2016 Public Health Emergency Medical Countermeasures Enterprise Stakeholders Workshop Report

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Natcher Conference Center
William H. Natcher Building
45 Center Drive
Bethesda Campus, National Institutes of Health
Bethesda, MD 20894

U.S. Department of Health and Human Services
Office of the Assistant Secretary for Preparedness and Response
Public Health Emergency Medical Countermeasures Enterprise

Contents

Introduction

The Department of Health and Human Services (HHS) established the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) in July 2006, as a coordinated, interagency organization to define and prioritize requirements for public health emergency medical countermeasures (MCMs); to integrate and coordinate research, early- and late-stage product development, and procurement activities addressing the requirements; and to set deployment and use strategies for MCMs held in the Strategic National Stockpile (SNS). The Pandemic and All-Hazards Preparedness Act (PAHPA), enacted in December 2006, established the Office of the Assistant Secretary for Preparedness and Response (ASPR), under which the PHEMCE is managed and through which it operates.

The series of MCM-related Stakeholders Workshops sponsored by HHS began with the BioShield Stakeholders Workshop in September 2006,[1] with which then-HHS Secretary Michael O. Leavitt fulfilled a pledge to the U.S. Senate Committee on Health, Education, Labor, and Pensions to engage the public and industry about the priorities and opportunities afforded by the Project BioShield Act of 2004. Workshops were held thereafter annually as PHEMCE Stakeholders Workshops through January 2011, the last one prior to the 2016 Workshop. The Biomedical Advanced Research and Development Authority (BARDA) was also established by PAHPA in 2006, to foster advanced development of MCMs through administration of Project BioShield and other sources of funding. Although BARDA, an office within the Office of the ASPR, continued to host frequent stakeholder engagements with industry by several means,[2] the 2016 event is the first broad-based PHEMCE Stakeholders Workshop since 2011. The workshop afforded the PHEMCE an opportunity both to update these communities on the many advances that have been realized over the intervening period and to hear from these groups about current concerns, needs, and coordination efforts. Given the positive response and clear value of this engagement to the government and to attendees (see Survey results), the PHEMCE will plan to resume the series on a biennial basis, with a next meeting around 2018.

Goal

The goal of the 2016 PHEMCE Stakeholders Workshop was to provide a forum within which a broad spectrum of stakeholders in the PHEMCE mission of effective provision of emergency medical countermeasures could learn about PHEMCE activities, interact, and provide input to PHEMCE partners about their interests, issues, concerns, and priorities.

Support and planning

The 2016 PHEMCE Stakeholders Workshop was supported by BARDA. The planning committee comprised representatives from all major PHEMCE partner agencies (see *Appendix 4: 2016 PHEMCE Stakeholders Workshop Planning Committee*). On-site support was provided by staff of the Division of Medical Countermeasure Strategy and Requirements, Office of Policy and Planning, Office of the ASPR.

Meeting resources

Resources, including access to this report, are available at the website for the 2016 PHEMCE Stakeholders Workshop. Links to resources associated with previous stakeholder engagements are provided in *Appendix 3: MCM-related stakeholder engagements*.

[1] The 2006 BioShield Stakeholders Workshop Report (https://www.medicalcountermeasures.gov/BARDA/documents/2006bswreportfinal.pdf) is available, accessed March 1, 2016.

[2] See *Appendix 3: MCM-related stakeholder engagements* on p. 27.

Attendance

Figure 1 shows the numbers and relative proportions of the various stakeholder populations that attended the workshop. Of the 359 attendees, the majority (219 = 61 percent) were government personnel, mostly federal (189 = 53 percent of the total), but with appreciable state and local representation (30 = 8 percent). Nineteen percent of the participants (69) were from industry and about six percent (21) were from academia. The remainder of the attendees represented non-profit organizations (15 = 4.2 percent), health care providers (2 = 0.6 percent), first responders (1 = 0.3 percent), media representatives (1 = 0.3 percent), the international community (6 = 1.7 percent), or other categories (25 = 7 percent).

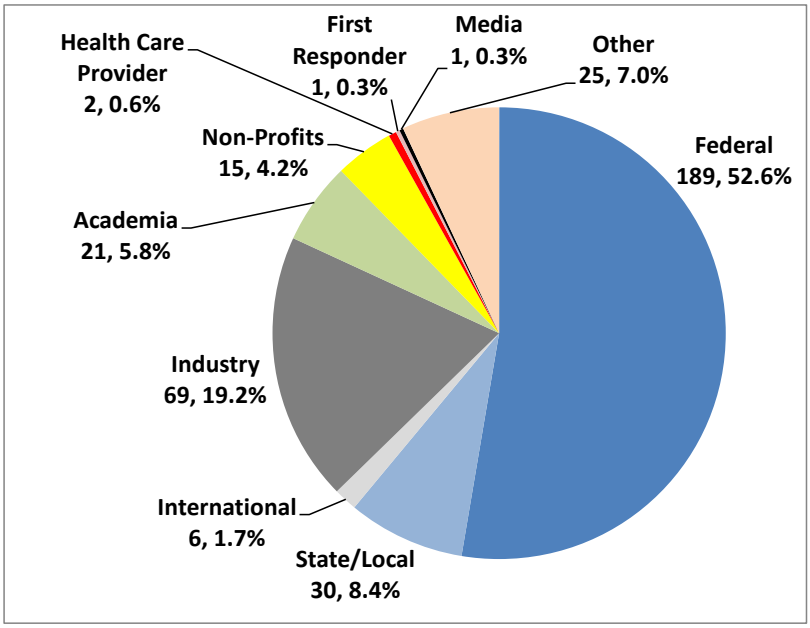

Figure 1. Attendance by groups

Plenary sessions

Plenary sessions were designed to provide a broad overview and context for PHEMCE programs and their impact. These sessions were delivered by senior leadership from across the various organizations that constitute the PHEMCE.

Day 1: Federal initiatives and progress

Opening and welcome

Dr. Sally Phillips and Dr. George Korch, co-chairs of the PHEMCE Executive Committee, opened the Workshop. Dr. Phillips welcomed attendees. Dr. Korch noted the diversity of stakeholders attending, that the PHEMCE had accomplished much since the previous workshop in 2011, and that much remains to be done.

Alice C. Hill, JD, Special Assistant to the President and Senior Director for Resilience Policy, National Security Council, White House
Judge (retired) Hill, representing the view from the White House, emphasized the criticality of MCMs in response to naturally occurring incidents; to chemical, biological, radiological, or nuclear (CBRN)

intentional threats; and to the continuing complexity of seasonal influenza. She noted challenges, lessons learned, and capabilities and systems developed during the Ebola response. The PHEMCE community supported and developed previously unavailable Ebola diagnostics and critical MCMs. The U.S. MCM response, essential to bringing the Ebola outbreak under control, was only possible because of the infrastructure already built to address other threats. In general, critical capabilities for effective response beyond stockpiling MCMs ready for use in the response include: (a) distribution, mass-dispensing, and appropriate utilization of the necessary MCMs; (b) clear and factual communication to the public; (c) rapid diagnostics; (d) rapid manufacturing; and (e) travel screening. Global health requires continual broad-based collaboration, with particular attention to emerging threats.

George Korch, PhD, Senior Science Advisor, Office of the ASPR
Dr. Korch reviewed the history of the PHEMCE, noting the events and legislation that led to development of the Office of the ASPR and of the PHEMCE. He noted the evolution of various PHEMCE processes and progress made toward MCM preparedness and response, including threat analysis, requirements development, advanced development, and acquisition. Dr. Korch emphasized how the PHEMCE focuses on full MCM life-cycle considerations with broad interagency participation and how the 2015 PHEMCE Strategy and Implementation Plan provides the necessary goals, objectives, and priority activities to ensure success. Dr. Korch reviewed major accomplishments and priorities for future development and acquisition. The focus of the PHEMCE has shifted from threat-based considerations exclusively to a capabilities-based emphasis that seeks to be responsive to multiple potential threats, including those traditionally deemed of greatest concern. This approach also places greater focus on operational capacity; portfolio priorities; SNS sustainability; regulatory research; communication with external stakeholders; and approaches to potential future threats through basic research and investment in capacity to rapidly scale up commercial output.

D. Christian Hassell, PhD, Deputy Assistant Secretary of Defense for Chemical and Biological Defense
Dr. Hassell discussed how activities of the U.S. Department of Defense's (DoD's) Office of Chemical and Biological Defense (CBD) are designed to achieve a layered and integrated biodefense portfolio for the warfighter. Goals to address weapons of mass destruction (WMDs) include: (a) non-proliferation (no new WMDs); (b) counter-terrorism (no WMD use); and (c) mitigation (minimization of effects of WMD use). MCMs are tools for mitigation. Dr. Hassell noted the need for collaboration and integration of MCM development, with both interagency and international partners for a "whole of society" approach. In the integrated portfolio, some threats are unique to the DoD (particularly prophylaxis), some to HHS (e.g., smallpox vaccine for special populations), and some are of important concern to both agencies. The PHEMCE Portfolio Advisory Committee coordinates the programs of HHS and DoD. In the DoD, successful MCM development depends on public-private partnerships, on DoD's Advanced Development and Manufacturing Capability, and on DoD-based core services.

Day 2: Emerging infectious disease responses lessons learned: Interagency coordination to recent outbreaks

RADM Nicole Lurie, MD, MSPH (USPHS), Assistant Secretary for Preparedness and Response (ASPR)
RADM Lurie opened the plenary session for the second day of the Workshop with an overview of the office of the ASPR, the evolution of the PHEMCE, and global emergency response challenges. Organizational and portfolio reviews have helped direct and focus the PHEMCE's ability to identify and address challenges as they develop. Improvements include a shift from threat-based to capabilities-based approaches to investment, emphasis on seeking MCMs with utility in non-biodefense applications as well as for public health emergency use, and to foster cost-effective solutions with broad benefits. Global challenges will require an international governance structure with financial accountability among

multiple governments, regulating bodies, and industry. A global "PHEMCE-like" entity would have a significant role in addressing neglected diseases of public health significance, emerging and re-emerging diseases, combatting antibiotic resistance, and science preparedness.

RADM Stephen Redd, MD (USPHS), Director, Office of Public Health Preparedness and Response (OPHPR), Centers for Disease Control and Prevention (CDC)
RADM Redd provided an overview of CDC public health emergency response activities. CDC facilitates PHEMCE coordination with state, local, tribal, and territorial partners, and coordinates an integrated network of state and local public health, federal, military, and international laboratories to detect CBRN and other public health threats. CDC played a key role in identifying and responding to the 2009 H1N1 influenza pandemic, including advances in assessing clinical severity and relating it to transmissibility. During the Ebola outbreak, CDC provided guidance for airport screening, personal protective equipment, and monitoring patients and movement. To enhance overall MCM-related preparedness, CDC oversees and manages the SNS, serving as a co-lead with ASPR in an annual review of its contents in relationship to requirements. Operational readiness reviews (ORRs) assess the ability to execute medical countermeasure plans of jurisdictions awarded Public Health Emergency Preparedness (PHEP) grants. A goal is for all 62 jurisdictions with PHEP grants to establish satisfactory implementation by June 2022.

Robin Robinson, PhD, Director, Biomedical Advanced Research and Development Authority (BARDA), Office of the ASPR
Dr. Robinson provided an overview of BARDA's capabilities to enhance MCM preparedness in the face of inherent challenges. As exemplified by recent outbreaks of Ebola and Zika viruses, diseases will continue to emerge as issues for public health, requiring MCMs for response. MCM development is expensive, risky, and lengthy; a key function of BARDA's mission is to support industry partners to cross the "valley of death" during which lack of support can halt promising, potentially important solutions. BARDA has developed essential capabilities to support developers with milestones such as nonclinical development, clinical studies, analytical decision-making, regulatory and quality affairs, and manufacturing. While the SNS procures emergency MCMs that are FDA-approved, BARDA has authority to acquire useful products that can be deployed under Emergency Use Authorization (EUA; i.e., prior to FDA approval). BARDA has reduced the number of doses needed for efficacy of some vaccines, making compliance simpler and more likely and per-patient cost lower. Also contributing to lower costs for more rapid response is the ability to store bulk product rather than in final formulation, which would be prepared when needed. BARDA has played crucial roles in response to influenza (e.g., H7N9, with very rapid vaccine development), the Ebola outbreak (clinical trials of vaccines and therapeutics), and MERS-CoV (Middle East respiratory syndrome coronavirus).

Breakout sessions

The PHEMCE covers a wide range of policy, science, operational, and regulatory issues. Both to cover as much program breadth as possible in a two-day workshop and to tailor information that serves different interests across the broad stakeholder communities attending, the program was organized into simultaneous breakout sessions covering four separate tracks: end-user considerations; federal policy initiatives and progress; industry partnerships; and emerging infectious diseases and pandemic influenza. The multiple topics addressed under each of these tracks were each organized by one or two coordinators who are recognized leaders in their respective areas.

Track 1: End-user considerations

The PHEMCE preparedness assessment process and distribution and dispensing planning

Session coordinator [Breakout session I]: **Joanna Prasher, PhD** (ASPR/OPP)
David Howell, PhD (ASPR/OPP) A description of preparedness assessment processes: Five determinants of MCM preparedness and data sources being used in assessments
Joanna Prasher, PhD (ASPR/OPP) Strengths and gaps identified to date and a preview of priorities in this area in the 2016 PHEMCE Strategy and Implementation Plan
Christine Kosmos, RN, BSN, MS (CDC/OPHPR/DSLR) Public Health Emergency Preparedness (PHEP) grant MCM-related capabilities: State-level examples of addressing shortfalls with PHEP resources

Simply holding MCMs is not sufficient for preparedness – they have to traverse the "last mile" to get to the person needing them and be used effectively. To assure comprehensive preparedness associated with MCMs, the PHEMCE assesses MCM preparedness in terms of the national capacity to: (1) develop, (2) produce, (3) buy, (4) plan for and (5) effectively use MCMs in an emergency. Capacity to produce, buy, and use MCMs is measured relative to need-based quantities, which is the number of people who would benefit from their use as determined by modeled responses to planning scenarios. Capabilities to develop MCMs and plan for their use are measured relative to other standardized metrics. The results from this process are used to prioritize critical initiatives to improve MCM preparedness. To assure these priorities are addressed, they are incorporated into the annually updated PHEMCE Strategy and Implementation Plan, which serves as a roadmap for critical activities.

CDC's Division of State and Local Readiness (DSLR) is a key interface between (a) federal and (b) state and local public health activities, addressing state and local planning needs in federal public health planning. DSLR's mission is to assure that the nation's public health system is prepared and capable for responding to and recovering from public health emergencies.

The Public Health Emergency Preparedness (PHEP) program is a cooperative agreement providing grant funding, federal guidance, technical assistance, and field staff to enable scientific evidence-based state, local, tribal, and territorial (SLTT) operational capabilities. DSLR uses ORRs to assess and enhance public health preparedness associated with SLTT capabilities. DSLR developed and is implementing an MCM ORR tool to assess and enhance public health preparedness associated with SLTT capabilities, in collaboration with CDC's Division of the Strategic National Stockpile (DSNS). DSLR anticipates completing collection of baseline data using the ORR tool by July 2016. CDC has set a national goal to have all 62 PHEP jurisdictions achieve a "satisfactory" status level on the ORR assessment by 2022.

The Strategic National Stockpile: The right stuff at the right time to the right people

Session coordinator [Breakout session IV]: **Susan Gorman, PharmD, MS** (CDC/OPHPR/DSNS)
Susan Gorman, PharmD, MS, DABAT, FAACT (CDC/DSNS) SNS assets and SNS formulary review
Scott Drexler (CDC/OPHPR/DSNS) SNS training
Rocco Casagrande, PhD (Gryphon Scientific - supporting DHS) DHS/CDC formulary risk assessment

The SNS is the nation's provider of emergency MCMs for which the available supply would otherwise be inadequate. Dr. Gorman identified the scope, scale, and rationale for the SNS, and priority threats it addresses. A legislatively mandated SNS annual review is conducted to identify and prioritize MCMs for the SNS, providing a defensible portfolio for the annual HHS budget submission. The SNS addresses logistics and supply chain considerations (e.g., time frame for clinically effective use; cold-chain shipping) and the ways in which the SNS can deploy MCMs to respond to a public health emergency (e.g., forward-deployed caches, 12-hour push-packages, SNS-managed inventory). Nearly all of the SNS is managed as inventory in its possession; some is vendor-managed inventory (VMI), which requires a commercial market great enough to rotate the needed supply under vendor management without expiration. During the Ebola response, the SNS utilized the commercial supply chain for personal protective equipment (PPE) needed to protect health care workers treating patients both at home and abroad.

There are risks and costs associated with MCMs that must be assessed using an informed process. Dr. Casagrande provided an overview of the risk-mitigation study developed by the Department of Homeland Security (DHS) at the request of CDC to inform procurement decision-making for the SNS. The study utilized scenarios modeled previously by DHS for the Integrated Terrorism Risk Assessment mandated by Homeland Security Presidential Directive- (HSPD-) 18. The various interagency modeling groups (in CDC, DHS, and ASPR/BARDA) collaborate and communicate to reduce redundancy. The study used a probabilistic risk assessment methodology to compare MCM utility across threat areas. Information is used to assist in review of the SNS formulary during the annual review process to evaluate how much risk could be avoided with various formulary options. Ultimately, this information may inform agency solicitations and acquisitions affecting public health response, aiming to reduce risk as much as possible across the spectrum of threats.

Improvements in emergency management are continuously being sought leveraging lessons learned from exercises and actual incidents. Mr. Drexler reviewed training resources available through the SNS for emergency response personnel and coordinators. The DSNS is revamping its training programs, due to changes in processes and technology, and based on lessons learned. It plans to assess consequent performance changes. Discussion included potential coordination of DSNS's programs with the Medical Reserve Corps (MRC), which is coordinated through the ASPR's Office of Emergency Management (OEM). Future steps may include evaluation of training methods, programs, and audiences to see where efforts could be combined or strengthened to provide the maximum impact for state and local planners.

Clinical guidance on the use of medical countermeasures

Session coordinator [Breakout session II]: **CDR Satish Pillai, MD, MPH** (USPHS) (CDC/OID/NCEZID)
CDR Satish Pillai, MD, MPH (USPHS) (CDC/OID/NCEZID) CDC's general approach to developing countermeasure guidance
CDR Brett Petersen, MD (USPHS) (CDC/OID/NCEZID) An example: Development of guidance on post-event smallpox vaccine use
LCDR Kevin Chatham-Stephens, MD, MPH (USPHS) (CDC/OID/NCEZID) Use of systematic reviews to inform the guidance development process

LCDR Stephanie Griese, MD, MPH (USPHS) (CDC/OPHPR/ OD) Unique considerations for special and vulnerable populations

Dr. Pillai provided an overview of a framework for development of clinical guidelines for the use of MCMs held in the SNS for bio-threat agents. Clinical guidelines are needed for appropriate diagnosis, prevention, and treatment of threat agent-induced illness or injury during public health emergencies. CDC's Countermeasures Working Group (CMWG) uses an evidence-based, systematic, rigorous, and transparent process for developing clinical guidelines for use of MCMs for bio-threat agents. Recent guidance documents have been developed for MCM use during an anthrax mass-casualty incident"[3] and for smallpox vaccine use.[4] The CMWG is composed of CDC staff with expertise in multiple bio-threats and special populations.

LCDR Chatham-Stephens provided a detailed overview of how systematic reviews are used to inform the guidance development process. Important steps in a systematic review include defining the questions, developing an analytic framework, searching the literature, abstracting data, cleaning data, grading the evidence, and interpreting the findings. Systematic reviews to inform clinical guidelines can require a substantial commitment of personnel, time, and resources.

LCDR Griese noted that development of clinical guidelines should include consideration of at-risk populations, especially children and pregnant women. MCM considerations specific to children include weight-based dosing, child-consumable drug formulations, and alternative regulatory mechanisms for emergency use of drugs that are not FDA-approved for children. Pregnant women undergo changes in drug metabolism and clearance that may require MCM dosing adjustments, and MCMs may cross the placenta and reach the developing fetus. Ethical challenges of research on children and pregnant women contribute to difficulty determining appropriate dosing and efficacy for them, and consequent gaps in knowledge.

CDR Petersen provided information on CDC's now-published (Feb 2015) first-ever clinical guidance for smallpox vaccine use post-incident, and on the process developing it. The document provides recommendations on the use of all three smallpox vaccines contained in the SNS.

Discussion following the presentations addressed the essential role of public health communication during a public health emergency, including effective clinical guidance.

Challenges with monitoring and assessment of public health emergency medical countermeasures

Session coordinator [Breakout session III]: **RADM Carmen Maher, MA, BNS, RN** (USPHS) (FDA/OC) **RADM Carmen Maher, MA, BSN, RN,** (USPHS) (FDA/OC) and **Bruce Gellin, MD, MPH** (OASH) How do we conduct MCM data collection, post-market studies, and run clinical trials during a response?

RADM Maher and Dr. Gellin co-chair the PHEMCE MCM Monitoring and Assessment Integrated Program Team (MA IPT). Established in 2014, the MA IPT was tasked to develop a PHEMCE-wide strategy for a coordinated capability to monitor and assess MCMs through data collection and analysis, to inform

[3] Bower, WA, K Hendricks, S Pillai, J Guarnizo, and D Meany-Delman, 2015, Clinical framework and medical countermeasure use during an anthrax mass-casualty incident: CDC recommendations, Morbidity and Mortality Weekly Report (MMWR), 64(RR04): 1-28 (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6404a1.htm), accessed April 14, 2016.

[4] Petersen, BW, IK Damon, CA Pertowski, D Meany-Delman, JT Guarnizo, RH Beigi, KM Edwards, MC Fisher, SE Frey, R Lynfield, and RE Willoughby, 2015, Clinical guidance for smallpox vaccine use in a postevent vaccination program, Morbidity and Mortality Weekly Report (MMWR), 65(RR02): 1-26 (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6402a1.htm), accessed April 14, 2016.

decision-making during and after an emergency response. A key to success will be having infrastructures in place before an incident to integrate with response activities without interfering substantially with the primary goal of patient care. The MA IPT is considering how existing U.S. government-supported networks can be leveraged to develop a "network-of-networks" for data collection during a response. MA IPT working groups are assisting with developing how to do this, focusing on antiviral agents, pandemic vaccines, and anthrax vaccine and antibiotics. Additional working groups are looking at how to integrate electronic health records data into MCM monitoring and assessment processes and how "big data" can inform and enhance these processes.

Track 2: Federal initiatives and progress

The evolving biosafety and biosecurity landscape

Session coordinators [Breakout session II]: **Theresa Lawrence, PhD** (USPHS) (ASPR/OPP) and **Jeffrey 'Clem' Fortman, PhD** (DoD)
Susan Coller-Monarez, PhD (OSTP) National strategic efforts in biosafety and biosecurity
June Sellers (DoD) Biosafety and biosecurity: A DoD perspective
Edward You, MS (FBI) Evolving biosecurity challenges

The current framework for biosafety of microbiological laboratories, with regulations regarding "select agents," has evolved over decades.[5] In response to recent laboratory biosafety/biosecurity incidents, the White House-issued Holdren-Monaco Memorandum[6] outlines steps that the U.S. government plans, to identify and address the underlying causes of these incidents. For the longer-term, the Federal Experts Security Advisory Panel recommended identifying needs and gaps, with recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for biological select agents and toxins (BSATs); actions and regulatory changes to improve biosafety and biosecurity; and an approach to determine the number of high-containment U.S. laboratories needed to possess, use, or transfer BSATs. The Fast Track Action Committee on Select Agent Regulations recommended conducting a comprehensive review of the impact that the Select Agent Regulations have had on science, technology, and national security. A follow-up memorandum[7] to the initial Holdren-Monaco Memorandum called for transparency of the nation's laboratory system for public safety and security, incident reporting and accountability to the public, material stewardship, and application of these principles to other biological agents that could pose a serious threat to public health or agriculture.

In 2012, the White House Office of Science and Technology Policy (OSTP) outlined oversight requirements for dual-use research (DUR), which generates knowledge, information, or products that can be utilized either for benevolent or harmful purposes. Dual-use research of concern (DURC) may pose a significant threat with broad potential consequences to public health safety. The DUR and DURC policies preserve benefits of life sciences research while minimizing the risk of the knowledge being misused.

The DoD Biosecurity mission is critical to ensure that research and development can be performed safely and securely. This policy complements civilian biosafety policy.

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[5] See website for Science, Safety, Security (http://www.phe.gov/S3), accessed March 4, 2016
[6] August 18, 2014, Enhancing biosafety and biosecurity in the United States (https://www.whitehouse.gov/sites/default/files/microsites/ostp/enhancing_biosafety_and_biosecurity_19aug2014_final.pdf) accessed March 4, 2016
[7] October 29, 2015, Next steps to enhance biosafety and biosecuirty in the United States (https://www.whitehouse.gov/sites/default/files/docs/10-2015_biosafety_and_biosecurity_memo.pdf), accessed March 4, 2016

After issuance of Executive Order 13546 in July 2010, *Optimizing the Security of BSAT in the U.S.,* DoD analyzed CDC Select Agent Regulations and DoD requirements to identify issues and differences. DoD simultaneously revised existing chemical and biological policies while harmonizing them with CDC rules. At the time of this Stakeholders Workshop, finalization of the policy was pending. The new biosecurity policy will be implemented at all DoD laboratories and the next version of this policy will incorporate new roles and lessons learned from recent incidents.

One such incident involved inadequately inactivated anthrax spores shipped to a number of DoD laboratories to test detection equipment, from 2005 to 2015. An FBI investigation did not identify any biosecurity incidents. DoD performed a comprehensive review focusing on the root cause analysis for the incomplete inactivation of anthrax, DoD laboratory biohazard safety procedures and protocols, laboratory adherence to established procedures and protocols, and identification of systemic problems.

Criminal statutes were crafted by Congress to fulfill commitments to the Biological Weapons Convention.[8] Possession of a biological or chemical agent without a scientific/academic reason and with malicious intent is a violation of federal law.

With advances in biotechnology, biosecurity in the U.S. has to be redefined. For example, Galanie et al. (2015) recently published methodology on engineering yeast to produce opioids. [9] This technology has both positive and negative potential consequences. It could be used to mass-produce narcotics for commercial medical purposes or by terrorists or other malefactors for nefarious purposes. The FBI has a role in addressing synthetic biology issues associated with life science workers and the health care system. FBI coordinators are trained in biochemical issues, and can be contacted for response to activities of concern.

New technologies stimulate innovations to improve health care. One example is development of individually personalized health care plans based on genetic, family, and medical histories. The potential increasing value and availability of personal health information highlights accompanying risks evidenced by recent health records system hacks. Little discussion is underway about security implications of increasing availability and use of digitized personal health information. A potentially narrow window of opportunity exists to evaluate these threats and come up with solutions.

The revised MCM requirements process and updated risk assessments with the Material Threat Assessment 2.0 process

Session coordinator [Breakout session I]: **Richard Jaffe, PhD, MT, ASCP** (ASPR/OPP)
P. Scott White, PhD (DHS) Overview of risk assessments and the Material Threat Assessment 2.0 process
Jessica Appler, PhD (ASPR/BARDA) Medical and public health consequence assessments
David McClimans and **Elaine Wencil, PhD** (ASPR/OPP) Overview of the PHEMCE requirements process

MCMs are needed to protect the health of the U.S. population from the consequences of potential threat agents and emerging infectious diseases. The Project BioShield Act of 2004 established authorities that support the development and stockpiling of critical security MCMs. To exercise these authorities, Project BioShield mandates an evaluation of current and emerging threats, an assessment of the potential public health consequences, and defining of the requirements for these critical MCMs. DHS and HHS made recent advances in conducting these assessments. DHS, in collaboration with HHS, conducts material threat assessments (MTAs) as part of prioritizing which threats to address and how to address them. Previous methods of developing MTAs have been enhanced. “MTA 2.0” includes: (a)

[8] See Biological Weapons Convention (http://www.un.org/disarmament/WMD/Bio/), accessed March 4, 2016
[9] Galanie, S, K Thodey, IJ Trenchard, MF Interrante, CD Smolke, 2015, Complete biosynthesis of opioids in yeast, Science, 349 (6252): 1095–1100; DOI: 10.1126/science.aac9373.

multiple scenarios that vary in consequence, size, and location, and (b) an assessment of scenario plausibility based on potential actor capabilities. Within ASPR, BARDA's Division of Analytic Decision Support develops modeling, visualization tools, and decision-making tools for medical consequence and public health assessments across the risk spectrum for preparedness and in a response. These tools help leadership make transparent, evidence-based, and defensible MCM policies. ASPR's Office of Policy and Planning, Division of Medical Countermeasure Strategy and Requirements, develops MCM requirements, with PHEMCE's Integrated Program Teams (IPTs) providing critical guidance and subject-matter expertise. This updated process reflects threat assessments, public health consequence modeling, and subject matter expert input to determine not only which and how many MCMs we need, but how many can be used in an incident, and how many should be stockpiled. Prioritization of requirement activities is driven by leadership directives, the PHEMCE Strategy and Implementation Plan, IPT work plans, plans for advanced research and development, and acquisition plans. PHEMCE partners engage industry in addressing product development challenges. Attendees questioned whether economic considerations associated with acquisition decisions are now being incorporated into analyses. Dr. Jaffe acknowledged the importance of economic analyses and indicated that they are being incorporated into PHEMCE analyses to support decisions on resource allocation. Additionally, attendees expressed interest in greater transparency of the MTA and requirement processes and results, stressing the importance of this session and the need for continued conversation between federal and non-federal partners.

A focus on at-risk populations: The National Advisory Committee on Children and Disasters (NACCD) and the National Preparedness and Response Science Board (NPRSB)

Session coordinators [Breakout session IV] : **CAPT Charlotte Spires** (USPHS) (ASPR/OPP) and **LCDR Evelyn Seel, MPH** (USPHS) (ASPR/OPP)
Dr. Anne Zajicek, MD, Pharm.D. (NACCD) Overview of the NACCD and reports to the ASPR
Dr. John S. Bradley, MD, FAAP, FIDSA (NPRSB) Overview of the NPRSB and reports to the ASPR focusing on at-risk populations

LCDR Seel presented an overview of the Federal Advisory Committee process. The Federal Advisory Committee Act of 1972 established how federal agencies receive advice and guidance from the private sector and the general public. More than 1,000 federal advisory committees across federal agencies provide transparent and balanced input, usually in the form of reports and recommendations. The National Preparedness and Response Science Board (NPRSB) is a Federal Advisory Committee that has provided extensive insight for HHS into public health emergency preparedness.

Dr. Bradley presented an overview of the NPRSB, which was established initially by PAHPA in 2006 as the National Biodefense Science Board (NBSB),[10] a group of scientific, public health, and medical experts convened to consider questions posed by the ASPR and to make policy recommendations. Over the last decade, the NPRSB moved the agency forward by providing scientific and technical guidance regarding preparing for, responding to, and recovering from adverse health effects of natural and man-made disasters. [11]

Goal 4 of the 2014 and 2015 releases of the PHEMCE Strategy and Implementation Plan describes the need to develop MCM requirements and support MCM advanced development and acquisition for all sectors of the U.S. population, including at-risk individuals, "people with access and functional needs that may interfere with their ability to access or receive medical care before, during, or after a disaster

[10] In 2014, the board was renamed to reflect a broader mission.
[11] NPRSB reports and recommendations are available online at National Preparedness and Response Science Board (http://www.phe.gov/Preparedness/legal/boards/nprsb/Pages/default.aspx), accessed March 4, 2016.

or emergency."[12] This includes children, pregnant women, and people with disabilities, as well as people with other needs. The NPRSB made specific recommendations related to using the anthrax vaccine on children. Although the NPRSB has not been asked to address other at-risk populations, the board is poised to provide guidance and recommendations in meeting the emergency preparedness needs of other populations at-risk due to pregnancy, pre-existing medical conditions, advanced age, limited English skills, homelessness, physical or mental disabilities, or other physical, mental, communication, or transportation challenges. Due to special needs and considerations, advanced development and acquisition of MCMs for some types of at-risk individuals, including children, requires stable, dedicated resources.

The Pandemic All-Hazards Preparedness Reauthorization Act (PAHPRA) of 2013 designated the National Advisory Committee on Children and Disasters (NACCD) to provide advice and recommendations to the Secretary of HHS regarding children's medical and public health needs during disasters. Dr. Zajicek, a member of the NACCD, noted that it is prepared to make recommendations related to grants and cooperative agreements, as well as disaster drills and exercises. The NACCD assessed (a) pediatric surge capacity for a potential large-scale infectious disease outbreak and (b) the state of health care preparedness to care for large numbers of ill or injured children in the face of a natural or man-made disaster of any type.

Dr. Zajicek described the NIH-FDA Pediatric Formulations Platform.[13] It is a model inter-agency agreement to develop an approach for producing clinically useful oral formulations and dosage increments of various Biopharmaceutical Classification System-class drugs. The goal is for the formulations to be palatable to and usable for children and stable in heat and humidity. These formulations are also suitable for adults needing easy-to-take formulations.

Ready … Go: Science during crisis response

Session coordinator [Breakout session III]: **Diane DiEuliis, PhD** (NDU)
LT Marcienne Wright, PhD (USPHS) (ASPR/OPP) Hurricane Sandy science preparedness grants
Robert Fisher, PhD (FDA/OC) Monitoring and assessment

Establishing and sustaining a scientific research framework before, during, and after emergencies is important to identify, collect, and analyze critical and time-sensitive data and information needed to protect the health and safety of responders, communities, and the U.S. population. Within the PHEMCE, these activities are called "science preparedness initiatives."

Dr. DiEuliis discussed science preparedness initiatives within ASPR and the PHEMCE since Hurricane Sandy in 2012. In the aftermath of Hurricane Sandy, the Disaster Relief Appropriation Act advanced post-disaster research opportunities and funding, specifically for research aimed at aiding the long-term recovery of areas hit hard by the storm. Mechanisms and infrastructure were developed to expedite and enhance rapid research efforts in response to an emergency. The Public Health Emergency Review Board was created in 2012 with the goal of establishing rapid, centralized, rigorous institutional review board capabilities following a public health emergency. Science preparedness work continued throughout the PHEMCE during the Ebola outbreak and response.

LT Wright discussed ASPR's award of $8.6 million to 23 awardees in the form of two-year research grants to examine long-term recovery of health systems and communities in areas of the country

[12] At-Risk Individuals (http://www.phe.gov/preparedness/planning/abc/pages/at-risk.aspx), accessed March 4, 2016.
[13] Pediatric Formulations Platform (http://bpca.nichd.nih.gov/collaborativeefforts/initiatives/pages/index.aspx), accessed March 4, 2016.

affected by Hurricane Sandy. Collaboration amongst awardees was important; LT Wright described examples of some of the resulting research. Outcomes from the two-year grants included peer-reviewed publications, preparedness tool-kits and models, and training materials.

Dr. Fisher outlined some challenges associated with the collection of safety and efficacy data during a public health emergency, specifically in connection with MCM-dispensing activities. This type of data is particularly important for MCMs utilized under EUA or Investigational New Drug (IND) procedures. Dr. Fisher identified ways the FDA advances preparedness through regulatory science including: (1) intramural grants to FDA and other U.S. government scientists, (2) extramural contracts to support academic and industry partners, (3) participating in PHEMCE monitoring and assessment planning and activities.

Track 3: Industry partnerships

Accelerating research transitions

Session coordinator [Breakout session II]: **Michael Kurilla, MD, PhD** (NIH/NIAID)
David Jett, PhD (NIH/NINDS) MCM product development support for chemical threats
Bert Maidment, PhD (NIH/NIAID) MCM product development support for rad/nuc threats
Michael Schaefer, PhD (NIH/NIAID) Support for basic research and development to enable MCM product development for biological threats
Tina Guina, PhD (NIH/NIAID) MCM product development support for biological threats

Dr. Kurilla, Director of the Office of Biodefense Research Resources and Translational Research at NIH/NIAID, explained that a primary mission of his office is to partner with industry and academia researchers to accelerate biodefense science. Four of his NIH colleagues described unique aspects of their mission spaces.

Dr. Jett described the CounterAct Program, which conducts basic research on chemical threats and therapeutic targets and facilitates the maturation of the chemical threat MCM pipeline through translational research. CounterAct Program partners in industry and academia are working with NIH to develop numerous potential MCMs. One example is a tissue plasminogen activator (tPA) product recently transitioned from the CounterAct Program to BARDA for advanced development as a sulfur mustard poisoning antidote. In response to questions, Dr. Jett noted that the CounterAct Program does not typically do research on specific delivery devices separate from research on the MCM being delivered; and does not currently evaluate existing drugs for new applications against chemical threats, although such work might be fruitful.

Dr. Maidment described NIAID's support for investigation of candidate MCMs to mitigate the lethal effects of radiation exposure. The support includes company collaboration contracts, as well as inter- and intra-agency collaborations. During the program's 11 years, more than 150 MCM candidates have been identified for further evaluation and development; of these, 20 MCM candidates and six biodosimetry candidates have been transitioned to BARDA for advanced development. Recently, the FDA approved supplemental Biologics License Applications for Neupogen® and Neulasta®, respectively, as treatments for people who have received high doses of radiation and who may experience bone marrow destruction, possibly resulting in infection and uncontrolled bleeding. Asked about research on radioprotectants, Dr. Maidment replied that the NIAID program focuses on civilian MCM requirements, which do not call for radioprotectants to be administered prior to radiation exposure, although such countermeasures may be appropriate for a military population.

Dr. Schaefer described NIAID's support for basic research and development on MCMs for biological threats. The translational research activities include Regional Centers of Excellence across the U.S.

designed to expand the pool of researchers and technical personnel for biodefense and emerging infectious diseases research. Currently, more than 825 projects are supported, with almost 500 principal investigators. To date, the Centers of Excellence have produced more than 3,500 publications about their research in biodefense science. In addition to the Regional Centers, 14 Centers of Excellence for Translational Research focus on synergistic and broad-spectrum MCM approaches to bacterial infection (e.g., antibiotic treatment and vaccine), viral infection (e.g., filoviruses), technology solutions (e.g., nanoparticle delivery systems), and diagnostic testing. Beyond the Centers, Partnership Programs have made more than 500 awards to early- and late-stage translation programs, many of which are higher risk and innovative discovery programs. NIAID has a Small Business Program and a Small Business Technology Transfer Program to partner with qualifying small research entities.

Dr. Guina, of NIAID's Biodefense Drug Development Section, described the Extramural Research Services available to biodefense industry partners involved in developing broad-spectrum MCMs that address biodefense and emerging infectious diseases. Innovators from academia, non-profit organizations, industry, and government are eligible to benefit from Extramural Research Services. Possible funding mechanisms include grants, contracts, requests for actions, and broad agency announcements. The range of preclinical services provided by NIAID includes expertise in product development, lowering the risk for developers, testing and screening products, therapeutics development services, and vaccine development services.

Past, present, and future of the MCM initiative at FDA

Session coordinator [Breakout session IV]: **Rebecca Lipsitz, PhD** (FDA/OC)
Robert Fisher, PhD (FDA/OC) Linking the scientific and regulatory environments for PHEMCE stakeholders: MCMi Regulatory Science
Drusilla Burns, PhD (FDA/CBER) Center for Biologics Evaluation and Research (CBER) MCM research and a case study: Prolonging anthrax vaccine shelf life
Kevin Krudys, PhD (FDA/CDER) Determining the dose of MCM products in special populations
Heike Sichtig, PhD (FDA/CDRH) Regulatory perspective for infectious disease diagnostics and FDA-ARGOS database

Dr. Fisher noted that the FDA supports and complements the PHEMCE by ensuring that MCMs to counter CBRN and emerging infectious disease (EID) threats are safe, effective, and secure. The FDA seeks to help assist stakeholders by identifying appropriate regulatory pathways for approval of MCMs. The FDA Medical Countermeasures Initiative (MCMi) promotes the development and availability of safe and effective MCMs such as drugs, vaccines, diagnostic tests, and PPE. The FDA launched MCMi in late 2010 in response to a PHEMCE review of the nation's readiness for public health emergencies. The FDA Office of Counterterrorism and Emerging Threats (OCET) coordinates all MCMi activities to include MCM development, approval, availability, and security. OCET also leads MCM emergency use activities. Examples of FDA's MCMi activities include: (a) establishment of agreements between FDA and its international counterparts enabling information-sharing and effective collaboration and (b) extension of expiry dating for certain MCMs such as oral doxycycline for the prevention of anthrax disease held by state and local public health preparedness stakeholders.

Dr. Burns noted that CBER research areas include manufacturing, product quality, assay development (especially potency and other lot release assays), animal models, biomarkers and correlates of protection, clinical trial design, and post-marketing safety. While developing the new generation anthrax vaccine, two types of changes upon storage were noted: structural changes and compositional changes. Structural changes were detected by melting point analysis, intrinsic protein fluorescence, and immunogenicity of specific regions of the protein. Multiple factors may play a role in recombinant protein A (rPA) vaccine instability. Significant structural changes that affect immunogenicity can occur

when proteins are bound to aluminum adjuvant, and compositional changes resulting in non-enzymatic protein modifications that affect immunogenicity occur slowly over time; "deamidation" of proteins is the most common change. Mitigation of rPA vaccine instability appears to be possible with the use of adjuvants that allow retention of structure and use of conditions that slow deamination, resulting in the extension of the vaccine longevity.

Dr. Krudys noted that under the animal rule, a thorough understanding of the pharmacokinetic/ pharmacodynamic (PK/PD) data for the investigational drug or biologic is essential in selection of a dose regimen expected to be effective in humans. Clinical trials in healthy humans should evaluate safety and PK data over a range of doses. Quantitative methods, such as PK modeling can be used to derive dosing of MCM products in special populations. For example, to determine the pediatric dose of Raxibacumab to match the adult dosing using PK modeling, one would start with the adult population PK analysis, simulate pediatric PK profiles using different dosing regimens, and select a pediatric dosing regimen to match adult exposures. The effects of intrinsic and extrinsic factors on dosing in special populations should be considered.

Dr. Sichtig noted that the Center for Devices and Radiological Health (CDRH) established a Multiplex and Microbial Sequencing In Vitro Diagnostics Action Team to facilitate development of multiplex microbial DNA sequence-based *in vitro* diagnostic tests, which could test for multiple pathogens simultaneously from a single clinical specimen, using next-generation sequencing (NGS). FDA is working to establish a policy for regulating such tests; a current challenge is determining a policy for U.S. marketing authorization for such NGS-based diagnostics. FDA's general concept of diagnostic device evaluation is that each possible organism needs confirmation by a reference method. FDA is developing a regulatory-grade reference database FDA ARGOS (FDA dAtabase for Regulatory Grade micrObial Sequences), to support use of NGS to diagnose infectious diseases. Its goal is to add 2,000 high-quality MCM and clinically relevant pathogen sequences to the database. Pilot sequencing has been done on Ebola isolates from the recent Ebola outbreak.[14]

Beating back the bugs: Combating antibiotic-resistant bacteria

Session coordinator [Breakout session III]: **Christopher Houchens, PhD** (ASPR/BARDA)
Discussants: **Erin Reichert, PhD** (DoD/DTRA); **Jane Knisely, PhD** (NIH/NIAID)

Roundtable discussion

Drug-resistant bacterial infections pose a significant risk to public health, and, by extension, to emergency response capabilities. A White House priority is a national action plan for Combating Antibiotic-Resistant Bacteria (CARB). The threat of increased microbial drug resistance is compounded by decreased development and production of newer and more effective antibiotics. To address the global threat of drug-resistant bacterial infections, BARDA is partnering with industry to support the late-stage development of promising and effective novel classes of life-saving antibiotics. In addition, BARDA and NIAID are working together to establish an Antimicrobial Resistance Biopharmaceutical Incubator, a consortium of academic, biotechnology and pharmaceutical industry participants that will foster innovation in the early-stage discovery and pre-clinical research and development of promising antibiotic candidates that will provide new products for the late-stage drug development pipeline. Through both of these approaches, BARDA is supporting the end-to-end research, development and

[14] Decoding Ebola: Next-Generation Sequencing of the Ebola Genome for the FDA ARGOS Database (http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm452650.htm), accessed March 4, 2016.

approval of new antibiotics to counter the current threat and likely continued emergence of antimicrobial resistant bacteria.

In DoD, the Defense Threat Reduction Agency (DTRA), the Joint Program Executive Office (JPEO), and the Office of the Secretary of Defense/Chem-Bio Defense (OSD/CBD) support the warfighter, but also focus on antimicrobial resistance as a threat to the warfighter as well as to the general population.

NIAID aims to move beyond small molecule therapeutics, which can lead to drug resistance. NIAID participates in the Antibacterial Resistance Leadership Group, which has a mission to prioritize, design, and execute clinical studies that will reduce the public health threat of antibacterial resistance. In support of the CARB National Strategy, NIAID focuses on (a) advanced development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria and (b) accelerating basic and applied research and development for new antibiotics, other therapeutics, and vaccines. Gene expression signatures can be used to distinguish between viral and bacterial infections, for targeted antibiotic use. [15] NIAID's Division of Microbiology and Infectious Diseases (DMID) has product development services, research tools, biological materials, and funding opportunities available to researchers.

"How can we help you make that product?"

Session coordinator [Breakout session I]: **Richard Hatchett, MD** (ASPR/BARDA)
Discussants: **Christopher Houchens, PhD** (ASPR/BARDA)**; Arlene Joyner, MS** (ASPR/BARDA); **Tim Belski** (DoD/JPM MCS)**; Gerry Parker, DVM, PhD, MS** (TAMUS); and **Robert Lindblad, MD** (Emmes)

A roundtable discussion on product development, building manufacturing capacity, and services the government can provide to encourage the development of specific countermeasures

The federal government, specifically BARDA and the DoD, continues to partner with industry and academia to support the advanced development and manufacturing of MCMs against CBRN and emerging infectious disease threats.

Dr. Hatchett described the development of Core Services Programs within the PHEMCE, including the HHS Centers for Innovation in Advanced Development and Manufacturing (CIADMs) in 2012, the DoD Medical Countermeasure Advanced Development and Manufacturing consortium in 2013, the HHS Fill Finish Manufacturing Network (FFMN) in 2013, and the HHS Non-Clinical (NCSN) and Clinical (CSN) Studies Networks established in 2011 and 2014, respectively. Dr. Hatchett distinguished use of these capabilities in "peace-time" such as for smallpox preparedness and in "crisis," such as during the Ebola response.

Dr. Houchens illustrated the role of the BARDA NCSN in supporting the development of smallpox antiviral agents. The BARDA NCSN, in concert with the FDA and with the NCSN's contract laboratories, has developed reproducible animal models of orthopox virus infection in mice and rabbits that can be used to evaluate the efficacy of smallpox MCMs. Two product developers are currently using these models to conduct pivotal studies under the FDA's animal rule. Unique benefits are associated with BARDA-developed animal models for both the U.S. government and the private sector, including avoiding duplication of efforts, ensuring standardization for drug evaluation, and making reagents and models available for other product developers.

Dr. Lindblad of the Emmes Organization discussed the role of the BARDA CSN during the Ebola response. Emmes is one of five CROs within the BARDA CSN. During the Ebola response, Emmes and Technical

[15] Zaas, AK, T Burke, et al., 2013, A host-based RT-PCR gene expression signature to identify acute respiratory viral infection, Science Translational Medicine, 5 (203): 203ra126; DOI:10.1126/scitranslmed.3006280.

Resources International, Inc. were awarded contracts to support the Sierra Leone Trial to introduce a vaccine against Ebola with the goals of estimating the efficacy of the vaccine in preventing laboratory-confirmed Ebola and of assessing serious adverse events following administration of the vaccine. Over 8,600 participants enrolled in the study across seven clinical sites. Dr. Lindblad noted the importance of collaboration between the CROs, the government of Sierra Leone, CDC, and BARDA throughout the trial.

Ms. Joyner discussed BARDA's manufacturing core services in more specific detail including BARDA's three CIADMs and the FFMN. Specific achievements of the CIADMs include transferring of pandemic influenza vaccine candidate for bulk manufacturing and two monoclonal antibody projects for Ebola therapeutics. Achievements of the FFMN include Zmapp fill-finish services to support BARDA's Ebola response activities, as well as fill and finishing services for multiple pandemic influenza candidates.

Mr. Tim Belski provided an overview of DoD advanced development and manufacturing capabilities, highlighting DoD's contract with Nanotheropeutics, Inc. to develop a "greenfield" manufacturing facility. This facility will be used to facilitate advanced development of MCMs. It will also support large-scale manufacturing for development and sustainment of medical countermeasure production capabilities at a biosafety level (BSL) 3.

Dr. Parker outlined the specific contract structure of the Texas A&M University System (TAMUS) CIADM, including the various partner biopharmaceutical companies, academic institutions, non-profit institutions, and commercial enterprises, and how to gain access to CIADM product development support services. The National Center for Therapeutics Manufacturing is managed by TAMUS, but privately operated to serve as a biopharmaceutical process and manufacturing facility. Dr. Parker described the development, capabilities, and current status of the Pandemic Influenza Vaccine Facility and the Live Virus Vaccine Facility. A range of potential platforms and product classes can be developed by these various facilities within the CIADM. The TAMUS CIADM also supports biopharmaceutical workforce development.

In discussion, the panelists emphasized the importance of early and active communication of prospective product developers with government partners, as well as the need for product developers to be collaborative and flexible.

Track 4: Emerging infectious diseases and pandemic influenza

Influenza and respiratory pathogens update

Session coordinators [Breakout session IV]: **Rick Bright, PhD** (ASPR/BARDA) and **Jonathan Ban** (ASPR/OPP)
Ruben Donis, DVM, PhD [substituting for **Rick Bright, PhD**] (ASPR/BARDA) Update on pandemic influenza vaccine capacity and response → New initiative towards more effective influenza vaccines with universal potential
Lisa Koonin, DrPH, MN, MPH (CDC/OID/NCIRD) Update on pandemic influenza preparedness and response capabilities
Jonathan Ban (ASPR/OPP) An update of the HHS Pandemic Influenza Plan: Where do we need to go over the next 10 years?
Armen Donabedian, PhD (ASPR/BARDA) Seasonal Influenza Vaccine Improvement Initiative

Dr. Donis provided an overview of the public health effect of influenza and reviewed the pandemic influenza response capabilities prior to 2005, highlighting the various strategic response documents. Currently, over 200 products are in the MCM pipeline with support from BARDA. Implementing BARDA's Pandemic Influenza Strategy, BARDA has increased domestic influenza vaccine manufacturing surge capacity, increased international influenza vaccine manufacturing capacity, and developed a more

effective influenza vaccine. BARDA also built a faster response capability through its Centers for Innovation in Advanced Development and Manufacturing, Influenza Vaccine Manufacturing Improvement Initiative, and Fill Finish Manufacturing Network initiatives. The Pandemic Vaccine Stockpile has incorporated risk assessment tools to inform the timing and scale of stockpiling decisions and actions. BARDA is working to develop more effective influenza vaccines, using a transformative approach, linking vaccine design, adjuvants, and administration.

Dr. Koonin provided an overview of the pandemic planning assumptions, noting that the 2009 H1N1 pandemic was not what was planned for. Lessons learned from the 2009 pandemic include the need for and value of early epidemiological information and guidance on the severity of the pandemic (noting that this is difficult due to the lack of information and an evolving situation), flexible and coordinated decision-making, and appropriate inventions (specifically MCMs that fit the severity of the disease or situation). The Influenza Risk Assessment tool was used to assess the potential risk of novel influenza A viruses circulating in animals to cause a pandemic. The tool accounts for the pathogen's potential for human-to-human transmissions and its potential public health effect. The goal of the tool is to understand what actions could be taken, pre-pandemic, to mitigate the risk. The Pandemic Severity Framework allows for the comparison of characteristics of an emerging influenza virus and the disease it causes to the characteristics of past seasonal and pandemic viruses. The tool assists with determining the potential impact of a pandemic and helps leadership ascertain what actions could mitigate the impact.

Mr. Ban provided an overview of activity to update the 2005 HHS Pandemic Influenza Plan. The U.S. National Security Strategy has evolved to include health issues. The first National Health Security Strategy (NHSS) was released in 2009 and recently updated in 2015. The 2015 strategy includes five overarching objectives addressing the whole health care system, domestically and globally. Associated with the third strategic objective, enhancing situational awareness, HHS is updating the Pandemic Influenza Plan. The plan includes 10 domains ranging from building science infrastructure to public communications. Mr. Ban reviewed in more detail the MCM domain and its eight priorities, with the overall goal of creating MCMs that work better and faster.

Dr. Donabedian provided an overview of the seasonal influenza vaccine improvement initiative. Regarding the 2014 vaccine mismatch, challenges with H3N2 viruses are that antigenic characterization and development of candidate vaccine virus are difficult. During the H3N2 surveillance that led to the mismatch, a change occurred in relative prevalence of H3N2 subgroups during vaccine development; this change was recognized too late for availability of the pertinent strains to the manufacturers. In January 2015, vaccine effectiveness was estimated at 23 percent. The PHEMCE's Influenza (Flu) Risk Management Meeting prepared an influenza vaccine improvement action plan recommending development of a risk assessment framework and improved communications between HHS and industry. A table-top exercise was conducted to assess the vaccine manufacturing and vaccination process. The HHS recommendations were shared with the participants at the Fourth World Health Organization (WHO) Informal Consultation on Improving Influenza Vaccine Virus Selection,[16] which emphasized formulating improvement actions.

The MERS-CoV connection

Session coordinator [Breakout session I]: **George Korch, PhD** (ASPR/IO)
George Korch, PhD (ASPR/IO) General background and current epidemiology of MERS-CoV

[16] 4th WHO Informal Consultation on Improving Influenza Vaccine Virus Selection (http://www.who.int/influenza/vaccines/virus/4thmtg_improve_vaccine_virus_selection/en/), accessed March 10, 2016.

David Spiro, PhD (NIH/NIAID) Development of animal models for MERS-CoV
Rosemary Humes, MS (ASPR/BARDA) Point-of-care diagnostics efforts
Robert Walker, MD (ASPR/BARDA) [substitute for **Rick Bright, PhD** (ASPR/BARDA)] Creation of a clinical trials network for MCM testing

Dr. Korch, ASPR Senior Science Advisor, presented the general background and current epidemiology of Middle East respiratory syndrome coronavirus (MERS-CoV) in terms of MCM planning. While devoting major attention to the Ebola outbreak last year, PHEMCE partners nevertheless recognized the public health threat of MERS-CoV and started to evaluate its epidemiologic status and assess the needs for infrastructure to support and focus on MERS-CoV MCMs. An epidemiological pattern is not yet clear; in general, no well-established seasonality or periodic patterns are apparent. From 2012 through 2015, over 1,200 cases of MERS-CoV have been laboratory-confirmed, from 13 countries, resulting in 550 deaths (57 percent), three currently active cases (0.2 percent), and no demonstration of sustained human-to-human community transmission.

Dr. Spiro, section chief of the Influenza, SARS, and Related Viral Respiratory Diseases Section in the Respiratory Diseases Branch at DMID, NIAID, addressed the importance of investing in further animal model development as a key component of MCM evaluation. This needs to include both private and public investments. MERS-CoV can infect a range of animals such as bats, rabbits, camels, marmosets, and macaques, while other species commonly used as animal models, such as mice, rats, hamsters, and ferrets, do not support infection. Modification of dipeptidyl peptidase (DPP4), the receptor for MERS-CoV, to mimic the human sequence can allow viral entry in mouse and ferret cells. Transgenic mouse models expressing the human DPP4 receptor allow MERS-CoV infection and pathogenesis.

Animal model selection depends on a range of variables and needs, such as the pathogenesis being replicated, logistical constraints, and ethical issues. Working with some large animals (e.g., camels) is limited because of geographic considerations or difficulty to maintain in a controlled laboratory setting. However, progress has been made in MERS-CoV animal models using camels, marmosets, African green monkeys, and rhesus macaques. Although marmosets seem to afford a good animal model, challenges include limitation in supply and limitations on sample volume using the smaller animal. Among small animals, transgenic "humanized" mice are the model of choice because of high levels of virus replication and pathology in the lung that resembles human disease. Mice are useful for screening MCMs in evaluation of pre- and post-exposure efficacy of human antibodies against spike protein. Substantial time and money has been invested to develop the humanized mouse model. NIAID's DMID has a contract open to the research community for screening MCMs using this model.[17] Another mouse model was studied at the University of Texas. [18] A NIAID-sponsored MERS-CoV animal model standardization workshop on February 29-March 1, 2016, in Rockville, Maryland, brings together partners to identify gaps and barriers and to outline the future of MCM development.

Ms. Humes described the importance of diagnostic development and test results in decisions for care of individuals and populations. This is especially important for unique threat- and incident-specific concepts of operations (ConOps), which involves platforms or systems that cut across routine pathogens, biothreat agents, and emerging infections. Development of diagnostics must take into account complex and different logistical constraints, regulatory considerations, and payer-provider

[17] Zhao, J, K Li,_et_al., 2014, Rapid generation of a mouse model for Middle East respiratory syndrome, PNAS, 111(13): 4970-4975.
[18] Agrawal, AS, T Garron, X Tao, B-H Peng, M Wakamiya, T-S Chan, RB Couch, C-TK Tseng., 2015, Generation of a transgenic mouse model of Middle East respiratory syndrome coronavirus infection and disease, J. Virology, 89(7): 3659-3670.

issues. The PHEMCE seeks tests that can be used at the national level, as well as tests that will be useful in a clinical office setting at the point of care. The success of a diagnostic test depends on the level of exposure, need and capabilities for infection rule-in/rule-out, signs and symptoms of early disease, treatment utility/impact, and disease progression. Regarding strategy and policy issues, ConOps determine where diagnostics might add value in a CBRN or EID incident. Important considerations are sensitivity, specificity, and predictive value of the assay. Major issues for diagnostics development are why you are testing, whom you are testing, and how many you are testing. Do we have the right analyte? What constitutes timely responses to the incident, tests, and interpretations? How might results transfer to physicians? These questions help assess what the sensitivity and specificity should be in the context of logistical and regulatory issues.

Obstacles to development of diagnostic tests for biological threats include rarity of agents needed to develop the tests and lack of materials, many of which are highly regulated. Demand is low for tests for rare biological threats. Ebola exemplifies all these challenges. The DoD had an existing pre-EUA for an Ebola diagnostic test, based on their long-standing needs for deployment of field-ready assays. The pre-EUA allowed an EUA to be issued immediately upon declaration of the Ebola emergency. However, the complexity of the global response to Ebola raised other challenges for diagnostics developers. The WHO was supporting commercial test development, leading to challenges in setting of standard sensitivity and specificity parameters across different countries, and then regarding diagnostic interpretation and liability. No international consensus exists about clinical settings, and regulatory requirements vary among countries. The WHO and the FDA also have different requirements for clinical settings. The federal government learned a great deal during the Ebola response about creating inactivated virus panels for developers. These lessons are now being applied to panels being created for MERS-CoV. Even with these guidelines and substantial technical support, only the U.S. is in a position to address continuing technical problems and lack of developed materials.

Dr. Walker, the acting director of the BARDA Division of Clinical Studies, discussed BARDA's development and oversight of a clinical studies network (CSN), including capabilities to conduct overseas clinical trials in resource-limited settings, which were done in Africa for Ebola and may be useful for MERS-CoV. The CSN is a network of contracted clinical research organizations that enables collection of comprehensive data informing phase I-IV safety, dosage, PK/PD, and efficacy of MCM candidates; to conduct clinical studies in both preparedness and response environments; and to collaborate with other core services and PHEMCE partners to contribute to the national MCM response infrastructure. BARDA, through contractors, ensures multiple talents in rural communities as well as training and monitoring for staff.

The hits just keep coming: Dealing with emerging infectious diseases

Session coordinators [Breakout session II]: **Segaran Pillai, PhD, MS** (FDA/OC) and **Steve Monroe, PhD** (CDC/OADLSS)
Pierre Rollin, MD (CDC/OID/NCEZID) **-** New Ebola diagnostic tools
Katherine Laughlin, PhD (NIH) **–** Chikungunya diagnostics and medical countermeasures
Steve Monroe, PhD (CDC/OADLSS) **–** Emerging Infectious Diseases Working Group

Dr. Rollin provided an overview of the new Ebola diagnostic tools. Prior to the 2014/2015 outbreak, diagnostic tests were available for Ebola only in reference laboratories. Although the virus can be found throughout the patient's life, different tests are required at different phases of the disease. Reverse-transcriptase polymerase chain reaction (RT-PCR) is typically used to detect the virus in serum in the acute phase; the technique has changed little over the years, and every reference laboratory uses it. ELISA IgM and IgG tests are typically used to detect evidence of the immunologic response during the convalescent phase and specimen quality may affect test results. A DoD-developed assay was the first to

be approved by FDA, in August 2014, five months after the first cases in the outbreak. Most of the diagnostic tests work only for the Zaire virus, the strain in this outbreak, not for all Ebola strains; thus, new tests will need to be developed for detection of other strains. Most of the laboratories available during the outbreak were supported by international laboratories; a gap will occur when the support ends. Diagnostic tests need to be rapid, cost effective, easy to use, and not cold chain-dependent. Rapid screening tests, although lower in sensitivity, may be more effective, and long-term plans for their use, inventory, and funding are being developed. Therapeutics were not available prior to the outbreak, except for compassionate use. Phase 2 and 3 trials are in progress for convalescent plasma therapeutics and phase 2 trails are in progress for Zmapp. However, as the end of the outbreak nears, patient enrollment has been low and trials may be interrupted or ended as a result. Multiple diagnostic platforms and possible therapeutics are now available. However, all are for the Zaire virus, leaving challenges for a potential outbreak of a different strain, e.g., Sudan or Bundibugyo strain.

Dr. Laughlin provided an overview of the diagnostic and MCM projects underway at NIH for chikungunya. The majority of chikungunya projects receiving NIH funding in Fiscal Year 2014 focused on vaccines, therapeutics, and basic research. Diagnostic projects are largely left to CDC, though NIH has a few underway. Of the basic research projects, 50 that focus on chikungunya address structural virology; animal models; and early development of vaccines, diagnostics, and therapeutics. Clinical trials are being conducted for two vaccines for chikungunya. Diagnostics need to be simple, easy to use, and not cold chain-dependent. Pre-clinical development services are available at NIH. Because of limited chikungunya outbreaks, no market exists, and therefore manufacturers are not interested in investing in this type of development, due to anticipated low return on investment. DMID preclinical services at NIH work to lower the risk of the development process and to encourage developers to develop new products, particularly those with greatly limited resources (e.g., academics, small bio-tech firms).

Dr. Monroe provided an overview the Emerging Infectious Disease Working Group. The group was established in 2014 and was charged with creating a process and framework that can be used to assess the public health risk posed by any emerging infectious disease. The goal is to provide information to help inform future PHEMCE actions and investments. Additionally, the framework accounts for a level of uncertainty, so that pathogens can be addressed as new information emerges. Dr. Monroe reviewed the scenario, action, and outputs to be provided to senior leadership and described the framework development process. Four consensus parameters are pathogen characteristics, MCMs, disease impact, and transmission. The draft framework was scheduled to be presented to the PHEMCE Executive Committee in January or February 2016.

Federal response to recent threats through interactions with state, local, and international partners

Session coordinators [Breakout session III]: **Gary Disbrow, PhD** (ASPR/BARDA) and **Jeffrey "Clem" Fortman, PhD** (DoD)
CDR Franca Jones, PhD, MS (DoD/USN); **Peter Morris, MPS, MS** (USAID); **Melissa Harvey, RN, MSPH** (ASPR/OPP); **CAPT Inger Damon, MD, PhD** (USPHS) (CDC/OID/NCEZID)

Roundtable discussion on the responses to Ebola, MERS, and H1N1

Chemical and Biological Defense Program (CBDP), Office of the Secretary of Defense

CDR Jones focused on her experience as the Director of Medical Programs (DoD) during the Ebola outbreak, and described her current role as it relates to global emerging infections surveillance. The CBDP has worked on vaccines, therapeutics, and diagnostics for Ebola for years. CBDP Ebola investments were critical to several MCMs moving from the pipeline and into clinical trials, including the first Phase 1 trial for the recombinant vesicular stomatitis virus-Ebola virus vaccine. CDR Jones and Dr. Disbrow led a

working group that prioritized the vaccines and therapeutics that were furthest along in the pipeline, highlighting those that warranted additional funding. The Ebola response in West Africa was unique in being "whole of the world." CBDP collaborated with agencies within the U.S., national agencies, and intergovernmental organizations such as the WHO. The Ebola response involved each part of the U.S. government, with multiple levels of response, from the tactical level up to the White House.

DoD programs fund surveillance activities in 60 countries around the world. These programs are primarily military-to-military engagements but include some surveillance program initiatives with national ministries of health. As part of a network based at the Naval Medical Research Unit, DoD leveraged its assets to provide diagnostics support for the Ebola outbreak, and also support for addressing other threats (e.g., Lhasa, malaria, tuberculosis) that assumed lower priority once the Ebola outbreak occurred. CDR Jones works to strengthen and expand DoD's activities to work with more countries and partners to detect the next disease or epidemic.

Long-standing collaborations, such as those within the PHEMCE, were critical to the quick response to the outbreak. However, DoD clinical trial assets in Africa could have been better utilized. Earlier leveraging of DoD's existing large clinical network would have allowed the clinical trials to begin sooner.

U.S. Agency for International Development (USAID)/ Office of U.S. Foreign Disaster Assistance (OFDA)

USAID/OFDA is the lead U.S. humanitarian coordinator for assistance in response to international disasters. Its mission is not in initial outbreak response, but rather to address an associated humanitarian crisis beyond the ability of the affected countries to respond, as happened with the Ebola outbreak. OFDA was involved in the H1N1, MERS-CoV, and Ebola outbreaks because of their magnitudes and the wide scope of players. The OFDA mandate is to save lives, alleviate suffering, and reduce the social and economic impact of disasters. The OFDA director can authorize funding for humanitarian response. OFDA also has borrowing authority from other parts of the USAID budget, if necessary, for fulfilling its response mission.

Hospital Preparedness Program (HPP)

The HPP is the sole source of funding to provide the U.S. health care system protection against EIDs. It provides funding annually through state health departments, cities, and freely associated states and territories. From there, the funding filters down to the health systems. This helps ensure a consistency of approach to EID protection among health systems. HPP provided guidance to health care facilities and, importantly, shaped and designed regional and tiered systems for response to Ebola and other pathogens. This tiered system begins with frontline health care facilities. They need to know how rapidly symptoms arose, where patients were originally located, and how to stabilize them. At the next level of the system, assessment hospitals have capabilities and resources for testing and have the ability to hold a patient for several days, given the risk of infection.

HPP identified facilities in the U.S. willing to house Ebola patients under certain conditions. Some were willing to take in only patients from their states or jurisdictions, while others were only willing to take those who were part of their hospital networks. This forced HPP to consider regional approaches. Although regional systems are in place for other conditions, with requirements that facilities treat anyone from the region, this is not the case for EIDs.

HPP received funding for this tiered system. States and jurisdictions with designated Ebola treatment centers, assessment hospitals, and healthcare coalitions received $162 million for overall health care system preparedness. Each state was required to have at least one assessment hospital. Funds were used to compensate health care facilities for Ebola preparedness activities beginning in July 2014, to build additional health care facility capabilities for Ebola and Ebola-like incidents, to develop state

ConOps for Ebola patient care, and to ensure the EMS system is capable of safely transporting Ebola patients. Another $32.5 million supported development of 10 regional Ebola treatment centers. Joint funding from ASPR and CDC totaling $12 million supported establishment of the National Ebola Training and Education Center.

The following lessons were learned from the Ebola response: the government should consider a broader-tiered health care system for EIDs, because not all hospitals have the same capabilities, and a need exists to ensure that a greater number of domestic health care facilities are both willing and able to accept and care for patients who need to be evacuated from overseas; infection control needs improvement; consensus is required regarding when biocontainment is necessary; regional coordination of hospitals needs improvement; risk communication strategies are essential; and early enrollment of facilities in research protocols can be beneficial.

CDC Role in Ebola Response

CDC's overall goals during the Ebola outbreak response were to stop human-to-human transmission (case identification, contact tracing, infection control, safe burials, and health communication) and to improve patient care (triaging, providing experienced staff, and strict use of PPE). CDC deployed staff to West Africa to assist in surveillance, contact tracing, lab testing, incident management, emergency outpatient department development, safe isolation, and health education. Because relatively few people in the area were previously knowledgeable about Ebola, CDC also trained local African health workers, volunteers, and others in these activities and deployed staff to non-affected border countries to conduct assessments of Ebola preparedness.

During the response, CDC learned the importance of the connection between disaster assistance response teams (DARTs) and use of OFDA resources. CDC had few people in West Africa and did not know the major players very well. OFDA has the capacity to connect CDC with the major players and help guide activities on the ground. The DARTs supported the CDC public health assessment and response. In the U.S., public health system training was provided in person and also online to hundreds of thousands of people. CDC activated the laboratory response network (LRN) labs to provide quick turnaround on testing.

Lessons learned during the Ebola outbreak include the importance of quick action, of incident command strategies to coordinate activities and functions at both the international and domestic levels, and of risk-communication strategies to communicate uncertainty and empower action.

Survey results

We received responses from 80 people (22 percent of attendees) to a survey sent to attendees after the meeting. The distribution among population categories for survey respondents was similar to that of all workshop attendees (see Appendix 2, *Figure 2*).

Among those responding to the survey, 19 percent (15 of 79 answers) indicated that they had been to a previous PHEMCE Stakeholders Workshop (Appendix 2, *Figure 3*a).Of these, the distribution of those who judged this workshop to be more, equally, or less useful than previously attended workshops or to be generally useful was positive overall (Appendix 2, *Figure 3*b).

About 94 percent of respondents said they would be somewhat or very likely to attend another Stakeholders Workshop if it were held in the next two years (Appendix 2, *Figure 4*). The survey indicated that the structure, scope, quality, and value of the meeting was generally well regarded (Appendix 2, *Figure 5* through *Figure 11*), with from 75 percent to over 90 percent positive responses (satisfied or very satisfied). While multiple simultaneous sessions present dilemmas for some participants regarding which session to attend, overall satisfaction was positive with this format (Appendix 2, *Figure 12*).

We also received useful comments regarding access to the presentations during or after the meeting, as well as desires for more interactivity or dialogue during or after the sessions. Other important suggestions included that we host more frequent workshops, increase the presence of industry presentations, and shorten the plenary sessions. We plan to implement these suggestions in future workshops.

Appendices

Appendix 1: Acronyms and abbreviations

ARGOS	dAtabase for Regulatory Grade micrObial Sequences
ASPR	Assistant Secretary for Preparedness and Response
BARDA	Biomedical Advanced Research and Development Authority
BSL	biosafety level
BSAT(s)	biological select agent(s) and toxin(s)
CARB	Combating Antibiotic-Resistant Bacteria (a national action plan)
CBD	Office of Chemical and Biological Defense (of DoD)
CBDP	Chemical and Biological Defense Program (of DoD)
CBER	Center for Biologics Evaluation and Research (of FDA)
CBRN	chemical, biological, radiological, nuclear
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research (of FDA)
CDRH	Center for Devices and Radiological Health (of FDA)
CIADM(s)	Center(s) for Innovation in Advanced Development and Manufacturing (of BARDA)
CMWG	Countermeasures Working Group (of CDC)
CRO(s)	contract research organization(s)
CSN	Clinical Studies Network (of BARDA)
DART(s)	Disaster Assistance Response Team(s)
DHS	Department of Homeland Security
DMID	Division of Microbiology and Infectious Diseases (of NIH/NIAID)
DoD	Department of Defense
DPP4	dipeptidyl peptidase, the receptor for MERS-CoV infection
DSLR	Division of State and Local Readiness (of CDC's OPHPR)
DSNS	Division of the Strategic National Stockpile (of CDC's OPHPR)
DTRA	Defense Threat Reduction Agency (of DoD)
DUR	dual-use research
DURC	dual-use research of concern
EUA	Emergency Use Authorization (issued by the FDA)
FBI	Federal Bureau of Investigation
FDA	U.S. Food and Drug Administration
FFMN	Fill Finish Manufacturing Network (of BARDA)
HHS	Department of Health and Human Services
HPP	Hospital Preparedness Program (of ASPR/OEM)
HSPD	Homeland Security Presidential Directive
IND	Investigational New Drug
IO	Immediate Office (of the ASPR)
IPT	Integrated Program Team (a PHEMCE interagency group of subject-matter experts)
JPEO	Joint Program Office (of DoD)
JPM	Joint Project Manager (DoD)

MA IPT	MCM Monitoring and Assessment Integrated Program Team (of the PHEMCE)
MCM(s)	medical countermeasure(s)
MCMi	Medical Countermeasures Initiative (of FDA)
MCS	Medical Countermeasure Systems (of DoD)
MERS-CoV	Middle East respiratory syndrome coronavirus
MTA(s)	material threat assessment(s) (of DHS)
NACCD	National Advisory Committee on Children and Disasters
NBSB	National Biodefense Science Board (subsequently NPRSB)
NCEZID	National Center for Emerging and Zoonotic Infectious Diseases (of CDC's OID)
NCIRD	National Center for Immunization and Respiratory Diseases (of CDC's OID)
NDU	National Defense University
NGS	next-generation sequencing
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NPRSB	National Preparedness and Response Science Board (previously NBSB)
NSN	Non-clinical Studies Network (of BARDA)
OADLSS	Office of the Associate Director for Laboratory Science and Safety (of CDC's
OC	Office of the Commissioner (of FDA)
OCET	Office of Counterterrorism and Emerging Threats (of FDA)
OD	Office of the Director (of CDC's OPHPR)
OEM	Office of Emergency Management (of ASPR)
OFDA	Office of Foreign Disaster Assistance (of USAID)
OID	Office of Infectious Diseases (of CDC)
OPHPR	Office of Public Health Preparedness and Response (of CDC)
ORR(s)	operational readiness review(s)
OSD	Office of the Secretary of Defense (of DoD)
OSTP	Office of Science and Technology Policy (of the White House)
PAHPA	Pandemic and All-Hazards Preparedness Act (2006)
PAHPRA	Pandemic and All-Hazards Preparedness Reauthorization Act (2013)
PD	pharmacodynamic
PHE	public health emergency
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHEP	Public Health Emergency Preparedness (grant program of CDC)
PK	pharmacokinetic
rPA	recombinant protein A (a type of anthrax vaccine)
SLTT	state, local, tribal, and territorial
SNS	Strategic National Stockpile
TAMUS	Texas A&M University System
USAID	U.S. Agency for International Development
USN	U.S. Navy
USPHS	U.S. Public Health Service
WHO	World Health Organization
WMD(s)	weapon(s) of mass destruction

Appendix 2: Survey result details

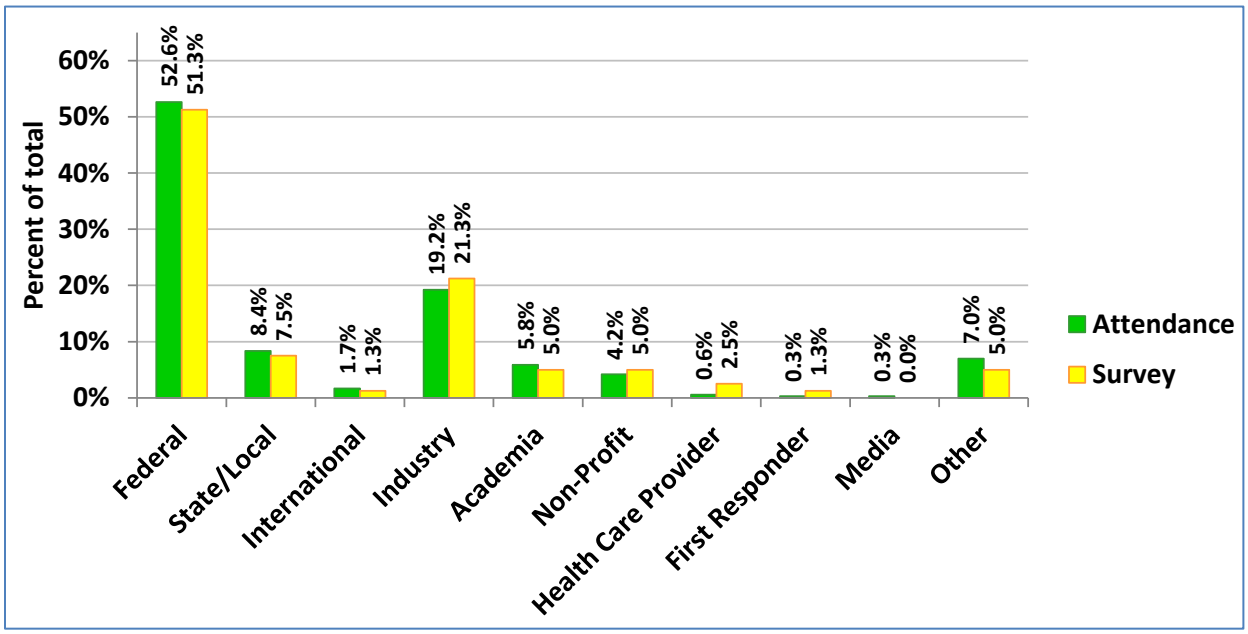

Figure 2. Comparison of population sectors for attendance and for the survey.

Figure 2 displays similarities of group percentages for (a) attendance at the workshop and (b) survey respondents, compared using side-by-side bars representing group percentages of the totals. The following values for the groups of attendees and survey respondents, respectively, are displayed: Federal: 52.6% and 51.3%; State/Local: 8.4% and 7.5%; International: 1.7% and 1.3%; Industry: 19.2% and 21.3%; Academia: 5.8% and 5.0%; Non-Profit: 4.2% and 5.0%; Health Care Provider: 0.6% and 2.5%; First Responder: 0.3% and 1.3%; Media: 0.3% and 0.0%; Other: 7.0% and 5.0%.

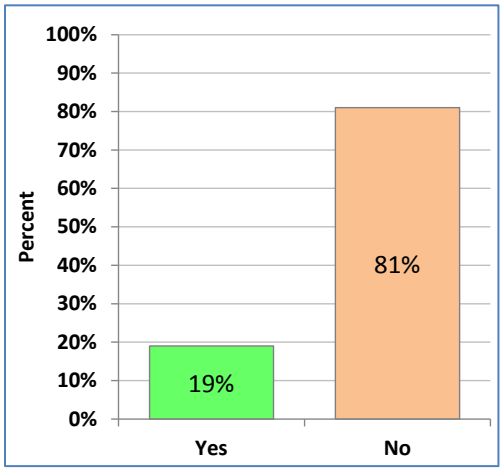

Figure 3a. Proportion attending previous Stakeholders Workshops

Figure 3b. Assessment by previous attendees of usefulness of Stakeholders Workshops

Figure 3a is a bar chart representing the 19 percent of attendees who attended at least one previous PHEMCE Stakeholders Workshop, and the 81 percent who did not.

The assessment of usefulness shown in Figure 3b was made by the 15 attendees who had attended previous Stakeholder Workshops. The average score of 0.3 is for those assessing it as more, equally, or less useful than previous workshops, based on scores assigned as shown in the x-axis legend (five with a value of +2 for more useful, four with a value of 0 for equally useful, three with a value of −2 for less useful). The fourth category (three with responses of "useful") is for those who indicated it was useful, without relating it to the previous workshop(s) attended.

For Figures 4 through 12, the average scores shown are calculated by assigning the scores shown in the legends to the various answers: +2 for very satisfied or very likely, +1 for satisfied or somewhat likely, 0 for neutral or unsure, −1 for dissatisfied or not likely, and −2 for very dissatisfied.

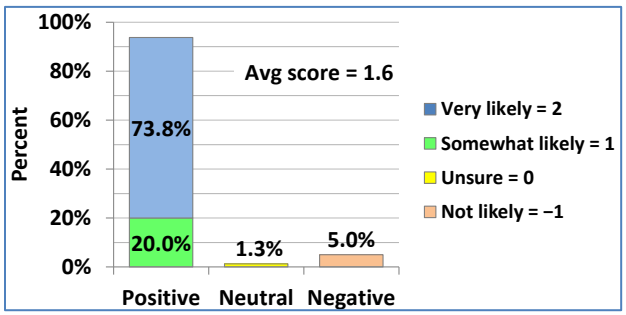

Figure 4. Likelihood to attend another Stakeholders Workshop if in the next two years
Positive: 93.8% = very likely: 73.8% and likely: 20.0%
Neutral: unsure: 1.3%; Negative: not likely: 5.0%
Average score: 1.6

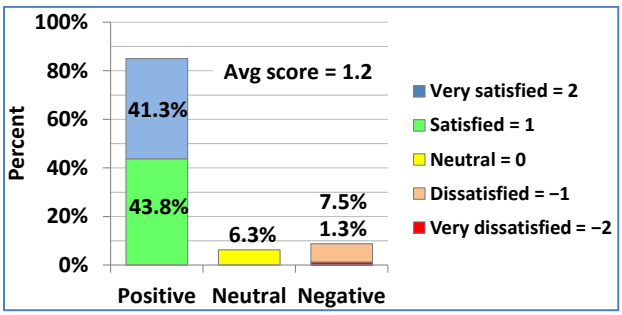

Figure 7. Usefulness of the information
Positive: 85.1% = very satisfied: 41.3% and satisfied: 43.8%
Neutral: 6.3%
Negative: 8.8% = dissatisfied: 7.5% and very dissatisfied: 1.3%
Average score: 1.2

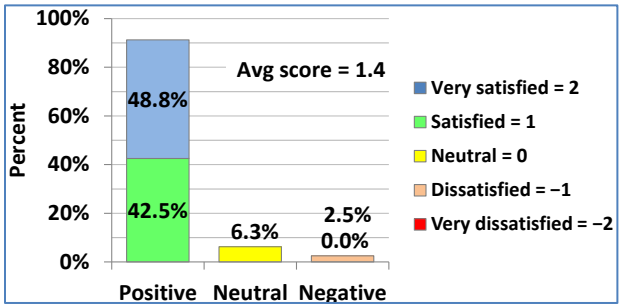

Figure 5. Quality of overall event
Positive: 91.3% = very satisfied: 48.8% and satisfied: 42.5%
Neutral: 6.3%
Negative: 2.5% = dissatisfied: 2.5% and very dissatisfied: 0.0%
Average score: 1.4

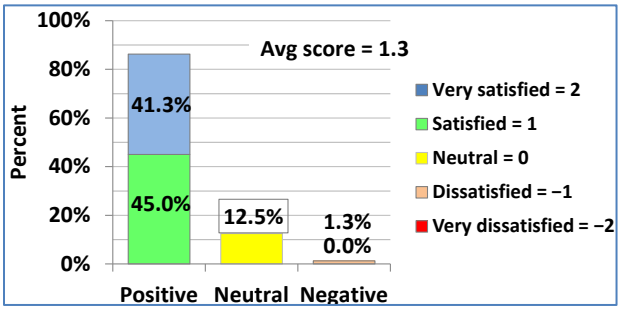

Figure 8. Quality of presentations in plenary sessions
Positive: 86.3% = very satisfied: 41.3% and satisfied: 45.0%
Neutral: 12.5%
Negative: 1.3% = dissatisfied: 1.3% and very dissatisfied: 0.0%
Average score: 1.3

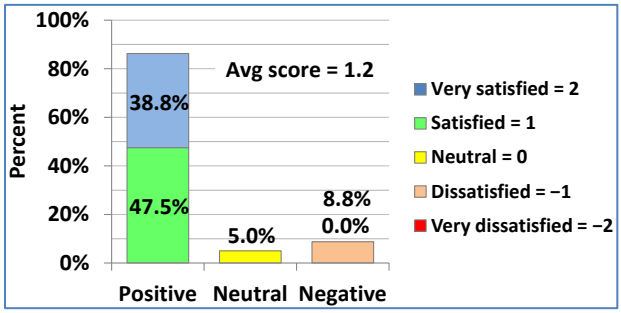

Figure 6. Scope of information presented
Positive: 86.3% = very satisfied: 38.8% and satisfied: 47.5%
Neutral: 5.0%
Negative: 8.8% = dissatisfied: 8.8% and very dissatisfied: 0.0%
Average score: 1.2

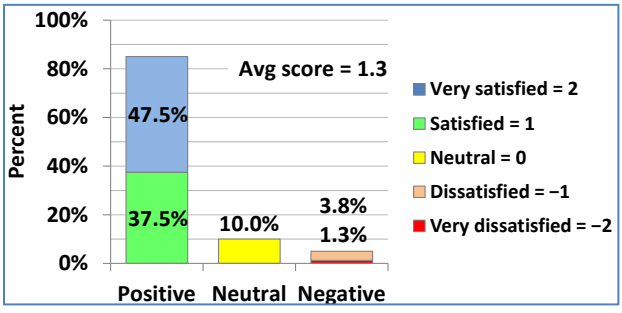

Figure 9. Overall meeting format
Positive: 85.0% = very satisfied: 47.5% and satisfied: 37.5%
Neutral: 10.0%
Negative: 5.1% = dissatisfied: 3.8% and very dissatisfied: 1.3%
Average score: 1.3

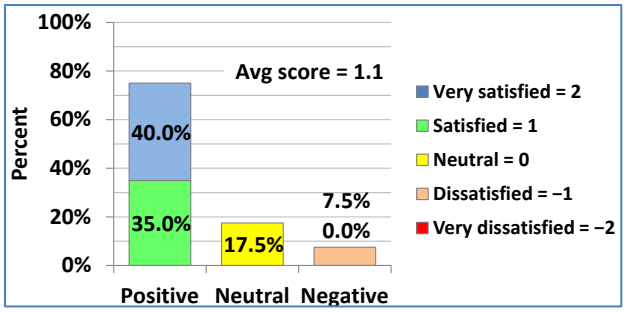

Figure 10. Sufficient time to network with stakeholders
Positive: 75.0% = very satisfied: 40.0% and satisfied: 35.0%
Neutral: 17.5%
Negative: 7.5% = dissatisfied: 7.5% and very dissatisfied: 0.0%
Average score: 1.1

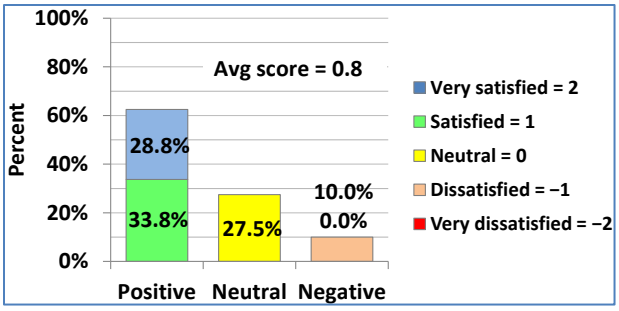

Figure 12. Simultaneous sessions presentations
Positive: 62.6% = very satisfied: 28.8% and satisfied: 33.8%
Neutral: 27.5%
Negative: 10.0% = dissatisfied: 10.0% and very dissatisfied: 0.0%
Average score: 0.8

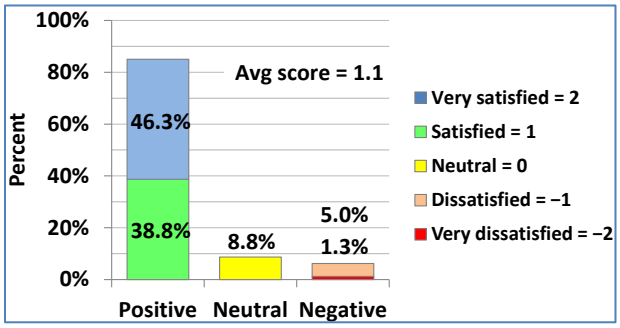

Figure 11. Meeting's overall value to advance public health preparedness
Positive: 85.1% = very satisfied: 46.3% and satisfied: 38.8%
Neutral: 8.8%
Negative: 6.3% = dissatisfied: 5.0% and very dissatisfied: 1.3%
Average score: 1.1

Appendix 3: MCM-related stakeholder engagements

Links to information on public meetings and conferences associated with medical countermeasures:
Public Meetings and Conferences (https://www.medicalcountermeasures.gov/federal-initiatives/public-meetings-and-conferences.aspx, accessed March 2, 2016)

Information on previous BioShield and PHEMCE Stakeholders Workshops

2006 BioShield Stakeholders Workshop

- Website for materials: BioShield Stakeholders Workshop (https://www.medicalcountermeasures.gov/barda/phemce-management/2006-bioshield-stakeholders-workshop.aspx, accessed March 1, 2016)
- Report: 2006 BioShield Stakeholders Workshop Report (https://www.medicalcountermeasures.gov/BARDA/documents/2006bswreportfinal.pdf, accessed March 1, 2016)

2007 HHS PHEMCE Stakeholders Workshop

- Website for materials: HHS Public Health Emergency Medical Countermeasures (PHEMC) Enterprise Stakeholders Workshop (https://www.medicalcountermeasures.gov/barda/phemce-management/2007-phemce-stakeholders-workshop.aspx, accessed March 1, 2016)
- Report: 2007 HHS PHEMCE Stakeholders Workshop Report (https://www.medicalcountermeasures.gov/BARDA/documents/phemc-workshopagenda-01172008.pdf, accessed March 1, 2016)

2008 PHEMCE Stakeholders Workshop

- Website for materials: HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Stakeholders Workshop 2008 and BARDA Industry Day (https://www.medicalcountermeasures.gov/barda/phemce-management/2008-phemce-stakeholders-workshop.aspx, accessed March 2, 2016)
- Report: HHS PHEMCE Stakeholders Workshop 2008 & BARDA Industry Day Report (https://www.medicalcountermeasures.gov/barda/documents/PHEMCE_08_Report.pdf, accessed March 2, 2016)

2009 PHEMCE Stakeholders Workshop

- Website for information: HHS PHEMCE Stakeholders Workshop 2009 & BARDA Industry Day (https://www.medicalcountermeasures.gov/barda/phemce-management/2009-phemce-stakeholders-workshop.aspx, accessed March 2, 2016)

2011 – PHEMCE Fifth Annual Stakeholders Workshop and BARDA Industry Day

- Website for information: Fifth Annual PHEMCE Stakeholders Workshop and BARDA Industry Day (https://www.medicalcountermeasures.gov/barda/phemce-management/2010-phemce-stateholders-workshop.aspx, accessed March 2, 2016)

2016 PHEMCE Stakeholders Workshop (this conference)

- Website for information: PHEMCE Stakeholders Workshop 2016 (http://www.phe.gov/Preparedness/mcm/phemce/PHEMCEworkshop/Pages/default.aspx, accessed March 2, 2016)

Appendix 4: 2016 PHEMCE Stakeholders Workshop Planning Committee

Chair: George Korch, PhD (ASPR)

ASPR

- Diane DiEuliis, PhD (OPP)
- Gary Disbrow, PhD (BARDA)
- Melissa Harvey, RN, MSPH (OEM)
- Charmaine Richman, PhD (AMCG)
- L. Paige Ezernack (OPP)

CDC

- Sue Gorman, PharmD, MS (OPHPR/DSNS)
- Tracee Treadwell, RN, DVM, MPH (OD)

FDA

- Rebecca Lipsitz, PhD (OCET)
- Nicolette deVore, PhD (CBER)

NIH

- Rose Aurigemma, PhD (NIAID)

DHS

- Segaran Pillai, MD

DoD

- CDR Franca Jones, PhD, MS
- Ashley Grant, PhD
- Jeffrey “Clem” Fortman, PhD

Appendix 5: Workshop agenda

2016 Public Health Emergency Medical Countermeasures Enterprise Stakeholders Workshop

January 6-7, 2016

KEYNOTE SPEAKERS

RADM Nicole Lurie, MD, MSPH (USPHS)
Assistant Secretary of Health and Human Services for Preparedness and Response

RADM Stephen Redd, MD (USPHS)
Director, Office of Public Health Preparedness and Response, Centers for Disease Control and Prevention

Robin Robinson, PhD
Director, Biomedical Advanced Research and Development Authority, Office of the Assistant Secretary for Preparedness and Response

Alice C. Hill, JD
Special Assistant to the President and Senior Director for Resilience Policy, National Security Council, the White House

D. Christian Hassell, PhD
Deputy Assistant Secretary of Defense for Chemical and Biological Defense

George Korch, PhD
Senior Science Advisor, Office of the Assistant Secretary for Preparedness and Response

AGENDA AT A GLANCE

Time	Wednesday, January 6th	Thursday, January 7th
8:30 - 11:30am	Plenary session I: **Federal initiatives and progress** Alice C. Hill D. Christian Hassel George Korch	Plenary session II: **Emerging infectious disease response lessons learned** Nicole Lurie Stephen Redd Robin Robinson
11:30am- 1:00pm	Lunch	Lunch
1:00-2:15pm	Breakout session I	Breakout session III
2:15-2:30pm	Break	Break
2:30-4:00pm	Breakout session II	Breakout session IV
4:00-4:30pm	Poster session and exhibit hall	Closing session: George Korch
4:30-5:00pm	Poster session and exhibit hall	Poster session and exhibit hall

DAY 1

8:30-11:30am

KEYNOTE ADDRESSES

Federal initiatives and progress: PHEMCE interagency leadership will discuss governmental partnerships (DHS, DoD), PHEMCE initiatives/priorities and preparedness level; multi-year budget development; DoD/HHS partnerships in planning; and capacity building.

Opening and welcome

Alice C. Hill, JD
Special Assistant to the President and Senior Director for Resilience Policy,
National Security Council, the White House

George Korch, PhD
Senior Science Advisor, Office of the Assistant Secretary for Preparedness and Response

D. Christian Hassell, PhD
Deputy Assistant Secretary of Defense for Chemical and Biological Defense

11:30am-1:00pm
Lunch

1:00-2:15pm
BREAKOUT SESSION I

TRACK 1 – END-USER CONSIDERATIONS

The PHEMCE preparedness assessment process and distribution and dispensing planning
Session coordinator: **Joanna Prasher, PhD** (ASPR/OPP) [email: joanna.prasher@hhs.gov]

David Howell, PhD (ASPR/OPP)
A description of preparedness assessment processes: Five determinants of MCM preparedness and data sources being used in assessments

Joanna Prasher, PhD (ASPR/OPP)
Strengths and gaps identified to date and a preview of priorities in this area in the 2016 PHEMCE Strategy and Implementation Plan

Christine Kosmos, RN, BSN, MS (CDC/OPHPR/DSLR)
PHEP grant MCM-related capabilities: State-level examples of addressing shortfalls with PHEP resources

Q&A

TRACK 2 – FEDERAL INITIATIVES AND PROGRESS

The revised MCM requirements process and updated risk assessments with the Material Threat Assessment 2.0 process

Session coordinator: **Richard Jaffe, PhD, MT, ASCP** (ASPR/OPP) [email: richard.jaffe@hhs.gov]

P. Scott White, PhD (DHS)
Overview of risk assessments and the Material Threat Assessment 2.0 process

Jessica Appler, PhD (ASPR/BARDA)
Medical and public health consequence assessments

David McClimans and **Elaine Wencil, PhD** (ASPR/OPP)
Overview of the PHEMCE requirements process

Q&A

TRACK 3 – INDUSTRY PARTNERSHIPS

"How can we help you make that product?"
Session coordinator: **Richard Hatchett, MD** (ASPR/BARDA) [email: richard.hatchett@hhs.gov]

Richard Hatchett, MD (ASPR/BARDA); **Christopher Houchens, PhD** (ASPR/BARDA)**;**
Arlene Joyner, MS (ASPR/BARDA); **Tim Belski** (DoD/JPM MCS)**;**
Gerry Parker, DVM, PhD, MS (TAMUS); and **Robert Lindblad, MD** (Emmes)

A roundtable discussion on product development, building manufacturing capacity, and services the government can provide to encourage the development of specific countermeasures

Q&A

TRACK 4 – EMERGING INFECTIOUS DISEASES AND PANDEMIC INFLUENZA

The MERS-CoV connection
Session coordinator: **George Korch, PhD** (ASPR/IO) [email: george.korch@hhs.gov]

George Korch, PhD (ASPR/IO)
General background and current epidemiology of MERS-CoV

David Spiro, PhD (NIAID)
Development of animal models for MERS-CoV

Rosemary Humes, MS (ASPR/BARDA)
Point-of-care diagnostics efforts

Rick Bright, PhD (ASPR/BARDA)
Creation of a clinical trials network for MCM testing

Q&A

2:15-2:30pm
Break

2:30-4:00pm
Breakout Session II

TRACK 1 – END-USER CONSIDERATIONS

Clinical guidance on the use of medical countermeasures
Session coordinator: **CDR Satish Pillai, MD, MPH** (USPHS) (CDC/OID/NCEZID) [email: vig8@cdc.gov]

CDR Satish Pillai, MD, MPH (USPHS) (CDC/OID/NCEZID)
CDC's general approach to developing countermeasure guidance

CDR Brett Petersen, MD (USPHS) (CDC/OID/NCEZID)
An example: Development of guidance on post-event smallpox vaccine use

LCDR Kevin Chatham-Stephens, MD, MPH (USPHS) (CDC/OID/NCEZID)
Use of systematic reviews to inform the guidance development process

LCDR Stephanie Griese, MD, MPH (USPHS) (CDC/OPHPR/OD)
Unique considerations for special and vulnerable populations

Q&A

TRACK 2 – FEDERAL INITIATIVES AND PROGRESS

The evolving biosafety and biosecurity landscape

Session coordinators: **Theresa Lawrence, PhD** (USPHS) (ASPR/OPP) [email: theresa.lawrence@hhs.gov] and **Jeffrey 'Clem' Fortman, PhD** (DoD) [email: jeffrey.l.fortman.ctr@mail.mil]

Susan Coller-Monarez, PhD (OSTP) National strategic efforts in biosafety and biosecurity
June Sellers (DoD) Biosafety and biosecurity: A DoD perspective
Edward You, MS (FBI) Evolving biosecurity challenges

Q&A

TRACK 3 – INDUSTRY PARTNERSHIPS

Accelerating research transitions

Session coordinator: **Michael Kurilla, MD, PhD** (NIH/NIAID) [email: mkurilla@niaid.nih.gov]

David Jett, PhD (NIH/NINDS) MCM product development support for chemical threats
Bert Maidment, PhD (NIH/NIAID) MCM product development support for rad/nuc threats
Michael Schaefer, PhD (NIH/NIAID) Support for basic research and development to enable MCM product development for biological threats
Tina Guina, PhD (NIH/NIAID) MCM product development support for biological threats

Q&A

TRACK 4 – EMERGING INFECTIOUS DISEASES AND PANDEMIC INFLUENZA *The hits just keep coming: Dealing with emerging infectious diseases*

Session coordinators: **Segaran Pillai, PhD, MS** (FDA/OC) [email: segaran.pillai@fda.hhs.gov] and **Steve Monroe, PhD** (CDC/OADLSS) [email: stm2@cdc.gov]

Roundtable discussion

Q&A

4:00-5:30pm Poster Session and Exhibit Hall

DAY 2

8:30-11:30am

KEYNOTE ADDRESSES

Emerging infectious disease responses lessons learned: Interagency coordination to recent outbreaks

RADM Nicole Lurie, MD, MSPH (USPHS)
Assistant Secretary for Preparedness and Response

RADM Stephen Redd, MD (USPHS)
Director, Office of Public Health Preparedness and Response, Centers for Disease Control and Prevention

Robin Robinson, PhD (ASPR/BARDA)
Director, Biomedical Advanced Research and Development Authority

11:30am-1:00pm
Lunch

1:00-2:15pm Breakout Session III

TRACK 1 – END-USER CONSIDERATIONS

Challenges with monitoring and assessment of public health emergency (PHE) MCMs
Session coordinator: **RADM Carmen Maher, MA, BNS, RN** (USPHS) (FDA/OC) [email: carmen.maher@fda.hhs.gov]

RADM Carmen Maher, MA, BSN, RN, (USPHS) (FDA/OC) and **Bruce Gellin, MD, MPH** (OASH)
How do we conduct MCM data collection, post-market studies, and run clinical trials during a response?

Q&A

TRACK 2 – FEDERAL INITIATIVES AND PROGRESS

Ready … Go: Science during crisis response
Session coordinator: **Diane DiEuliis, PhD** (NDU) [email: diane.dieuliis@ndu.edu]

LT Marcienne Wright, PhD (USPHS) (ASPR/OPP)
Hurricane Sandy science preparedness grants

Robert Fisher, PhD (FDA/OC)
Monitoring and assessment

Q&A

TRACK 3 – INDUSTRY PARTNERSHIPS

Beating back the bugs: Combating antibiotic-resistant bacteria

Session coordinator: **Christopher Houchens, PhD** (ASPR/BARDA) [email: christopher.houchens@hhs.gov]

Erin Reichert, PhD (DoD/DTRA); **Jane Knisely, PhD** (NIH/NIAID); and **Christopher Houchens, PhD** (ASPR/BARDA)

Roundtable discussion

Q&A

TRACK 4 – FEDERAL AGENCY'S RESPONSE TO EBOLA AND OTHER EMERGING AND INFECTIOUS DISEASES

Federal response to recent threats through interactions with state, local, and international partners
Session coordinators: **Gary Disbrow, PhD** (ASPR/BARDA) [email: gary.disbrow@hhs.gov] and **Jeffrey "Clem" Fortman, PhD** (DoD) [email: jeffrey.l.fortman.ctr@mail.mil]

CDR Franca Jones, PhD, MS (DoD/USN); **Peter Morris, MPS, MS** (USAID);
Melissa Harvey, RN, MSPH (ASPR/OPP); and **CAPT Inger Damon, MD, PhD** (USPHS) (CDC/OID/NCEZID)

Roundtable discussion on the responses to Ebola, MERS, and H1N1

Q&A

2:15-2:30pm
Break

2:30-4:00pm
Breakout Session IV

TRACK 1 – END-USER CONSIDERATIONS

The Strategic National Stockpile: The right stuff at the right time to the right people
Session coordinator: **Susan Gorman, PharmD, MS** (CDC/OPHPR/DSNS) [email: spg4@cdc.gov]

Susan Gorman, PharmD, MS, DABAT, FAACT (CDC/OPHPR/DSNS)
SNS assets and SNS formulary review

Scott Drexler (CDC/OPHPR/DSNS)
SNS training

Rocco Casagrande, PhD (Gryphon Scientific - supporting DHS)
DHS/CDC formulary risk assessment

Q&A

TRACK 2 – FEDERAL INITIATIVES AND PROGRESS

A focus on at-risk populations: The National Advisory Committee on Children and Disasters (NACCD) and the National Preparedness and Response Science Board (NPRSB)

Session coordinator: **CAPT Charlotte Spires** (USPHS) (ASPR/OPP) [email: charlotte.spires@hhs.gov] and **LCDR Evelyn Seel, MPH** (USPHS) (ASPR/OPP) [email: evelyn.seel@hhs.gov]

Dr. Anne Zajicek, MD, Pharm.D. (NACCD)
Overview of the NACCD and reports to the ASPR

Dr. John S. Bradley, MD, FAAP, FIDSA (NPRSB)
Overview of the NPRSB and reports to the ASPR focusing on at-risk populations

Q&A

TRACK 3 – INDUSTRY PARTNERSHIPS

Past, present and future of the MCM Initiative at FDA

Session coordinator: **Rebecca Lipsitz, PhD** (FDA/OC) [email: rebecca.lipsitz@fda.hhs.gov]

Robert Fisher, PhD (FDA/OC)
Linking the scientific and regulatory environments for PHEMCE stakeholders: MCMi regulatory science

Drusilla Burns, PhD (FDA/CBER)
CBER MCM research and a case study: Prolonging anthrax vaccine shelf life

Kevin Krudys, PhD (FDA/CDER)
Determining the dose of MCM products in special populations

Heike Sichtig, PhD (FDA/CDRH)
Regulatory perspective for infectious disease diagnostics and FDA-ARGOS database

Q&A

TRACK 4 – EMERGING INFECTIOUS DISEASES AND PANDEMIC INFLUENZA

Influenza and respiratory pathogens update

Session coordinators: **Rick Bright, PhD** (ASPR/BARDA) [email: rick.bright@hhs.gov] and **Jonathan Ban** (ASPR/OPP) [email: jonathan.ban@hhs.gov]

Ruben Donis, DVM, PhD (ASPR/BARDA)
Update on pandemic influenza vaccine capacity and response → New initiative towards more effective influenza vaccines with universal potential

Lisa Koonin, DrPH, MN, MPH (CDC/OID/NCIRD)
Update on pandemic influenza preparedness and response capabilities

Jonathan Ban (ASPR/OPP)
An update of the HHS Pandemic Influenza Plan: Where do we need to go over the next 10 years?

Armen Donabedian, PhD (ASPR/BARDA)
Seasonal Influenza Vaccine Improvement Initiative

Q&A

4:00-4:30pm

Closing session: Report-outs from breakout sessions and closing remarks

George Korch, PhD (ASPR/IO)
Senior Advisor, Office of the Assistant Secretary for Preparedness and Response

4:30-5:30pm

Poster Session and Exhibit Hall