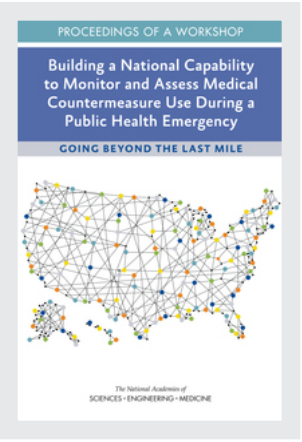

Building a National Capability to Monitor and Assess Medical Countermeasure Use During a Public Health Emergency: Going Beyond the Last Mile: Proceedings of a Workshop (2017)

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CONTRIBUTORS

Morgan Boname, Theresa Wizemann, and Justin Snair, Rapporteurs; Board on Health Sciences Policy; Health and Medicine Division; National Academies of Sciences, Engineering, and Medicine

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Building a National Capability to Monitor and Assess Medical Countermeasure Use During a Public Health Emergency

GOING BEYOND THE LAST MILE

PROCEEDINGS OF A WORKSHOP

Morgan Boname, Theresa Wizemann, and Justin Snair, *Rapporteurs*

Board on Health Sciences Policy

Health and Medicine Division

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PLANNING COMMITTEE ON BUILDING A NATIONAL CAPABILITY TO MONITOR AND ASSESS MEDICAL COUNTERMEASURE USE IN RESPONSE TO PUBLIC HEALTH EMERGENCIES[1]

BORIS LUSHNIAK (*Chair*), Dean and Professor, University of Maryland School of Public Health
PHYLLIS ARTHUR, Managing Director, Infectious Diseases and Diagnostics Policy, Biotechnology Innovation Organization
SUZANNE BAKKEN, Alumni Professor of Nursing; Professor of Biomedical Informatics, Columbia University
JEREMY BROWN, Director, Office of Emergency Care Research, National Institute of General Medical Sciences, National Institutes of Health
J. PERREN COBB, Professor, Clinical Surgery; Director, University of Southern California Critical Care Institute; Director, Keck Surgical Intensive Care Unit, University of Southern California
JEFFREY COUGHLIN, Senior Director, Federal and State Affairs, Healthcare Information Management and Systems Society
AMANDA PEPPERCORN, Senior Medical Director, Infectious Diseases Research and Development, GlaxoSmithKline
RICHARD PLATT, Professor and Chair, Department of Population Medicine, Harvard Medical School
KIMBERLEY RICKETTS, Public Health Advisor, U.S. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services
PAUL SELIGMAN, Executive Director, Amgen
UMAIR SHAH, Executive Director, Harris County Public Health and Environmental Services
YON YU, Associate Director, Regulatory Affairs, National Center for Emerging and Zoonotic Infectious Diseases, U.S. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services

Health and Medicine Division Staff

JUSTIN SNAIR, Senior Program Officer (until September 2017)
SCOTT WOLLEK, Senior Program Officer

[1] The National Academies of Sciences, Engineering, and Medicine's planning committees are solely responsible for organizing the workshop, identifying topics, and choosing speakers. The responsibility for the published Proceedings of a Workshop rests with the workshop rapporteurs and the institution.

MORGAN BONAME, Associate Program Officer
ALEXA EDMIER, Research Assistant
ANDREW POPE, Director, Board on Health Sciences Policy

Consultants

LAURA RUNNELS, LAR Consulting
THERESA WIZEMANN, Consulting Writer

Reviewers

This Proceedings of a Workshop was reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise. The purpose of this independent review is to provide candid and critical comments that will assist the National Academies of Sciences, Engineering, and Medicine in making each published proceedings as sound as possible and to ensure that it meets the institutional standards for quality, objectivity, evidence, and responsiveness to the charge. The review comments and draft manuscript remain confidential to protect the integrity of the process.

We thank the following individuals for their review of this proceedings:

SUZANNE BAKKEN, Columbia University
JAY C. BUTLER, Alaska Department of Health and Social Services
J. PERREN COBB, University of Southern California
EVA LEE, Georgia Institute of Technology
BORIS LUSHNIAK, University of Maryland School of Public Health
VINIT P. NAIR, Humana

Although the reviewers listed above provided many constructive comments and suggestions, they were not asked to endorse the content of the proceedings nor did they see the final draft before its release. The review of this proceedings was overseen by **LINDA C. DEGUTIS,** Henry M. Jackson Foundation. She was responsible for making certain that an independent examination of this proceedings was carried out in accordance with stan-

dards of the National Academies and that all review comments were carefully considered. Responsibility for the final content rests entirely with the rapporteurs and the National Academies.

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Acronyms and Abbreviations

ASPR	Office of the Assistant Secretary for Preparedness and Response (HHS)
BARDA	Biomedical Advanced Research and Development Authority
CBRN	chemical, biological, radiological, nuclear
CDC	U.S. Centers for Disease Control and Prevention
CONOPS	concept of operations
CMS	Centers for Medicare & Medicaid Services
CTSA	Clinical and Translational Science Awards
EHR	electronic health record
EMS	emergency medical services
EUA	Emergency Use Authorization
FDA	U.S. Food and Drug Administration
GSK	GlaxoSmithKline
HHS	U.S. Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act of 1996
IPT	integrated program team
IRB	institutional review board

IT	information technology
MCM	medical countermeasure
NCATS	National Center for Advancing Translational Sciences (NIH)
NIAID	National Institute of Allergy and Infectious Diseases (NIH)
NIH	National Institutes of Health
NLM	National Library of Medicine (NIH)
OCR	Office for Civil Rights (HHS)
ONC	Office of the National Coordinator for Health Information Technology
PHE	public health emergency
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
POD	point of dispensing
SNS	Strategic National Stockpile

1

Introduction and Overview[1]

During public health emergencies (PHEs) involving chemical, biological, radiological, or nuclear (CBRN) threats or emerging infectious diseases, medical countermeasures (MCMs) (e.g., drugs, vaccines, devices) may need to be dispensed or administered to affected populations to help mitigate the human health impact of the threat. The optimal MCMs determined for use during an emergency might be U.S. Food and Drug Administration (FDA) approved but used in unapproved ways (e.g., in a new age group or against a new agent); FDA approved using animal models because human efficacy testing is not ethical or feasible; or not yet FDA approved for any situation. Current medical product surveillance systems are typically passive systems that were not designed to provide information in the time frame necessitated by emergencies.

As part of the United States' scientific and research preparedness enterprise, there is an imperative to go "beyond the last mile" of MCM dispensing and administration to build and maintain a national capability to monitor and assess the use of MCMs (e.g., safety, compliance, clinical benefit) after they have been dispensed during PHEs. This need was first recognized in 2010 by then-Secretary of the U.S. Department of Health and

[1] This workshop was organized by an independent planning committee whose role was limited to identification of topics and speakers. This Proceedings of a Workshop was prepared by the rapporteurs as a factual summary of the presentations and discussions that took place at the workshop. Statements, recommendations, and opinions expressed are those of individual presenters and participants, and are not necessarily endorsed or verified by the National Academies of Sciences, Engineering, and Medicine, or the Health and Medicine Division, and they should not be construed as reflecting any group consensus.

Human Services (HHS) Kathleen Sebelius,[2] whose recognition led to the development of the *Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Action Plan for Developing an Enhanced National Capability for Monitoring and Assessing Medical Countermeasures During Public Health Emergencies*[3] in 2013. The PHEMCE action plan helped to identify the current core capabilities for MCM monitoring and assessment: data collection and reporting (i.e., surveillance systems), receipt and management of information, analysis of information, regulatory decision making, and communication.

In 2014, HHS Assistant Secretary for Preparedness and Response (ASPR) leadership established an MCM monitoring and assessment integrated program team (IPT) to develop a comprehensive, PHEMCE-wide coordinated capability to monitor and assess MCM use through data collection and analysis during and after an emergency to enable assessment and decision making during present and future PHEs. The IPT is actively working on this issue and has identified, engaged, and partnered with numerous stakeholders to advance its goals. IPT membership includes FDA, the U.S. Centers for Disease Control and Prevention (CDC), ASPR, the U.S. Department of Defense, the U.S. Department of Veterans Affairs, and the National Institutes of Health (NIH). Because of its representation on IPT and concomitant role in regulating MCMs, FDA has been an instrumental partner in working to develop the needed national capability for monitoring and assessing MCMs.

Looking forward, stakeholders could consider strategies to bridge the data collection gap between distributing and monitoring and surveilling MCMs during a PHE. Addressing this issue could better inform ongoing and future PHE responses, including the ability to use such information for clinical and regulatory decision making in near real time. This information could also advance efforts to protect and promote public health, particularly in light of the fact that there may be very limited human safety and efficacy data available for some MCMs prior to their use during PHEs. Boris Lushniak, dean and professor, University of Maryland School of Public Health, remarked that successfully developing and advancing a national MCM monitoring and assessment capability will require engagement with and by stakeholders from diverse sectors, including but not limited to local, state, tribal, and federal public health and emergency response agencies (including those involved in MCM planning and response); academia;

[2] *The Public Health Emergency Medical Countermeasures Enterprise Review: Transforming the Enterprise to Meet Long-Range National Needs*. 2010. Washington, DC: U.S. Department of Health and Human Services. https://www.medicalcountermeasures.gov/media/1138/mcmreviewfinalcover-508.pdf (accessed September 22, 2017).

[3] See https://www.phe.gov/Preparedness/mcm/phemce/Documents/2015-PHEMCE-SIP.pdf (accessed September 12, 2017).

clinical trial networks; contract research organizations; health information technology; electronic health records (EHRs); big data; drug sponsors; and health care–related professional organizations (e.g., medical, public health, and health care organizations and boards).

WORKSHOP BACKGROUND AND OBJECTIVES

To further the discussion on the need for a more robust national capability for monitoring and assessing MCMs following their distribution and use during PHEs, the Board on Health Sciences Policy of the National Academies of Sciences, Engineering, and Medicine (the National Academies) hosted a 2-day public workshop, Building a National Capability to Monitor and Assess Medical Countermeasure Use in Response to Public Health Emergencies.[4] The workshop, sponsored by FDA, was held on June 6–7, 2017, in Washington, DC. The statement of task for the workshop can be found in Box 1-1. The workshop was organized into five panel sessions (see Appendix B for the workshop agenda), which were followed by periods of open discussion with workshop participants facilitated by Laura Runnels of LAR Consulting.

ORGANIZATION OF THIS PROCEEDINGS OF A WORKSHOP

This Proceedings of a Workshop was prepared by the rapporteurs as a factual summary of what occurred at the workshop. Statements, recommendations, and opinions expressed are those of individual workshop participants and have not been endorsed or verified by the National Academies, and they should not be construed as reflecting any group consensus. The workshop was webcast live and the slide presentations and videos are archived on the meeting website.[5]

As previously noted, the workshop was organized into five panel sessions. However, to best reflect the workshop discussions and themes that arose over the 2 days, the rapporteurs for this proceedings chose to structure the discussions conceptually as follows:

- The final section of this chapter provides workshop sponsor FDA's perspective on MCM monitoring and assessment during PHEs, which set the stage for workshop discussions.

[4] See https://www.phe.gov/Preparedness/mcm/phemce/Documents/2015-PHEMCE-SIP.pdf (accessed September 12, 2017).

[5] See http://nationalacademies.org/hmd/Activities/PublicHealth/MedicalCounterMeasures/2017-JUNE-06.aspx (accessed September 22, 2017).

- Chapter 2 introduces the concepts of electronic health data, big data, operations for response, and clinical networks and explains how each of these terms was defined for the purposes of the workshop. This chapter also provides stakeholder perspectives from federal, state, and local health agencies; health care; the pharmaceutical industry; and academia.
- Chapter 3 summarizes workshop discussions that characterized data needs, sources, and collection methodologies for stakeholder decision making, with consideration of topics such as leveraging

BOX 1-1
Workshop Statement of Task

An ad hoc committee will organize a 2-day public workshop in Washington, DC. Through this workshop, the committee will convene experts representing a selection of government, academia and other researchers, the private sector, and public health and health care stakeholders and organizations currently involved with, or who have an interest in the concept of, building a national capability to monitor and assess public health emergency (PHE) medical countermeasure (MCM) use after dispensing/administration during public health emergencies. The workshop will focus on the topics of electronic health record (EHR) capabilities, the role of big data (i.e., large, complex, and unstructured datasets often precluded from conventional approaches to analysis that could be used for identifying patterns and associations), clinical trials networks, and concepts of operations for threat response and the utility of each to actively monitor and assess MCM use during actual or potential PHE responses.

The workshop will address the following objectives:

- Discuss the roles and efforts (both current and future) of the federal government and of relevant stakeholders with an interest in building and maintaining a national PHE MCM active monitoring and assessment capability;
- Discuss federal monitoring and assessment efforts (completed and ongoing) and opportunities for future work in areas, including
  - EHR capabilities,
  - the role of big data,
  - clinical trial networks, and
  - concept of operations for threat response; and
- Help inform the development of MCM active monitoring and assessment strategic plans for public health emergencies.

The committee will develop the agenda for workshop sessions, select and invite speakers and discussants, and moderate the discussions. A proceedings of the presentations and discussions at the workshop will be prepared by a designated rapporteur in accordance with institutional guidelines.

existing datasets, disseminating data and information, and unique challenges for data collection.

- Chapter 4 provides an overview of workshop discussions that centered on considerations for conducting rapid clinical research on MCMs during a PHE. Workshop speakers and panelists contemplated how operations for threat response could be adapted and how the current clinical trial infrastructure could be leveraged to facilitate MCM monitoring and assessment in PHEs, with discussion of topics such as data and information sharing, protocol design, and governance.
- Chapter 5 summarizes both the perspectives of federal stakeholders on key workshop takeaways, including barriers and opportunities for promoting monitoring and assessment of MCM use within their respective agencies, and reflections from individual workshop participants.

VIEWPOINT FROM THE U.S. FOOD AND DRUG ADMINISTRATION ON MCM MONITORING AND ASSESSMENT DURING A PHE

Rear Admiral Carmen Maher, acting assistant commissioner for counterterrorism policy and acting director of the Office of Counterterrorism and Emerging Threats at FDA, set the stage for the workshop by providing an FDA perspective on monitoring and assessment of MCMs. The pace of potential threats has increased since the 2001 anthrax attack, she noted, including several infectious disease threats that have emerged or reemerged in the past 5 years, such as Ebola virus, Zika virus, Middle East respiratory syndrome coronavirus, highly pathogenic avian influenza, enterovirus D68, measles, and H7N9 influenza. In response to these threats, the MCM field has advanced significantly in the last 15 years. For example, a comprehensive framework[6] was developed by stakeholders to rapidly identify the requisite MCM for a given threat and to help facilitate the development, manufacturing, stockpiling, and deployment of those MCMs. More recently, Maher noted, efforts have focused on how to conduct advanced product development in the midst of responding to a PHE (e.g., during the recent Ebola virus and Zika virus outbreaks). As is the case with any new medical product, when assessing MCMs, FDA must balance the potential benefits and risks of a product in light of the available scientific data, the public health needs, and the regulatory framework. When monitoring and assessing MCMs, however, all aspects of this process occur within a com-

[6] See https://www.phe.gov/Preparedness/mcm/phemce/Documents/2015-PHEMCE-SIP.pdf (accessed September 12, 2017).

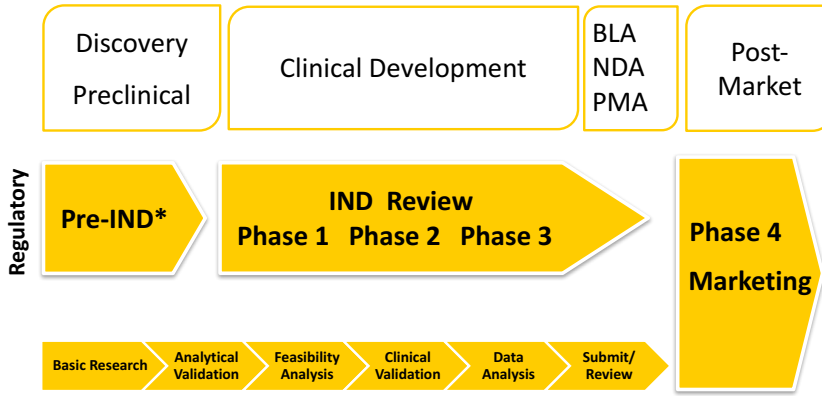

FIGURE 1-1 Traditional medical product life cycle.
NOTE: BLA = Biologics License Application; IND = Investigational New Drug; NDA = New Drug Application; PMA = Pre-Market Approval.
* Pre-submission for medical devices.
SOURCE: Maher presentation, June 6, 2017.

pressed timeframe. Furthermore, FDA must be cognizant of accessing the information needed to fulfill his goal without disrupting on-the-ground responses, said Maher.

Role of FDA Across the MCM Product Life Cycle

Maher discussed key elements of FDA's role in the development, review, and distribution of MCMs and the need to go beyond the last mile to monitor and assess them for safety and effectiveness. The traditional medical product life cycle is a tightly controlled, iterative process, Maher said, and decisions are made by FDA at each developmental stage regarding whether a product advances (see Figure 1-1). FDA has several legal and regulatory mechanisms that can be applied during the development and review of MCMs to accelerate medical product approval and availability, such as the Animal Rule, Emergency Use Authorization (EUA), Expanded Access provisions, and various authorities provided under Investigational New Drug Application and Investigational Device Exemption pathways.[7] After a product is approved, FDA has a variety of mechanisms for post-market

[7] More information about FDA's legal and regulatory MCM authority is available at https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/default.htm (accessed August 23, 2017).

surveillance, including passive and active surveillance systems and voluntary and mandatory reporting. Maher reiterated that most of the capabilities for post-market monitoring of medical products were not designed for use in PHEs. Still, FDA is currently reliant on those systems as there is no comprehensive strategy or framework for monitoring and assessment of MCM use during a PHE.

Medical products typically proceed through the preclinical and clinical developmental steps outlined in Figure 1-1 with the end goal of being approved and marketed. In recent responses to PHEs, however, FDA has been faced with making approval decisions farther left along the pathway than ever before (i.e., closer to the discovery and preclinical phases), with information on safety and effectiveness being collected after the product has been made available for use in the target population, said Maher. In some cases, such as a mass casualty event, she added, such a product might have been made widely available. Maher highlighted several potential key challenges in developing MCMs, including the following:

- The affected population is only available for clinical research during a PHE, so traditional clinical trials are not feasible.
- Products may have been approved under the Animal Rule,[8] so the first opportunity to gather data on MCM efficacy and safety in the affected population might be during a PHE.
- Post-marketing commitments or requirements may accompany the MCM for which the requisite data may be difficult to collect during a PHE.
- No MCMs are available for the threat at hand, so an early research and development product that could potentially address the threat must be identified and a determination made as to if, and how quickly, it could be developed.
- Human efficacy tests might be deemed unethical, further complicating the planning and conduct of clinical trials in a PHE.

Despite these challenges, and although regulatory decisions might be made based on limited data, Maher emphasized that such decisions are carefully considered by FDA and are made based on informed benefit–risk calculations using sound scientific data. Because information is often limited, however, it is essential to collect as much robust, credible data as possible during product use in a PHE to complete the safety and efficacy profile, she said.

[8] For more information about the Animal Rule, see https://www.fda.gov/emergencypreparedness/counterterrorism/medicalcountermeasures/mcmregulatoryscience/ucm391604.htm (accessed August 23, 2017).

TABLE 1-1 Differences Between FDA Product Assessment in a PHE Versus Traditional Research and Development

Public Health Emergency	Traditional Research and Development
• Intent—respond and mitigate • Unplanned and/or unexpected • Uncontrolled or no data collection • Large numbers of individuals • Simultaneous administration and/or multiple products • Rapid decision making and/or response • Little or no tracking and/or monitoring • Lack of primary provider oversight and/or interaction • Limited reporting or information dissemination	• Intent—generalizable knowledge • Planned and deliberate • Well-controlled clinical trials • Smaller numbers of individuals • Stepwise progression and a single product • Careful decision making and adequate time • Strict oversight and monitoring o Informed consent and process o Institutional review board review and approval o Adverse event reporting

SOURCE: Maher presentation, June 6, 2017.

Maher highlighted some of the key differences between assessing a new medical product developed via a traditional research and development pathway and an MCM developed in anticipation of or in response to a PHE (see Table 1-1). The intent in a PHE is to mitigate and respond, Maher reiterated, and decisions are made quickly. PHEs are often unpredictable in terms of their timing, location, and severity, even PHEs that have been planned for with preparedness activities. Maher also noted that during a PHE there is often simultaneous administration of multiple products to large numbers of the general public. Furthermore, during an emergency response, there is little or no tracking or monitoring of products that have been used as many MCMs are dispensed on scene by first responders or at mass points of dispensing (PODs). In contrast, in the traditional research and development pathway, a single product is studied in specific populations in a very controlled clinical setting.

Looking Beyond the Last Mile in the MCM Product Life Cycle

Within the federal government, emphasis has traditionally been placed on the dispensing and distribution of MCMs—commonly referred to as the "last mile" of the MCM product life cycle—rather than on their monitoring and assessment. The focus of this workshop, Maher said, is what happens beyond the last mile. Although tools and capabilities are available with which to monitor and assess medical products, these tools were not originally developed with the purpose of rapidly collecting, analyzing, and gathering data in the midst of PHEs or using that information in real-time to inform decisions on the use of that product within present (and future)

PHEs. Importantly, Maher said, data are needed that can show if the countermeasure is not performing as expected, or if there are unanticipated adverse events. Maher challenged workshop participants to consider how and where such information about MCM performance could be captured and rapidly assessed without disrupting the ongoing emergency response. To move beyond the last mile and integrate monitoring and assessment into the MCM life cycle, FDA is reviewing its current capabilities and identifying opportunities in four main areas: electronic health data, unstructured/big data, operations for response, and clinical networks.

There has been much progress to date, Maher said, including a host of PHEMCE, Department of Defense, and other initiatives that are under way or in development (see Box 1-2). Over the past 10 years, stakeholders within PHEMCE have made significant progress in coordinating response efforts in PHEs, with a mutual recognition of the contributions each stakeholder can bring to bear. She noted that managing and prioritizing differing commitments and priorities among stakeholders in a way that provides for a coordinated, rapid response are critical to these efforts. However, Maher noted, this coordination has been more successful in development and distribution of MCMs than in gathering the requisite data for monitoring and assessing MCMs.

Finally, Maher reemphasized that FDA does not intend to create a new system of monitoring and assessing medical products. Rather, their goal is to build a PHEMCE monitoring and assessment component into existing infrastructure. For example, how could current EHR capabilities or handheld device capabilities be used to collect information on MCM product performance in a real-world setting? How could clinical trial networks be linked? What roles could machine learning, social media, crowd sourcing, and smart technology play? Ultimately, Maher concluded, how do we leverage and coordinate all the many elements and partners during a PHE response to collect safety and efficacy data about MCMs?

OVERVIEW OF CROSS-CUTTING TOPICS HIGHLIGHTED DURING PRESENTATIONS AND DISCUSSIONS[9]

Various themes emerged across multiple panel sessions and discussions as workshop participants considered the various aspects of monitoring and assessing MCMs in PHEs. The themes and opportunities highlighted below,

[9] The rapporteurs' summary of the main topics and recurring themes is drawn from the presentations, discussions, and summary remarks by the workshop panelists and participants. Items on this list should not be construed as reflecting any consensus of the workshop participants or any endorsement by the National Academies of Sciences, Engineering, and Medicine.

BOX 1-2
H1N1 Influenza as a Case Study in MCM Development, Deployment, Monitoring, and Assessment

The response to the 2009 H1N1 influenza pandemic could serve as an example of the rapid pace of development and assessment of MCMs and the important roles of different government partners, said Maher (see Figure 1-2). The

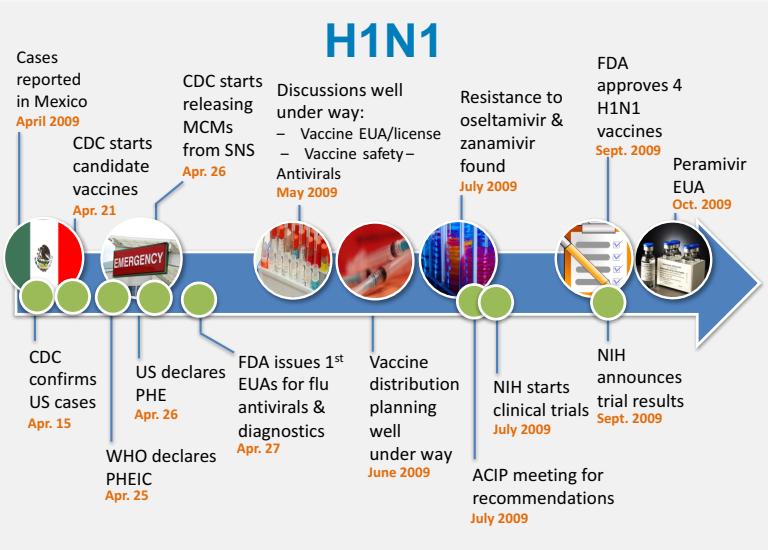

FIGURE 1-2 Timeline of FDA response to the 2009 H1N1 influenza pandemic.
NOTE: ACIP = Advisory Committee on Immunization Practices; CDC = U.S. Centers for Disease Control and Prevention; FDA = U.S. Food and Drug Administration; EUA = Emergency Use Authorization; MCM = medical countermeasure; NIH = National Institutes of Health; PHE = public health emergency; PHEIC = Public Health Emergency of International Concern; SNS = Strategic National Stockpile; WHO = World Health Organization.
SOURCE: Maher presentation, June 6, 2017.

drawn from individual panelist remarks and open discussions, are discussed further throughout this proceedings.

Benefits and Risks of MCMs

A key stage-setting question considered by workshop participants was whether an MCM deployed during a PHE is providing benefit (i.e., acting

first cases of H1N1 influenza in the United States were confirmed in April 2009. By September 2009, FDA had approved four H1N1 vaccines, and by October 2009, the agency had issued EUAs for an investigational product (peramivir), as well as for new, previously unapproved uses of products already on the market. Maher noted that although the H1N1 vaccine was handled as a strain change to an existing vaccine (very similar to how the seasonal influenza vaccine is developed each year), there were differences with the H1N1 strain that required clinical trials be performed, which is not typical of a seasonal strain change. In retrospect, however, FDA was not prepared to monitor and assess the performance of peramivir and other products that were being used, and it is still not clear whether peramivir helped, hindered, or had no effect, said Maher.

Lushniak and Maher discussed lessons learned from the 2009 H1N1 pandemic experience, specifically regarding assessing and monitoring MCM use. Maher said she was impressed by the intensity with which government, academic, and industry partners came together to assess the epidemiology of the virus and to consider what therapeutics were in the development pipeline, what countermeasures were in the stockpile, what products were already on the market, and how these resources could be used. The pace of the collaboration and the drive to intervene within a very compressed timeframe were striking, she said.

Lushniak noted the frustration around not having information about the effectiveness of peramivir. This experience exemplified that data collected should be prioritized according to what information clinicians and other decision makers need. For example, clinicians need to determine whether to continue to use the MCM, or perhaps switch to a different MCM. Government decision makers need to determine if or when to release a product from the Strategic National Stockpile. This information needs to be timely to enable decision making in real time, Lushniak added. Ideally, Maher said, all stakeholders would be using all the tools at their disposal to rapidly collect key information for different levels of decision makers about the use of the medical product. For example, information about the use of MCMs could be captured in EHRs, and crowdsourcing data might be used to understand compliance and patient experience with the MCM.

SOURCE: Maher presentation, June 6, 2017.

as expected), or causing harm. Discussions at the workshop centered on performing research and collecting data to inform the benefit–risk profile of MCMs, which may be deployed during PHEs at varying developmental stages (i.e., an investigational product with limited preclinical data, a product approved under the Animal Rule, or an FDA-approved product that may have post-marketing commitments and requirements) and with varying levels of safety and efficacy data. Because PHEs dictate a rapid timeline for

collecting data on safety and efficacy to inform MCM benefit–risk profiles, several workshop participants noted that discussions should consider how existing infrastructure and data sources could be leveraged and adapted for this setting.

Clinical Development for MCMs Versus Traditional Medical Product Development

As various workshop participants noted, a PHE might be the only opportunity to collect clinical safety and efficacy data on MCMs in humans. However, the uncertainty of when and how an MCM will be used makes it difficult to prospectively craft protocol designs and determine elements of clinical research that will be adaptable to a broad range of situations. Topics raised throughout the workshop related to clinical research on MCM use included elements of predefined study protocols, predefined variables for collecting data, and pre-identification of clinical trial sites. Elizabeth Higgs, global health science advisor for the Division of Clinical Research at the National Institute of Allergy and Infectious Diseases (NIAID) at NIH, noted that clinical research on MCMs requires increased efficiency, expediency, and adaptability, relative to routine clinical development. In light of these requirements, however, stakeholders must ensure that data collection efforts are as robust as possible and that rigor is not sacrificed at the expense of being faster and more adaptive in collecting data and/or implementing trials, she said.

Question-Driven Data Collection

A common theme throughout workshop discussions was that data collection should be driven by the questions that need to be answered in order to inform MCM use. However, data also inform the development of questions, and issues can arise when questions are driven by the availability of data, rather than by what needs to be known. Understanding the bidirectionality between crafting the right questions and understanding the availability and applicability of data sources to answer those questions is critical to monitoring and assessment efforts.

Potential Challenges to Identifying Data Needs and Data Collection

Several workshop participants noted that it is often not possible to prospectively determine what data need to be collected on MCM use during PHEs. Anita Patel, senior advisor and lead in the Pandemic Medical Care and Countermeasures Influenza Coordination Unit of the National Center for Immunization and Respiratory Diseases at CDC, noted that although

baseline data are needed for any PHE, depending on the specifics of the PHE—for example, the severity of the threat and known benefit–risk profile of the MCM—additional categories of information may be required. Furthermore, she said, different data users need different types of data, and data sources used will shift as data needs evolve over the course of an event.

In considering how best to collect data, several key themes arose, including understanding who the end users of the data are; determining where the best physical locations for collecting data are (i.e., in the field or in inpatient or outpatient facilities); how to best align data collection with timing and sequences of PHEs; identifying missing or unknown data; integration of data from different sources into an evolving response structure; and leveraging machine learning and artificial intelligence, as well as innovative modeling, for collecting and interpreting health data. Some of these concepts are discussed in this section, as well as throughout the proceedings.

Data Gaps and Equity

In consideration of what data are needed and the potential sources for gathering these data, individual participants emphasized that stakeholders should also be cognizant of what data are *not* being collected and how these missing data affect information-gathering efforts. For example, which patient populations are underrepresented during PHEs, how could this underrepresentation bias the data, and how could this issue be addressed in future data collection efforts? At a more granular level, participants noted that certain types of data are currently missing that would benefit MCM monitoring and assessment efforts, including medical histories and symptomatology.

It was emphasized that stakeholders would benefit from increasing their understanding of data collection methods and potential biases in data samples. Individual participants highlighted the need to recognize the differences between data that are collected for a specific purpose (following a predefined methodology) and data that are collected and analyzed retrospectively, and to interpret findings accordingly.

Data Standardization, Integration, and Interoperability

The health care system in the United States is complex and heterogeneous, and there is no single unified system with common standards for collecting and sharing data, said Eva Lee, director of the Center for Operations Research in Medicine and Health Care at the H. Milton Stuart School of Industrial and System Engineering at the Georgia Institute of Technology. Even local health departments within a state or individual hospitals

under the same network face challenges sharing information. At the present time, the electronic health data sources available to stakeholders are not completely interoperable, so the current task is to assemble a patchwork of data sources into a comprehensive surveillance system for MCMs that can be rapidly activated and cover a large portion of the population. Looking forward, several workshop participants emphasized that stakeholders should work toward interoperability between EHR systems and between EHR and other data systems. Integration of data could occur at various time points: early (at data input), intermediate (mapping multiple sources to a common data model), or late (after separate analysis).

Legal, propriety, and governance barriers present challenges to interoperability of systems, however, and it will take effort and good will to find ways to make these systems work together for purposes other than that for which they were primarily designed and in a way that remains consistent with their original missions. Issues to be considered and surmounted include data standardization and careful consideration of patient privacy and data security.

Data Privacy and Security

There is a clear need to balance patient privacy and data security with sharing of information; however, it was acknowledged by individual workshop participants that the Health Insurance Portability and Accountability Act of 1996 (HIPAA) is often subject to misinterpretation, overinterpretation, or is used as a reason not to share information. Furthermore, it was noted that there is often confusion among institutional review boards (IRBs) about when sharing of information is considered research and when it is considered public health practice. Several participants discussed the need to raise awareness that public health practice is not human subjects research and does not require IRB review.

Existing Data Sources, Datasets, and Clinical Trial Infrastructure

FDA noted at the outset of the workshop that its goal is not to create a new system to monitor and assess MCMs, but to build a PHEMCE monitoring and assessment component into existing infrastructure. However, most existing data sources are part of the traditional care delivery setting, and MCM dispensing often takes place in non-traditional settings. Therefore, tools routinely used for medical product surveillance settings are not immediately amenable to the rapid collection, aggregation, and analysis needed to enable real-time use of data for decision making in a PHE. Consideration could be paid as to how these data and tools could be adapted for this setting.

Throughout the workshop, individual participants highlighted some of the many existing data sources that could be leveraged for monitoring and assessing the outcomes of MCM use, including point-of-care patient narratives, EHRs, government surveillance and tracking systems, big data, emergency medical services (EMS), pharmacy databases, social media, and mobile health applications. Challenges, limitations, and the potential for these opportunities were discussed.

The use of existing clinical trial networks will be important to achieving rapid connectivity throughout the MCM monitoring and assessment enterprise, noted individual workshop participants. For example, in a PHE, predesigned protocols could be sent to predetermined, experienced clinical sites, and existing "networks of networks" could be adapted for this purpose.

Workforce and Training

The field of data science requires a broad range of skill sets and specific subject-matter expertise in the health sciences. No single individual has all the skills and expertise needed to be able to address any given problem. Participants discussed training programs that could enable more effective use of data systems and incorporating data science in undergraduate and graduate education to develop a pipeline of individuals who have data science and informatics competencies to complement their domain knowledge. Participants also remarked that an introduction to clinical research techniques could be incorporated into preparedness training for PHE responders to provide them with a broader perspective and increased familiarity with performing data collection on MCM use in the context of a PHE.

Leadership and Administrative Preparedness

Moving forward, leadership and responsibility around MCM monitoring and assessment during PHEs are needed to promote coordination of efforts, said Higgs. These efforts are generally more developed at the international than at the domestic level, she added. Similarly, remarked Ray Barishansky, Deputy Secretary of Health, Pennsylvania Department of Health, although public health preparedness and response has become quite robust over the past 15 years, there is an "administrative preparedness" angle to MCM monitoring and assessment that is often not as robust as it could be. At the state and local levels, he said, efforts can be decentralized, and there can be confusion around who the primary authority is during a response, including in areas such as data sharing.

Continuous Testing of Critical Infrastructure Systems

The importance of routine testing and exercising of systems to develop proficiency among users and establish the capacity of these systems was a common theme among workshop participants. Incorporating awareness of practices, policies, and regulations into everyday health practice could serve to ensure their understanding and identify risks and concerns before a crisis occurs.

Effective Communication Among Stakeholders

Individual participants called for better communication across stakeholders, including better processes for disseminating changes in policy and guidance from federal agencies down to local health departments, as well as ways to communicate information and questions back upstream. In consideration of collecting the best data possible, several participants observed that researchers could do better at articulating the value of data collection to health systems administrators, including explaining why they should share data from their systems and similarly articulating the value of public health preparedness effort to policy makers (see Policy and Regulation [Dis] Incentives in Chapter 3).

In the context of communicating to the public during a PHE, data are needed by local authorities to enable timely risk communication to affected populations. Alison Levy, emergency operations manager for Public Health–Seattle and King County, Washington, noted that cross-jurisdictional coordination is essential, as an uncoordinated message across a region could confuse the public on the necessary actions and damage public trust. In a similar vein, participants also discussed the importance of timely return of findings from data analysis to stakeholders, including research participants.

Funding

It was observed by individual workshop participants that medium, small, and rural health agencies are willing to participate in data collection, but they often lack the funding, staffing, and technology to do so. This gap could be addressed so that smaller health jurisdictions can collect and report their data and understand what the data mean for them on the local level. In support of this effort, potential costs of data collection and funding sources for these data collection efforts could be determined before a PHE occurs. Bringing the PHEMCE perspective to stakeholder activities that are already being funded to collect data could be a solution to implement cost savings through coordination of efforts.

2

Setting the Stage: Defining Terminologies and Sharing Stakeholder Perspectives

The workshop began with presenters providing stage-setting definitions and background information, which are summarized in the first half of this chapter. Richard Platt, professor and chair of the Department of Population Medicine at the Harvard Medical School and Sue Bakken, alumni professor of nursing and professor of biomedical informatics at Columbia University, provided definitions and general background on electronic health data, big data, and data science. Lushniak and Perren Cobb, director of Surgical Critical Care Institute and clinical professor of surgery and anesthesiology at the Keck School of Medicine, University of Southern California, provided definitions and general background on operations for response and clinical networks, respectively.

To set the stage for the workshop discussions, Yon Yu, associate director, Regulatory Affairs, National Center for Emerging and Zoonotic Infectious Diseases, CDC, HHS, asked a panel of stakeholders to consider the primary data sources discussed during the lightning terminology presentations and share perspectives on how their sector might contribute to a coordinated MCM monitoring and assessment effort during a PHE, which is presented in the second half of this chapter. Levy discussed her perspective as a local public health official. Theresa Cullen, associate director of the Global Health Informatics Program at Regenstrief Institute, Inc., offered perspectives both from health information technology (IT) and informatics and of a health care provider in the community. Patel provided a federal-level perspective, and Paul Petersen, director of the Emergency Preparedness Program of the Tennessee Department of Health, spoke from the perspective of a state health department. An industry perspective was provided by

Quazi Ataher, senior director of epidemiology in Worldwide Safety Strategy at Pfizer Inc. Finally, Adam Wilcox, chief analytics officer at the University of Washington, shared his perspective as an academic researcher.

DEFINING TERMINOLOGIES USED THROUGHOUT THE WORKSHOP

Electronic Health Data

Platt offered a framework for thinking about electronic health data in which he highlighted five key types of electronic health data that are developed principally during the delivery of health care: EHR, electronic

BOX 2-1
Types of Electronic Health Data

Electronic Health Records

- Practice and hospital-based systems (e.g., EpicCare, Meditech, Cerner)
- Timeliness: potentially same day; often next day
- Salient positive features (selected): substantial population penetration and clinical detail
- Salient negative features (selected):
  - Only capture care delivered by the individual provider organization (most people have more than one EHR)
  - Interoperability of EHR systems is limited
  - Optimized for individual care, not population health

Electronic Laboratory Data

- Practice and hospital-based systems, freestanding laboratories (e.g., Quest, LabCorp)
- Timeliness: potentially same day; often next day
- Salient positive features (selected): readily available, independently or incorporated into EHR data
- Salient negative features (selected):
  - Requires linkage to EHR or claims to be actionable
  - Substantial variability in coding practice

Administrative and Claims Data

- Data supporting payment for clinical care of insured individuals (e.g., Medicare, commercial)
  - Demographics (age, sex, address)
  - Diagnosis codes, procedures, dispensed medications
- Timeliness: weeks to months

laboratory data, administrative and claims data, prescription drug dispensing records, and public health registries (see Box 2-1). These types of health data exist in electronic form for substantial portions of the population, he said.

Platt expressed optimism that, in the future, data sources will be interoperable and information will be available about whole populations in real time. At present, however, the task is to consider how to assemble a patchwork of data sources into a comprehensive surveillance system for MCMs that can be activated rapidly, at any location, and covering a large fraction of the population. One consideration is that existing data sources are often part of the conventional care delivery system, while MCM dispensing often takes place in non-traditional settings.

- Salient positive features (selected):
  - Can define an eligible population
  - Allows assessment of billed care in all locations
- Salient negative features (selected):
  - Limited to covered population
  - Limited clinical detail

Prescription Drug Dispensing Records

- Information about medication fills (versus prescribed)
- Timeliness: weekly, possibly more frequent
- Salient positive features (selected):
  - Relatively complete for medications dispensed in the ambulatory setting
  - Includes dosage, form, and amount dispensed
- Salient negative features (selected):
  - Does not capture many vaccines or medications dispensed as part of an MCM program
  - Does not reliably capture drugs with low co-pays
  - Does not capture over-the-counter drugs

Public Health Registries

- State or other agency information reported directly by providers
- Timeliness: highly variable
- Salient positive features (selected): may be the most complete record in a jurisdiction
- Salient negative features (selected):
  - High variability between states in what is recorded and how it is recorded
  - Highly variable laws govern their use

SOURCE: Platt presentation, June 6, 2017.

Substantial technical challenges must be overcome to make incompatible data systems work with one another and work more rapidly than during routine surveillance, Platt said. Legal, propriety, and governance barriers present an even greater challenge to interoperability of systems. It will take effort and good will to find ways to make these systems work together for purposes other than that for which they were primarily designed and in a way that is still consistent with their original missions, Platt said.

There are a variety of potential solutions to increasing EHR interoperability, including standardization. Platt observed that EHRs were designed for use in individual health care settings, making it difficult to extract and analyze compatible population data for surveillance efforts. This is not an informatics problem, he continued, but an information problem.

Big Data

Bakken described the four dimensions of big data as volume (scale of data), velocity (analysis of streaming data), variety (different types of data), and veracity (uncertainty of data). She highlighted several considerations for best leveraging big data:

- Promoting data models, sharing, and standardization;
- Ensuring trustworthiness, security, and privacy of the data;
- Maintaining and distributing knowledge derived from data; and
- Appreciating the importance of learning organizations and organizational learning.

In conjunction with traditional data sources, an increasing number of novel big data sources can be useful for detection, surveillance, management, and evaluation of MCM use, said Bakken. However, integration is necessary to take advantage of this wide variety of data sources, she said, and can occur at different time points. In some systems, data are integrated early on by standardizing multiple data sources at input. In other instances, integration might occur at an intermediate time point by mapping multiple data sources to a common data model for analysis. Late integration can occur after data sources have been separately analyzed and are brought together to create a larger analytical dataset.

The ability to analyze vast quantities of data, rather than smaller datasets, could enable population-level analysis during PHEs, said Bakken. She emphasized that working with big data requires a willingness to embrace the "real-world messiness" of the data and accept the usefulness of identifying correlations rather than causation.

In concluding her remarks, Bakken posed several questions to foster discussion: How do we harness big data and implement the right infrastruc-

ture for generating actionable insights? What are the privacy and security considerations that need to be addressed? What are the strategies for normalization and integration for unstructured data? What are the potential roles for crowdsourcing and mining of non-traditional sources?

Concept of Operations for Threat Response

Concept of operations (CONOPS) for threat response is a description of how a set of capabilities can be employed to achieve desired objectives or an end state, Lushniak said. It is a document that describes the characteristics of a proposed system from the viewpoint of an individual who will use that system. CONOPS are used to communicate quantitative and qualitative system characteristics to all stakeholders. It is widely used in the military, governmental services, and other fields, Lushniak noted, and the term CONOPS has multiple uses and multiple definitions within those systems. A CONOPS includes

- A statement of the goals and objectives of the system;
- Strategies, tactics, policies, and constraints affecting the system;
- Organizations, activities, and interactions amongst participants and stakeholders;
- A clear statement of responsibilities and authorities; and
- Specific operational processes for fielding the system and processes for initiating, developing, maintaining, and retiring the system.

There are CONOPS for many different threat response capabilities, Lushniak explained, and the task of this workshop is to discuss how to build big data, electronic health data, and clinical networks for MCM monitoring and assessment into these operations. Coordination of operations across local, state, and national levels and across all stakeholders is needed, he said.

A CONOPS is developed to provide a narrative of the process to be followed in implementing a system; define the roles of the stakeholders involved; and offer a clear methodology to realize the goals and objectives of the system. PHE responses are all-hazards approaches, Lushniak said, with an overarching goal being an active MCM monitoring and assessment capability that will allow the pooling, analysis, and sharing of information to guide MCM use during the same event or future events. Lushniak emphasized the importance of building this system into a CONOPS.

Clinical Networks

Cobb began his discussion of clinical networks with the following quotation from a *New England Journal of Medicine* article discussing research as a part of PHE response:

> Although responses to recent events have typically used the best available science at the time, additional research, done in parallel with and after the response itself, is often essential to address the most pressing knowledge gaps presented by public health emergencies, and to ensure that they are addressed by the time another similar disaster strikes. Recent events, however, have illustrated gaps in the planning for, and rapidly executing, scientific research in the context of the disaster response. (Lurie et al., 2013, p. 1251)

In a follow-up to this article, Nicole Lurie, former ASPR, charged the U.S. Critical Illness and Injury Trials Group to bring together individuals and subject-matter experts from the federal government, academia, industry, and the community to identify key clinical questions that need to be answered in response to any type of PHE, across all hazards. The group developed a list of six questions they believed would be useful to clinicians and researchers and persons responsible for systems and operational evaluations (Murphy et al., 2015):

- Clinician end-users and researchers
  - What was the nature of the insult and the resulting phenotype?
  - As a responder, what, if anything, did you have to do differently?
  - Did diagnostics, countermeasures, and therapies work as expected?
  - What was the impact on the patient and care setting?
- Systems and operational evaluations
  - Was there anything essential needed that you did not get?
  - What is the best/worst case that could happen next time?

Using these questions as a starting point, stakeholders must next determine what data and infrastructure are needed to provide answers to these questions. A significant amount of work and funding has been under the general umbrella of PHEMCE, Cobb said, to build an infrastructure that supports a "network of networks," including

- A national network of acute and critical care research organizations of academic and community hospitals for adults and children, across the care continuum, from pre-hospital through rehabilitation;

- A rapid communication network with quarterly queries to assess national health system stress;
- Infrastructure for prospective trials for national PHEs, such as influenza and anthrax;
- National data coordinating centers;
- Human subjects research review with local and national IRBs, through the NIH Public Health Emergency Review Board; and
- Coordination of efforts with international organizations and clinical trials groups.

Overlaying a series of maps,[1] Cobb showed how this network of networks is geographically distributed across the country. Networks shown included sites of the U.S. Critical Illness and Injury Trials Group (recently renamed the Discovery Research Network of the Society of Critical Care Medicine); CDC National Ebola Training and Education Center; sites of the Johns Hopkins University Research Network; Pediatric Emergency Care and Research Network sites; Pediatric Acute Lung Injury and Sepsis Network Investigators; and the National Heart, Lung, and Blood Institute (NHLBI)-funded Prevention and Early Treatment of Acute Lung Injury Research Network. The United States is well covered by existing clinical trial networks, Cobb observed, although there are opportunities for better geographic representation. Importantly, he said, large numbers of centers are interested in clinical research during PHE response. However, he continued, there is not an opportunity for the leadership from these various networks to share information (e.g., lessons learned or efficient use of available resources) and coordinate efforts. In closing, Cobb referred workshop participants to a list of the key topic areas discussed at a 2015 Institute of Medicine (IOM) workshop, Enabling Rapid and Sustainable Public Health Research During Disasters (IOM, 2015). What is needed now, Cobb concluded, is an action plan that identifies metrics of success for these priorities and outlines exercises that test capabilities and capacity.

STAKEHOLDER PERSPECTIVES

Local Public Health Perspective

Levy described the role of her department, Public Health–Seattle and King County, as carrying out the local response to a PHE and ensuring that the measures implemented meet the needs of the local population. She

[1] The maps from Cobb's presentation are available at www.nationalacademies.org/hmd/~/media/Files/Activity%20Files/PublicHealth/MedPrep/4_Cobb.pdf (accessed October 14, 2017).

emphasized a need for equity and an awareness of which members of the local community may not be represented in the datasets discussed throughout the workshop. Information gathered during a PHE is primarily needed at the local level to understand more about the incident that occurred; the types of MCMs available for both prophylaxis and treatment; what MCMs are accessible in the supply chain that will influence the response; and what is known about the effectiveness of the MCMs being used.

Local health departments face a variety of challenges in communicating to the public during a rapidly evolving situation. Levy noted the struggle among MCM sponsors and developers to balance obtaining "perfect data" for research and development and approval with getting data out to local residents quickly. Similarly, she said, local health departments struggle with risk calculations regarding messaging for promoting healthy behavior in the public during a PHE. Considerations for this calculation include noting that there are many different ways people prefer to receive information, differing functional and access needs, and language barriers. Risk communication needs to be succinct, she added, by being simplified to a few key messages that promote healthy behavior by the public during the event.

In the short term, policy and decision making are influenced by several factors: who was affected (e.g., closed or open population), whether other areas were affected, and whether the exposure was accidental or intentional, said Levy. She challenged the commonly held notion that all incidents are local by stating that "all incidents are regional," and accordingly, cross-jurisdictional coordination is essential. Potentially affected populations cross county boundaries every day for work and for health care, she noted, and an uncoordinated message across the region could confuse the public on the proper course of action. Yu added that the public's perception and acceptance of their role in contributing to data collection on MCM use is an important part of that messaging, as well.

Community Provider Perspective

Cullen shared her perspective as a family medicine doctor who works shifts in a local hospital emergency department, the prior chief information officer of the Indian Health Service, and the prior chief medical informatics officer of the U.S. Department of Veterans Affairs; she is presently in health informatics and health research at Regenstrief. Health care providers and responders are dealing with the individual patient, an N-of-1, and data collected for that N-of-1 form a narrative that stems from the many different questions the provider asks when trying to establish a diagnosis, said Cullen. The narrative that evolves at the point of care provides an opportunity for early recognition as part of the public health and MCM response to an emerging event. Currently, she said, this un-

structured narrative, oftentimes captured within EHRs, is not accurately leveraged in PHE responses.

Federal Health Perspective

Patel remarked that stakeholders should consider the timing of events during a PHE and how data needs might change as a response evolves. Often, data needs change throughout a response, and being clear about what is needed on the front-end and how needs may change over time is important. Patel noted that the very early stages of a PHE response are critical for the federal government to be able to mobilize emergency operation centers, which streamline coordination efforts and allow cross-talk among government agencies. Furthermore, a key concern at the onset of a response is the identification of regulatory and policy needs, because much of what happens at the local level is contingent on these set rules and regulations, she said. Information gathered in the early stages of a PHE could influence decisions regarding declaration of states of emergency (e.g., invoking the Public Readiness and Emergency Preparedness Act Declaration[2]) and other regulatory mechanisms, such as EUA for MCMs. In response to a question on how coordination across the federal government could be done more effectively, Patel noted that the more stakeholders and their systems are exercised and tested in situations in which data sharing is essential and flows in different ways, the better and more coordinated responses become.

State Health Department Perspective

Petersen shared his viewpoint on data needs at the state level, including three major takeaways: the importance of timely risk communication to affected populations, clarification on the scale and scope of a PHE, and identification of the resource needs (including MCMs) that are not readily available for response efforts. He emphasized the importance of providing action steps that the public can take for themselves, and being transparent regarding any prioritization for MCM dispensing. Communicating MCM prioritization helps to foster public trust and adherence with any MCM dispensed. All emergencies start locally, Petersen added, and decisions (e.g., policy development, data collection requests) made at the federal and state levels can have significant impact on those working at the local level. Furthermore, Petersen emphasized that data sharing among stakeholders,

[2] For information on the Public Readiness and Emergency Preparedness (PREP) Act, see https://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx (accessed August 23, 2017).

BOX 2-2
Collaboration Between a State Health Department and the Health Care Community During the 2012 Nationwide Fungal Infection Outbreak

In September 2012, contaminated epidural steroid injections led to a nationwide fungal infection outbreak that resulted in 750 confirmed cases and 64 deaths, Petersen explained. In response to the crisis, the Tennessee Department of Health received daily lists of individuals who were exposed to these products from the health care community and assigned public health nurses to more than 1,100 patients. These patients were tracked by the Department of Health over a 3-month period and informed about symptoms that should prompt them to receive immediate care. Mortality was reduced from 31 percent to 4 percent just by getting people into care, Petersen said. The ability to monitor those individuals and to have a seamless connectivity to EHRs at the health care facility level was essential to the response and prompted Tennessee to adopt legislation to allow health information exchange to facilitate follow up of patients.

SOURCE: Petersen presentation, June 6, 2017.

including between state and local health care providers, can significantly improve monitoring efforts during a PHE (see Box 2-2).

Pharmaceutical Industry Perspective

Ataher said the pharmaceutical industry is always concerned with the benefit–risk balance of its products. During the usual drug approval process, there is ample time to assess the benefit and risk profile of a product, and post-approval studies, in which large datasets are gathered to study effectiveness, may last up to 5 years. In a PHE setting, however, the time for such assessment is limited. The key to success, Ataher suggested, is to plan for the unexpected by understanding what data will be needed in order to develop predefined clinical protocols that can be deployed for individual products in an emergency setting.

One difficulty in conducting clinical research during PHEs is the inability to conduct randomized clinical trials in defined populations; rather, products are administered to a generalized group of patients with limited background health data at the time of MCM administration, said Ataher. Furthermore, he remarked, from an epidemiological standpoint, confounding variables increase the difficulty in analyzing data from this research.

Ataher suggested that potential solutions to these issues could include having a predefined set of variables on what types of data should be collected, developing predefined study protocols, and identifying target sites and an accompanying "SWAT team for data collection" that could be readily activated to collect data without interfering with the administration of the MCM.

Academic Research Perspective

Wilcox noted that academic researchers have an important role to play during the course of a PHE response, parallel to the role of first responders, by providing observational research and analytical capabilities. For example, Wilcox noted that during the 2009 H1N1 influenza pandemic, a research team at Columbia University quickly assessed incoming data from CDC to assess the origins, diversification, and spread of the virus. Using innovative bioinformatics techniques, the team was able to decipher the genetic origins of the virus and determine that in the recent past, the virus was endemic to pigs—that is, swine flu—and not birds, as originally thought. This information was critical to monitoring the spread of the disease because it prompted public health officials to increase surveillance efforts in pigs and provided valuable information for studying and developing vaccinations for flu viruses of related structure in the future.

Wilcox concurred with Levy about the importance of understanding which populations are represented (or not represented) in a given data sample. Traditionally, research and health care delivery has focused on the population that happened to be coming in for care, he said. Population health initiatives throughout the country are beginning to take into consideration the populations that are not accessing care, however, and this shift has affected the way data systems are designed and increased attention to using the correct methodologies to link the data (see Box 2-3 for a case study on this issue).

FDA Perspective: Data for Regulatory Decision Making

Maher described what information FDA needs to make regulatory decisions related to MCM use. For PHEs, there is a general idea of the types of questions that should be asked, she said, as listed by Patel. However, it is difficult to define questions with more granularity in advance of a PHE. One challenge, also noted by Wilcox, is that data are used to answer the questions, but they also inform the development of the questions. It is a cycle of researchers asking for the data and data holders asking what questions the researchers are trying to answer, said Maher.

BOX 2-3
Understanding Methodologies and Biases in Data Collection: Lessons Learned from a Depression Study

Wilcox cited a study that examined the effectiveness of care regimens on the management of depression. Although the resulting retrospective data were first interpreted to show an increase in depression remission in response to care, researchers actually found that increasing their data collection ability resulted in an increased observance of remission rates—that is, patients who were in remission were more accurately captured in the expanded dataset. Wilcox noted that this is a common phenomenon across the board: increased data collection can result in increased capture of the target population, which should not be misinterpreted as increased treatment effect. Understanding data collection methodologies and associated biases, such as those represented in this depression study, are similarly important for MCM monitoring and assessment efforts, emphasized Wilcox.

SOURCE: Wilcox presentation, June 6, 2017.

One piece that is missing, she said, is the conversation about the many different places data might be, and whether and how that data might be accessed and used in a way that is not disruptive to the ongoing response operations. Maher raised several questions from a regulatory standpoint: How can all data, regardless of its location, be harvested and leveraged to answer not only regulatory questions, but also response-related questions? How can systems already in place be used and leveraged to answer questions? How can disconnected data sources be connected? Maher noted that a key question for monitoring and assessing MCM use is whether the MCM is providing a benefit (i.e., acting as expected) or causing more harm, and she pointed out another important question: How quickly can targeted studies be designed, using the detected safety and efficacy signals, to conduct research during the emergency to answer this question?

Ben Eloff, deputy director of epidemiology in the Center for Devices and Radiological Health at FDA, added that with regard to devices, regulatory decision making would be better informed if there were more detailed identification of the medical product and the exposure to that medical product. Drugs and biologics are relatively easy to identify, Eloff said, and he referred to systems such as the National Drug Code, which clearly identifies all drug products by an exclusive number. Medical devices span the gamut from tongue depressors and stethoscopes to implanted devices and defibrillators. It is more difficult to understand what role a given device might have

in the identification of or response to an emergency. Having more granular information about the specific devices used would be of value, he said. For example, if one manufacturer's meter has an error in their algorithm that is providing erroneous results, and other meters are not, this error can only be detected if the specific device is known.

3

Data Needs, Data Sources, and Collection Methodologies for Stakeholder Decision Making

When monitoring and assessing MCM use during a PHE, different stakeholders have different data and information needs (see Stakeholder Perspectives in Chapter 2). Throughout the workshop, panelists and participants discussed potential sources of data to answer questions important to monitoring and assessing MCM use and opportunities and challenges around their use. This chapter is organized conceptually according to the following four areas:

1. Defining and answering questions to inform data needs for MCM distribution and monitoring;
2. Considerations and approaches to data collection;
3. Existing data sources and datasets; and
4. Disseminating data and information.

DEFINING AND ANSWERING QUESTIONS TO INFORM DATA NEEDS FOR MCM DISTRIBUTION AND MONITORING

Yu called on panelists to describe, from their sector's perspective, key questions that should be asked and the corresponding data needed to inform the monitoring and assessment of MCM use when responding to a PHE. The bidirectionality between crafting the right questions and understanding the applicability of data sources to answer those questions is critical to monitoring and assessment efforts, she said. Key takeaways from individual workshop panelists and participants are described throughout this section.

Operational Questions That Drive Data Needs

From his experience managing cross-state EHR databases with upward of 15 million patients and fielding data requests from researchers, Wilcox noted the importance of understanding what data are needed to answer pre-defined questions. He referred participants to the 2013 PCORI Methodology Report,[1] which stated that problems can arise when research questions are driven by the availability of data, rather than by what needs to be known.

From the federal standpoint, Patel said, broad operational questions apply to MCMs in every PHE response that must be answered before a distribution plan can be developed:

- (Do)es the "right" product(s) exist?
- Is there sufficient confidence in the safety and efficacy profile of the MCM to proceed with its deployment?
- Are there adequate supplies to deploy the MCM (i.e., is the product commercially available, or does it need to be stockpiled)?
- What regulatory considerations apply to distribution and use of the MCM (e.g., EUA, investigational new drug application, mass dispending orders)?

Once these operational questions have been considered, a distribution plan can be crafted to support the use of the MCMs as governed by the appropriate regulatory mechanism. Decisions made regarding access to MCMs are fully contingent on the safety and efficacy profile of the products (see Box 3-1 for a case study of this issue) and include the following considerations, noted Patel and Petersen:

- How should the MCM be made accessible (e.g., access points, level of triage)?
- If an MCM is in limited supply, what are the ethical considerations underlying how distribution should be prioritized to populations with the greatest potential benefit, and how can the decision-making process be made as transparent as possible?
- What is the risk communication and action plan for the public, including consideration of the current acceptance level of the MCM by patients and providers?
- How can administration, adherence, and compliance be tracked? What communications channels will deliver data back to decision

[1] The PCORI Methodology Report is available at http://www.pcori.org/sites/default/files/PCORI-Methodology-Report.pdf (accessed August 23, 2017). This report is currently under revision with an updated version forthcoming.

makers (i.e., patient to provider to local, regional, or state level health agencies), and what is the level of understanding by patients and providers for reporting this information?

Data Needs and Data Elements

As summarized by Wilcox, three key questions to consider when considering data needs for monitoring and assessing MCM use include

1. What data do you need based on questions that have been identified?
2. How can you feed the data to the requisite stakeholders as quickly as possible?
3. What is a good metric for determining if you are using the right data?

Certain baseline data are needed for any PHE, said Patel; however, depending on the specifics of the PHE (e.g., the severity and accompanying benefit–risk profile of an MCM), additional categories of information may be required. Henry "Skip" Francis, director of Data Mining and Informatics Evaluation and Research at the Center for Drug Evaluation and

BOX 3-1
Examining the Impact of Safety and Efficacy Profiles on MCM Distribution: Lessons from Anthrax and H1N1

Patel described two scenarios that highlight how a product's safety and efficacy profile influences the operational aspects of MCM distribution. In a potential anthrax scenario, two FDA-approved drugs are available with mass dispensing orders available for their distribution. This regulatory approach is based on a high level of confidence in the products' safety and efficacy so that MCMs can be mass dispensed as quickly as possible. In contrast, in the 2009 H1N1 influenza pandemic, there were limited safety and efficacy data available for the MCM peramivir, so it was distributed under an EUA. Because the MCM was used under an EUA, the distribution process required individual clinicians to make requests to the federal government for the product on a patient-by-patient basis. Patel emphasized that the goal of this particular program was access, not collection of safety and efficacy data.

SOURCE: Patel presentation, June 6, 2017.

Research at FDA added that different stakeholders need different types of data. For example, at a national level, organizations such as the Biomedical Advanced Research and Development Authority (BARDA) need data on cases, locations, and association of a PHE to the MCMs available in the Strategic National Stockpile (SNS). Hospitals have a more situational and regional focus and need data on cases relevant to their area, he added, and FDA looks at as many information sources as possible. Three main categories of data discussed by workshop panelists and participants for answering key operational questions for MCM monitoring and assessment included medical history data, symptomatology data, and data to inform threat containment.

Ataher noted that in many PHEs, there may be limited safety and efficacy information available for an MCM. The product may be FDA approved, but it is being distributed for an unapproved indication, and/or the product may be dispensed in a less than rigorously monitored setting (e.g., a POD). To fill this data gap for MCMs that may only have investigational-level data, one should consider the short-term data needs for dispensing the MCM and the long-term data needs for properly assessing the safety and effectiveness of the MCM for the indication for which it is being prescribed or distributed, added Ataher.

Medical History

Baseline medical information is needed on the patient at the point of distribution in an emergency situation, said Ataher, including both prior medical conditions and symptomatology (see next section). EHRs may contain this information for the affected population and could be accessed after the event. In most cases, it is unlikely at the present time that EHRs will be readily available in an emergency situation to inform MCM treatment decisions, he added. However, Cobb remarked that stakeholders should continue to look for ways to better incorporate EHRs into PHE preparedness and response efforts.

Symptomatology

Cullen highlighted the need to better capture symptomatology data. Data on diagnoses, treatments, laboratory test results, and vital signs are generally well captured. Symptomatology is more challenging to capture as definitions are not standardized (e.g., one provider's definition of a cough may be different than another's). In the early stages of an event, a patient's clinical course and their symptomatic response to an intervention are important, Cullen said.

Petersen suggested leveraging existing IT resources for syndromic sur-

veillance and monitoring that are already available at local health care facilities to help inform decision making, and Levy suggested that 911 call dispatch records could be tapped for symptomatology data (see Existing Data Sources and Datasets later in this chapter). Levy added that data from 911 calls are used by local public health departments when dealing with a variety of incidents, including monitoring for carbon monoxide poisoning, power outages, or potential Ebola patients.

Threat Containment

In the face of no available MCMs, Lee highlighted the diverse types of data that could inform the containment of a pandemic or emergent threat. Data of interest could include epidemiology data from the affected area, human travel patterns, social behavior patterns, clinical data, and information about vectors and the disease cycle, as well as information about the environmental conditions that support the disease cycle. These data provide a picture of the population and how they interact, allowing operational aspects to be overlaid to determine how to achieve containment. Containment was critical at the start of the Zika outbreak, for example, when no MCMs were available, she said.

CONSIDERATIONS AND APPROACHES TO DATA COLLECTION

Just because data can be collected does not mean they should be collected, said workshop participant Sheldon Jacobson at the University of Illinois. Furthermore, he added, data are not evidence; they are potential for evidence. All data are not created equally, Wilcox said, and data can be generally divided into two categories based on their collection and analysis:

- Data that are collected for a specific purpose following a predefined methodology (prospective data collection and analysis), and
- Data that happen to be available because there are systems that collect them, most likely for a purpose other than surveillance (retrospective data collection and analysis).

It is important to recognize the difference between these two types of data, develop ways to segment data based on this criterion, and determine which data can be used in what ways, said Wilcox. Exemplifying these points, Lance shared an example of an all-hazards approach to data collection in New York State from which lessons could be learned about systems for collecting and disseminating data (see Box 3-2). Throughout the workshop, individual workshop panelists and participants highlighted important considerations when collecting data to answer specific questions

BOX 3-2
A Routine, All-Hazards Approach to Data Collection During a PHE in New York State

New York State's Countermeasure Data Management System was originally designed to collect MCM dispensing data, said Lou Anne Lance, public health program nurse in clinical operations at the New York State Public Health Department, including medical screening information and demographic information. The system takes an all-hazards approach to data collection during PHEs and includes clinical algorithms and protocols to streamline decision making. Routine use of the system develops proficiency among the users, said Lance, and helps identify gaps to be addressed before a PHE occurs. Another feature is the capability to seamlessly transition vaccine-related response data to the state's immunization registry (i.e., separate data entry is not needed). This capability was useful during a major hepatitis A outbreak in a small town in New York, where nurses could access the immunization information to determine whether those presenting for vaccination were already adequately immunized or only needed a second dose of the hepatitis A vaccine.

SOURCE: Lance presentation, June 6, 2017.

(see Operational Questions That Drive Data Needs on p. 32), as well as approaches for collecting that data.

Understanding the End User of Data

When determining what data infrastructure is needed for monitoring MCM use, Jeff Brown, associate professor at Harvard Pilgrim Healthcare Institute, suggested considering three questions: Who is the user or the audience? What questions do they need to answer, and with what level of precision? How quickly do they need the information? Answering these three questions will determine the type of information to obtain, he said. If the users need the rigor of a clinical trial, they must understand it will take months to years to obtain the data. If that level of rigor is not needed, and the users can work with data that show signals and trends, there may be data already being collected (i.e., immediately available) that could be relevant. It is a matter of matching the question to the data and to the method and the timing.

Determining the Physical Location for Point-of-Care Data Collection

Rather than focusing efforts on data collection at "outpatient" MCM dispensing centers (e.g., PODs), where there is a lack of infrastructure and resources to collect these data, Petersen suggested that efforts be focused on data collection by health care providers, such as those in physicians' offices or hospitals. Tools are already available for tracking upticks in admission and adverse events at these locations, he added, and they could be leveraged for monitoring and assessing MCM use. Lee proposed an intermediate solution of registering individuals who are treated at a POD and having that registration linked to their EHR and the corresponding immunization registry, as appropriate.

Aligning Data Collection with Timing and Sequence of PHEs

Data are often collected late in the chain of events because they are easy to collect at that point, but they are often more valuable early in the course of a PHE, said Jacobson. Yu observed that some key data elements are needed in support of clinical endpoints (e.g., for registration-enabling studies or post-marketing requirements or commitments) that can only be collected during the course of a PHE, that is, at the time of disease onset or exposure.

Multiple sources of data could be used in parallel during a PHE, said Yu. Collection from one data source could result in a sequence of events leading to different types of data collection, she noted, including observational studies, patient registries, electronic health data, big data, and clinical studies. In terms of how these different data streams are used, timing of data collection becomes an important issue, said Cullen. Can a system be designed so that the data points, the manner in which they are collected, and the way in which they are aggregated are responsive to the timing needs of each?

Lee emphasized the need for a feedback system to facilitate continuous improvement and real-time decision making and that data modelers must learn to manage evolving data and real-time information. Francis added that databases must adapt over time as an event evolves (see Box 3-3). Having a feedback system in the data collection and analysis process is valuable, Lee added. Analyzing data early during the course of a PHE can help to prioritize data needs and detect key data elements, allowing for allocation of resources to collect those elements. A feedback system could also facilitate adaptation of data models as new information is incorporated.

BOX 3-3
Modifying a CDC Database to Meet Evolving Data Needs in the 2009 H1N1 Influenza Pandemic

During the 2009 H1N1 influenza pandemic, early response decisions were informed by capturing data from existing CDC and state epidemiologic databases to develop an understanding of the anatomy of the early epidemic and population data and choose appropriate interventions. As the pandemic evolved, resistant virus strains emerged, so it was necessary to modify databases to identify other options for interventions, including unapproved MCMs, and estimate their anticipated safety and efficacy profile. When peramivir was selected for use under an EUA late in the pandemic, a cloud-based database system was created to acquire safety information that could be assessed in real time.

SOURCE: Francis presentation, June 6, 2017.

INTEGRATING DATA FROM DIFFERENT SOURCES

Patel emphasized the need for better integration of all levels of data from PHE responses into the evolving response structure. These data could be better integrated into distribution, dispensing, and upstream activities from MCM development to regulatory decisions. For example, the National Collaborative for Biopreparedness, funded by the U.S. Department of Homeland Security, has developed a system that collects and analyzes EMS data, 911 call center data, emergency department data, and other relevant information. This system aids both in syndromic surveillance and also establishes baselines, and it has fairly sophisticated analytic tools that can detect deviations.[2]

Identifying Missing or Unknown Data

Scott Proestel, director of the Division of Epidemiology, Office of Biostatistics and Epidemiology at the Center for Biologics Evaluations and Research at FDA, remarked that a key challenge in data collection efforts is capturing data that are missing or unknown. Lee added that, in some cases, data that are not collected can also provide helpful information. For example, patients not returning for follow-up care could indicate they are doing well after the intervention. It is important to use both known and unknown data to predict what is happening in the population, Lee said.

[2] See https://www.bioprep.us (accessed August 23, 2017).

Understanding the importance of and finding missing data are also important, said workshop participant Harlan Dolgin of the Bio-Defense Network. For example, if an MCM for anthrax were distributed at PODs, he said, important data points would be how many affected persons did not come to the PODs, the adherence rate of those who did receive treatment at a POD, and how many people experienced adverse effects of the MCM but did not report them to a doctor. Avenues such as social media and polling could be helpful to collect these data after MCM distribution, he said.

Using Machine Learning and Artificial Intelligence

Francis suggested that machine learning strategies or artificial intelligence could identify data sources for MCM monitoring and assessment that would not normally be considered. Joe Vasey, an epidemiologist and biostatistician with Practice Fusion, observed that some artificial intelligence and deep learning technologies are already being used in other fields, such as finance or defense, which also work with large amounts of "noisy" data. The question raised is whether and how such technologies could be applied to health data. Lee said that most models are designed for a specific type of data, instead of using all available data in a systematic and integrative way. The technology from artificial intelligence is not developed enough for health care data, Lee said, which are noisier than other sectors' data.

Modeling and Interpreting the Data

Levy said having better methods for modeling data before a disaster occurs would be helpful, as response plans are often based on these data-modeling assumptions. She suggested local partnerships with academic research centers to test and validate assumptions prior to a PHE and noted the need to have all relevant stakeholders at the table when data modeling is developed. Rhona Cooper, public health preparedness clinical coordinator with the Philadelphia Department of Public Health, shared an example of an algorithm for a dual-model anthrax response composed of a flow chart with basic questions to be answered by entering data into fields in a database. This algorithm drives the production of a database that is usable at every level, she said.

When developing systems to monitor or detect safety signals, it is important to understand the expected error rate, said Wilcox. When tracking the safety or efficacy of a medical product, he emphasized, it is critical to predict what the expected rates should be. Until you observe a signal above the expected error rate, he added, "Your problem isn't that you don't have a problem, your problem is that you can't see it," and the monitoring system is ineffectual.

EXISTING DATA SOURCES AND DATASETS

Stakeholders should have a robust understanding of existing data sources, what the capability and interoperability of data systems are, who has access to these data systems, and how existing technology can be used in different ways, said Patel. Ataher added that predesigning programs for rapid queries of multiple datasets in parallel could pool requisite information quickly. Because current data collection systems were not designed for monitoring medical products during a crisis situation, however, rapidly deployable health IT architectural designs should be developed and retrofit into existing systems, as appropriate, to detect and report unexpected signals, said Cullen (see Box 3-4 for a case study in this issue). Workshop panelists and participants discussed some of the many types of data and existing datasets that could be leveraged for monitoring and assessing the outcomes of MCM use, including patient narratives, EHRs, pharmacy databases, federal surveillance systems, big data, and social media.

Point-of-Care Patient Narrative

From a local health department point of view, Cooper noted that the most raw source of data is the patient interview. Stakeholders should consider the following questions when soliciting data from a patient: Who is the patient? What do they need? What are their individual issues? She noted that Medical Reserve Corps volunteers are trained to conduct patient interviews and enter the resulting data into an electronic database, and

BOX 3-4
Using Existing Data Collection Systems for Tracking MCM Distribution at the U.S. Department of Defense

John Grabenstein, executive director in Medical Affairs at Merck Vaccines, described a scenario in which the U.S. Department of Defense built into its immunization monitoring system—which is used for tracking widespread smallpox and anthrax vaccinations—an ability to monitor MCM distribution. Additional nonvaccine information was included in the system as a contingency in the event of an emergency situation in which a nonvaccine MCM (e.g., ciprofloxacin) would need to be distributed to National Guard bases across the country. This adaptation provided the ability to record medication administration and drug exposure in existing information systems.

SOURCE: Grabenstein presentation, June 6, 2017.

patients' driver's licenses are scanned to automatically enter demographic information.

Electronic Health Records

Limitations

Data in EHRs are collected purposefully and are usually the most consistent and least biased data sources, said Wilcox. However, EHR data are time intensive to collect, so they may not be as expansive as other data sources, and they are not amenable to large pattern-recognition algorithms because they are retrospectively analyzed, he added. Although there is a place for EHR data in conducting research on MCMs in PHEs, it is not in determining safety and efficacy, Higgs said. EHR systems were built to assist the physician and not the researcher, said Vasey, and data are generally not collected in the same way they would be collected for research purposes. In general, Francis added, EHR systems work well for claims data, but it is not always clear if the right medical information is being collected. Lee also noted that EHR systems include many unstructured tags, meaning there could potentially be hundreds of different ways for providers to characterize the same thing. It takes significant text-mining to merge all of these data, Lee observed. Furthermore, some EHR formats force providers to enter data at a level of specificity that may run counter to the care delivery goals in a PHE, noted Francis, because of time constraints at the point of care and in following up on data entries.

Groom of the Indian Health Service reiterated that EHR systems were designed for billing, not public health, although they have been evolving in response to Centers for Medicare & Medicaid Services (CMS) meaningful use requirements. She suggested the need for policies that would enable EHR vendors to respond in an emergency situation, assist with the development of solutions that could be broadly shared, and eliminate the need for third-party workarounds to extract data from the systems. Lushniak said that, in his experience, EHR vendors are very interested in helping public health move forward, but there are technical barriers that make it very hard to be nimble. The deployment of new software, for example, is subject to regulatory and certification processes. There is also tremendous variability in how institutions implement EHR systems, making it unlikely that any single solution could be deployed effectively across diverse systems.

Strengths

Despite these limitations, Cobb noted that EHRs will continue to evolve to better serve the needs of preparedness and response efforts. One

workshop participant noted that EHR data can help to establish baselines (e.g., baseline morbidity and mortality rates in the affected population). Baseline data are critical to interpreting the clinical implications of an emerging infectious disease outbreak, and they could inform adaptive clinical trial designs and allow for some level of generalizability of trial findings beyond the trial setting. Maher added that EHR data could detect important signals to help define the focus of response preparations, such as what protocols to develop and where to preposition them to enhance response in an event. Higgs noted EHR data might be helpful in supporting observational studies in the real-world setting in order to identify additional indications or patient populations.

Cloud-Based EHR Systems

Cloud-based EHR systems represent an opportunity for more rapid transfer of information collected during PHEs. Cloud-based EHR systems are more adaptable and flexible than systems based on servers, noted Vasey, and the continuous data feed that results from entries by system users allows for MCM monitoring. Modules can be added to the system to monitor for certain signals in real time and to provide relevant educational materials for users. During the Zika epidemic, for example, Practice Fusion's cloud-based EHR system allowed for a module of educational materials to be added for providers, said Vasey. Providers were also asked questions about their experiences and actions related to Zika. For future influenza outbreaks, cloud-based EHR systems can provide day-by-day monitoring of where illness is being reported, who is becoming ill, how many people are ill, what interventions are given, and so forth. He added that routine adverse event monitoring for medications allows physicians to record the adverse event occurrence in the EHR in real time, as they are talking to a patient. Another analogous system from which to derive lessons learned could be the Web-based countermeasure and response administration system being developed by CDC,[3] which is customizable to a specific disaster scenario.

Government Surveillance and Tracking Systems

Brown highlighted Sentinel, FDA's network of safety surveillance for the medical products it regulates, as a system that is currently leveraged by FDA in emergency situations. Systems such as this can be designed to be responsive in an emergency scenario when a PHE is declared and information is needed quickly. Platt noted that although the FDA Sentinel system is

[3] See https://www.cdc.gov/cts/cra (accessed August 23, 2017).

a public health initiative, it is interpreted as research by many stakeholders. He recalled that one-on-one meetings and calls were held with the IRBs of the 20 systems that participate in Sentinel to explain that IRBs do not have jurisdiction over Sentinel's data collection. Letters were obtained from the HHS Office for Human Research Protections confirming that Sentinel was not research covered by the Common Rule and from FDA stating that Sentinel was public health practice.

Cooper noted the lack of interoperability between concurrently utilized systems, such as the Pennsylvania Statewide Immunization Information System and the Knowledge Center (a software platform for real-time incident management). She mentioned that barcoded wristbands are used in mass casualty responses in Philadelphia through the Knowledge Center capabilities, allowing hospitals and EMS to communicate patient information. However, health officials have not yet been able to feed these data back into local PHE responses.

When the Philadelphia Department of Public Health activates a POD or conducts a POD exercise, Cooper said, it is required to create a new database using the Microsoft Access system. This is time consuming, she said, and during a PHE there is neither the time nor expertise to create more than a primitive database using questions and algorithms from federal sources. Furthermore, these databases currently lack long-term follow-up components (e.g., next vaccination appointment). She suggested the development of ready-made databases for already stockpiled, available, or approved MCMs that any local jurisdiction could use depending on the scenario.

Big Data[4]

Wilcox suggested that a potentially useful aspect of big data, in addition to mining data to answer specific questions, is the potential to identify changes in data flows and detect when data are changing in an unexpected way. Patel highlighted the need for innovative ways to look at the vast volumes of existing, unstructured big data and consider the interoperability between these data and other data systems. She referred workshop participants to a recent study of Yelp reviews of foodservice businesses that included reports of food-borne illness (Nsoesie et al., 2014), and asked whether and how such an approach could be applied to MCM monitoring and assessment: What information could be gleaned from big data, and is this type of data robust enough to inform monitoring and assessment efforts?

[4] See Big Data, Chapter 2, for background on how this terminology was defined at the workshop.

Emergency Medical Services

Workshop participant Rob Lawrence of the National Association of Emergency Medical Technicians highlighted the potential role of EMS in MCM monitoring and data collection. For example, EMS works at the epicenter of the opioid crisis, he said, and has the ability to conduct biosurveillance and syndromic surveillance to identify the point of consumption of opioids. A significant amount of data could aid opioid taskforces that are under way, he said. EMS also works closely with local public health departments. From a syndromic surveillance perspective, he said, EMS is often the first to see the signs of what is to come.

Pharmacy Databases

An example of an existing system that could be better leveraged is the pharmacy data system, Brown said. Pharmacy data systems are incredibly good in the United States, he said, and operate essentially in real time. Many people now get flu vaccinations at their pharmacy, and the data system could provide an almost "live" view of the status of flu vaccination across the country. He suggested that pharmacies could potentially be leveraged for mass vaccinations or mass dispensing, as an appropriate system for collecting dispensing data is already in place.

Social Media

There is untapped potential in patient-collected data, whether it is collected by a mobile health application (see next section) or from social media, said Vasey. For example, social media data can be useful for reconstructing an epidemic, added Francis. Bakken shared a recent article on content and structural mining of tweets during the Ebola outbreak (Odlum and Yoon, 2015). The authors were able to collect data about public knowledge, sentiment, and the spread of information during the outbreak. Bakken emphasized that from the perspective of health equity, it is important to understand the demographics of a social media outlet when mining data or when considering using social media as an intervention strategy. For example, data suggest that Latinos and African Americans use Twitter more heavily than whites, Bakken noted. Bakken noted that Twitter provides a daily public sample that can be downloaded and used retrospectively. She pointed out that Twitter data are not necessarily unstructured. For example, the use of hashtags in tweets would be considered structured. She reiterated the importance of understanding the user demographics of any technology to be aware of how the sample might be skewed.

Lee noted that younger generations seem eager to share their experi-

ences and voice their opinions, and they can often be engaged to complete online surveys or post comments as a follow-up to medical interventions. A challenge is how to merge such data with more objectively collected data, she said, given that they are highly unstandardized and difficult to fit into a structured framework that make them amenable to analytic tools. Vasey suggested working with hardware manufacturers and software developers to make those data sources more capable of being integrated with other data sources (e.g., EHR or imaging data). Greg Burel, director of the CDC Division of SNS, suggested that social media could be mined to gather data on how receptive people are to taking the MCMs that were dispensed to them. For example, opinion polling suggests that the public will accept MCMs that are provided to them, but they will wait to see if they get sick before taking them. He pointed out that the issue of monitoring MCM use is not just what happens after people take MCMs, but also whether they take it at all, a question that could potentially be answered by social media.

Mobile Health Applications

The more nimble, user-friendly capabilities of mobile health applications on portable devices (smartphones in particular) provide opportunities to engage the public and collect data from individuals, said Cobb. Lee added that countries in Africa rely heavily on smartphone capabilities for health care events (e.g., screening, sharing test results, and follow-up activities). She suggested that the United States could similarly use this technology, though there are potential hurdles in terms of patient confidentiality concerns. Some U.S. patients are already connected to their providers through remote patient-monitoring devices for chronic diseases (e.g., blood glucose meters that automatically send a patient's readings to their provider). Although user-based capabilities will not be evenly distributed across sociodemographic lines, Lee said, it is important to move forward and start to build the networks of knowledge and capability.

DISSEMINATING DATA AND INFORMATION

Delivering Data to the Correct End-User

How can the right data get to the people who could use them the best? What data are on-the-ground responders receiving? How are they using the data, and do the data look correct to them? The closer the data are to the point of care, the better, Wilcox said. It is critical that the people who are most familiar with what the data represent have the tools to navigate them, Wilcox added, and in many cases, stakeholders do not have the capability to query relevant datasets to meet their needs. Ataher added that

just having data is not enough: data need to be in the hands of the right person, someone who is capable of understanding, analyzing, and using the data. Wilcox also pointed out that sharing data across organizations is good, but linking volumes of standardized data does not necessarily mean there are more comprehensive data on any individual.

Direct Access to Information Sources

Levy pointed out that in a PHE, such as the recent Zika and Ebola outbreaks, information about the threat, MCMs, and the impact on the population comes through surveillance systems, to CDC, then to Public Health Emergency Preparedness awardees, and then to the local-level partners. At each level, nuances are lost, she said, and local health departments do not have the ability to directly question those who performed the research and the data collection. This inability handicaps local decision making, and she advocated for the local level to have more direct access to the source of information.

Guidance Updates

Petersen highlighted the challenges of dealing with guidance changes and updates during a PHE, which affects the implementation of plans and operations at the state and local levels. He called for better processes for disseminating guidance updates and informing the affected population, including clinicians who have to implement the guidance. For example, over the course of the Ebola outbreak, the guidance for use of personal protective equipment changed, and there was confusion about how organizations should be protecting health care workers.

Maher asked workshop participants how FDA and other agencies could better communicate changes in guidance and communicate information and questions upstream from local health systems to federal agencies. A variety of tools are available to gather information from local providers and health care facilities, Petersen said. For example, the Tennessee Joint Information Center works with health and association partners to push information out to stakeholders, and information is gathered through the Emergency Operations Center. Information gathered through these mechanisms is shared through webinars, conference calls, and other approaches.

UNIQUE CHALLENGES AND OPPORTUNITIES FOR DATA COLLECTION

Collection of health data is different from the collection of data in other sectors. Runnels summarized some of the challenges around MCM

data collection that were raised throughout the workshop discussions, including lack of standardization of health data; the difficulties of connecting databases and integrating data (and a variety of challenges specific to EHR systems); the dispersal of the data across many different sources during an event; the reliability and validity of the data; shortcomings of crowdsourcing and data mining; use and availability of analytical tools; and managing structured versus unstructured data. Some of these barriers and potential solutions for addressing them are detailed throughout this section.

Time and Resource Limitations

Other challenges to data collection during PHEs, said Amanda Peppercorn, senior medical director in Infectious Disease Research and Development at GlaxoSmithKline (GSK), are that health systems are stressed and physicians in a critical care situation do not have the capacity to enter large amounts of data in real time. As a potential solution, she said, GSK is now working with a clinical research organization to keep a particular MCM protocol up and running for the immediate future in order to test the protocol during an appropriate PHE.

Local health departments do not have the funding for sophisticated data collection, nor do they have the personnel to provide the epidemiological oversight needed to answer the questions asked by researchers, said Cooper. She emphasized that most local health systems do not have the capacity to collect the data requested of them for those who wish to analyze the data, and described data collection in MCM dispensing operations as early days. She cautioned that unless local health departments receive better guidance and assistance, they will continue to use unstandardized, self-created data collection formats. Staff can be trained to use basic electronic data systems, but local health departments generally have limited ability to collect data and could use support in this area. Researchers should be clear regarding what they want to know, Cooper added, and local jurisdictions can encompass those fields within their databases for their response operations. Ideally, she said, researchers would provide local-level health departments with all-hazards or MCM-specific databases.

Workshop participant Nick Boukas of the National Association of County and City Health Officials added that medium, small, and rural health agencies do not have the funding to make use of cloud-based IT systems to collect MCM data. In addition, they often do not have a full-time staff person dedicated to preparedness activities. Many county and city health officials serve dual roles; for example, the environmental health director might also serve as the preparedness coordinator and cover other assigned duties. Many of these communities do not have academic institutions they can partner with for analysis of the data they collect. Boukas

said his organization has been promoting a regional approach so that more rural communities have access to an academic institution that is not in their community, or even in their region. Boukas reminded participants that, although workshop discussions have been about what data needs to be collected, large segments of the country are largely unable to collect data the requisite data at this point. This gap needs to be addressed so that smaller health jurisdictions can collect and report their data and understand what the data mean for them on the local level.

Standardization

The health care system in the United States is complex and heterogeneous, said Lee. There is no one unified system with common standards for collecting and sharing data. Even local health departments within a state, or individual hospitals under the same network, face challenges sharing information, she added. There are many operational limitations to be overcome, and the barriers are both vertical and horizontal, but progress must be made and should not be stunted by the search for the perfect solution.

A workshop participant said that different researchers, with the same or similar technology, might take different approaches to address the same questions and may define the necessary data elements differently. Similarly, community physicians (during an emergency response or for routine health care) have multiple ways to answer the same set of questions. The focus needs to be on first defining the questions and then collecting data to answer them.

There is also a range of idiosyncrasies across the various health data streams, Vasey said, and the way each individual or system collects data is different. When designing and developing data collection systems, it is important to keep in mind the multiple potential uses for those systems, he added.

Capturing Symptomatology

Health data differs from other sectors' data because they stem from the human condition; Francis observed that, in 30 years of clinical practice, he has never seen pneumonia present in exactly the same way. General surveillance of EHR data for a particular event can be very difficult because of that variety in symptomatology. The diversity of the treatment effect within patient populations also causes lot of confusion and fuzziness in the data, Francis said. Nonetheless, noted Vasey and Cooper, focusing on a particular MCM could make it somewhat easier to define a set of data that might be useful for monitoring and assessment.

Policy and Regulation (Dis)Incentives

Workshop participant Jessica Keralis of the Cadence Group suggested that lack of political will is a barrier to data collection. Political buy-in is needed to support the development of data systems that can function toward public health preparedness. Money follows politics, she said, and the form of the data collection systems follows the money. For example, EHRs were designed for billing, and many nurses and doctors resisted EHRs until financial incentives for implementation became available through the Patient Protection and Affordable Care Act (ACA). Software developers are now building EHR systems according to the requirements of the ACA, and it appears there is still no public health functionality forthcoming. Data scientists need to sell the importance of public health preparedness to the politicians who make the policies that influence the design of these products, she added.

Data Science Training

The most undeveloped resource is not necessarily a particular database or data source, Francis said, but our own expertise in working with the available data and the available IT tools. Joelle Simpson noted that Children's National Health System has volumes of data, but it has been struggling to help staff develop the skills to use the data and produce the information being requested. Charles Cairns of the University of Arizona College of Medicine agreed that having educational and training programs are a necessary component of using data systems most effectively.

The field of data science requires a broad range of skill sets, including computer science, mathematics and statistics, machine learning, and traditional research methodologies, as well as specific subject-matter expertise, said Bakken. No single individual has all the skills and expertise needed to be able to address a given problem, she added. There are both statistical and computational challenges to working with big data, and there is a need for information visualization (applying visualization techniques to help detect signals and help experts understand the data).

Bakken also noted that many data science programs are being developed at both the undergraduate and graduate levels. She added that it has become a popular field, and admission to master's programs is highly competitive. There are also mechanisms in place to augment existing doctoral and post-doctoral training grants with data science supplements, and there are excellent online training programs for those already in the field who need to advance their skills. Bakken also noted that informatics competencies exist for public health professionals. To advance data science for MCM monitoring and assessment, it would be helpful to identify the existing

knowledge and skills gaps, she said, and what might be done at both undergraduate and graduate levels to offer better training and develop a pipeline of individuals with data science and informatics competencies, along with their domain knowledge. Lee reminded participants of NIH training grant opportunities in this area.

4

Considerations for Conducting Rapid Clinical Research on MCMs During a PHE

A PHE might be the only opportunity to collect clinical safety and efficacy data in humans; therefore, it is important to consider what questions should be answered (see Chapter 3) and leverage existing systems and infrastructure as much as possible to collect informative and actionable data on MCM use, said Runnels. Higgs added that three critical goals of conducting clinical research during a PHE are mitigating mortality, ending the outbreak, and developing rigorous, regulatory-level data for future outbreaks. Meeting these goals requires increased efficiency, expediency, and adaptability compared to routine clinical drug development. For studies conducted rapidly during a PHE, it is more difficult to answer questions about how the product fits into the larger paradigm of care, what combination of therapies might be effective, how the product is best administered and dosed, or which subpopulations may benefit the most, said Peppercorn. Participants throughout the workshop considered these issues, including how operations for threat response could be adapted and how the current clinical trial infrastructure could be leveraged to facilitate rapid monitoring and assessment of MCM use in a PHE. This chapter is organized conceptually into the following three areas:

- Potential elements of clinical research on MCM use;
- Data and information sharing; and
- Governance.

POTENTIAL ELEMENTS OF CLINICAL RESEARCH ON MCM USE

Although an MCM may be developed and potentially approved for an intended indication (or indications), the specific situation in which it will be used remains unknown until the time of a PHE. This uncertainty makes it difficult to prospectively craft protocol designs and determine elements of clinical research that will be adaptable to a broad range of situations, said Proestel. Individual workshop panelists and participants discussed potential elements of predefined protocols and other considerations for clinical research on MCMs, such as comparator arms, prescreening for contraindications, and leveraging existing clinical networks.

Predefined, Prepositioned Protocols

Proestel noted the importance of having protocols and site agreements prepared in advance of a PHE; however, some aspects of trial design cannot be expedited, said Higgs, including that IRB review and considerations on sharing data can cause delays. Proestel also said that working with a research site that does not have prior experience in PHEs has challenges, compared to working with a site that can rapidly receive and implement a protocol with minimal training. When possible, working with sites that are already up and running is most effective, Higgs added, though lessons can be learned from successful use cases in rapidly standing up clinical research sites in PHEs (see Box 4-1).

Elements to consider when prospectively designing trial protocols for use in monitoring and assessing MCM use during PHEs could include the following:

- Applying Bayesian statistical approaches to data analysis (Higgs);
- Closely involving an independent data and safety monitoring board that regularly reviews data for safety signals (Higgs);
- Availability of the MCM (Higgs); and
- Considering the impact of disaster scale on the appropriateness of the protocol design; for example, a large simple trial versus case reports (Grabenstein).

Higgs referenced an independent panel review of the Ebola response[1] that identified lessons learned from the recent outbreak and six areas for improvement, including MCM development. Accordingly, one interagency deliverable currently being addressed is the development of disease- and

[1] See https://www.phe.gov/Preparedness/responders/ebola/Documents/EbolaIP.pdf (accessed August 23, 2017).

BOX 4-1
Rapid Development of Clinical Research Protocols During the 2009 H1N1 Pandemic: Federal Perspective

During the 2009 H1N1 influenza pandemic, Higgs noted that NIAID coordinated an effective, cohesive, and rapid response to the crisis in mobilizing clinical research sites. An interagency NIAID working group identified MCM candidates that needed further study, and NIAID worked closely with FDA, CDC, BARDA, and industry to develop an EUA-enabling clinical protocol. Competitive indefinite delivery, indefinite quantity contracts were used to set up clinical research sites. However, even with EUA-enabling protocols in place, there were difficulties initiating the studies because of data access issues between the contracted clinical research sites and the companies whose products were being assessed. Eventually two lead candidate MCMs, one of which became an FDA-approved product, were entered into the same research study in comparison to a placebo (instead of each other).

SOURCE: Higgs presentation, June 6, 2017.

pathogen-agnostic interagency protocols for use during future outbreaks or pandemics. Although many stakeholders agree that having a protocol in advance of a PHE is valuable (see Box 4-2), there is some debate about the usefulness of this exercise, she said, given that the end products will need to be further adapted to each specific scenario. Higgs also emphasized that this exercise is for international, not domestic scenarios, but it provides important lessons on the need for leadership and responsibility during PHEs.

Comparator Arms

When designing clinical protocols for products approved under the Animal Rule, it can be difficult to define a comparator for establishing efficacy, said Proestel. Even when there are well-collected, standardized data on the use of an MCM in an emergency, it is difficult to determine the effectiveness of an MCM without a comparator. However, a placebo arm may not be a viable option in a PHE. Two options for control arms, both notably imperfect, could be individuals who declined administration of the MCM or trial arms based on data collected on patients who were administered the MCM from time of exposure to the hazard to first MCM dosage, said Proestel.

Based on her work within different biopreparedness programs at GSK, Peppercorn noted that having an appropriate control group for MCM

BOX 4-2
Highlighting the Importance of Predefined Protocols in the 2009 H1N1 Pandemic: Industry Perspective

Peppercorn shared an example of the challenges of not having predefined protocols. At the start of the 2009 H1N1 influenza pandemic, FDA and other public health agencies approached GSK to restart its intravenous neuraminidase inhibitor program, which was inactive at the time. This request required GSK to rapidly design a study, identify trial sites, establish contracts, secure approvals of IRBs and ethics committees, and start the emergency investigational new drug application process for a global compassionate use program. Even in the face of an emerging pandemic, she said, there was no special attention paid by IRBs to the research program. In fact, there was perhaps heightened scrutiny of the protocols, she said, because vulnerable populations were included (pregnant women, critically ill patients, children).

SOURCE: Peppercorn presentation, June 6, 2017.

clinical studies is essential to interpreting the data. For example, the MCM antibody to the anthrax toxin was approved under the Animal Rule and has not yet been administered to patients infected with anthrax. Assessment of safety and effectiveness in a field study are among the post-approval commitments for this product, she said. If and when the antibody is deployed from SNS, whether for a confined local or mass exposure event, GSK is prepared to collect safety and efficacy data. As previously noted, however, she stated that such a study is difficult to design when the location and the scale of the event are unknown.

Prescreening for Contraindications

In considering how to safely deliver MCMs to affected populations, it is important to know what medical screening is necessary to safely deliver an MCM to the public, said Lance. Previously performed pre-clinical or clinical research should provide as much information as possible on potential contraindications. These and other potential risks should be built into an algorithm to support safe administration of an MCM. For example, during the 2003 smallpox vaccination campaign, CDC reported that data gathered through its Vaccine Adverse Event Reporting System indicated increased risk for adverse cardiac events in response to vaccination. At the time, CDC noted a need for increased surveillance to confirm a relationship between the vaccination and adverse event.

Leveraging Existing Clinical Networks

Cobb recalled a point made by Lushniak about the need for connectivity throughout MCM monitoring and assessment, creating a feedback loop from the local to state to national levels (see Chapter 2). From a research operations standpoint, Proestel emphasized the importance of using existing clinical trial networks to achieve this connectivity. Setting up a new study site takes a long time, he said, especially with regard to training new site staff. In an emergency, predesigned protocols that could be sent to predetermined, experienced clinical sites, would be the most efficient approach, he said (see earlier section in this chapter on Predefined, Prepositioned Protocols and the Leveraging Existing Resources to Supply Data Needs section in Chapter 5).

Maher said FDA and others have been working to understand how clinical trial networks could be used most effectively in a PHE. One potential challenge would occur if the affected population is not located near a site where the clinical trial network has prepositioned protocols. What will it take to shift the protocol to a new site? A workshop participant suggested that the clinical research capacities of NIH grantees should be catalogued to be leveraged in the event of a PHE.

DATA AND INFORMATION SHARING

Lushniak emphasized the need to accelerate data sharing. He asked whether CMS and the Office of the National Coordinator for Health Information Technology (ONC) could accelerate sharing capabilities by the EHR vendors, particularly as CMS is paying for these systems.

Higgs suggested creating a historical database of the best IT development practices that have allowed EHR systems to share information that is traditionally in the domain of public health data or monitoring data. What is the best architecture to make a data system that is extensible, so that it is independent of the original domain?

Leremy Colf of HHS pointed out that the Paperwork Reduction Act prevents federal agencies from giving local jurisdictions a list of questions and information to be collected in a disaster. Any forms, questions, or surveys must be approved by the Office of Management and Budget before they can be disseminated to prevent them from being overly burdensome on the public. The approval process generally takes about 8 months, he said, which is not suitable in a disaster scenario. HHS has been working to decrease the regulatory time it takes to get local jurisdictions the information they want, and the 21st Century Cures Act, passed in December 2016, allows for waivers of the Paperwork Reduction Act in a PHE.

Communication and Outreach to Affected Populations

Higgs emphasized that the rules of clinical science do not change in an emergency. Safety and efficacy must be determined using data that are collected in a systematic way through rigorously designed studies, and there is an ethical obligation to communicate to affected populations the inherent risk of the proposed research.

Amanda Fuller Moore of Public Health Preparedness and Response, Division of Public Health, North Carolina Department of Health and Human Services, said every resident of a state is a stakeholder. After North Carolina authorities recognized that segments of the population were being missed during public health messaging campaigns, the state began looking at how to best get information to individuals. For example, newspapers had fallen out of favor as a public health communication medium until it was learned that a large segment of the population of North Carolina receive their news from print newspapers. The state has also taken on a project to engage individual community leaders and community groups as potential partners in sharing information with their neighbors.

It is important to understand needs and communicate across stakeholders at all levels (federal to local) to ensure not only that everyone is receiving a message, but receiving the correct message for their situation, said Moore. She added that information shared with other states is not necessarily the same information needed by local jurisdictions where the event is happening.

Cooper stressed the importance of returning the results of any data analysis back to the community. Communities will engage, but it is reasonable for them to expect to get something back from that investment of their time and resources.

Barriers to Information Sharing

Data Security

Deven McGraw, deputy director, Health Information Privacy, Office for Civil Rights (OCR), HHS, raised the issue of data security. Data collection creates targets for cyberattacks, and it will be important to ensure that data are stored and accessed under reasonable security measures, she said. Data breaches reduce public trust in sharing their data and affects future data collection efforts. It is not possible to have zero risk, she said, but there are approaches that can reduce the risk of a data breach considerably. Cobb suggested there will need to be a culture shift in how health information is handled that addresses patient protection and privacy. He noted that other nations have addressed this issue through a unique patient identifier.

Balancing Patient Privacy and Public Health Efforts

Scott Needle, member of the American Academy of Pediatrics and a primary care pediatrician, remarked that there is sometimes a tension between maintaining patient privacy and furthering public health efforts that results in decreased sharing of information. For example, the Florida state surgeon general released a statement during the Zika epidemic saying that there were seven babies born in the state who had been neurologically affected by the Zika virus, he said. However, the state was steadfast against releasing further details, such as disclosing the region in which the cases were identified and whether the cases were contracted locally or were travel related. Access to this kind of information would help providers better care for their patients and better assess and communicate risks to patients, said Needle. In order for health care providers to assist in public health efforts, he said, there needs to be a culture of increased data sharing.

Health Insurance Portability and Accountability Act

Workshop participants discussed the potential implications of HIPAA[2] on sharing patient-level medical data on MCM use during PHEs (see Box 4-3). As the entity responsible for enforcing HIPAA, OCR regulates most of the potential data sources for monitoring and assessing MCM use, McGraw said. Most hospitals, physicians, and all health plans are covered by HIPAA rules that govern how they use and share data, and the vendors they work with are also largely covered as business associates. However, HIPAA provisions governing the sharing of information for public health practice are fairly permissive. Furthermore, once the data are shared, the entity that shared them is not responsible for any subsequent use, so long as they provided the data in a way that was HIPAA compliant. There are pathways for data disclosure, as well as regulations, standards, and methodology for de-identification of data, if necessary, that stakeholders should understand to ensure that information sharing or analysis is consistent with the law, said McGraw. Other HIPAA issues discussed by individual workshop participants included the impact of state laws, consumer-shared data, and emergency department data.

State law HIPAA governs many of the entities that would contribute or use data for MCM monitoring and assessment; however, state law also plays a strong role, McGraw said. First, HIPAA does not preempt stronger state privacy laws (e.g., if state laws governing particular types of health

[2] For more information, see https://www.hhs.gov/hipaa/index.html (accessed August 23, 2017).

BOX 4-3
MCM Data and HIPAA: Human Subjects Research or Public Health Practice?

McGraw noted the potential uncertainty around when analysis and/or sharing of health data is considered research and when is it considered public health practice, which are treated differently under HIPAA rules. OCR believes that the pathways for the sharing and use of MCM data among stakeholders for the purpose of assessing safety and efficacy of MCMs are covered under public health practice, McGraw said. McGraw also clarified that public health practice is not human subjects research, which means that research conducted on MCM use that falls under the definition of public health practice does not require IRB review and does not need to be declared exempt by an IRB. She noted, however, that OCR cannot influence how an IRB within an institution determines when their authority applies (i.e., whether the activity is public health practice or human subjects research). This decision is made at the institutional level and is often based on the level of legal risk tolerance that each institution accepts.

HIPAA rules do not require that data be disclosed when shared or used for public health practice, but the rules do allow for them to be disclosed, if desired, McGraw said. Organizations are permitted to add additional disclosure requirements, which may relate to competitive and business issues as much as to maintaining the privacy of patient medical information.

If there is confusion regarding how HIPAA should be applied to MCM data sharing and use, said McGraw, OCR wants to know, so that additional guidance can be released to address misinterpretation or overinterpretations of the rules that might be barriers to progress.

SOURCE: McGraw presentation, June 7, 2017.

information place greater restrictions on sharing without the expressed consent of the patient). Second, state laws must conform with the public health permission clause in HIPAA, which allows entities covered by the rule to use and share information for public health purposes. This provision is very much reliant on the scope of authority of the public health entity involved, McGraw said. If the public health authority in a state is fairly constrained, then a sophisticated compliance officer will question whether there is enough permission in the law for them to be able to use or disclose protected health information. Less sophisticated staff, who might not read the regulations to the letter, might readily interpret the public health permitted use to mean they can release the information. This variety of interpretation of the law creates a dilemma for HHS with regard to enforcement if, in fact, the authority for the public health department to collect and use that information is not in the law, she said. However, the intent is for entities to

be able to share information for public health purposes, and it is unlikely that such a case would be pursued. Nevertheless, if state laws can provide that authority, and the pathway for disclosure is clear, it does reduce delays and allows information to flow without any uncertainty.

Consumer-shared health data McGraw pointed out that data collected by consumer-facing technologies such as wearable health devices and data from social media and social networking sites would not be covered by HIPAA. Their policies regarding sharing of user information are set in their user agreements. User agreements are enforced by the Federal Trade Commission and are expected to be transparent with regard to how the data are accessed, used, and shared. In response to a suggestion by Jeff Coughlin, senior director, Federal and State Affairs, Healthcare Information Management and Systems Society, in order to empower patients to voluntarily contribute their information, McGraw noted that HIPAA provides a pathway for the individual contribution of health data: patients have the right to obtain a copy of their medical data and to have it sent directly to the entity of their choice, which could include a public health authority.

Emergency department data Needle said it can be time-consuming for providers to obtain information from local emergency departments. Though such sharing is permitted under HIPAA, providers must first obtain a release from their patient to be able to receive their information.

GOVERNANCE

Leadership and Collaboration

In addition to clinical science expertise, leadership and responsibility during PHEs are needed moving forward, said Higgs. Establishing leadership is currently being done for international responses, but not domestic responses, she added. The Ebola response exemplified the necessity of identifying a lead U.S. government agency for a given crisis and providing clarity regarding the respective responsibilities of government agencies for both preparedness and response efforts. As previously noted in this section, an independent panel review following the Ebola crisis identified different government agencies as leads for future international PHEs, including tasking NIH with leading biomedical research during crises. Higgs also stressed the importance of working with local emergency operations systems, listening to the local experts, and establishing partnerships based on trust and agreement on the principles for the conduct of the research.

Keralis said the human tendency is to want to work with people who speak the same technical language, and she emphasized the need to bring

people together across silos for planning and exercises in advance of an emergency. Peer-to-peer sessions are also very helpful, she said, and may be more effective than top-down communication approaches. For example, state legal departments can be brought together to share cautionary tales, solutions, and best practices from past experiences. Marc Overhage, chief health informatics officer at Cerner, said that information silos often result in limited levels of education and awareness at the local level. He reiterated the importance of practicing response plans before a PHE to ensure that stakeholders are aware of regulations and their implications. Lee agreed with the importance of bringing the key stakeholders to the table, but she added that it can be logistically difficult to assemble such a large group, and meetings tend to be hours long. In addition, stakeholders are very enthusiastic at the table, but are often frustrated when they return home and try to implement ideas. Several weeks later they may have given up, she said, not because they have given up on the issue, but they simply do not know how to move forward.

Funding

Cobb added that in addition to filling leadership gaps, there is also a need to address funding. He said that none of the groups in the network of networks he described (see Chapter 2) exist solely to conduct preparedness research. Each group conducts research in their particular domain; however, they are able to pivot rapidly to initiate pre-defined clinical trial protocols, if needed. A potential concern is that these networks are not exercising the preparedness systems on a regular basis due to a lack of leadership, funding, or both. The investigators and professional organizations encompassed in these networks are committed to moving forward if funding were available, Cobb added, but at present it is not justifiable to dedicate 20 to 40 percent of their time to work on an initiative that is unfunded. David Reddick, chief strategy officer and co-founder of Bio-Defense Network, pointed out that the new CMS Emergency Preparedness Rule requires all CMS providers to have participated in a major community preparedness exercise.[3] Perhaps that will be the impetus for clinical networks to begin their preparedness exercises, said Reddick.

Funding is a perennial challenge, said Barishansky. Most health departments are stretched financially, and future funding for some critical public health preparedness grants will only remain stable or will be reduced. He added that many state and local health departments fund their public health preparedness programs entirely with these grants. Moore added that

[3] See https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertEmergPrep/Emergency-Prep-Rule.html (accessed August 23, 2017).

preparedness funding is also used to support everyday activities that are key systems in a PHE as well. For example, data from routine surveillance systems and inpatient monitoring systems can provide potential signals of emerging events or product safety issues.

Clinical Research Training

Cairns suggested that including a research component in disaster preparedness and response training could introduce disaster responders to clinical research in disaster settings and increase their comfort level with collecting data for research. As there is limited time for disaster response training, Cairns said, the intent would not be to develop responders into researchers, but to provide a broader perspective. He recalled comments by Chip Hughes of the National Institute of Environmental Health Sciences at an IOM workshop regarding the challenges of collecting data from the point of initial contact in environmental disasters (e.g., the Gulf oil spill or hurricanes). Cairns recalled that Hughes mentioned the availability of a standardized disaster response training module for chemical environmental disasters and had proposed adding a research module. Higgs noted there are discussions about integrating basic training on research into disaster training and preparedness at the global response level within the Office of U.S. Foreign Disaster Assistance.

Chris Kratochvil, a principal investigator for the National Ebola Training Education Center, said the center conducts training, education, and site visits for regional Ebola treatment centers across the United States, with funding from CDC and ASPR.[4] Recent efforts have focused on setting up a research infrastructure within that network, including a central IRB, case report forms, and a data repository. They are also developing training protocols for the nurses at the Ebola treatment centers to be able to support clinical research. The initiative is now being expanded beyond Ebola to encompass highly infectious diseases in general. Although this initiative is on a small scale, including just the 10 regional treatment centers, it is a model that could be useful more broadly.

Colf said relevant training programs are available, and he referred participants to the National Center for Disaster Medicine and Public Health, which conducts education, training, and research around disaster medicine and public health preparedness.[5] Another example is the Department of the Interior, which trains researchers on how to follow the incident command system in a disaster so they can better collect data without hindering responders.

[4] See https://netec.org (accessed August 23, 2017).
[5] See https://www.usuhs.edu/ncdmph (accessed August 23, 2017).

A participant added that responses at the federal public health level and the local health care facility level are entirely different (e.g., Ebola and pandemic influenza). Being prepared for one does not necessarily translate to being prepared for the other. Organizationally, the right kind of training needs to be provided at the right time to support local health organizations. Communities cannot be expected to be well-prepared to respond to every type of challenge that federal public health agencies are responsible for responding to.

Administrative Preparedness

Public health preparedness and response has become quite robust over the past 15 years, Barishansky said. However, there is an "administrative preparedness" angle to MCM monitoring and assessment that is often not as robust as it should be, he said. How do existing administrative functions (e.g., policies and authorities) affect response and the ability to collect the necessary information? Moore agreed that administrative preparedness is a concern and is often not thought of until an event occurs and information is not being shared as needed. For example, the public health system in North Carolina is decentralized, she said, and local health directors have

BOX 4-4
Exercising for Administrative Preparedness in PHEs

Cobb described a preparedness exercise held in 2012 at the request of ASPR. A study was designed to enroll 150 patients across 10 institutions within a 24-hour period and provide data back to ASPR within the next 24 hours. It was quickly determined that this could not be done using technologies from EHR providers such as Cerner and Epic, and instead, REDCap was used to manage patient information. Another challenge was balancing the decisions of the 12 participating IRBs. For example, one IRB determined it was ethical to collect information, but no samples, while another IRB said it was ethical to collect samples, but no information. He noted that, despite those and other challenges, the exercise was a success. Cobb also mentioned a current national preparedness exercise focused on influenza and anthrax, for which the case report forms do not include any protected health information because of the challenges of working with IRBs for these exercises. The bottom line is that workarounds are being developed for preparedness exercises, instead of using the large EHR vendors. As a solution, Cobb suggested convening an advisory board for administrative preparedness to help inform those working on preparedness studies.

SOURCE: Cobb presentation, June 6, 2017.

the primary authority in response and surveillance efforts. As such, there are often delays and confusion around sharing of data among hospitals, local jurisdictions, and state agencies. She emphasized the need to prepare in advance of the next PHE to determine how administrative preparedness can be addressed to inform how information can best be collected and shared. Cobb highlighted what he called a "healthy tension" between obtaining information needed during a health emergency and protecting the privacy of patients (see Box 4-4).

Barishansky said that a state department of health serves its constituents and visitors to the state and strives to ensure that they remain healthy. In this regard, the Commonwealth of Pennsylvania Department of Health considers MCMs to be a critical component of public health preparedness. When considering the ramifications of a PHE, he asks how will it impact the state, the neighboring states, or a certain area of the state (county, town), with the intent of understanding how communities might be made more resilient from a public health perspective. Barishansky remarked that many states lack the necessary statutory authority to conduct MCM monitoring and assessment. He suggested that a template could be developed to assist states in developing statutory language.

5

Inspiring Collective Action: Perspectives from Federal Stakeholders and Reflections from Individual Workshop Participants

The aspiration of achieving a national capability to monitor and assess MCM use is a shared responsibility among stakeholders, Lushniak observed, which starts with leadership and direction from within the federal system. In the final panel session of the workshop, federal government stakeholders reflected on the workshop discussions and shared their observations on the gaps, challenges, and opportunities around monitoring and assessing MCM use in the midst of PHEs. Panelists included Stacey Arnesen, chief of the Disaster Information Management Research Center in the Specialized Information Services of the National Library of Medicine (NLM) at NIH; Greg Burel; Redonna Chandler, deputy director of the Division of Clinical Innovation at the National Center for Advancing Translational Sciences (NCATS) at NIH; John Fleming, deputy assistant secretary for Health Technology Reform at ONC; Joseph Larsen, deputy director of the Division of CBRN Medical Countermeasures at BARDA; and Carmen Maher. The panel discussion was followed by an open discussion with workshop participants, facilitated by Lushniak.

Following the federal panel session, participants divided into breakout groups to discuss priority issues and potential actions for moving forward. Upon reconvening in plenary session at the close of the workshop, breakout group moderators Lushniak, Cobb, and Bakken reflected on the main points of discussion from their groups.

FEDERAL STAKEHOLDER PERSPECTIVES ON MOVING FORWARD

Biomedical Advanced Research and Development Authority

BARDA works toward filling gaps in preparedness and seeks to make investments that will be transformative in increasing the capacity to respond, Larsen said. In reflecting on the workshop, he observed that hurdles to collecting data on MCM use are more policy related than technological. Larsen recognized that there is a need to engage industry in discussions because medical product sponsors can provide valuable feedback on the design and conduct of post-marketing (Phase 4) studies. He also emphasized the importance of determining what type of information is absolutely necessary to collect and what information would be nice to have. Accountability is needed, said Larsen, and one agency (possibly CDC or FDA) should be designated as the lead agency responsible for collecting information. Larsen suggested piloting an MCM data collection system around an existing surveillance program, such as the routine monitoring of botulism cases in the United States. Botulism is going to continue to occur naturally, he said, and a pilot program for monitoring and assessing use of an approved MCM (heptavalent botulism antitoxin) for this indication could be launched.

Larsen also noted the need to determine costs associated with data collection, identify funding sources, and consider the sustainability of the enterprise. As an example of potential costs, he said that BARDA recently funded an expanded access protocol for the Ebola treatment ZMapp, including funding for data collection in two countries in West Africa and 11 sites in the United States. Capping the study at a maximum of 35 potential patients, it will cost $3 million per year for data collection, even if the capability is not used. This investment is not insignificant when it must be applied to 10 or 15 MCMs. Larsen noted that BARDA is already facing challenges in sustaining the investments it has made in companies and product development. Companies need to be assured of continued procurement of their product in the future, which drives commercial returns and enables them to continue to devote resources to MCM development.

Strategic National Stockpile

When discussing monitoring and assessing MCM use, the focus is generally on efficacy and safety data, Burel said. However, there is a spectrum of information needed throughout a PHE to inform the ongoing response and enable rapid changes to meet emerging needs. He noted, for example, that antiviral drugs were distributed to states during the 2009 H1N1 influenza pandemic, but there was no rapid feedback on what happened after the states received the products.

Various systems can be leveraged for monitoring the use of MCMs administered in a more traditional medical setting. When MCMs are administered in nonmedical settings, there is currently a dearth of any kind of useable data, Burel said. As discussed over the course of the workshop, however, data on MCM use might be found in non-traditional places, such as social media. Burel asked: Are there data to suggest people have confidence in the MCM? Are they receiving the product, and if so, what is the level of compliance? The data to answer such immediate questions about the response might already exist, he said.

Burel called for collaborative efforts among federal, state, and local authorities and industry to develop simple, easy-to-use reporting. For example, could a mobile app be developed that integrates into dispensing operations at a POD? Patients could enter follow-up information on their use of the MCM they received, providing valuable data on compliance and experience.

We do not know everything we need to know, Burel said, but there is a big block of data that we know we need. It is important to start now, and not wait until the day of an event to decide what questions to ask.

National Center for Advancing Translational Sciences

Part of the mission of NCATS is developing innovations that aid health research of all types, particularly tools that speed up the process of clinical research and data capture, Chandler said.[1] NCATS is an excellent resource for the clinical networks aspect of MCM monitoring and assessment efforts, she said. For example, the NCATS Clinical and Translational Science Awards (CTSA) Program supports a network of more than 50 academic medical centers across the country. CTSA facilitates collaboration, allowing researchers across institutions to come together as a clinical research enterprise. NCATS is currently working to create interoperable data warehouses across CTSA program awardees, which Chandler said could be invaluable for addressing many different types of research questions. In addition, the data could help to facilitate rapid recruitment for clinical studies.

All CTSA program sites have signed an agreement to streamline IRB review for multisite studies by relying on a single IRB.[2] The concept was tested in a pilot study and used by the Harvard-affiliated CTSA programs following the Boston Marathon bombing to rapidly initiate a clinical study, Chandler said. A group of investigators was interested in studying hearing impairment and repair in individuals who were at the exact site of the blast and in geographical circles around the blast. The ethical review process for

[1] For more information, see https://ncats.nih.gov/index.php (accessed August 23, 2017).
[2] See https://ncats.nih.gov/expertise/clinical/smartirb (accessed August 23, 2017).

the multisite study, which might normally take months (or longer), was completed in a matter of days because the sites had previously formed a network and agreed to a single IRB review. This exemplified a point that individual participants raised often during the workshop: there are certain research questions that can only be answered in the context of a PHE.

Chandler noted that there is a tension in a PHE between the government responders and local community. Another valuable aspect of the CTSA network, she said, is that NCATS has existing relationships with the local centers of excellence it funds and an understanding of the resources they have available, the service delivery system in their area, and the needs of their patient population.

Regarding monitoring and assessment of MCM use, Chandler said there is always room for more collaboration and engagement and suggested looking at what capacity across NCATS might be applied during a PHE. For example, NCATS intramural researchers have significant expertise in subjects such as screening libraries of approved compounds for repurposing existing drugs.

Office of the National Coordinator for Health Information Technology

One area of focus for ONC is information transfer, particularly in emergencies, Fleming said. One of the lessons learned from the response to Hurricane Katrina was the need for a system that can retrieve and share patient information from a range of sources during a disaster response. Residents of nursing homes and assisted living, for example, were sent to care facilities in Mississippi, Texas, and elsewhere, and the nurses and doctors receiving these patients were without information regarding medications or diagnoses for these patients. To address this unmet need, ONC is currently pilot testing the Patient Unified Lookup System for Emergencies, which provides connectivity with health information exchange systems.

The United States is lagging behind the rest of the world when it comes to interoperability of health care data systems, Fleming noted. EHR includes structured data and unstructured data; structured data are more interoperable than unstructured data (such as imaging files and free text). ONC is focused on improving the interoperability of data systems without compromising privacy and security, which requires vigilance when developing policies and standards to ensure that records cannot be hacked or misused, he said.

From a funding perspective, ONC is working on implementing rules and regulations for the 21st Century Cures Act.[3] Fleming explained that

[3] See https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf (accessed October 23, 2017).

ONC serves a coordination function that includes coordinating distribution of funding; establishing standards, quality measurement, and measurement of interoperability; and overcoming deliberate information blocking.

National Library of Medicine

Arnesen reiterated an earlier comment that the field of data science requires a broad range of skill sets and specific health subject-matter expertise (see Data Science Training in Chapter 3). She suggested that the NLM Disaster Information Management Research Center could help to address that need. Some themes that consistently emerge in discussions of disaster preparedness and response are data, information, and communication, she said. Information and communication are core components of library sciences, Arnesen added, and data science will feature significantly in the forthcoming NLM strategic plan.

NLM has evolved from simply collecting information, to organizing and indexing the information, to discovering what can be done with data and considering issues around data sharing, open data, data analysis tools, and other areas. NLM has a lot to offer in the area of "data preparedness," Arnesen added, and in helping to develop tools for response operations that can be ready-to-go for data collection and data analysis.

Although NLM is often not thought of when discussing response operations and MCMs, it has been engaged, for example, in working with ASPR on Radiation Emergency Medical Management and Chemical Hazards Emergency Medical Management toolsets, which provide information on MCMs. Arnesen noted that she looks forward to increased engagement of NLM by those working on MCM monitoring and assessment.

Discussion

In the discussion that followed the federal stakeholder perspectives, the federal panelists further discussed the data needs and resources available to decision makers, as well as the funding, costs, and interoperability of the data systems proposed throughout the workshop. John Tegeris of BARDA noted that the task at hand is not to design a theoretical solution and put it on the shelf. It must be built, exercised, and refined, he said. He suggested incorporating data collection infrastructure activities into a study of a product in development, thereby accomplishing several goals across agencies, industry, and other stakeholders.

Operational Questions, Data Needs, and Collection Methodologies

FDA, BARDA, and SNS are federal decision makers in need of data and information on MCMs, Lushniak said, and NCATS, ONC, and NLM are in positions to help provide access to that data. He prompted Maher, Burel, and Larsen, of FDA, SNS, and BARDA, respectively, to identify questions they need answered with regard to MCM use. Key questions for CDC and SNS, Burel said, are whether and how people are making use of an MCM that has been provided to them and whether the MCM is having the immediate desired effect.

Some MCMs are approved and entered into the SNS based on limited human effectiveness data, Maher added, and a PHE is likely the only time the MCM will be used in its intended population. Therefore, it is important to gather requisite data to quickly assess whether the performance expectations extrapolated from preclinical studies are, in fact, correlated with how the MCM is performing in the real world. Decisions can then be made by state and local authorities regarding whether to continue use of the MCM or to stop deployment, she said. These data are also needed to enable regulatory decision making, said Maher. For products administered under an EUA, for example, data are needed to ultimately support FDA regulatory review and approval, said Larsen. For an approved product, data are needed to provide greater confidence that the product is safe and effective.

Maher raised several questions regarding leveraging existing tools and systems for data collection. Who owns each of these systems or tools? How can independently owned tools be coordinated? Who coordinates them? Who are the decision makers, and what information do those decision makers need from these systems? How is that information normally obtained, and are there data gaps created by using these existing systems? What might need to be built into the existing systems? How is the information prioritized and communicated back to stakeholders?

Leveraging Existing Resources to Supply Data Needs

Lushniak asked Chandler, Fleming, and Arnesen what capabilities NCATS, ONC, and NLM, respectively, might have to fulfill the needs of MCM decision makers. Fleming observed that an "information highway" is needed—an infrastructure for MCM data. He noted that it is not the job of ONC to build that highway, but to see that it is built through ONC's coordination function. What is most essential, he said, is standardizing information transfer and protecting privacy and security so that information can get from point A to point B for the purposes of providing care and conducting research.

NLM is partially responsible for helping build that information high-

way and considering what data are collected and what data are stored, Arnesen said. She mentioned the FAIR principles of data management, which emphasize that scientific data should be findable, accessible, interoperable, and reusable (i.e., collected once and used multiple times, by different researchers). NLM is looking across the spectrum of research as it pertains to storing, accessing, and sharing data, and Arnesen suggested that MCM monitoring and assessment could be used as a pilot or test case. NLM is also working closely with ONC in developing standards both for interoperability and in establishing common ontologies, she added, and the development of standards could be an area in which MCMs could be used as a test case.

Chandler elaborated on the CTSA Program at NCATS as a resource for the integration of clinical care delivery and research and the collection of data. CTSA researchers understand both data collection and the delivery of clinical care, she said. Structurally, the CTSA Program provides funding to academic medical centers to serve as hubs within their localities; they are then networked to hospitals, federally qualified health centers, and other points-of-care delivery locations. NCATS is beginning to work on data interoperability across its academic medical centers hubs and ultimately plans to incorporate all of their network organizations. She explained that these institutions provide different types of care and thus have the potential to be involved in the collection of different types of data.

Entrepreneurship exists across the CTSA Program, Chandler said. CTSA awardees, in partnership with industry, bring medical products through development, regulatory approval, and post-approval monitoring, and then feed data and information back in support of a learning health system. Bakken added that each CTSA Program hub has extensive resources for engaging the local communities, and she suggested that these resources could be brought to bear for MCM monitoring and assessment.

Funding and Costs

Cooper and Lushniak prompted the federal panelists to consider how the changes and strategies being discussed could realistically be implemented in the context of a rapidly changing fiscal environment, which includes threatened cuts to public health funding. Burel noted that funding is a persistent issue, and discussions of developing critical monitoring and assessment capability do not become theoretical simply because of declining budgetary resources. There is a need to think innovatively about funding, he said, instead of relying solely on federally appropriated funds. For example, Burel said, there could be cooperative funding among states to develop a tool to meet broad stakeholder needs, which would also leverage foundation support.

Burel pointed out that it is not yet known what the actual costs of an MCM monitoring and assessment system will be, which is essential information when discussing funding. He suggested defining the essential data elements, data that would be nice to have but that are less essential, and information that would be difficult to obtain. After this exercise, one could identify existing sources that might contain this information, potentially looking beyond the health care system. He suggested engaging the National Academy of Public Administration to better understand what other departments, agencies, states, and localities have done to collect information and perhaps identifying how to leverage those resources. Fleming noted the potential of leveraging IT to lower costs and deliver more. Other industries, particularly in the private sector, have lowered costs by using IT, he observed.

Maher reiterated the importance of defining ownership or coordinating responsibility for the tools and solutions. Who is empowered to assemble the different pieces from where funding already exists? Additional funding would be ideal, but potential solutions exist that can be adopted in the absence of substantial additional funding. Maher highlighted the need for public health to become much more efficient at bringing the PHEMCE perspective to stakeholder activities that are already being funded. For example, how might MCM data collection be incorporated as part of the recent implementation of a new EHR system at the U.S. Department of Veterans Affairs? In other words, show other stakeholders how this problem is also their problem, and how helping to solve it serves them as well, she said.

PRIORITIZING ISSUES FOR ACTION: REFLECTIONS FROM INDIVIDUAL WORKSHOP PARTICIPANTS

Following the final panel session, workshop speakers and attendees were invited to discuss potential strategies and actions in the areas of CONOPS, clinical networks, and sources of data (both electronic health data and big data). At the end of the workshop, Lushniak, Cobb, and Bakken shared their individual reflections on the discussions held in these breakout sessions and throughout the workshop.

Concept of Operations[4]

In the context of CONOPS, Lushniak shared his observations on what could be done to make the system ready to determine the safety and effectiveness of a given MCM when the next PHE happens, as well as potential solutions and action steps. He likened CONOPS to a machine with a set of levers that one must pull to instruct the machine what to do. Similarly,

[4] All comments in this section are directly attributable to Lushniak.

determinations on the type of CONOPS needed for monitoring and assessment of MCMs during PHEs involves an understanding of key parameters that will define the scope of the problem, including the scale of the PHE, the type and regulatory status of the MCM, and how and in what locations the MCM will be distributed.

Lushniak noted there could be resistance or opposition by certain stakeholders to operational aspects of MCM monitoring and assessment. For example, state and local partners may resist some CONOPS activities because they may already be overburdened and have limited or insufficient resources (e.g., time, staffing, funding, or supplies) to participate in these operations. There may also be concern raised from groups on specific issues (e.g., opposition to vaccinations or data privacy advocates).

A primary challenge to CONOPS for MCM monitoring and assessment is funding, said Lushniak. Other challenges, he observed, include politics and political will; personnel and workload issues; siloing of data or lack of collaboration; communication; education and training; bureaucracy; scalability and flexibility of plans; differing missions, priorities, and authorities across stakeholders; technology; and exercising and evaluation of CONOPS.

There are present opportunities for CONOPS in MCM monitoring and assessment, said Lushniak, including the potential to validate regulatory approaches for regulating medical products (e.g., the Animal Rule); collecting data and information to inform, refine approaches, and set priorities for PHE responses; standardizing information; potentially decreasing the risk of products if positive safety and efficacy data were collected; demonstrating return on investment; building systems for future scenarios; and saving lives.

Lushniak described steps that could be undertaken within the coming year related to CONOPS for MCM monitoring and assessment, including

- *Explore the use of clinical trial networks for MCM monitoring and assessment and share lessons learned* (potentially as part of a BARDA tabletop exercise);
- *Understand and define the data needed for monitoring and assessing MCMs, which could be informed by exploring a specific MCM as a use case* (potentially as an SNS workshop);
- *Develop communications strategies to illustrate the challenges and opportunities for MCM CONOPS* (potentially at upcoming forums such as the Health 2.0 conference);
- *Leverage industry resources and expertise;*
- *Conduct a landscape evaluation of existing systems at the state and local levels* (potentially working through the National Association of County and City Health Officials); and

- *Build or expand partnerships with stakeholders that are often underrepresented or not represented at workshops such as this one* (e.g., CMS, private payers, or IRBs).

Clinical Networks[5]

Cobb shared his observations on how an extensible clinical system for monitoring and assessing MCMs that is rapid, adaptable, scientifically robust, and minimally disruptive to the course of care during a PHE could be developed. Cobb noted that considerations for realizing such a system could include

- *The developmental stage of the MCM and level of evidence available* (e.g., investigational product, approved under Animal Rule, or FDA approved);
- *The type of research to be conducted* (e.g., interventional or observational; acute, real-time data collection or ongoing study of long-term outcomes);
- *The nature and scale of the PHE* (e.g., national versus local; infectious disease versus natural disaster); and
- *The class of MCM* (e.g., drug, biologic, device, or combination product).

There are several strengths of the current system and potential opportunities to consider when developing a clinical trial network for MCM monitoring and assessment, said Cobb. From a resource standpoint, there is an existing clinical trial infrastructure that could be leveraged; expertise that could be brought to bear; new innovations on the horizon; a movement toward public–private partnerships; and global experience with past PHEs, domestically and globally, that can inform the process. A variety of opportunities are available, including case studies from past PHEs (e.g., Ebola); testing protocols in benign, predictable threat situations (e.g., seasonal influenza); socializing the issue to engage and educate the public; and the opportunity to conduct annual exercises.

Cobb also highlighted several weaknesses of the current system and threats that could affect progress, including a lack of leadership or ownership; lack of commercial models or incentives; fragmentation of the health care system; funding cuts and uncertain sustainability of existing structures; the risk of unknown public health threats; and dissemination of misinformation.

[5] All comments in this section are directly attributable to Cobb.

Several potential solutions and next steps could be undertaken within the next year to advance a clinical trial of networks for MCM monitoring and assessment, noted Cobb:

- Draft a playbook of potential scenarios and a framework for evaluating them against available data sources.
- Begin annual exercises and tabletops to test the feasibility of pilot efforts and provide proof of concept of a "network of networks" approach.
- Identify and address leadership gaps, including designating an organization or agency to be tasked with the authority to create or leverage clinical trial networks to conduct research during PHEs.
- Build private–public partnerships and mechanisms for conversation among stakeholders, including product sponsors.
- Create an advisory board for administrative preparedness that would address issues around human subjects protection in public health practice versus research.
- Leverage existing surveillance systems.

Data Sources[6]

Bakken presented her perspective on how existing data sources, systems, and technical and human infrastructures can be leveraged to meet the needs of MCM monitoring and assessment for safety and effectiveness. She noted some key parameters, stakeholders, context, and potential solutions and action steps that could be considered.

One could consider this topic from the perspective of a broad set of stakeholders and their needs, Bakken said, and indeed some stakeholders are both data suppliers and data users. A vast range of stakeholders collect and use data that could potentially be leveraged for MCM monitoring and assessment, said Bakken, and the particular stakeholders involved in any one effort are driven by the scenario. There is a particular need for representation for special or vulnerable populations, whose data are not always captured, as well as those still facing technology barriers to inclusion in research, Bakken added. For example, certain areas of the country, including tribal areas, continue to lack broadband Internet access, which is a hindrance to capturing or delivering data.

Bakken noted that challenges to adequately leveraging data in monitoring and assessing of MCMs could be categorized as technical or nontechnical. She highlighted a lack of adequate standards for semantic operability across data systems as a main technical challenge. Other techni-

[6] All comments in this section are directly attributable to Bakken.

cal challenges include text mining; terminology; timeliness of data delivery; time to enact a change of data system vendor; the volume of available data; governance of data sharing; time needed to set up data use agreements and renewals; training of data collectors; pockets of data that are not being collected; and configuration of databases.

Other primary, non-technical challenges, she added, are workforce development in data science and the lack of a prospective plan to test the readiness of data collection and transfer processes. The volume of available data presents a challenge, but it is also an opportunity, said Bakken, though there are certain populations that are not presently included in datasets, including some international and tribal populations.

Based on the workshop discussions, Bakken listed several potential opportunities, solutions, and next steps that could be leveraged, built upon, or undertaken within the next year:

- *Data preparedness framework and testing plan*—Consider which data sources, and what level of data veracity, are needed for which purposes.
- *Data sharing governance*—As part of a data preparedness plan, establish priority data use agreements with identified partners, such as pharmacy benefit managers or insurance systems, and exercise the agreements ahead of time to establish relationships and build trust.
- *Data standardization*—Identify and address gaps in current standards and develop a common ontology as they relate to data collection for MCMs.
- *Data storage and use*—Encourage continued refinement of models for mapping datasets and maintenance data coordinating centers.
- *Commercial pharmacies to fill unmet data needs*—For example, consider placing "pop-up pharmacies," which have existing data collections capabilities, in underserved areas.
- *Patient- and consumer-generated data collection*—Take advantage of non-traditional data sources such as wearables, self-reported data, social media information, and search engines.
- *Data science*—Leverage the current heightened interest in data science as an opportunity to build a data science workforce. Look to existing bodies of knowledge, such as the U.S. Digital Service, for support in this area. Promote financial incentives, including student loan forgiveness, for health care workers.

CLOSING REMARKS

Lushniak closed the workshop by thanking the various groups that made it a success: the planning committee, for volunteering their time for several months to plan and convene the workshop; the workshop speakers, who volunteered their knowledge and experience; the workshop sponsor, FDA, for bringing to light this important topic; the workshop participants for taking part in the discussions; National Academies staff; and workshop facilitator Laura Runnels.

Many potential solutions were discussed throughout the workshop, said Lushniak, including a wide array of challenges and potential solutions and next steps. He added that when it comes to MCMs, the health and safety of our nation, and the national security of our country, the work does not stop here.

Appendix A

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Appendix B

Workshop Agenda

Building a National Capability to Monitor and Assess Medical Countermeasure Use in Response to Public Health Emergencies: A Workshop

June 6–7, 2017

AGENDA

National Academy of Sciences Building, Kavli Auditorium
2101 Constitution Avenue, NW, Washington, DC 20418

WORKSHOP OBJECTIVES

- Discuss the roles and efforts of the federal government and relevant stakeholders who have an interest in building and maintaining a national medical countermeasure (MCM) monitoring and assessment capability for public health emergencies.
- Discuss federal monitoring and assessment efforts and opportunities for future work in areas including electronic health record capabilities, big data, clinical networks, and operations for response.
- Help inform the development of strategic MCM monitoring and assessment plans for public health emergencies.

June 6, 2017

8:30 am **OPENING REMARKS**
Boris Lushniak, Dean and Professor, School of Public Health, University of Maryland

8:45 am **KEYNOTE PRESENTATION: BACKGROUND ON FEDERAL MCM AND MONITORING/ASSESSMENT**
Carmen T. Maher, Acting Assistant Commissioner for Counterterrorism Policy, U.S. Food and Drug Administration

AUDIENCE Q/A
Moderator: *Boris Lushniak, Dean and Professor, School of Public Health, University of Maryland*

9:30 am **LIGHTNING PRESENTATIONS: ESTABLISHING DEFINITIONS OPERATIONS FOR RESPONSE**
Boris Lushniak, Dean and Professor, School of Public Health, University of Maryland

ELECTRONIC HEALTH DATA
Richard Platt, Professor and Chair, Department of Population Medicine, Harvard Medical School

UNSTRUCTURED/BIG DATA
Suzanne Bakken, Alumni Professor of Nursing; Professor of Biomedical Informatics, Columbia University

CLINICAL NETWORKS
Perren Cobb, Professor of Clinical Surgery; Director, University of Southern California Critical Care Institute; Director, Keck Surgical Intensive Care Unit, University of Southern California

FACILITATED DISCUSSION
Laura Runnels, LAR Consulting

10:30 am **BREAK**

11:00 am **PANEL DISCUSSION I: WHAT DATA ARE NEEDED TO MAKE DECISIONS?**
Moderator: *Yon C. Yu, Associate Director, Regulatory Affairs, National Center for Emerging and Zoonotic Infectious Diseases, U.S. Centers for Disease Control and Prevention*

Quazi Ataher, Senior Director of Epidemiology in Worldwide Safety Strategy, Pfizer Inc.

Theresa Cullen, Associate Director, Global Health Informatics Program, Regenstrief Institute, Inc.

Alison Levy, Emergency Operations Manager, Public Health–Seattle and King County

Anita Patel, Senior Advisor, Lead, Pandemic Medical Care and Countermeasures Influenza Coordination Unit, National Center for Immunization and Respiratory Diseases, U.S. Centers for Disease Control and Prevention

Paul Petersen, Director, Emergency Preparedness Program, Tennessee Department of Health

Adam Wilcox, Professor, Biomedical Informatics and Medical Education, Chief Analytics Officer, University of Washington

FACILITATED DISCUSSION WITH AUDIENCE
Laura Runnels, LAR Consulting

12:30 pm **LUNCH** *(on your own)*

1:30 pm **PANEL DISCUSSION II: EXISTING DATASETS AND CHALLENGES WITH THE SOURCES**
Moderator: *Laura Runnels, LAR Consulting*

Rhona Cooper, Public Health Preparedness Clinical Coordinator, Philadelphia Department of Public Health

Henry "Skip" Francis, Director, Data Mining and Informatics Evaluation and Research, Center for Drug Evaluation and Research, U.S. Food and Drug Administration

Eva Lee, Director, Center for Operations Research in Medicine and HealthCare, H. Milton Stewart School of Industrial and Systems Engineering, Georgia Institute of Technology

Joe Vasey, Epidemiologist and Biostatistician, Practice Fusion

FACILITATED DISCUSSION WITH AUDIENCE
Laura Runnels, LAR Consulting

3:00 pm **BREAK**

3:30 pm **PANEL DISCUSSION III: EXISTING SYSTEMS AND INFRASTRUCTURE FOR CLINICAL NETWORKS AND OPERATIONS FOR THREAT RESPONSE: ADVANTAGES AND CHALLENGES**
Moderator: *Laura Runnels, LAR Consulting*

Jeff Brown, Associate Professor, Harvard Pilgrim Health Care Institute

John Grabenstein, Executive Director, Medical Affairs, Merck Vaccines

Elizabeth S. Higgs, Global Health Science Advisor, Division of Clinical Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Lou Ann Lance, Public Health Program Nurse, Clinical Operations, Bureau of Communicable Disease Control, New York State Health Department

Amanda Peppercorn, Senior Medical Director, Infectious Diseases Research and Development, GlaxoSmithKline

Scott Proestel, Director, Division of Epidemiology, Office of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration

FACILITATED DISCUSSION WITH AUDIENCE
Laura Runnels, LAR Consulting

5:00 pm **RECAP AND REVIEW**
Boris Lushniak, Dean and Professor, School of Public Health, University of Maryland

5:15 pm **ADJOURN DAY 1**

June 7, 2017

8:30 am **OPENING REMARKS**
Boris Lushniak, Dean and Professor, School of Public Health, University of Maryland

8:45 am **PANEL DISCUSSION IV: LAWS AND INCENTIVES TO PROMOTE ADOPTION AND STANDARDIZATION**
Moderator: *Laura Runnels, LAR Consulting*

Ray Barishansky, Deputy Secretary of Health, Pennsylvania Department of Health

Jeff Coughlin, Senior Director, Federal and State Affairs, Healthcare Information Management and Systems Society

Deven McGraw, Deputy Director, Health Information Privacy, Office for Civil Rights, U.S. Department of Health and Human Services; Acting Chief Privacy Officer, Office of the National Coordinator for Health Information Technology

Amanda Fuller Moore, Public Health Preparedness and Response, Division of Public Health, North Carolina Department of Health and Human Services

J. Marc Overhage, Chief Health Informatics Officer, Cerner

FACILITATED DISCUSSION
Laura Runnels, LAR Consulting

10:15 am **BREAK**

10:45 am **KEYNOTE PANEL DISCUSSION: INSPIRING COLLECTIVE ACTION**
Moderator: *Boris Lushniak, Dean and Professor, School of Public Health, University of Maryland*

Stacey Arnesen, Chief, Disaster Information Management Research Center, Specialized Information Services, National Library of Medicine, National Institutes of Health

Greg Burel, Director, Division of Strategic National Stockpile, U.S. Centers for Disease Control and Prevention

Redonna Chandler, Deputy Director, Division of Clinical Innovation, National Center for Advancing Translational Sciences, National Institutes of Health

John Fleming, Deputy Assistant Secretary for Health Technology Reform, Office of the National Coordinator for Health Information Technology

Joseph Larsen, Deputy Director, Division of CBRN Medical Countermeasures, Biomedical Advanced Research and Development Authority, Office of the Assistant Secretary for Preparedness and Response

Carmen T. Maher, Acting Assistant Commissioner for Counterterrorism Policy, U.S. Food and Drug Administration

11:45 am **ACTIVITY: PRIORITIZING ISSUES FOR STRATEGY BREAKOUTS**
Laura Runnels, LAR Consulting

12:15 pm **LUNCH** *(on your own)*

1:15 pm **BREAKOUT EXERCISE** *(Rooms to Be Announced)*
Moderators:

Suzanne Bakken, Alumni Professor of Nursing; Professor of Biomedical Informatics, Columbia University

Perren Cobb, Professor of Clinical Surgery; Director, University of Southern California Critical Care Institute; Director, Keck Surgical Intensive Care Unit, University of Southern California

Boris Lushniak, Dean and Professor, School of Public Health, University of Maryland

Richard Platt, Professor and Chair, Department of Population Medicine, Harvard Medical School

3:30 pm **BREAK**

4:00 pm **BREAKOUT EXERCISE—REPORT BACK**
Suzanne Bakken, Alumni Professor of Nursing; Professor of Biomedical Informatics, Columbia University

Perren Cobb, Professor of Clinical Surgery; Director, University of Southern California Critical Care Institute; Director, Keck Surgical Intensive Care Unit, University of Southern California

Boris Lushniak, Dean and Professor, School of Public Health, University of Maryland

Richard Platt, Professor and Chair, Department of Population Medicine, Harvard Medical School

5:00 pm **RECAP AND REVIEW**
Boris Lushniak, Dean and Professor, School of Public Health, University of Maryland

5:15 pm **ADJOURN DAY 2**

Appendix C

Biographical Sketches of Workshop Speakers and Moderators

Stacey J. Arnesen, M.S., is the chief of the Disaster Information Management Research Center in the Specialized Information Services Division of the NLM, NIH. She has worked at NLM for 30 years, the past 15 years in the area of disaster information management. Her work includes the coordination of tools and resources to improve access to disaster medicine and public health information including disaster health literature, tools and apps for hazmat and CBRN incidents, and disaster information management research. Ms. Arnesen oversees the development of a gray literature database on disaster medicine and public health (http://disasterlit.nlm.nih.gov). Ms. Arnesen received her M.S. in neurobiology and behavior from Cornell University and her A.B. from Smith College.

Quazi Ataher, M.B.B.S., M.H.S., Ph.D., is a senior director of epidemiology in Worldwide Safety Strategy at Pfizer Inc. He is the epidemiology group lead for the Pfizer Essential Health and Pfizer Consumer Health businesses. He leads a group of epidemiologists responsible for developing pharmacoepidemiology programs to support drug development and safety assessment. He has more than 10 years of experience in designing and conducting epidemiology studies for multiple products in various therapeutic areas. Additionally, he is involved in the study and use of quantitative methods of product benefit–risk assessment at Pfizer. Prior to joining the pharmaceutical industry, Dr. Ataher practiced medicine in Bangladesh. He received his medical degree from Chittagong Medical College in Bangladesh, an M.H.S. in molecular microbiology and immunology from the Johns Hopkins Uni-

versity School of Hygiene and Public Health, and a Ph.D. in epidemiology from Emory University.

Suzanne Bakken, RN, Ph.D., FAAN, FACMI, is the alumni professor of nursing and professor of biomedical informatics at Columbia University. Following doctoral study in nursing at the University of California, San Francisco, she completed an NLM postdoctoral fellowship in medical informatics at Stanford University. She currently directs the Precision in Symptom Self-Management Center. In 2010, she received the Pathfinder Award from the Friends of the National Institute of Nursing Research. She is the past president of the American College of Medical Informatics, a fellow of the American Academy of Nursing, and a member of the National Academy of Medicine.

Raphael Barishansky, M.P.H., M.S., CPM, is the deputy secretary for health planning and assessment at the Pennsylvania Department of Health. He is a nationally recognized EMS and PHE preparedness leader, author, speaker, and advocate. From 2012 to 2015, he served as the director of the Office of Emergency Medical Services for the Connecticut Department of Public Health. Prior to that, he served as the chief of Public Health Emergency Preparedness and Response for the Prince George's County (Maryland) Health Department from 2008 to 2012. Mr. Barishansky holds a B.A. from Touro College, an M.P.H. from New York Medical College, and an M.S. in homeland security studies from Long Island University. He is a graduate of the Senior Executives in State and Local Government program held at the John F. Kennedy School of Government at Harvard University (2006) and the Healthcare Leadership and Administrative Decision Making class held at the Center for Domestic Preparedness in Anniston, Alabama (2009). He has also earned a certified public manager (CPM) certification through Arizona State University. Mr. Barishansky has authored more than 300 articles in such publications as *EMS Magazine*, *Journal of Emergency Medical Services*, *EMS Insider*, *Domestic Preparedness Journal*, *Journal of Homeland Security and Emergency Management*, *Emergency Management Magazine*, *Public Safety Communications*, and *Crisis Response Journal* (UK). He is a nationally known speaker and has made more than 100 public presentations at various EMS and public health conferences.

Jeffrey Brown, Ph.D., is an associate professor in the Department of Population Medicine (DPM) at Harvard Medical School and the Harvard Pilgrim Healthcare Institute. He is research director of the Therapeutics Research and Infectious Disease program at DPM and chief operating officer and a member of the executive committee of the FDA Sentinel project. Dr. Brown is a health services researcher with expertise in pharmacoepidemiology

and medical product safety, with primary research interests in the development of approaches to facilitate multi-institutional medical product safety surveillance and research using electronic health data. He is co-lead of the PCORnet Distributed Research Network Operations Center, co-chair of the Informatics Core of the NCI Cancer Research Network, and co-lead of the EHR Core of the NIH Healthcare System Research Collaboratory. Dr. Brown is the lead architect and inventor of PopMedNet, an open-source software platform that facilitates the creation and operation of large-scale distributed health data networks. He holds a master's degree in economics from Tufts University and a Ph.D. in social policy from Brandeis University.

Greg Burel, currently serves as the director of the Division of Strategic National Stockpile (DSNS), Office of Public Health Preparedness and Response, CDC. Prior to his leadership at DSNS, Mr. Burel developed an extensive background in supply chain management in the federal government beginning in 1982. In addition to CDC, his service includes management roles with increasing responsibility with the Internal Revenue Service, General Services Administration, and the Federal Emergency Management Agency. Mr. Burel was selected as a member of the Senior Executive Service and joined CDC in April 2005. In March 2007, he assumed his current position. In this role, Mr. Burel directs the nation's premier medical materiel preparedness and response organization charged with supply chain management delivering critical medical assets to the site of a national emergency. Mr. Burel holds a bachelor's of business administration degree from Georgia State University. He is a graduate of the Federal Executive Institute's Leadership for a Democratic Society and Harvard University's Kennedy School of Government National Preparedness Leadership Initiative. In 2016, Mr. Burel was awarded the Samuel J. Heyman Service to America Medal for Management Excellence. He is an elected Fellow of the National Academy of Public Administration.

Redonna Chandler, Ph.D., joined NCATS as the deputy director of the Division of Clinical Innovation (DCI) in April 2015. She brings extensive scientific and organizational leadership and supports coordination, collaboration, and communication for DCI and the CTSA Program. Dr. Chandler earned her Ph.D. in psychology from the University of Kentucky and is a licensed psychologist. As a clinician, she has treated those struggling with addiction, serious mental health issues, and infertility. She has been at NIH since 2002, serving in positions of increasing responsibility and leadership at the National Institute on Drug Abuse. Prior to joining NCATS, Dr. Chandler served as the acting deputy director for the Division of Epidemiology, Services and Prevention Research and as the chief of the Services Research Branch at the National Institute on Drug Abuse. She worked for the U.S.

Department of Justice from 1996 to 2002, directing large drug treatment programs.

Perren Cobb, M.D., FACS, FCCM, is the director of Surgical Critical Care at Keck Medicine of the University of Southern California. At the Keck School of Medicine, he holds the rank of clinical professor of surgery and of anesthesiology. Dr. Cobb is founding director of the U.S. Critical Illness and Injury Trials Group, which fosters investigator-initiated hypothesis testing and strategic planning at the national level for critical illness and injury research. His academic interest is systems approaches to clinical quality improvement and preparedness for research emergencies. Dr. Cobb was an undergraduate at Vanderbilt University and received his medical degree from the University of Louisville School of Medicine. He trained in general surgery at the University of California, San Francisco, and completed fellowships in critical care at NIH and the University of Pittsburgh. His early research focus was the treatment of sepsis; he worked nationally with trauma collaborators to develop a novel sepsis diagnostic, the riboleukogram, which uses contemporary genomics and microfluidics technology to track the host response to injury and infection. More recently, he has worked with federal partners to establish new capabilities to conduct clinical research during public health emergencies, in the process standardizing data collection, analysis, and reporting tools. Dr. Cobb's work has been supported by NIH, CDC, ASPR, FDA, BARDA, the American Association for the Surgery of Trauma, the Society of Critical Care Medicine, and the Barnes Jewish Hospital Foundation. His awards include the Research Scholarship Award of the American Association for the Surgery of Trauma, the Founders Grant for Critical Care Research of the Society of Critical Care Medicine, the George H.A. Clowes, Jr. Memorial Research Career Development Award of the American College of Surgeons, and the 2nd Annual Critical Care Medicine Distinguished Alumnus of the University of Pittsburgh. Dr. Cobb is a former president of the Association for Academic Surgery.

Rhona H. Cooper, M.S.N., M.A., RN, is the clinical coordinator on the Bioterrorism–Public Health Preparedness team at the Philadelphia Department of Public Health (PDPH), Division of Disease Control. She is responsible for the development and implementation of all plans relevant to the procurement, distribution, and dispensing of MCMs during a PHE in Philadelphia. She has a lead role in collaboration with state and federal partners, including the SNS, and coordinates with public and private agencies to expand mass medication capacity and readiness. Most recently, Ms. Cooper participated in the City of Philadelphia's public health readiness planning and operations for the Papal visit in 2015 and the Democratic

National Convention in 2016. Ms. Cooper received her master's degree in nursing from La Salle University and her master of arts in education from Arcadia University. Prior to joining PDPH, Ms. Cooper worked for the School District of Philadelphia, first as a school nurse and later as school nurse coordinator, where she had responsibility to oversee the health services provided by 200 certified school nurses in more than 350 public and nonpublic schools serving more than 150,000 school children in the City of Philadelphia.

Jeffrey R. Coughlin, M.P.P., is the senior director of Federal and State Affairs at the Healthcare Information and Management Systems Society (HIMSS). In this position, he leads HIMSS's efforts to build stronger relationships with federal agencies and facilitates the building of a nationwide network of advocates for state-based initiatives that affect all aspects of health IT. Before joining HIMSS, Mr. Coughlin was the team leader for corporate accounts at the Marwood Group, where he worked with nonprofit health systems, health IT vendors, professional societies, and trade associations, analyzing how they could most effectively influence legislative and regulatory processes and focus their advocacy efforts. His career also included several years in the health care nonprofit advocacy world, where he led efforts in policy development, directed outreach to Congress and Executive Branch agencies, built advocacy coalitions with like-minded organizations, and created robust grassroots networks. Mr. Coughlin also worked for HHS, where he was part of the team responsible for the development, implementation, and management of the Government Performance and Results Act within HHS. Mr. Coughlin's educational background includes a master's degree in public policy from the College of William and Mary and a bachelor's degree in political science from Providence College.

Theresa Cullen, M.D., M.S., is a family physician who retired from the U.S. Public Health Service (USPHS) in 2012 after more than 25 years of active duty. During her tenure with USPHS, she was a practicing family physician on multiple rural American Indian and Alaska Native reservations. She also led multiple software development and deployment initiatives within the Indian Health Service. When she was chief information officer for the Indian Health Service, RPMS (the Service's health IT system) became the only ONC-certified health IT software suite within the federal government. Between 2012 and 2015, Dr. Cullen worked as the chief medical information officer for the Veterans Health Administration, where she developed a new model for field and community involvement in health IT, as well as supporting and expanding work in multiple areas of health IT, including interoperability and data sharing, standards and terminology, and informatics patient safety. She has worked to develop population health IT software

suites since 2002, including electronic clinical quality measures and expanded population health capabilities at the point of care. Her interests are in using health IT to help achieve health equity throughout the globe as well as ensure the use of appropriate technology to meet identified clinical needs. Dr. Cullen currently serves as the associate director for the Global Health Informatics Program at Regenstrief Institute, Inc., as well as visiting associate professor of family medicine at Indiana University School of Medicine.

John Fleming, M.D., serves as ONC's deputy assistant secretary for Health Technology Reform. Prior to serving at ONC, Dr. Fleming served as a Representative from Louisiana's 4th Congressional District from 2009 to 2017. He is an early adopter and supporter of health IT, having implemented an EHR in his Minden, Louisiana, practice in 1997. His public career also includes medical service in the U.S. Navy. Dr. Fleming was the 2007 Louisiana Family Practice Physician of the Year. Dr. Fleming earned his B.S. and M.D. at the University of Mississippi.

Henry "Skip" Francis, M.D., has been the director of the Data Mining and Informatics Evaluation and Research Group in the Office of Translational Sciences, Center for Drug Evaluation and Research (CDER), FDA, since March 11, 2013. In that capacity he directs a transdisciplinary group of senior sciences to test, create, and operate data analysis programs facilitating the efficient use of scientific methods to evaluate complex data information in order to make regulatory decisions for drug approval and drug safety. From October 2007 until March 10, 2013, Dr. Francis was the deputy director of the Office of Surveillance and Epidemiology (OSE) in CDER. Dr. Francis worked with the OSE director to lead five divisions of pharmacy and clinical scientists in the detection and study of adverse medical events occurring after the release of new drugs into the American health market (the post-market period). Dr. Francis's specific interest is in the development of data mining techniques to enhance pharmaco vigilance capabilities in national medication use and health care databases. Prior to working in FDA, Dr. Francis was a basic and clinical researcher in NIAID, NIH. He worked in several clinical and epidemiologic research projects conducting AIDS and tropical research projects in the Democratic Republic of the Congo (DRC) and other projects in the Caribbean and the South Pacific. Dr. Francis was the director of the USPHS and Belgian Project SIDA (AIDS research) Research Laboratories in Kinshasa, DRC.

John D. Grabenstein, Ph.D., is the executive director for Medical Affairs for Merck Vaccines. He leads medical affairs and scientific policy activities for Merck's and MSD's global vaccine enterprise of more than 150 million doses annually for 12 vaccines to help reduce the burden of vaccine-preventable

diseases worldwide. A pharmacist with 37 years' experience, he has served on multiple committees advising the U.S. government and published more than 400 articles and 9 books, primarily on topics of immunization, public health, and leadership. Dr. Grabenstein received his pharmacy degree from Duquesne University in 1980, a master's degree in education from Boston University in 1988, and his doctorate in epidemiology from the University of North Carolina in 1999. Previously, as a colonel in the U.S. Army, Dr. Grabenstein directed the Military Vaccine Agency, where he organized "Immunization University" to train clinicians from many health disciplines. He oversaw U.S. Department of Defense immunization programs for 9 million troops, retirees, and family members spread across four continents and dozens of ships at sea. In 1996, he wrote the curriculum for "Pharmacy-Based Immunization Delivery," a CDC-recognized 20-hour course coordinated by the American Pharmacists Association.

Elizabeth S. Higgs, M.D., MIA, DTMH, is a global health science advisor for the Division of Clinical Research (DCR), NIAID, NIH, HHS. During the 2014–2015 West African Ebola outbreak, Dr. Higgs was part of the NIAID DCR senior team designated to establish and advance the clinical research response for HHS under the Liberia–U.S. Joint Clinical Research Program, also known as PREVAIL in West Africa. During the outbreak, the PREVAIL program established research capacity and conducted clinical trials for Ebola vaccines and therapeutics, and it is currently conducting an Ebola natural history study for survivors. PREVAIL launched a study in summer 2016 to assess the ability of a novel compound to eradicate persistent Ebola viral RNA from semen. Dr. Higgs serves as the DCR liaison for the World Health Organization and collaborates with U.S. government agencies, including an interagency White House endeavor to mitigate the risk of Ebola transmission from survivors in West Africa. Dr. Higgs provided leadership for NIH collaborative international infectious disease research, including the Southeast Asia Infectious Disease Clinical Research Network and International Collaborations in Tropical Disease Research Network. She led the U.S. government interagency clinical design group on influenza therapeutics during the H1N1 2009 pandemic. She was formerly seconded by NIH to the U.S. Agency for International Development (USAID) as science advisor for research and innovation to the U.S. government Global Heath Initiative and the USAID Global Health Bureau, where she focused on science for development issues, including U.S. government Global Health Evidence Summits, evidence evaluation frameworks for global health decision making, and smart linkages between U.S. government development and science agencies, such as Partnerships for Enhanced Engagement in Research's Implementation Science for Child Survival. Dr. Higgs initiated and is helping to steer a multilateral effort to

establish norms for social sciences in global health with a particular focus on integration with biomedical interventions for women and children. A career focus includes the development of independent research capacity in low- to middle-income countries. Research interests have focused broadly on influenza therapeutics, HIV, tropical diseases, nutrition, emerging infectious diseases, Ebola, and research responses to pandemics. She is trained in internal medicine and infectious diseases. She received a doctorate in medicine from the University of Virginia (UVA), a master's degree in international affairs from Columbia University, an interdisciplinary bachelor's degree in bioethics from UVA, and a diploma in tropical medicine and hygiene from the London School of Tropical Medicine & Hygiene.

Lou Ann Lance, RN, M.S.N., is a public health program nurse at the New York State Department of Health in the Bureau of Communicable Disease Control, Division of Epidemiology. She serves as a nurse epidemiologist and provides technical assistance and clinical guidance to local and state jurisdictions for MCM screening and dispensing operations, including PODs and community reception center sites. She is responsible for developing medical and epidemiological data collection and screening protocols, including clinical algorithms, and serves as a member of the program leadership team to guide all-hazard development priorities for the New York State Countermeasure Data Management System. She routinely provides onsite clinical leadership for large-scale immunization and mass dispensing events. Until 2011, Ms. Lance served as the clinical director for a local health department where she led a team of public health professionals responsible for all jurisdictional public health education and prevention activities as well as communicable disease, nutrition, and emergency preparedness and response programs. She also provided administrative and clinical oversight for the Article 28 dental clinic and a certified home health agency. Ms. Lance previously served as an adjunct professor at Elmira College and a clinical associate at the State University of New York at Binghamton, Decker School of Nursing. Ms. Lance received her bachelor's degree from Cedar Crest College, Allentown, Pennsylvania, and completed her M.S.N. degree at Syracuse University.

Joseph Larsen, Ph.D., is the acting director of the Division of CBRN Medical Countermeasures within the BARDA. In that role, he oversees a $2.8 billion fund for the development and procurement of medical products for use during public health emergencies. He is also the BARDA lead for BARDA's work on combating antibiotic-resistant bacteria and is an executive member of CARB-X, a novel $450 million public–private partnership focused on promoting innovation in antibacterial drug development. Dr. Larsen has been actively involved in discussing potential reforms to the

economic incentive structures for antibacterial drug development. Previously Dr. Larsen served as deputy director of BARDA's CBRN Division. During 2010–2014, Dr. Larsen served as chief of the Broad Spectrum Antimicrobials program at BARDA. The goal of this program is to develop additional antimicrobial treatment options needed to counter the growing threat of antimicrobial resistance. In that role, he oversaw a portfolio of approximately $1.2 billion in programs that support the development of novel antibacterial and antiviral drugs. Dr. Larsen also serves as the BARDA representative on the U.S. Transatlantic Task Force on Antimicrobial Resistance. Dr. Larsen received his Ph.D. in microbiology from the Uniformed Services University of the Health Sciences and his B.A. with honors from the University of Kansas.

Eva K. Lee, Ph.D., is the Virginia C. and Joseph C. Mello chair (for health care delivery and operations) and professor in the H. Milton Stewart School of Industrial and Systems Engineering at Georgia Institute of Technology, and director of the Center for Operations Research in Medicine and HealthCare, a center established through sponsorships from the National Science Foundation (NSF) and the Whitaker Foundation. The center focuses on biomedicine, public health, and defense, advancing domains from basic science to translational medical research; intelligent, quality, and cost-effective delivery; and medical preparedness and protection of critical infrastructures. She is a distinguished scholar in Health Systems, Health System Institute at Georgia Tech and Emory University. She is also the co-director of the Center for Health Organization Transformation, an NSF Industry/University Cooperative Research Center. Dr. Lee partners with hospital leaders to develop novel transformational strategies in delivery, quality, safety, operations efficiency, information management, change management, and organizational learning. Her research focuses on mathematical programming, information technology, and computational algorithms for risk assessment, decision making, predictive analytics and knowledge discovery, and systems optimization. She has made major contributions in advances to medical care and procedures, emergency response and medical preparedness, health care operations, and business operations transformation. Dr. Lee serves on the National Preparedness and Response Science Board, a federal advisory committee that provides advice and guidance to ASPR within the HHS, and to the HHS secretary on preventing, preparing for, and responding to adverse health effects of emergencies. She is the principal investigator of an online interoperable information exchange and decision support system for mass dispensing, emergency response, and casualty mitigation. The system integrates disease-spread modeling with response processes and human behavior and offers efficiency and quality assurance in operations and logistics performance. It currently has more than 10,000

public health site users. Dr. Lee has also performed field work within the United States on mass dispensing design and evaluation, and she worked with local emergency responders and affected populations after Hurricane Katrina, the Haiti earthquake, the Fukushima Japan radiological disaster, and Hurricane Sandy. Dr. Lee has received prestigious analytics and practice excellence awards including, the INFORMS Franz Edelman award and the Daniel H. Wagner prizes for novel cancer therapeutics, bioterrorism emergency response dispensing for mass casualty mitigation, optimizing and transforming clinical workflow and patient care, vaccine immunity prediction, and reducing hospital-acquired conditions. She is an INFORMS fellow and has received seven patents on innovative medical systems and devices.

Alison Levy, M.P.P., CEM, is the emergency operations manager for Public Health–Seattle and King County, a metropolitan health department serving a diverse jurisdiction of more than 2 million people. As the second in command for the public health preparedness program, she oversees a suite of capabilities, including emergency operations, medical materiel management, MCM dispensing, responder health, volunteer management, and training and exercise. She is a past chair of the National Association of County and City Health Officials' MCM work group and serves as a mentor to new public health preparedness coordinators across the country. She is a frequent national speaker on alternative dispensing modalities, including pharmacy- and health care–based mass dispensing and closed points of dispensing. Ms. Levy has worked in the field of PHE preparedness since 2002, and in that time has coordinated the health and medical response to more than 50 emergencies. Prior to working in public health preparedness, she was a health policy analyst with AARP in Washington, DC. She completed her master's degree in public policy at American University.

Boris D. Lushniak, M.D., M.P.H., Rear Admiral (retired), has been the dean of the School of Public Health at the University of Maryland since January 2017. Prior to that, he served as a professor and chair of the Department of Preventive Medicine and Biostatistics and Professor of Dermatology, F. Edward Hébert School of Medicine at the Uniformed Services University of the Health Sciences in Bethesda, Maryland. Dr. Lushniak was the U.S. Deputy Surgeon General from November 2010 to September 2015, assisting the Surgeon General to articulate the best available scientific information to the public to improve personal health and the health of the nation. He also oversaw the operations of the USPHS Commissioned Corps, comprising approximately 6,700 uniformed health officers who serve in locations around the world to promote, protect, and advance the health and safety of our nation. Dr. Lushniak served as acting surgeon general from July 2013 to December 2014 and was responsible for the release of the

50th Anniversary Surgeon General's Report on Smoking and Health and the first-ever Surgeon General's Call to Action to Prevent Skin Cancer. From January to March 2015 he served as commander of the USPHS Monrovia Medical Unit in Liberia, the only U.S. government hospital providing care to Ebola patients. Dr. Lushniak began his USPHS career in 1988 in the Epidemic Intelligence Service and initially served with CDC's National Institute for Occupational Safety and Health (NIOSH) in Cincinnati, Ohio, where he conducted epidemiological investigations of workplace hazards. In 1993 he completed a dermatology residency at the University of Cincinnati and established an occupational skin disease program at NIOSH. He also served on assignments in Bangladesh, St. Croix, Russia, and Kosovo, was part of the CDC/NIOSH team at Ground Zero and part of the CDC anthrax team in Washington, DC. In 2004 he transitioned from CDC to FDA in the Office of Counterterrorism and was appointed FDA assistant commissioner in 2005. He was deployed to Hurricane Katrina and also served as the FDA deputy incident commander for the 2009 pandemic response. He was promoted to Rear Admiral, Lower Half in 2006 and attained the rank of Rear Admiral, Upper Half in 2010. He retired from USPHS On October 1, 2015, after 27 years of service. He was admitted to the 6-year Honors Program in Medical Education at Northwestern University and completed his B.S. degree in 1981 and M.D. in 1983. In 1984 he completed an M.P.H. degree at Harvard University. He completed a residency in family medicine in 1987 (St. Joseph Hospital, Chicago) and maintains certifications in dermatology and preventive medicine (occupational). A firm believer in leadership by example, Dr. Lushniak promotes the core messages of the National Prevention Strategy via his active lifestyle.

Carmen Maher, M.A., RN, RAC, is a nurse officer in the USPHS Commissioned Corps. She is an assistant surgeon general and is currently serving as acting assistant commissioner for counterterrorism policy and acting director of the Office of Counterterrorism and Emerging Threats in the Office of the Chief Scientist, FDA. In this capacity, Rear Admiral (RADM) Maher is responsible for providing leadership, coordination, and oversight for FDA's national and global health security, counterterrorism, and emerging threat portfolios. She serves as FDA's point of entry on policy and planning matters concerning counterterrorism and emerging threats and collaborates across the U.S. government and internationally on actions to advance global health security and U.S. national security. RADM Maher works in collaboration with other U.S. government agencies to define and prioritize requirements for MCMs to respond to public health emergencies, coordinate research for evaluating MCMs, set strategies for deployment and use of MCMs, and facilitate access to MCMs during public health emergencies. RADM Maher also leads FDA's Medical Countermeasures Initiative, a key component of

a broad U.S. government program to improve the United States' capacity to respond quickly and effectively to public health emergencies. RADM Maher has supported MCM and counterterrorism programs at FDA since 2006. From 2002 to 2006, she served as nurse officer and lead regulatory officer for preclinical and early clinical development of infectious disease vaccines and therapeutics at the Division of Microbiology and Infectious Diseases, NIAID, NIH. RADM Maher began her nursing career in 1993 as an ensign in the U.S. Navy, assigned to the National Naval Medical Center in Bethesda, Maryland. She has more than 20 years' experience in nursing, regulatory affairs, clinical trials and medical product development, public health, and emergency response. RADM Maher earned an associate's degree and B.S.N. from the University of Puerto Rico. She earned an M.A. in national security and strategic studies with highest distinction from the U.S. Naval War College in Rhode Island, and holds a regulatory affairs certification in U.S. health care product regulations.

Deven McGraw, J.D., M.P.H., L.L.M., is the deputy director for Health Information Privacy at the HHS OCR and is the acting chief privacy officer for the ONC. She is a well-respected expert on HIPAA rules and brings to her positions a wealth of experience in both the private sector and the nonprofit advocacy world. Prior to joining HHS, she was a partner in the health care practice of Manatt, Phelps & Phillips, LLP. She previously served as the director of the Health Privacy Project at the Center for Democracy and Technology, which is a leading consumer voice on health privacy and security policy issues, and as the chief operating officer at the National Partnership for Women and Families, where she provided strategic leadership and substantive policy expertise for the partnership's health policy agenda. Ms. McGraw graduated magna cum laude from the University of Maryland. She earned her J.D., magna cum laude, and her L.L.M. from Georgetown University Law Center and was executive editor of the *Georgetown Law Journal*. She has an M.P.H. from the Johns Hopkins University School of Hygiene and Public Health.

Amanda Fuller Moore, Pharm.D., served as the North Carolina SNS, CHEMPACK, and Cities Readiness Initiative coordinator for 11 years. Currently, she is the interim bioterrorism coordinator for the North Carolina (NC) Department of Health and Human Services Division of Public Health and will transition to serve as the NC Division of Public Health Pharmacist. After graduating from the University of North Carolina School of Pharmacy in 2003, she completed two pharmacy residencies at Wake Forest University Baptist Medical Center in Winston Salem, NC, where she specialized in critical care. After gaining hands on experience with

SNS after Hurricane Katrina, Dr. Moore joined the NC Division of Public Health's Office of Public Health Preparedness and Response. As part of her responsibilities, she worked with all local health departments and hospitals in North Carolina to ensure they met CDC requirements for SNS. She also oversaw other pharmacy projects related to bioterrorism and natural disasters, including MCMs for radiation emergencies and pandemic planning. In addition, Dr. Moore works with the Epidemiology Section on 340b issues, serves as the Board of Pharmacy Liaison, and participates in the HHS Pharmacy Task Force.

J. Marc Overhage, M.D., Ph.D., is the chief medical informatics officer and vice president for Strategic Intelligence for Cerner. Prior to this role he was the founding chief executive officer of the Indiana Health Information Exchange and was director of Medical Informatics at the Regenstrief Institute, Inc., and the Sam Regenstrief Professor of Medical Informatics at the Indiana University School of Medicine. He has spent more than 25 years developing and implementing clinical and scientific systems and evaluating their value. Working at the Regenstrief Institute, he created a community-wide electronic medical record (the Indiana Network for Patient Care) containing data from many sources including laboratories, pharmacies, and hospitals in central Indiana. More than 104 acute care hospitals and more than 22,000 physicians participate in the system, which includes inpatient and outpatient encounter data, laboratory results, immunization data, and other selected data. To create a sustainable financial model, he helped create the Indiana Health Information Exchange, a not-for-profit corporation. In addition, Dr. Overhage has developed and evaluated clinical decision support including inpatient and outpatient computerized physician order entry and the underlying knowledge bases to support them. He practiced general internal medicine for more than 20 years in ambulatory, inpatient, and emergency care settings. Over the past decade, Dr. Overhage has played a significant regional and national leadership role in advancing the policy, standards, financing, and implementation of health information exchange. He serves on the HIMSS Board of Directors and has served on the HIT Standards Committee, the National Committee for Vital and Health Statistics, and the Board of Directors of the National Quality Forum, eHealth Initiative, and the American Medical Informatics Association. Dr. Overhage earned his M.D. and a doctorate in biophysics from the Indiana University School of Medicine, where he also completed a residency in internal medicine and served as chief resident in medicine, and he completed a fellowship in medical informatics at the Regenstrief Institute. He is a fellow of the National Academy of Medicine, a master of the American College of Physicians, and a fellow of the American College of Medical Informatics.

Anita Patel, Pharm.D., M.S., is a senior advisor and the lead for pandemic medical care and countermeasures with the Influenza Coordination Unit in the National Center for Immunization and Respiratory Disease (NCIRD), CDC. She is a clinical pharmacist with more than 13 years of experience in managing and improving programs related to public health response, including implementing new strategies and improving systems for drug and vaccine dispensing and administration, creating new tools for communication and surveillance, and science-based operational solutions. Prior to her role in NCIRD, Dr. Patel spent more than 10 years providing scientific oversight, management, strategic development, and budget planning for the CDC's SNS. Her past experience also includes having a key role in CDC's MCM response efforts for various responses, including Hurricane Katrina, the 2009 H1N1 influenza pandemic, and the 2014 Ebola response. Dr. Patel graduated with a doctorate in pharmacy from the University of the Sciences, Philadelphia College of Pharmacy, and completed a 2-year Rutgers post-doctoral pharmaceutical industry fellowship. She also holds a master's degree in biosecurity and disaster preparedness from Saint Louis University School of Public Health.

Amanda F. Peppercorn, M.D., is a late-stage clinical development leader at GSK. She attained her medical degree at Harvard Medical School in 1998 and completed her internal medicine residency and adult infectious diseases fellowship at Massachusetts General Hospital. She was on faculty at the University of North Carolina (UNC) at Chapel Hill, from 2005 to 2009, focusing on immune-compromised hosts (transplant infectious diseases and HIV), and she continued as an adjunct professor of medicine at UNC until 2014. Since joining GSK in 2009, she has played a leadership role in the development of biomedical countermeasures, leading the programs for raxibacumab, a monoclonal antibody treatment for anthrax, and intravenous zanamivir, an intravenous treatment for severe and/or pandemic influenza. She has experience leading a large cross-functional matrix team in the development and execution of Phase 2 and 3 clinical trials, engaging with U.S. and global regulatory agencies, and partnering with key public health agencies such as BARDA and CDC.

Paul E. Petersen, Pharm.D., is the director of the Tennessee Department of Health's Emergency Preparedness Program. He serves as principal for Tennessee's federally funded ASPR Hospital Preparedness Program (HPP) and the CDC Public Health Emergency Preparedness (PHEP) cooperative agreements. He oversees the operations and strategic direction of approximately 120 staff members statewide. Dr. Petersen serves as lead in Tennessee's response to all public health and medical emergencies. Tennessee has experienced a wide range of threats and public health emergencies requiring

decisive action by the HPP-PHEP–funded Emergency Preparedness program staff, health care coalitions, and partners. Events of the past 5 years include the 2012 fungal infections outbreak, 2013 Jefferson County Interstate bus crash, 2014–2015 Ebola infections, 2015 Blount County train derailment, 2016 Zika infections, and the 2016 Gatlinburg wildfire response. Each event has presented opportunities to demonstrate the life-saving impact of the infrastructure built by preparedness funding over time. Dr. Petersen earned his doctorate of pharmacy at the University of the Pacific Thomas J. Long School of Pharmacy and Health Sciences. He completed his post-graduate pharmacy practice residency at Saint Thomas Hospital in Nashville, where he also served as the clinical operating room pharmacist prior to his move to state government. He is an active member of several professional public health and pharmacy associations. He also serves on various national preparedness policy committees, including work with the National Academy of Sciences.

Richard Platt, M.D., M.Sc., is an internist and infectious disease clinician and epidemiologist. He is professor and chair of the Harvard Medical School Department of Population Medicine and executive director of the Harvard Pilgrim Healthcare Institute. He is principal investigator of the FDA Sentinel system, which has created a distributed data network based on information available to national insurers, health plans, and CMS. He led the development, with the Massachusetts Department of Public Health, of ESPnet, a system for doing real-time EHR-based surveillance for both syndromes of interest and individually notifiable conditions. This work was funded by a CDC National Center of Excellence in Public Health Informatics and ONC. He is also co-principal investigator of the National Patient-Centered Clinical Research Network Coordinating Center, which is developing standard methods for extracting and using EHR data for multiple uses. Dr. Platt co-leads the coordinating center of the NIH Healthcare System Research Collaboratory and leads a CDC Prevention Epicenter. He co-chairs the CER Innovation Collaborative of the National Academy of Medicine's Leadership Consortium for a Value and Science-Driven Health System, and he is a member of the American Medical Colleges Advisory Panel on Research.

Scott Proestel, M.D., is the director of the Division of Epidemiology at the FDA Center for Biologics Evaluation and Research. His division uses active and passive surveillance strategies to identify new safety issues with medical therapies approved for use in the United States. He is the primary investigator for a project exploring the use of IBM Watson to perform causality assessments of spontaneous adverse event reports submitted to the FDA Adverse Event Reporting System and the Vaccine Adverse Event

Reporting System. Dr. Proestel received his bachelor's degree in biology from Johns Hopkins University and his medical degree from Columbia University College of Physicians & Surgeons. He completed his internal medicine residency at Johns Hopkins Hospital.

Joe Vasey, Ph.D., is a health care epidemiologist with more than 25 years of experience in health outcomes and health care quality research. At Practice Fusion, Dr. Vasey is responsible for the design, planning, oversight, and interpretation of studies related to quality of care and outcomes of care based on data collected through the Practice Fusion platform. Before working at Practice Fusion, Dr. Vasey was with Quintiles and General Electric Healthcare. At Quintiles, he served as director of Epidemiology, Late Phase, and Real-World Evidence, where he was responsible for the development, planning, scientific oversight, and execution of programs and studies in clinical data services for the biopharmaceutical industry. He occupied a similar position at GE Healthcare IT. Prior to that, Dr. Vasey held a research scientist appointment at Penn State's Center for Healthcare and Policy Research, where, in addition to his research activities, he taught graduate-level courses in statistics and research methods.

Adam Wilcox, Ph.D., is the chief analytics officer at the University of Washington (UW) School of Medicine and a professor of biomedical informatics at UW. He has broad experience in applied and research informatics, with experience both in academia and health care delivery organizations. He leads efforts to develop and implement a data and analytics strategy to help UW Medicine effectively use data to improve care delivery and transformation. Nationally, he is noted for his work with designing, developing, and sustaining research data systems for populations with research and EHR data; for design and implementation of health information systems; and for advancing methods in sustainability of data systems. Previously, he was a director of medical informatics at Intermountain Healthcare, where he led Intermountain's clinical decision support efforts and directed its analytic health repository. At Columbia University and New York Presbyterian Hospital, he designed research systems that advanced patient-reported data for population health, and he was the director of clinical databases, managing both the clinical data repository and data warehouse. Prior to this role, he worked at Intermountain Healthcare where he led efforts in development of primary care and care management systems. He is an elected fellow of the American College of Medical Informatics, a senior editor for *eGEMs*, and a Clinical Informatics Subcommittee member for the American Board of Preventive Medicine, which administers the board examination for the clinical informatics subspecialty. He has authored more than 100 book chapters, peer-reviewed articles, and abstracts in clinical informatics. In

2015, he was appointed a member of the PCORI Methodology Committee, where he is a leader on that committee in informatics and investigating issues with the use of secondary data for outcomes research.

Yon C. Yu, Pharm.D., is the associate director for regulatory affairs in the National Center for Emerging and Zoonotic Infectious Diseases, CDC. She provides scientific regulatory expertise and programmatic support for CDC's oversight regarding stockpiled MCMs. Among other tasks, she coordinates to ensure that FDA-compliant regulatory mechanisms are in place for the stockpiled MCMs to facilitate their rapid deployment and optimal clinical use during potential public health emergencies involving high-consequence or emerging threats such as pandemic influenza, anthrax, and botulism. She also leads regulatory support for various experimental drugs that are only available through CDC for routine public health needs regarding rare diseases, such as Chagas disease, free-living amoebae infections, and malaria given the lack of approved treatment options. She coordinates CDC's assessment of unmet medical needs and most effective drugs for a given threat agent to develop the protocols that inform and guide the health care providers about the appropriate safe and effective use of the MCMs.