, and strengthen

¹⁴ Presidential Policy Directive 8 <http://www.whitehouse.gov/blog/2011/10/07/ppd-8-announcing-national-preparedness-goal>

¹⁵ *The Public Health Emergency Medical Countermeasures Enterprise Review: Transforming the Enterprise to Meet Long-Range National Needs*. August 2010. <http://www.phe.gov/preparedness/mcm/enterprisereview/Pages/default.aspx>

public health abroad.” These improvements are being pursued actively and are integrated into the current PHEMCE Strategy.

Additionally, HHS has made great strides in implementing the Public Readiness and Emergency Preparedness (PREP) Act¹⁶ authorities and continues to leverage and exercise its use of these authorities. The PREP Act authorizes the Secretary to provide liability immunity to medical countermeasure developers, manufacturers, distributors, program planners, and other qualified persons who prescribe, administer, or dispense covered countermeasures during or in anticipation of a public health emergency. Moreover, the PREP Act authorizes compensation for certain injuries resulting from the use of these countermeasures. HHS has repeatedly heard from stakeholders that liability protection is a necessary incentive for them to undertake activities to develop, manufacture, distribute, and dispense critical countermeasures. The protections provided under the PREP Act ensure that certain barriers (including the unavailability or prohibitive cost of liability insurance) do not limit the availability of critical countermeasures in a public health emergency.

Finally, significant investments have been made by HHS and its interagency partners in the medical countermeasure mission. Given currently available resources from the Federal to the state, local, tribal and territorial levels (SLTT) and existing public health infrastructure, the PHEMCE must work to ensure long-term sustainability of the mission, while maintaining and building a national capability to respond to national security threats. This includes assessing risks and establishing and communicating clear priorities, collaborating closely with SLTT partners, seeking multi-use solutions wherever possible, and working to develop innovative development, manufacturing, stockpiling, and fielding alternatives.

DEVELOPMENT OF THE 2012 PHEMCE STRATEGY

ASPR led the development of the 2012 PHEMCE Strategy through an interagency steering committee comprised of representatives from across the PHEMCE agencies. The steering committee reviewed existing strategies, implementation plans, and other documents with direct relevance to setting PHEMCE goals and objectives. The PHEMCE-wide strategic goals and objectives identified in this Strategy are consistent with these previously identified, agency-level strategies and priorities. Following review and input from across the PHEMCE, the Strategy was approved by HHS and publically released.

¹⁶ Enacted December 30, 2005 (P L. 109-148); Available at ftp://ftp.hrsa.gov/countermeasurescomp/Public_Readiness_and_Emergency_Preparedness_Act.pdf

STRATEGIC PRIORITIZATION FRAMEWORK

Two core principles guide the activities of the PHEMCE and are reflected in the strategic goals and objectives presented in this document:

- *Limit Adverse Health Impacts* – The ultimate benefit of investing in medical countermeasure preparedness activities is to limit the adverse health effects impacts (deaths, illness, etc.) caused by CBRN and naturally occurring threats to national health security. Programmatic prioritization will take into consideration the potential for each product or program to ultimately prevent fatalities and/or reduce morbidity, including the capability to address the needs of at-risk populations.
- *Stewardship of Resources that create an enduring capability* – To achieve our vision of a responsive and flexible capability to provide medical countermeasures for all hazards, it is important to create a sustainable assemblage of products and supporting infrastructure to reliably get the products to the point of need, especially as financial resources become more constrained. Enduring capability here captures both fiscal and operational meanings. Good stewardship of taxpayer resources demands that the PHEMCE identify and foster products or technologies that serve more than one purpose or that are less reliant on government-only sources of support where possible. The potential for commercial viability (e.g., use in routine public health and/or medical applications), advancement of platform technologies, and innovative, effective, and efficient approaches to inventory management and operational improvements that enhance life-cycle management of medical countermeasures are examples of avenues that help to strengthen the sustainability of the PHEMCE, and these will be considered when establishing program priorities.

Because resources are finite, and there are still a number of important needs, the PHEMCE must have a compelling and transparent set of criteria for assessing all investment decisions. PHEMCE Leadership has identified a strategic framework comprising three essential criteria against which all investments are to be prioritized. These include (1) the need to focus predominantly on addressing the most significant threats; (2) give greater priority to approaches, products, or technologies that are multi-functional; and (3) foster products that improve our ability to ease operational burdens in distribution and dispensing products to the end-user. PHEMCE leadership will thus apply these criteria to guide decisions on programmatic prioritization across the Enterprise:

1. The PHEMCE must still address the most significant threats (see list of high-priority threats in Box 1 below); however, significant progress has been made against anthrax, smallpox, and botulinum toxin, and while improvements to existing countermeasures are needed, a shifting of focus over time to the remaining threats is warranted.
2. The PHEMCE is in a transition point, moving from products that address single threats to a more agile and sustainable system that has the potential for expanded coverage of threats and that may provide capability against unknown pathogens. It will therefore be

important to prioritize efforts when and where possible that provide this capability (e.g., broad-spectrum, multi-functional, platform approaches).

3. A key PHEMCE focus must be to address end-user needs by clearly developing and communicating the concept of operations under which medical countermeasures will be used.

Box 1: High-Priority Threats

The PHEMCE will continue to address medical countermeasure needs to protect against the following high priority threats which have been determined by the Secretary of Homeland Security to pose a material threat sufficient to affect national security and/or which have the potential to seriously threaten national health security:

- *Bacillus anthracis* (anthrax)*
- Clostridium botulinum toxin (botulism)*
- Cyanide
- Emerging infectious diseases (including pandemic influenza)
- Gram negative organisms
 - *Francisella tularensis* (tularemia)
 - *Yersinia pestis* (plague)
 - *Burkholderia mallei* (glanders) and *B. pseudomallei* (melioidosis)
 - *Rickettsia prowazekii* (typhus)
- Multi-drug resistant *Bacillus anthracis* (MDR anthrax)
- Nerve agents
- Radiological agents (e.g., radiological dispersal devices)
- Nuclear agents
- Variola virus (smallpox)*
- Viral Hemorrhagic Fevers
 - Marburg
 - Ebola

* As significant progress accrues for these threats there will be greater attention paid to the next most important agents over time.

The *PHEMCE Implementation Plan* will further detail how these principles and criteria are further developed to assess investments for decisions about current and future products.

PHEMCE STRATEGIC GOALS AND OBJECTIVES

The following strategic goals and objectives will guide the policies and decisions of PHEMCE agencies to promote medical countermeasure capabilities that enhance preparedness for CBRN and emerging infectious disease threats to national health security, including pandemic influenza.

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

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

Effective use of medical countermeasures in a public health response is in part dependent on strategic decisions in research and development, manufacturing, and acquisition of medical countermeasures. Additionally, given the range of potential threats and the limited resources available to address them, prioritization of HHS and PHEMCE-wide resources across the medical countermeasure development, acquisition, and utilization continuum is necessary. The PHEMCE will employ a coordinated, strategic framework through which to focus investments across the PHEMCE mission space and will apply this framework to inform resource allocations for research, development, manufacturing, and procurement.

Objective 1.2 Utilize consistent approaches for medical consequence and public health response assessments and medical countermeasure requirement setting that include consideration of effective production, storage, deployment and administration strategies.

Simply stated, PHEMCE medical countermeasure requirements must address the questions of “Who needs what, when, and how?” They serve to improve the outcome of public health emergencies by focusing federal investments toward an aligned research, advanced development, acquisition, deployment, and use agenda by HHS agencies. Moreover, requirements inform private industry and academia about the civilian medical countermeasure needs and facilitate effective coordination of programs with PHEMCE interagency partners.

PHEMCE medical countermeasure requirements will continue to be informed by medical consequence and public health response assessments of the number of people who would likely benefit from being prophylaxed, diagnosed, or treated with a particular medical countermeasure under multiple planning scenarios. These estimates will continue to be vetted by Federal subject matter experts from across the PHEMCE in areas including microbiology, health physics, chemistry, toxicology, medicine, medical care, diagnostics, and by non-federal experts where needed and appropriate.

Medical countermeasure requirements will also continue to be informed by consultations with partners both within and beyond the Federal government to ensure that these requirements are based upon a sound understanding of the Concepts of Operations under which the medical countermeasures will be used. Such medical countermeasure requirements will inform development of countermeasures that can be safely and effectively used following a public health emergency and that will ultimately meet the needs of the American people.

Objective 1.3 Ensure a robust and sustainable product pipeline for medical countermeasures 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.

A robust product pipeline is one in which the number of product 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 support FDA approval¹⁷ for the desired indication(s). The PHEMCE will seek to maintain robust product pipelines where they exist and to build them in areas where critical gaps still remain. The PHEMCE will take a portfolio management approach to ensure that research and development activities are well-coordinated across agencies.

To ensure the enduring capabilities of the Enterprise over time, the PHEMCE will pursue wherever possible medical countermeasures that can address multiple high-priority threats and/or have routine public health applications (and thus commercial viability). The Enterprise is mindful that a “one bug, one drug” or fixed defense¹⁸ approach for medical countermeasure development is still required for some of the highest priority threats, such as anthrax and smallpox. However, a broad-spectrum approach, where 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 both the sustainability of the medical countermeasure mission and improve daily national health security.

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

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. Engaging international partners offers opportunities to leverage respective

¹⁷ For purposes of this document, the term “approval” refers to FDA-approval, licensure, or clearance under sections 505, 510(k), or 515 of the Federal Food, Drug, and Cosmetic Act or section 351 of the Public Health Service Act.

¹⁸ 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 medical countermeasure intended for use against a specific organism and not useful in scenarios that employ a different organism.

national and international proficiency and expertise to collectively address shortfalls and challenges in the CBRN medical countermeasure development area. Such partnerships are also crucial to create incentives and synergies for facilitating novel, nimble, and innovative solutions to complex problems. Government scientists from across 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 bottlenecks in the process.

The PHEMCE will seek to provide core services such as expertise in FDA regulatory affairs, product development, scale-up and manufacturing, and manufacturing capacity. Such services, while critical to the success of the PHEMCE mission, are often beyond the resources of many individual private entities.

<p>GOAL 2. Establish and communicate clear pathways to facilitate medical countermeasure development and use.</p>
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Reducing regulatory uncertainties is critical for fostering medical countermeasure development and availability. Regulatory oversight of medical product development for these high consequence but low frequency events includes both the stewardship that the government exercises to assure products are safe and effective, as well as the operating conditions established to ensure safe and secure access to work involving the threat agents themselves. This presents a complicated landscape for product development that the PHEMCE partners have worked to steadily address. The PHEMCE will continue support for regulatory science to develop new tools, standards, and approaches to accelerate the development and approval of a wide range of medical countermeasures for both emergency response and daily health needs, while maintaining the high standards for safety and efficacy that the American people expect.

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

The regulatory assessment of medical countermeasures by FDA for approval, clearance, licensure, or authorization¹⁹ is data-driven. However, there are often gaps in scientific knowledge that impede or prevent thorough assessment. These gaps in knowledge arise from multiple sources including intrinsic uncertainties about the biologic behavior of threat agents in potential public health emergencies, as well as from insufficient drug development tools, such as animal models, for creating the necessary data to support regulatory decision-making. Discrepancies in available scientific information and tools result in regulatory uncertainties that

¹⁹ In situations where potentially useful medical countermeasures are available but not yet FDA-approved, licensed, or cleared 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.

many developers perceive as contributing to a higher-than-typical risk environment for engaging in medical countermeasure development.

The FDA, through its Medical Countermeasures Initiative (MCMi), is actively engaged with PHEMCE partners in identifying regulatory and scientific challenges that impede medical countermeasure development and use for high-priority medical countermeasures.²⁰ The PHEMCE will coordinate and prioritize its activities to resolve these challenges based on near-, mid-, and long-term medical countermeasure priorities and requirements established through the PHEMCE coordinated strategic framework.

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

Most of the developers engaged in medical countermeasure development are small biotechnology companies that bring a nimble and innovative approach to the development of new products. However, these companies are often challenged by their limited experience in taking a product through advanced development to FDA licensure, approval, or clearance. For example, these companies often lack experience 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.

PHEMCE partners, in particular the National Institute of Allergy and Infectious Diseases (NIAID) within NIH, BARDA, DoD, and FDA, will continue to provide assistance to medical countermeasure developers in working interactively with FDA throughout the regulatory process to facilitate medical countermeasure development, regulatory assessment, and use. The PHEMCE will ensure these efforts are coordinated, consistent, and accurate.

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

The Nation must be prepared to appropriately use medical countermeasures in an emergency. This requires robust relationships among Federal planners and the SLTT stakeholders who would ultimately be at the operational edge of a public health emergency response. This includes development of optimal approaches for medical countermeasure inventory management and of plans, policies, procedures, and guidance to ensure timely, safe, and effective medical countermeasure distribution and utilization. This will also require administrative preparedness to ensure 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, modified, streamlined, and accountably managed at all levels of government. Achieving these objectives

²⁰ <http://www.fda.gov/EmergencyPreparedness/MedicalCountermeasures/default.htm>

will require communications, training, and education with response stakeholders and ultimately with the American people. In addition, strategies should be developed to evaluate and monitor the use, safety and performance of medical countermeasures during a response – to allow adjustment of operations as needed.

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

An effective national response to a public health emergency requires the capability to provide medical countermeasures to mitigate morbidity and mortality in a clinically relevant time frame. The SNS is the Federal medical countermeasure repository designed to supplement and re-supply State and local public health agencies if locally-held or commercial supplies are depleted during a public health emergency or to provide emergency medical countermeasures not available commercially. Medical countermeasure development must take into account product characteristics that will affect logistical and operational issues. Key product characteristics that affect these options include:

- storage requirements (e.g., room temperature, refrigerated, or frozen),
- transportation requirements,
- packaging and space requirements,
- associated ancillary supplies for administration,
- shelf-life,
- dosage forms for administration (e.g., tablets, suspensions, or injectables), and
- commercial applications (e.g., availability in the supply chain and alternative inventory management systems).

Currently the SNS employs several inventory management mechanisms including stockpile-managed inventory, where resources are held in private sector warehouses on behalf of the SNS, and vendor-managed inventory, in which supplies are rotated by the vendor through normal commercial supply chains. Alternative models of inventory management may also be appropriate in reducing the cost of stockpiling for specific medical countermeasures, notably those that are widely used in the daily U.S. pharmaceutical supply chain.

The PHEMCE will continue to evaluate medical countermeasure candidates for storage under alternative inventory management models and will explore the conditions where alternative models are robust and tested, where these may reduce life-cycle costs and improve the sustainability of the SNS. The PHEMCE will also continue to explore alternative strategies to supplement pre-event medical countermeasure stockpiling, including consideration of “just-in-time” production and/or procurement possibilities, especially for those situations where such mechanisms may provide sufficient medical countermeasure preparedness and significantly reduced costs over time.

Objective 3.2 Develop and communicate medical countermeasure utilization policy, guidance and response strategies, including FDA regulatory frameworks, that are responsive to end-user needs and that are integrated with SLTT and private sector response plans, and when possible international partners, and

that ensure timely, safe, and effective medical countermeasure distribution and utilization.

The success of the PHEMCE will be measured by the ability to quickly, safely, and effectively utilize medical countermeasures and to effectively develop, communicate, and provide guidance and education on the role of medical countermeasures in a public health emergency response. 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 medical countermeasure emergency response plans are flexible enough to fit into SLTT and private response partners' activities. The plans will also be standardized sufficiently to facilitate a rapid and effective response across all regions.

The decline in resources for public health preparedness activities and the need for capacity to distribute and utilize medical countermeasures is a challenge to the global community. The 2009 influenza pandemic exposed world-wide gaps in making vaccines and antivirals available for the global population in a timely fashion. The PHEMCE will support development of, to the extent possible and commensurate with U.S. national health security objectives, a collaboration framework with international organizations (like WHO) and partner countries for mutual assistance, harmonized preparedness plans, and guidance for international medical countermeasure distribution and utilization policies.

The PHEMCE will continue to drive product development and use practices by gaining input up-front and on a regular basis from key stakeholders at all levels and from multiple communities of interest both domestically and internationally. The PHEMCE will seek to further develop and strengthen the feedback loop between the end-users and developers of critical medical countermeasures. This will help support consideration by medical countermeasure developers of the most up-to-date information regarding the circumstances under which their products may be used in the field.

PHEMCE members and partners will identify opportunities to improve statutory, regulatory, and policy mechanisms with respect to medical countermeasure distribution, administration, and use.

Objective 3.3 Develop and provide medical countermeasure communications, training, and education information to inform all stakeholders.

The PHEMCE will continue to focus attention on ensuring that accurate evidence and science-based information and training are provided on the use of medical countermeasures during a public health emergency. The best practices in risk communication will be employed in providing medical countermeasure-specific communications that include relevant health information, response plans, and timing, and specific instructions regarding medical countermeasure use. The PHEMCE will enhance transparency and communication on policies regarding priorities for allocation of potentially limited medical countermeasures and overarching response strategies to assist partners and the American people in their preparedness and planning efforts.

Previous risk-communication and engagement activities show that the American people are willing to educate themselves on what to do in case of a public health emergency when the information is provided in a usable and trusted way. As demonstrated in past national emergencies, a prepared and engaged population creates less dependencies and can help PHEMCE partners focus resources on those most in need. The PHEMCE will ensure provision of well-defined and concise guidance, policies, and recommendations that support clear, accurate, and effective communication the American people can trust.

Objective 3.4 Develop and implement strategies to assess, evaluate, and monitor medical countermeasure safety, performance, and patient compliance during and after a public health emergency response.

Optimal use of medical countermeasures 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 real-time refinement 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. Monitoring systems and processes are critical for the success of the PHEMCE. To be effective, a monitoring system must take into account the demands of patient care in hospital and other emergency settings that may limit the resources available for data gathering and reporting activities; the system should also address the ways that acute care record-keeping could contribute to needed data generation, gathering, and analysis which in turn could help to improve patient care during as well as after the emergency. The PHEMCE will coordinate Federal development and implementation of tools and standards for tracking medical countermeasure performance and adjusting the emergency response in real-time as needed. This includes utilization of the SNS Inventory Tracking and Management System and NIH research centers to evaluate the safety, performance, and uptake of medical countermeasures used during public health emergencies.

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

At-risk individuals,²¹ who make up a significant proportion of the American civilian population at any given time, may have diverse and unique vulnerabilities and medical countermeasure needs. The PHEMCE remains fully committed to working towards the goal of protecting the U.S. population, including at-risk individuals, from intentional threats, pandemic influenza, and other emerging infectious diseases posing a threat to national health security. The following

²¹ At-risk individuals have needs in one or more of the following functional areas: communication, medical care, maintaining independence, supervision, and transportation. At-risk groups may include children, senior citizens, 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>

objectives outline how the PHEMCE will work toward better addressing and more fully integrating the needs of at-risk individuals into the medical countermeasure planning and acquisition processes – 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 setting for at-risk individuals.

The PHEMCE will increase consideration of and efforts to address the medical countermeasure needs of all individuals from across the various sectors of our population that have specific vulnerabilities or needs. These specific vulnerabilities and medical needs must be included in the medical consequence and public health response assessments that inform medical countermeasure requirements determinations within the PHEMCE. Specific vulnerabilities and medical needs include those of pediatric, geriatric, and obstetric populations, as well as people with chronic medical conditions or compromised immune systems.

Objective 4.2 Support medical countermeasure advanced development and procurement for at-risk individuals.

Investment in emergency medical countermeasure development for these populations has not been feasible for industry without the assistance of the U.S. government due to inherent business risks and ethical and regulatory challenges. The needs of at-risk populations pose challenges to the development and acquisition of medical countermeasures specifically formulated for these groups. The PHEMCE will continue to support evaluation of those medical countermeasures currently held in the SNS for use in these important segments of our population, as well as development of additional dosage forms where needed,²² including maximizing use of medical countermeasure dosage forms that are suitable for use in multiple populations. PHEMCE organizations will continue to support development-specific indications on medical countermeasures for at-risk populations.

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

People in at-risk populations must have coordinated and equitable access to medical countermeasures during public health emergencies. The PHEMCE will seek to ensure that Federal medical countermeasure emergency response plans consider the particular needs of these populations and are based on available medical countermeasure safety and efficacy data in those populations.

²² The SNS authority specifically requires that the emergency health security of children and other at-risk populations be taken into account in determining which medical countermeasures and supplies are needed for the SNS (Section 319F-2 of the Public Health Services Act (42 USC 247d-6b)).

IMPLEMENTATION OF THE STRATEGY

This *2012 PHEMCE Strategy* reflects the HHS commitment, in collaboration with its interagency partners in the PHEMCE, to provide the Nation with a nimble, flexible capacity to produce medical countermeasures rapidly in the face of any public health attack or threat, known or unknown. For the ultimate benefit of limiting adverse health effects to be realized, the PHEMCE must also be committed to ensuring that medical countermeasures are available and can be effectively and safely utilized by all populations in need. The Strategy provides strategic direction to the Department, signals the Department's intents and priorities to its governmental and private partners, and guides the development of the *2012 PHEMCE Implementation Plan*.

The *2012 PHEMCE Implementation Plan* will be released in summer 2012 and will detail those programs and initiatives throughout the Department that will be prioritized in pursuit of the goals and objectives presented in this document. Both documents together constitute the blueprints the PHEMCE will follow in the near-, mid-, and long-terms to make the best use of available resources to contribute to national health security.

APPENDIX 1 – GLOSSARY

<i>At-Risk Population</i>	At-risk individuals have needs in one or more of the following functional areas: communication, medical care, maintaining independence, supervision, and transportation. At-risk groups may include children, senior citizens, 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.
<i>Capabilities-Based Approach or Planning</i>	Preparing, under uncertainty, to provide agile systems across the PHEMCE components suitable for a wide range of known and unknown threats while working within an economic framework that necessitates prioritization in order to provide medical countermeasures in a timely manner and reduce adverse health impact of an emergency.
<i>Consequence Assessment</i>	The process of identifying or evaluating the potential or actual effects of an event, incident, or occurrence.
<i>Core Services</i>	Expertise and capabilities required to overcome the technical, regulatory, manufacturing, commercialization, and business challenges inherent in moving innovative medical countermeasures from laboratory to commercial scale production and through the regulatory approval process.
<i>Deployment</i>	To station people and/or pharmaceuticals systematically to an area or during an event.
<i>Dispensing</i>	The process of providing medical countermeasures from points of dispensing (PODs) or other sources directly to individuals or targeted populations in the community in various medical or potentially non-medical settings.
<i>Distribution</i>	The transport and delivery of medical countermeasures from SNS locations to state and regional Receipt, Staging and Storage (RSS) sites, and from RSS locations to points of dispensing (PODs) or other local sites that will handle dispensing to individuals.
<i>Emerging Infectious Diseases (EID)</i>	Emerging infectious diseases include “newly-emerging” infectious diseases (i.e., infectious diseases that heretofore had not been recognized in humans but that could pose a public health risk) and “re-emerging” infectious diseases (i.e., infectious diseases that have been recognized in humans but are increasing in incidence or geographic range), the emergence of which would threaten national health security and require a Federal response to ensure community resiliency.
<i>Material Threat Assessment (MTA)</i>	A DHS-led assessment that includes the number of individuals likely to be exposed to a threat agent in a plausible, high-consequence

	scenario. Formerly known as a Population Threat Assessment (PTA).
Material Threat Determination (MTD)	Issued by the Secretary of Homeland Security for threat agents deemed to pose a material threat sufficient to affect national security. The MTD is necessary, but not sufficient, to support a medical countermeasure acquisition under Project BioShield using the Special Reserve Fund (see Project BioShield).
Medical Consequence Assessment (MCA)	A process of evaluating the physiological effects for the affected population of a real or hypothetical incident or event that results in injury, illness, or loss of life. This process incorporates individual or group judgment of available information, which may include the quantitative results of medical consequence models.
Medical Countermeasures (MCMs)	Medical countermeasures include both pharmaceutical interventions, such as vaccines, antimicrobials, antidotes, and antitoxins, and non-pharmaceutical interventions, such as ventilators, diagnostics, personal protective equipment (PPE), 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.
Pandemic and All-Hazards Preparedness Act (PAHPA)	Passed by Congress in December 2006 “to improve the Nation’s public health and medical preparedness and response capabilities for emergencies, whether deliberate, accidental, or natural.” PAHPA amends the Public Health Service Act to require the Secretary of HHS to lead all Federal public health and medical response to public health emergencies and incidents covered by the (former) National Response Plan, or what is now the National Response Framework. Among its provisions, the Act established ASPR and provided authorities for a number of programs, including the advanced development and acquisition of medical countermeasures, and called for the establishment of a quadrennial National Health Security Strategy.
HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE)	The PHEMCE was established by HHS in 2006 to coordinate Federal efforts to enhance CBRN and EID preparedness from a medical countermeasure perspective. The PHEMCE’s mission is to advance national preparedness for CBRN and EID threats, including pandemic influenza, by coordinating medical countermeasure-related efforts within HHS and in cooperation with PHEMCE partners. The PHEMCE is led by the ASPR and includes three core HHS agency partners: CDC, FDA, and NIH. The PHEMCE also includes four interagency partners: DHS, DoD, VA, and USDA. PHEMCE agencies work to protect the American public from national health security threats through the use of medical countermeasures.
Public Health Response Assessment	A process of evaluating the public health response to a real or hypothetical incident or event by explicitly considering concepts of operations. This process incorporates individual or group judgment of

	available information, which may include the quantitative results of public health response models.
Point of Dispensing (POD)	A designated location for rapidly distributing medical countermeasures, usually antibiotics or vaccines, to high volumes of exposed and potentially exposed persons in a public health emergency. PODs represent the traditional mass prophylaxis distribution method and are not designed to deliver medical care.
PROJECT BIOSHIELD	<p>Signed into law on July 21, 2004, the Project BioShield Act of 2004 represents part of a broader strategy to defend America against the threat of weapons of mass destruction. Project BioShield approaches this goal in three ways:</p> <ul style="list-style-type: none"> • <u>Funding of Needed Countermeasures:</u> Project BioShield institutes a secure funding source and procedures for the purchase of critical medical countermeasures, such as vaccines, therapeutics, and diagnostics, targeted at threats for which an MTD has been issued by DHS (see MTDs). Project BioShield authorizes \$5.6 billion in funding through 2013 for the advanced development and purchase of priority medical countermeasures. Acquisitions using this "Special Reserve Fund" are managed by BARDA. • <u>Facilitating Research and Development:</u> Project BioShield grants the NIH/National Institute of Allergy and Infectious Diseases authorities to expedite and simplify the solicitation, review, and award of grants and contracts for the development of critical medical countermeasures. • <u>Facilitating the Use of Medical Countermeasures in an Emergency:</u> Project BioShield establishes the EUA mechanism to provide access to the best available medical countermeasures following the determination of an emergency by the Secretary of DoD, DHS, or HHS, a declaration justifying the EUA by the Secretary of HHS, and issuance of the EUA by the FDA Commissioner.
Recovery	Those capabilities necessary to assist communities affected by an incident to recover effectively, including but not limited to, rebuilding infrastructure systems; providing adequate interim and long-term housing for survivors; restoring health, social, and community services; promoting economic development; and restoring natural and cultural resources.
Response	Immediate actions to save lives, protect property and the environment, and meet basic human needs. Response also includes the execution of emergency plans and actions to support short-term recovery.
Risk	Potential for an adverse outcome assessed as a function of threats (likelihood), vulnerabilities, and consequences associated with an incident, event, or occurrence.

<i>Risk Assessment (RA)</i>	Product or process which collects information and assigns values to risks for the purpose of informing priorities, developing or comparing courses of action, and informing decision making.
<i>Scenario</i>	Hypothetical situation consisting of a hazard, an entity impacted by that hazard, and associated conditions including consequences when appropriate.
<i>Strategic National Stockpile (SNS)</i>	The statutory mission of the SNS is to provide for the emergency health security of the United States (42 USC 247d-6b(a)). The SNS is the Federal cache of pharmaceuticals, vaccines, medical supplies, equipment, and other items established to augment local supplies of critical medical countermeasures that may be needed for a public health emergency or disaster. The SNS is managed by the CDC and includes (1) the 12-Hour Push Packages positioned in strategically located, secure warehouses ready for immediate deployment to a designated site within 12 hours of the federal decision to deploy SNS assets, (2) SNS-managed inventory, and (3) vendor-managed inventory (to increase efficiency and reduce cost of stockpiling). SNS holdings are supplied to state and local jurisdictions at their request upon federal authorization. Formerly known as the National Pharmaceutical Stockpile (NPS).
<i>Terrorism Risk Assessment</i>	Comprehensive, quantitative assessment of terrorism risk within specified threat type (i.e., C-B-R-N) to inform investments; aid in identifying threats, vulnerabilities, and knowledge gaps; and support strategic risk management planning. DHS S&T conducts four formal terrorism risk assessments: <ul style="list-style-type: none"> • Biological Terrorism Risk Assessment (BTRA) • Chemical Terrorism Risk Assessment (CTRA) • Integrated Terrorism Risk Assessment (ITRA) • Radiological/Nuclear Terrorism Risk Assessment (RNTRA)
<i>Threat Assessment</i>	Product or process of identifying or evaluating entities, actions, or occurrences, whether natural or man-made, that has or indicates the potential to harm life, information, operations, and/or property.

APPENDIX 2 - ACRONYMS

Acronym	Definition
ARS/DEARE	Acute Radiation Syndrome and the Delayed Effects of Acute Radiation Exposure
ASPR	Assistant Secretary for Preparedness and Response
BARDA	Biomedical Advanced Research and Development Authority
CBRN	chemical, biological, radiological and nuclear
CDC	Centers for Disease Control and Prevention
CRI	Cities Readiness Initiative
DHS	Department of Homeland Security
DoD	U.S. Department of Defense
DTPA	Diethylenetriamine-pentaacetate
EEC	Enterprise Executive Committee
EID	Emerging infectious disease
ESC	Enterprise Senior Council
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
HHS	U.S. Department of Health and Human Services
IPR	In-process-review
IPTs	Integrated Program Teams
JRO	Joint Requirements Office
MCMi	Medical Countermeasure Initiative
MTD	Material threat determination
NBSB	National Biodefense Science Board
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
ODATSD(CBD)	Office of the Deputy Assistant to the Secretary of Defense for Chemical and Biological Defense
PAC	Integrated Portfolio Advisory Committee
PCT	Project coordination teams
PEP	Post-exposure prophylaxis
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PPE	Personal protective equipment
PREP	Public Readiness and Emergency Preparedness
SLTT	State, local tribal and territorial
SNS	Strategic National Stockpile
SRF	Special Reserve Fund
TAR	Technical assistance reviews
USDA	U.S. Department of Agriculture
USPS	U.S. Postal Service
VA	U.S. Department of Veterans Affairs
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WG	Working group

APPENDIX 3 – PHEMCE ORGANIZATIONAL STRUCTURE

In July 2006, HHS established the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE or Enterprise). The PHEMCE’s mission is to advance national preparedness against chemical, biological, radiological, and nuclear (CBRN) and emerging infectious disease (EID) threats, including pandemic influenza, by coordinating medical countermeasure related efforts within HHS and in cooperation with interagency PHEMCE partners. The forum for cooperation and overall mission fulfillment is the Enterprise Senior Council and its supporting infrastructure (Figure 1). Structurally, the ESC is led by the ASPR and comprised of the senior leadership of NIAID, CDC, and FDA with comparable senior level representatives from DoD, DHS, VA, and USDA. Additional HHS components 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 participate in a non-voting capacity. The PHEMCE activities are organized and governed using the hierarchy shown in this figure.

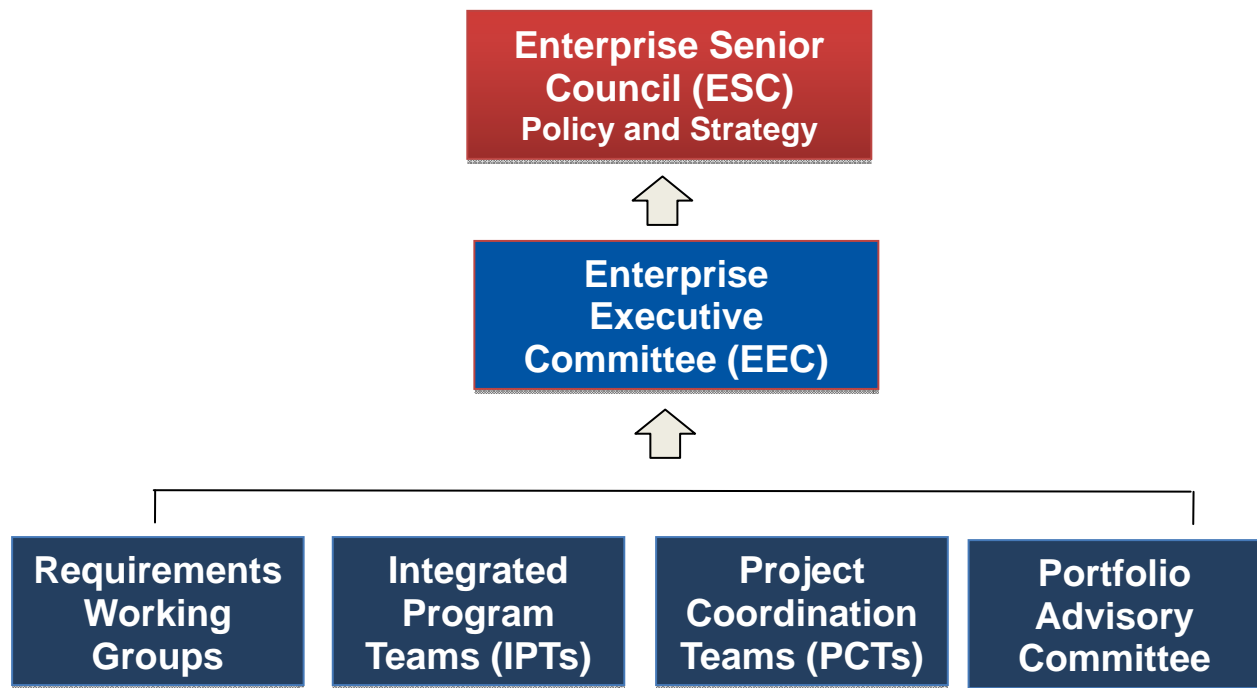


Figure 1. PHEMCE Governance Structure

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” medical countermeasure preparedness activities, defined as requirements generation, research, early- and late-stage product development, procurement, and utilization planning activities for all

threats including CBRN, pandemic influenza, and EID. 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 for 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). 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. As the most senior level in the PHEMCE structure, this group approves major policies, product requirements, and large-scale procurement actions. It also oversees strategic reviews of the activities in each of the major threat portfolios (e.g., anthrax, smallpox, rad/nuc) and is the final reporting body for high priority actions identified as gaps in these reviews.

Enterprise Executive Committee (EEC) – The EEC is an operational-level decision and coordination body for all policy and product-level issues in the Enterprise. The EEC is comprised of senior program managers across the partner agencies. It provides the critical interface and organizing capability between the strategic focus of the ESC and the tactical-level efforts conducted within the subordinate Integrated Program Teams (IPTs) and Working Groups (WGs). The EEC reports directly to, and receives guidance from, the ESC. The Executive Committee is co-chaired by two senior management officials appointed by the ASPR. The EEC is composed of senior staff from each PHEMCE agency selected by the ESC members. The EEC is responsible for assuring that important programmatic, procurement, requirements, and portfolio actions are fully vetted and that the solutions and recommended actions requiring approval at higher levels are well delineated for decisions. Additionally, the EEC manages the work at the lower IPT and subgroup levels, directly manages the annual assessment of the Strategic National Stockpile, and composes PHEMCE level documents, such as this Strategy and Implementation Plan.

Integrated Program Teams (IPTs) – The IPTs provide an end-to-end vision of medical countermeasures against a particular threat type (e.g., anthrax, smallpox) or capability (e.g., diagnostics) that ranges from requirements-setting (specifically quantity and product characteristics) through to stockpiling, delivery and dispensing, and monitoring and evaluating medical countermeasure effectiveness. The IPTs develop strategies for addressing key cross-cutting issues, in consideration of available programmatic resources at the Federal, state, local, tribal and territorial levels. IPTs serve as subject matter expert communities of practice for interagency vetting and input on issues within their purview. They report to the EEC.

Requirements Working Groups (WGs) – The Biological, Chemical, Radiological/Nuclear, and Blood/Tissue MCM Requirements Working Groups are established by the EEC to determine which types of medical countermeasures, including blood and tissue, are needed for response to public health emergencies and other threats to national health security. The Working Groups report to the EEC.

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

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 Principal Deputy Director and by the Medical Director of the Office of the Deputy Assistant to the Secretary of Defense for Chemical and Biological Defense (ODATSD(CBD)).

Specific PHEMCE mission components – and organizations with lead responsibilities and capabilities in these areas – are depicted below (Figure 2).²³ This figure shows the complex interconnectedness of the PHEMCE organizations and mission space.

²³ While capabilities from across the PHEMCE are utilized in many of these areas, the organizations with lead responsibility in particular areas are specifically depicted here.

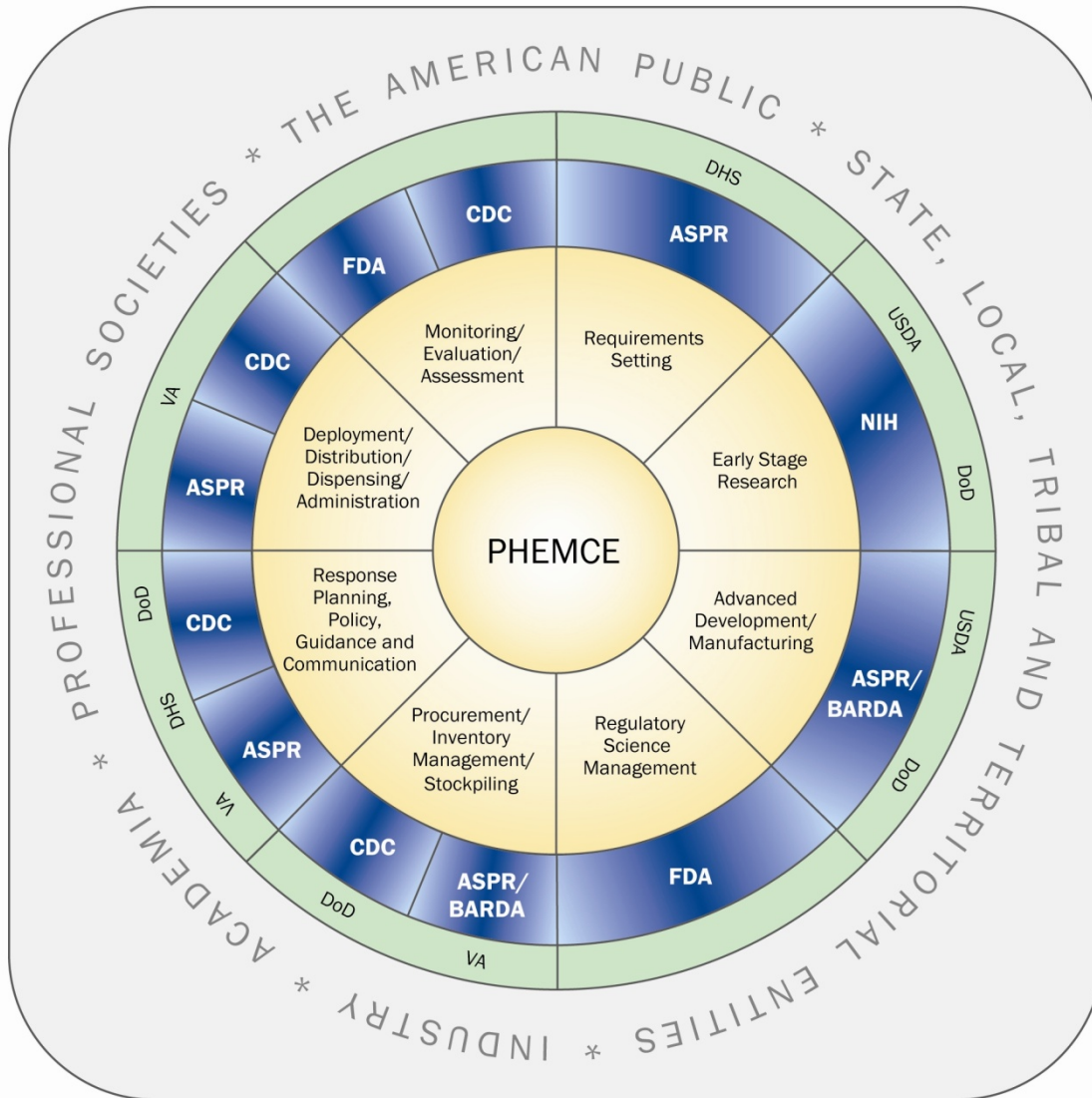


Figure 2: PHEMCE Agency Lead Roles

Key

PHEMCE Mission Components

HHS PHEMCE Agencies

Non-HHS PHEMCE Agencies

Non-Federal Stakeholders

Acronyms

PHEMCE: Public Health Emergency Medical Countermeasure Enterprise

DHS: Department of Homeland Security

DoD: Department of Defense

USDA: U.S. Department of Agriculture

VA: Department of Veterans' Affairs

HHS: Department of Health and Human Services

ASPR: Assistant Secretary for Preparedness and Response

BARDA: Biomedical Advanced Research & Development Authority

CDC: Centers for Disease Control and Prevention

FDA: Food and Drug Administration

NIH: National Institutes of Health

APPENDIX 4 – PROGRESS REPORT

MCM Program	2007 PHEMCE Implementation Plan Goals ²⁴	HHS Accomplishments Since 2007
Diagnostocs	Development and acquisition of <i>in vitro</i> diagnostics for biological agents	<ul style="list-style-type: none"> • Senior level interagency groups, to include a PHEMCE IPT, have been established to coordinate and leverage the development of specific requirements and diagnostic tools for biothreat diagnostics and ensure integration with the national architecture for the Laboratory Response Network and related networks.
Broad spectrum antibiotic(s)	Evaluation of SNS-held antibiotics and acquisition of commercially available antibiotics as needed; advanced development of broad spectrum antimicrobials addressing bacterial agent material threat determinations (MTDs), including regulatory approval for biodefense clinical indications	<ul style="list-style-type: none"> • BARDA established advanced development programs for new broad-spectrum antibiotics to address both biodefense and routine indications. • NIH developed and FDA accepted a new animal model to support licensure of currently stockpiled antibiotics for use against pneumonic plague. • NIH developed and submitted for FDA review efficacy data to support additional indications for currently available antibiotics. • FDA reviewed and processed several “pre-Emergency Use Authorization (EUA)” submissions for the use of antimicrobial products for first responders and affected populations as part of critical emergency preparedness activities for the 2008 Political Conventions and the 2009 Presidential Inauguration. • An EUA was issued in July 2011 for the emergency use of oral doxycycline for the post-exposure prophylaxis (PEP) of inhalational anthrax. This EUA remains in effect as of this writing. • An EUA was issued for the emergency use of doxycycline hyclate tablet emergency kits for PEP of inhalational anthrax for United States Postal Service (USPS) participants and their household members as part of the Cities Readiness Initiative (CRI) in October 2008. This EUA was revised in Feb 2009 and October 2011 and remains in effect as of this writing.

²⁴ HHS advanced development and acquisition goals proposed for the time period FY2007-FY2013.

MCM Program	2007 PHEMCE Implementation Plan Goals²⁴	HHS Accomplishments Since 2007
		<ul style="list-style-type: none"> • CDC conducts ongoing procurement of broad spectrum antibiotics to maintain inventory levels at, or above, PHEMCE requirements.
Broad Spectrum Antivirals	Prioritization of research and development of MCMs capable of addressing several MTD viruses	<ul style="list-style-type: none"> • BARDA is supporting development of two smallpox antivirals, one of which may also have routine public health applications for other double-stranded DNA viruses.
Anthrax Antitoxin(s)	Continue advanced development and phased acquisition program.	<ul style="list-style-type: none"> • NIH developed four anthrax antitoxin products through Phase I clinical trials with transition to BARDA for further advanced development. • BARDA supports advanced development of both monoclonal and polyclonal products and development of products with the potential for extended shelf-life, increased ease of administration, and decreased life cycle management cost. • BARDA acquired anthrax antitoxin (of two different types) for the SNS and the majority has been delivered to the SNS for potential use under EUA. • Anthrax antitoxin developed through NIH and BARDA efforts and now held in the SNS has already been used to treat patients with naturally-acquired pulmonary anthrax in the both the U.S. and Scotland.
Anthrax Vaccine	Advanced development and acquisition of current and next generation anthrax vaccines	<ul style="list-style-type: none"> • Promising candidates for improved anthrax vaccines that could greatly increase the amount of vaccine ready for use moved from the research bench at NIH to advanced development at BARDA. • NIH completed anthrax vaccine post-exposure prophylaxis (PEP) animal model efficacy development, including (in conjunction with FDA and CDC) utilization of a regulatory pathway validated by FDA's VRBPAC.²⁵ • BARDA supports advanced development of next generation anthrax vaccines, as well as enhancements to the current licensed vaccine and expansion of domestic manufacturing capacity for this product.

²⁵ Vaccines and Related Biological Products Advisory Committee

MCM Program	2007 PHEMCE Implementation Plan Goals²⁴	HHS Accomplishments Since 2007
		<ul style="list-style-type: none"> • HHS acquired the currently licensed anthrax vaccine for the SNS and CDC maintains a contract to support delivery (through 2015) at the maximum levels available within current production capacity to build the SNS holdings towards the existing PHEMCE requirement. • HHS and DoD have consolidated management of their once separate anthrax vaccine stockpiles through the SNS, thus reducing costs and improving the life-cycle management of these vaccines.
Filovirus MCM(s)²⁶	Research and development and acquisition of antivirals and/or vaccines	<ul style="list-style-type: none"> • NIH is funding early stage research in this area
Smallpox Antiviral(s)	Advanced development and acquisition	<ul style="list-style-type: none"> • NIH developed two smallpox antiviral candidates through Phase I and II, respectively, with transition to BARDA for further advanced development and acquisition. • BARDA is funding advanced research and development in this area (see also Broad Spectrum Antivirals) and has awarded a Project BioShield contract for acquisition of a smallpox antiviral.
Smallpox Vaccine	Advanced development and acquisition	<ul style="list-style-type: none"> • NIH developed a smallpox vaccine candidate through Phase II with transition to BARDA for further advanced development and acquisition. • BARDA funded advanced development of two smallpox vaccines. • BARDA supported advanced development and acquisition for the SNS of a smallpox vaccine for immunocompromised individuals. • HHS also provides the currently licensed smallpox vaccine to DoD through Economy Act orders.
ARS/DEARE²⁷ MCM(s)	Research, advanced development, and phased acquisition of	<ul style="list-style-type: none"> • BARDA has supported advanced research and development of over 32 different candidate products to mitigate the negative effects of radiation exposure. These products include MCMs to address radiation exposure injuries to the skin, lung, hematopoietic

²⁶ Medical countermeasures

²⁷ Acute Radiation Syndrome and the Delayed Effects of Acute Radiation Exposure

MCM Program	2007 PHEMCE Implementation Plan Goals ²⁴	HHS Accomplishments Since 2007
	ARS/DEARE MCM(s)	system, and gastrointestinal tract.
<i>Biodosimetry and Bioassay</i>	Advanced development and acquisition of on-scene triage biodosimetry assays; establishment of a system of laboratories	<ul style="list-style-type: none"> • BARDA supports advanced research and development of several different promising technologies in this area.
<i>Radionuclide-Specific Agent(s)</i>	Development of novel and improved formulations of decorporating agents; acquisition of an oral formulation of DTPA ²⁸	<ul style="list-style-type: none"> • BARDA acquired liquid Potassium Iodide (KI) (a blocking agent); delivery to the SNS is completed. • BARDA acquired two forms of DTPA; delivery to the SNS is completed. • BARDA supports advanced development of a new formulation of Prussian blue decorporation agent for use in children and of new formulations of DTPA.
<i>Enterprise CHEMPACKs</i>	Procurement and fielding of additional current CHEMPACK configurations; development of operations analysis to support an Enterprise CHEMPACK system; ²⁹ and development and acquisition of next-generation replacement products	<ul style="list-style-type: none"> • BARDA supports advanced development of a next-generation anticonvulsant product for CHEMPACKs. • CDC completed fielding of CHEMPACK caches to the 50 states, 4 directly-funded cities, all participating U.S. territories, and freely-associated island nations.

²⁸ Diethylenetriamine-pentaacetate, a chelating agent

²⁹ To include education, training, and exercise components and by optimizing the pre-positioning of antidotes

MCM Program	2007 PHEMCE Implementation Plan Goals²⁴	HHS Accomplishments Since 2007
<i>Volatile Nerve Agent Single Antidote</i>	Research and development	<ul style="list-style-type: none"> • In conjunction with NIH, BARDA supports advanced research and development of MCMs for chemical threats.

APPENDIX 5 – STRATEGIC ALIGNMENT

Goal 1: Identify, create, develop, manufacture, and procure critical medical countermeasures	
PHEMCE Mission Components	Requirements Setting; Early Stage Research; Advanced Development / Manufacturing; Procurement / Inventory Management / Stockpiling
HHS Strategic Plan	Goal 2: Advance Scientific Knowledge and Innovation, Objective A: Accelerate the process of scientific discovery to improve patient care
Secretary's Strategic Initiatives	Accelerate the Process of Scientific Discovery To Improve Patient Care
National Health Security Strategy	Strategic Objective 6: Promote an effective countermeasures enterprise
Goal 2: Establish and communicate clear regulatory pathways to facilitate medical countermeasure development and use	
PHEMCE Mission Components	Regulatory Science Management
HHS Strategic Plan	Goal 2: Advance Scientific Knowledge and Innovation, Objective C: Invest in the regulatory sciences to improve food and medical product safety
Secretary's Strategic Initiatives	Accelerate the Process of Scientific Discovery To Improve Patient Care
National Health Security Strategy	Strategic Objective 6: Promote an effective countermeasures enterprise
Goal 3: Develop logistics and operational plans for optimized use of medical countermeasures at all levels of response	
PHEMCE Mission Components	Procurement / Inventory Management / Stockpiling; Response Planning, Policy, Guidance, and Communication; Deployment / Distribution / Dispensing / Administration; Monitoring / Evaluation / Assessment
HHS Strategic Plan	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 in response to emergencies
Secretary's Strategic Initiatives	Protect Americans' Health and Safety during Emergencies, and Foster Resilience in Response to Emergencies
National Health Security Strategy	Strategic Objective 6: Promote an effective countermeasures enterprise

Goal 4: Address medical countermeasure gaps for all sectors of the American population	
PHEMCE Mission Components	Requirements Setting; Early Stage Research; Advanced Development / Manufacturing; Regulatory Science Management; Procurement / Inventory Management / Stockpiling; Response Planning, Policy, Guidance, and Communication; Deployment / Distribution / Dispensing / Administration; Monitoring / Evaluation / Assessment
HHS Strategic Plan	Goal 1: Strengthen Health Care, Objective E: Ensure access to quality, culturally competent care for vulnerable populations; Goal 2: Advance Scientific Knowledge and Innovation, Objective A: Accelerate the process of scientific discovery to improve patient care and Objective C: Invest in the regulatory sciences to improve food and medical product safety; 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 in response to emergencies
Secretary's Strategic Initiatives	Eliminate Health Disparities; Accelerate the Process of Scientific Discovery To Improve Patient Care; Protect Americans' Health and Safety during Emergencies, and Foster Resilience in Response to Emergencies
National Health Security Strategy	Strategic Objective 6: Promote an effective countermeasures enterprise