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**How to Steward Medical Countermeasures
and Public Trust in an Emergency –
A Communication Casebook for
FDA and Its Public Health Partners**

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Chapter One: Introduction

The nation must have the nimble, flexible capability to produce and effectively use MCMs in the face of any attack or threat, whether known or unknown, novel or reemerging, natural or intentional. These capabilities must be communicated to the American public before and during an emergency.

-- 2015 Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan, p. 7¹

Introduction

How FDA and other US government officials convey information about medical countermeasures (MCMs) will affect uptake, compliance, and ultimately survival in the aftermath of a natural disease emergency or a chemical, biological, radiological, or nuclear (CBRN) attack. Moreover, effective communication regarding MCMs has the potential to strengthen psychological resilience as well as engender public trust in science, government, and public health. The purpose of this casebook is to provide FDA and other officials who deliver public health information with “real world” inspired opportunities for reflective learning on the principles of effective MCM communication and on the wider contexts that influence the development, delivery, and consumption of accurate, timely, and meaningful MCM information in an emergency. Communication successes will better enable FDA to fulfill its regulatory role and activities and “facilitate the development of and access to safe, effective, and quality MCMs” to counter CBRN and emerging infectious disease threats (for more on FDA’s MCM-related mission, activities, and collaborators, see Table 1).²

This opening chapter previews the casebook findings, and it reviews expert-vetted, model practices in risk and crisis communication in order to provide a self-contained takeaway for FDA users seeking general advice on how to communicate effectively about MCMs in an emergency. In addition, this introduction describes the methods used to develop the casebook including integrating input from the Expert Working Group on MCM Emergency Communication Strategies (Table 2). Each of the 4 chapters that follow represents an in-depth case study of an emergency in which communication regarding MCMs was important: the recent Ebola outbreak, the 2011 Fukushima nuclear accident, the 2009-10 H1N1 influenza pandemic, and the 2001 anthrax letter attacks. The cases are comprised of a brief background on the emergency, a selection of serious communication challenges faced by FDA and its partners, and forward-looking implications, including action items for the FDA to help mitigate comparable issues in the future.

The 4 case studies are snapshots in time to memorialize the lessons learned from the experience, and they are not intended as a comprehensive assessment or history of after action implementation efforts by the FDA and US government in subsequent years. Like much of the leading crisis and risk

Table 1. FDA's MCM Mission and Collaborators –
Setting the Context for MCM Emergency Communication

The FDA's overarching objective in relation to MCMs is to "facilitate the development of and access to safe, effective, and quality MCMs" to manage the health impacts of CBRN emergencies and emerging infectious disease threats.² The organizational structure underpinning this objective is the Medical Countermeasures Initiative (MCMi), coordinated by the Office of Counterterrorism and Emerging Threats (OCET), within the FDA Office of the Chief Scientist, in partnership with other FDA offices and centers, including the Office of Regulatory Affairs (ORA) and the agency's 3 medical product centers – Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), and Center for Devices and Radiological Health (CDRH).³ The MCMi was launched in 2010 to capitalize upon the FDA's existing MCM programs, and by applying additional resources, to expand and strengthen the agency's MCM efforts even further, addressing many of the issues identified during the anthrax and H1N1 responses.³

The FDA engages in an array of activities to help advance the development and availability of MCMs. These activities stretch across the entire MCM life cycle and include:

- Expanding the scientific knowledge base to support regulatory decision-making. Through intra- and extramural research support and strategic partnerships with US government agencies, academia, and industry, FDA works to continuously improve the scientific and technical means for assessing MCM safety, efficacy, quality, and performance.²
- Conducting efficient and effective regulatory review. Tasks in this vein include clarifying for sponsors, applicants, and the federal agencies supporting product development the requirements for approving or making available investigational MCMs, as well as reviewing and approving MCM marketing applications that meet standards for safety, efficacy and quality.²
- Helping ensure an adequate supply of MCMs, as exemplified by granting expiry dating extensions for MCMs after testing them for stability and quality and by inspecting MCM production facilities to ensure the use of current good manufacturing practices and to proactively resolve issues that could lead to potential product shortages.²
- Facilitating a swift and effective emergency response. Illustrative tasks include expediting the regulatory review of data for critical products in the development pipeline; when necessary, enabling access to potentially available MCMs that are not approved by the FDA through an appropriate mechanism such as an Emergency Use Authorization (EUA); and monitoring the MCM supply chain to identify and forecast product shortages and potential promotion of fraudulent products.²
- Providing technical support, with regard to the regulatory matters within FDA's authority, to key MCM partners including the state, tribal, local, and territorial (STLT) stakeholders charged with stockpiling, distributing, and dispensing or administering MCMs during and in anticipation of a health emergency.⁴

Table 1. FDA’s MCM Mission and Collaborators –
Setting the Context for MCM Emergency Communication, continued

Along with the larger MCM community, the FDA participates in the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE). Led by the US Department of Health and Human Services (HHS) Assistant Secretary for Preparedness and Response (ASPR) in the interest of national health security, the PHEMCE is the body that coordinates the MCM-related efforts within HHS (ie, FDA, Centers for Disease Control and Prevention [CDC], and National Institutes of Health [NIH]) and in cooperation with interagency partners at the Departments of Veteran Affairs (VA), Defense (DoD), Homeland Security (DHS), and Agriculture (USDA).¹ The PHEMCE also engages non-Federal partners including STLT governments, public health systems, academia, private industry, and the larger US population.¹

Complex divisions of labor exist among the PHEMCE federal partners, with each agency at times playing either a leading or supporting role, depending upon the mission component as well as agency authority and jurisdiction.⁵ A sampling of HHS agencies and their leading roles in relation to MCMs for the civilian population follow below, to help put FDA’s contributions (and its communication role) in context; readers are encouraged to consult more comprehensive accounts¹ for further clarification and detail:

- ASPR is responsible for developing the strategic framework to prioritize PHEMCE resources and investments, based on the DHS-led threat and risk assessment, and other inputs such as medical consequence and public health response assessments.⁵ Via the Biomedical Advanced Research and Development Authority (BARDA), ASPR leads in supporting the advanced development and scale up of MCM manufacturing capacity and in the procurement of certain MCMs for the Strategic National Stockpile (SNS).⁵
- CDC leads the procurement and maintenance of the commercially available MCMs amassed for the SNS.⁵ In collaboration with ASPR, CDC also coordinates the development of federal response plans, policy, guidance, and communication; develops strategies for the allocation and clinical use of MCMs; and coordinates interactions with STLT and private entities “to provide timely and effective deployment, distribution, dispensing, and administration” of MCMs in an emergency.⁵
- NIH carries out and supports basic research on health threats; the knowledge generated then informs the development of medical products as well as strategies for prevention, diagnosis, and treatment.⁵ NIH plays an important support role in evaluating MCM safety and performance, such as through clinical trials management.⁵
- FDA’s role is to ensure MCMs are safe and effective, including – in conjunction with the CDC – monitoring the safety and performance of deployed MCMs during and after a public health emergency.⁵

Table 2. Expert Working Group on MCM Emergency Communication Strategies

- RADM Kenneth W. Bernard, MD, USPHS (Ret.), Special Advisor, White House National Security Council
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- Julie Casani, MD, MPH, Public Health Preparedness Director, North Carolina Division of Public Health, North Carolina Department of Health and Human Services
- Gail H. Cassell, PhD, Senior Lecturer, Department of Global Health and Social Medicine, Harvard Medical School; Senior Scientist, Division of Health Equity, Brigham and Women's Hospital
- Kevin Fain, JD, MPH, Senior Advisor for Policy and Research, ClinicalTrials.gov Program, National Library of Medicine, National Institutes of Health
- John D. Grabenstein, RPh, PhD, Executive Director, Global Health and Medical Affairs, Merck Vaccines
- Michelle Groman, JD, Director of Bioethics Grants, Strategy, and Special Projects, The Greenwall Foundation
- Dan Hanfling, MD, Special Advisor, Emergency Preparedness and Response, Inova Health System
- Lisa M. Koonin, DrPH, MN, MPH, Senior Advisor and Lead, Pandemic Medical Care and Countermeasures Task Force, Influenza Coordination Unit/Office of Infectious Diseases, Centers for Disease Control and Prevention
- Michael G. Kurilla, MD, PhD, Director, Office of BioDefense, Research Resources, and Translational Research; Associate Director BioDefense Product Development, Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health
- Heidi J. Larson, PhD, Senior Lecturer, Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine; Associate Clinical Professor, Department of Global Health, University of Washington
- CAPT Deborah Levy, PhD, MPH (USPHS), Lead, Healthcare Preparedness Activity, Division of State and Local Readiness, Centers for Disease Control and Prevention
- Meredith Li-Vollmer, PhD, Risk Communication Specialist, Public Health, Seattle and King County
- Linda M. MacIntyre, PhD, RN, Chief Nurse, American Red Cross
- Gretchen Michael, JD, Director of Communications, Office of the Chief Operating Officer, Office of the Assistant Secretary for Preparedness and Response, US Department of Health and Human Services
- Seth Mnookin, Associate Director, MIT's Graduate Program in Science Writing
- Ann Norwood, MD, COL, MC, USA (Ret.), Contributing Scholar, UPMC Center for Health Security
- Cynthia Pellegrini, Senior Vice President, Public Policy and Government Affairs, March of Dimes
- Greg Pratt, RPh, Emergency Preparedness Coordinator, Michigan Pharmacists Association
- Sandra Crouse Quinn, PhD, Associate Dean for Academic Affairs; Senior Associate Director, Maryland Center for Health Equity; Professor, Department of Family Science, School of Public Health, University of Maryland
- Richard Reed, MSW, Senior Vice President, Disaster Cycle Services, American Red Cross
- Mitch Rothholz, RPh, MBA, Chief Strategy Officer, American Pharmacists Association
- Sara E. Rubin, MPH, MA, Director, Research, National Association of Chain Drug Stores
- Lainie Rutkow, JD, PhD, MPH, Associate Professor, Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health
- Jeannette Sutton, PhD, Assistant Professor, Department of Communication; Director, Division of Risk Sciences, University of Kentucky
- Shari R. Veil, MBA, PhD, Associate Dean for Undergraduate Affairs; Associate Professor of Communication, College of Communication and Information, University of Kentucky

communication literature, the casebook relies upon real crises to illustrate successful or failed application of model communication practices. Accounts of actual events can accelerate learning: people reason effectively through analog and not just general, abstract principles; contextualization makes broader principles meaningful and memorable; and cases provide reflective thinking and reinforce users' ability to apply that knowledge in future settings.⁶⁻⁷ Moreover, industry-specific cases can motivate users who see direct, practical relevance to familiar issues and settings (eg, MCMs in emergency contexts).⁸

What Defines Good Stewardship of MCMs in a Public Health Emergency?

MCM stewardship comprises strategies to optimize population wellbeing in an emergency, including reduced morbidity and mortality, enhanced psychological resilience, and preserved faith in the institutions of science, government, and public health.

Medical countermeasures – the drugs, biologics (eg, vaccines), and devices (eg, in vitro diagnostics, respiratory protective devices) used to diagnose, prevent, or treat the human health impacts of CBRN emergencies and emerging infectious disease threats – are an essential part of national health security.⁹ Appropriate shepherding of countermeasures in an emergency entails the following objectives:

- Enabling citizens to make smart, informed decisions about MCM uptake;
- Maximizing benefit and minimizing harm, including psychological impacts;
- Getting MCMs to individuals and groups most in need of them;
- Allocating scarce MCMs in ways that preserve public lives and public trust;
- Protecting the public from fraudulent products and false product claims that can be harmful, feed unfounded hope, or waste scarce household money;
- Testing unproven MCMs in a scientifically rigorous way that provides interpretable data;
- Supporting non-pharmaceutical measures that empower people to protect themselves.

Why Do Emergencies Present Special Communication Challenges for Stewards of MCMs?

Public health emergencies are exceptional events, and many of the drugs, vaccines and medical devices now being developed to manage them are also outside the norm.

MCMs, as a class, are often novel products, rare in number, and limited in supply:

There are insufficient MCMs for preventive and therapeutic purposes, to match the number and diversity of high-priority threats to US health and security. While the nation's MCM inventory does include large quantities of some well-established products, many CBRN countermeasures are recent innovations, still under development, and/or not scaled for mass production. Some MCMs may be among the first being developed for a specific threat, potentially through innovative ways like

recombinant and molecular techniques and the use of flexible, disposable manufacturing component and multiuse facilities.¹⁰

MCMs target health threats that are themselves extraordinary:

MCMs are medical products intended to protect against high-priority threats that have the capacity to affect US national security.⁹ Such high-priority threats include agents that can lead to substantial illness and death and, by virtue of their lethality, unfamiliarity, and/or gruesome clinical presentation, can induce significant fear in the population. Among the current high priority threats are anthrax, smallpox, viral hemorrhagic fevers, nerve agents, and radiological agents. Development of a flexible infrastructure to support rapid production of MCMs for future, as-yet unknown threats is also a national goal.

MCMs used in an emergency may have limited prior clinical experience in humans:

Many of the high-priority threats for which MCMs are being developed do not occur naturally to an extent that would allow for field efficacy studies in humans, and it is not ethical to conduct human challenge studies with many threat agents. In these situations, efficacy data from animal studies may be used if the results can reasonably be extrapolated to expected human use. MCMs may have been FDA-approved on the basis of efficacy studies in animals, may be unapproved but authorized for use during the crisis, or may not have been previously used in certain populations (eg, pediatric populations).⁹ Helping to inform clinical decisions during the public health response requires near real-time monitoring and assessment of MCM performance such as through enhanced adverse event tracking, reporting, analysis, and communication.⁹

Typically time-consuming, product development and review processes can be accelerated for MCMs:

FDA applies its rigorous review and approval regulations and policies to MCMs, like all medical products. FDA does have the authority to help speed up MCM development and availability through processes that include fast track, breakthrough therapy, accelerated approval, priority review, and orphan designation, as well as through the enhanced authorities and resources specifically devoted to MCMs.^{9,11}

Prompt emergency access to MCMs may involve atypical procedures:

Even with an approved product, rapid distribution and administration to a large affected population may call for an unconventional approach: eg, extending the labeled expiration date; dispensing a product without an individual prescription; allowing deviations in storage temperatures during a response; enabling innovative delivery methods such as postal carriers equipping households with antibiotics in event of an anthrax attack; making available streamlined, easy to understand “emergency use instructions” concerning the product’s approved use.¹² In the case of an unapproved, investigational product, or the unapproved use of an approved product, FDA has certain mechanisms to facilitate emergency access (eg, through an Investigational New Drug [IND] or Device Exemption [IDE] process, as well as through Emergency Use Authorization [EUA]).⁹

Liability immunity can exist for a MCM-related claim of loss:

The Secretary of Health and Human Services can issue a PREP Act declaration to confer liability protection (absent willful misconduct) in relation to the manufacture, testing, development, distribution, and administration, and use of MCMs for an actual or potential emergency threat. Claimants may have recourse to the Countermeasures Injury Compensation Program.¹²

How Will MCM Communication Dynamics Evolve Over the Life Cycle of an Emergency?

People’s level of interest, topics of concern, emotional requirements, demand for information, capacity for processing information, and objective public health needs will evolve over the life cycle of an emergency, prompting the need for a phased approach to MCM communication.

Before the Emergency

1. Health threats are abstract and personally irrelevant. People commonly believe that they are, as a rule, “safe” and that a disaster only happens to “other” people.¹³
2. A person may be unaware of the risks and benefits of a specific MCM; if they are aware, then the risks of MCM use may be the more salient issue given that there is no imminent threat.
3. Communication that enables individuals to personalize a risk, envision how certain actions protect against that risk, and feel a degree of self-efficacy in performing such actions may motivate people to take protective measures in advance of an emergency (eg, learn more about a MCM or an entity involved in its distribution and administration).¹⁴⁻¹⁵
4. On-going, repetitive, and mutually reinforcing messages from diverse sources are necessary to break through everyday background noise and to prompt a desired public behavior (eg, seeking out more information about an agency’s role in stewarding MCMs).¹⁶
5. Engaging in a preparedness behavior (eg, learning about local plans for MCM dissemination) is the end result of many prior steps: ie, thinking about surprise events in advance, seeking out additional information, conferring with others, deciding to do something, and then taking action. A continuous stream of reinforcing messages helps people successfully complete this sequence.¹⁶
6. Human ties and social dynamics strongly influence preparedness communication and action. Once receiving preparedness messages, people typically confer with others to assess the significance and relevance of the information; conferral could occur in person or via social media. Moreover, a person is more likely to engage in a preparedness behavior when they see others around them doing the same.¹⁶
7. Community partners (eg, community- and faith-based organizations, health professionals, private industry, schools and universities, social service providers, volunteer groups) can broaden and deepen the reach and reception of official communication on MCMs. By collaborating with diverse partners, officials can better understand specific audiences and tailor

messages accordingly, enlist additional spokespersons who are already respected within their own communities, and enable the adoption of preparedness as a group's own social norm.¹⁶

8. People learn as they interact with the world, developing mental maps along the way that serve as heuristic devices (or shortcuts) for organizing information.^{14,17,18} The operating assumptions that individuals hold around health threats and MCMs in advance will shape how they later make sense of these things during an emergency.
9. The routine, non-crisis timeframe allows public health entities to be more proactive. The opportunity exists to develop careful messages about threats, MCMs, and regulatory processes as part of a longer-term awareness raising campaign.¹⁹⁻²⁰

During the Emergency

1. A health threat is present and potentially dangerous for the person. However, the perception of personal risk may not match the professional appraisal of risk (whether it is higher or lower).²¹⁻²²
2. Risk/benefit information about a MCM is more salient (ie, personally relevant and significant), and public demand and need for these facts becomes more acute.
3. At the outset of a crisis, an information deficit typically exists – circumstances are still unfolding, facts are few in number, media interest is piqued, the full scope of the problem is uncertain, communication channels may be disrupted, and only partial perspectives are possible.²³
4. When a threat is present, people are hungry for information, and they rarely if ever get too much information.²⁴ They want to know as much as they can about potential dangers for which officials have sounded an alarm, and they will turn to the media and sources they consider trustworthy to find out more details before protective actions are started.²⁵ In contrast, uninformed authorities may hesitate to sound any alarm, out of an unsubstantiated fear regarding the potential for public panic.¹⁶
5. The urgency of the situation coupled with heavy demand for information, by the media and the public, may be at odds with well-reasoned but protracted government procedures for “clearing” information before it can be shared publicly.²³ The delay can lead to an information vacuum that is potentially filled by unreliable sources and inaccurate information.
6. People who are worried and distressed due to a perceived threat have a reduced capacity to process information effectively and efficiently and to engage in complex decision-making.^{14,17,26} Protective action information, however, should not be simplistic and short out of fear people will be overwhelmed or confused; instead, messages should meet style and content criteria proven to prompt the desired public response (points 8-9 below).²⁴⁻²⁵
7. For the public to implement the protective behavior desired by officials, they typically undergo a sequence of perceptual, cognitive, and behavioral steps: hearing the warning, understanding the information, believing the warning is credible and accurate, concluding that the message applies to them (ie, they are at risk if they do not take protective action), confirming the warning is genuine and others are taking heed, deciding to take action, and carrying out that decision to act.²⁴⁻²⁷ Also affecting this process is whether the protective action is feasible.²⁸⁻²⁹

8. Five kinds of information are essential to motivate public compliance with official protective actions: what (ie, the actions the public should take), when (ie, by what time the action should be executed), where/who (ie, which people should or should not take the action as described in clear geospatial, age groups, and other everyday terms), why (ie, the threat and how the protective action will reduce its impact), and whose advice (ie, the person or entities providing the information).^{16,30}
9. People respond well to messages that are jargon-free and use wording that is specific (ie, precise and non-ambiguous), accurate (ie, free from errors that create confusion), certain (ie, authoritative and confident); and consistent.³⁰
10. Government-issued details on MCM risks/benefits and on recommended protective actions will not be the only information available to the public on those topics. Monitoring the “information sea” in which the public is immersed can help reveal if conflicting information is inhibiting the desired response and thus inform necessary corrective actions.¹⁶
11. Information on MCM benefits/risks may change during an emergency as MCMs are used and clinical information is received and analyzed, which could alter the response. Any change in public information regarding benefits/risks will require forthright explanation.
12. The time urgency and dynamic conditions put public health entities in a more reactive mode. Exigencies may require MCM-related message development on the fly, a focus on short-term problems, and quick delivery of information.¹⁹⁻²⁰

After the Emergency

1. Health concerns can shift from the emergency threat to the unintended and lingering consequences of the public health response, including the long-term effects of MCMs, if any.
2. People are in a state of reflection, as they try to make sense of what has happened and why. They rely on images, narratives, and frames of reference around them to help explain what has been seen, heard, and felt in connection with the calamity, and also to provide a meaningful framework for processes of coping, grieving, and rebounding.³¹⁻³²
3. Themes of causality, responsibility, accountability, and the in-/adequacy of the emergency response can dominate the post-crisis period of retrospection.^{19,23,31,33} In a world of instantaneous news and information saturation, the “framing and blaming” that tend to follow epidemics and disasters occur with increasing speed and reach.³³⁻³⁴
4. Communal narratives that give people’s experience of mass tragedy shared meaning and purpose help facilitate recovery after the event.³⁵⁻³⁷ Stories held in common that emphasize capability, adaptability, optimism, collective learning, and a focus on the future can help ease people’s experience of distress and restore their sense of well-being.^{19,35}
5. When the emergency is no longer front page news, the people who have been most affected continue to require emotional support as their feelings of loss and grief set in.²³ Themes of having had access (or not) to a MCM and/or whether the MCM has helped or not may figure prominently in their experiences and personal narratives of the public health emergency.

6. In the aftermath of an extreme event, a “window of opportunity” opens for moving messages that are otherwise ignored (eg, explanations of FDA processes to ensure MCM safety and efficacy before and during an emergency). Officials have people’s rapt attention.³⁸⁻³⁹

What MCM Communication Strategies Should FDA Prioritize for Each Phase of an Emergency?

The impacts of effective MCM emergency communication are largely seen during the crisis. Nonetheless, to be optimal, MCM communication requires groundwork before an emergency ever unfolds. Critical self-reflection and organizational retooling afterward also pre-position an agency like FDA for success during future emergencies.

FDA, in collaboration with its federal partners, is encouraged to implement broadly recommended “best practice” guidance (Table 3) when communicating about MCMs in the emergency context. At the same time, the following represent suggested priorities for FDA tackle in order to strengthen its emergency MCM communication. The action items derive from an analysis of MCM communication concerns emerging during recent emergencies covered at length in the casebook (Tables 4-7) and a larger typology of foreseeable communication dilemmas based upon prior experiences and best professional judgment (Table 8). Under-resourced and heavily burdened agencies like FDA are often forced to communicate in an emergency from a reactive position, rather than a proactive one. Nonetheless, FDA is strongly encouraged to implement as many pre-crisis, preparatory steps as possible so that it can be a nimble and influential communicator in moments of widespread distress.

Before the Emergency

1. **Build Up FDA’s Reputation and Credibility:** As part of everyday activities, enhance public familiarity with how the FDA regulatory mission applies in an emergency and what legal and administrative tools the agency can facilitate public access to MCMs in a crisis.

Repetitious messaging and readily-digestible publications concerning FDA’s “brand” and its response “toolkit” (eg, EUA) can prime people for the agency’s emergency role and help reduce the element of surprise. When a crisis arises, such materials can also be available for people to access without delay. Advance communication materials cannot anticipate every threat and MCM scenario or individual public concern. That is, a pre-prepared playbook of messages for every eventuality is not feasible (although development of high-stakes, audience-tested messages as noted below is advisable). FDA should therefore work to engender greater understanding of, and faith in the agency’s fundamental ability and commitment to protecting public health and safety. When unique, unforeseen circumstances arise, the agency can then rely on its established reputation when stewarding a MCM and implementing a EUA or other regulatory measure. An organization seen to be enacting proven core values in a crisis is more likely to enlist public support and to bolster its reputation.¹⁹

Table 3. Best Practices for Communicating Risk in an Emergency^{20,40-43}

1. Incorporate communication experts, insights, and goals at the outset when developing emergency management policies. Embrace communication as an essential part of “front-end” decision-making rather than the mere function of sharing policy decisions at the “back-end.”
2. Conduct pre-event communication planning that identifies potential threats or hazards, outlines risk reduction approaches, recognizes the resources needed to implement them, and spells out the responsibilities of principal actors.
3. Build pre-crisis partnerships and alliances with other stakeholder entities to coordinate communication resources and activities, enlist their help in better understanding and reaching target audiences, and establish trusted links that can be activated during the crisis period.
4. Accept the public as a legitimate partner in managing an emergency. Recognize the public’s right to know the risks that it faces as well as protective actions that it can take, and plan for the prompt sharing of this information so that people can freely carry out their own informed decisions.
5. Listen to the public before and during the emergency. Find out what people know, think, or want done about risks, and use this to inform communication and emergency response planning. Acknowledge people’s concerns, even if they do not conform to scientific risk assessments. Put yourself in their place and adapt messages.
6. Communicate with honesty, candor, and openness. Be truthful to foster credibility with the public and the media. Relate the truth as it is known, even if it may reflect poorly on the agency, and be frank about the potential severity of any crisis. Promptly make information accessible. Convey information uncertainties, strengths, and weaknesses.
7. Accept uncertainty and ambiguity. In an emergency, acknowledge the dynamism of the situation and the potential need to act before all the facts are known. Be prepared to explain the fluidity of conditions and the measures being taken to fill in the knowledge gaps. Address differing scientific perspectives and international variances as needed.
8. Communicate with compassion, concern, and empathy. Recognize the human dimensions of the emergency, acknowledge people’s distress and extend genuine sympathy and understanding.
9. Respect the unique communication needs of diverse audiences. Be mindful of differences in cultural background, immigrant status, education, technological adeptness, hearing and seeing abilities, and other factors that influence information uptake and processing. Use clear, non-technical language along with graphics to clarify messages; employ multiple language translations where appropriate.
10. Meet the needs of the media and remain accessible. Plan to work diligently with the media before and during an incident knowing that members of the public often rely on news outlets to learn about a crisis or risk.
11. Convey messages of self-efficacy. Provide specific information to the public on how to reduce any potential harm and what can be done to help others. Protective messages can reduce material harm as well as enhance morale by restoring a sense of control over uncertain and menacing conditions.
12. Monitor public responses and update communication efforts to meet people’s evolving information needs.

2. Widen and Reinforce Communication Partnerships: Continuously network with intra- and interagency partners as well as external stakeholder groups to comprehend diverse audiences, coordinate communication resources, and build up trust that can be tapped in an emergency.

FDA cannot be the sole communicator on MCM safety and efficacy to the US populace; it needs others to amplify its messages and to know what diverse audiences require of the agency. Doctors, nurses, pharmacists, state and local health officials, and other frontline professionals interpret MCM risks and benefits for the public, and individuals turn to these and other trusted sources for information. A host of traditional, new, and emerging media platforms transmit critical health information to diverse publics. FDA can bolster current stakeholder ties and create new ones: eg, strengthen the role of the Office for Minority Health in the MCMi to help uncover, understand, and address the MCM communication needs of vulnerable and historically underserved populations; reach further into health professional societies on top of FDA's ongoing participation in national level workshops, meetings, and webinars; and hold informational workshops for journalists to increase media awareness of current practices in regulatory science, including how MCMs are authorized and approved.

3. Anticipate Problems and Rehearse Solutions: Scan in advance for signs of novel communication dilemmas (or evidence of persisting ones), and with agency partners and stakeholders, develop and drill early solutions that can preempt failure and enhance real-time responses.¹⁹

Tabletops can focus on specific communication dilemmas, allowing agency personnel and its collaborators to rehearse challenges and solutions (eg, issuing a timely EUA that strikes the right balance between technical accuracy and ease of comprehension; explaining in an emergency why the government may still not authorize the use of foreign products already used in large populations overseas; addressing public concerns in an emergency about using clinical trials that involve placebos). Table 7 provides a rubric for thinking about MCM emergency communication dilemmas; many of these themes can be interwoven into simulations and used to generate collective ideas about comprehensive mitigation strategies.

4. Set a Research Agenda; Work from the Top Down: Study topics that affect the agency's ability to facilitate good outcomes in an emergency (eg, fewer illnesses and lost lives; preserved public trust); develop and test messages; investigate people's information consumption habits.

Advance research can fortify the agency's ability to communicate on MCMs in a crisis. Recent emergencies suggest that some topics and audiences require prompt, deeper understanding: in particular, the sensitivity among historically underserved populations about unfair distribution of either MCM risks or benefits, and the moral ambiguity that some people attach to randomized controlled trials for investigational products amidst mass tragedy. Other issues and topics also deserve further exploration, when resources allow (eg, polling on FDA as the gatekeeper for MCM safety and efficacy, design/testing of info-graphics to make the EUA process more intelligible). In general, to meet the information needs of citizens who come from diverse cultural, social, and demographic backgrounds, the agency should take steps to understand different audience segments and develop messages that address their concerns.⁴⁴⁻⁴⁵

In conjunction with efforts to “profile” the needs and preferences of intended audiences, the agency can pretest messages and materials as well as media planned for their dissemination, to determine if they resonate with end users.⁴⁶

5. Exceed the Limits of “Printed Statements” Communication: Expand modes of communication to reach a broader, non-technical audience: eg, balance published statements with public remarks, supplement heavy text with graphics, and design the agency website with end users in mind.

As a regulatory agency, FDA is under pressure to represent its public health activities and decisions in ways that are true to the science and in line with legal mandates. Partiality for highly precise terminology and the written word can lead to unintended opaqueness, when broader public understanding around MCMs is called for. Some steps to enhance the agency’s ability to convey messages that are meaningful to a broad audience include: enhancing risk and crisis communication training of individuals serving as the public face of the agency on MCM issues; engaging user experience experts to improve the accessibility and visibility of the FDA website which is the central archive for its key messages and where the agency drives consumers via twitter and other social media; supplementing text-heavy documents with infographics that can help make the agency’s regulatory decisions, processes, and complex topics intelligible to a wider array of audiences; and pre-testing communication with end users to check for comprehensibility.

During the Emergency

1. Keep Ear to the Ground on Responses to the MCM Campaign: Conduct real-time monitoring of traditional and social media to gauge public confidence in the MCM campaign, including rumors, knowledge gaps, and waxing/waning trust, and then adjust messages and outreach strategies.

A strong social media presence, in particular, will allow FDA to “listen” and anticipate potential communication issues before they become full-fledged crises (eg, concerns about MCM use or uptake of alternative or fraudulent products). Social media engagement is not a just-in-time endeavor; the relationships that make social media an effective tool in an emergency are built over time. While technology platforms will evolve, FDA should commit in the near term to provide messages to, and monitor information from the public (and providers) via social media.

2. Address Public Priorities around Self-Protection: During an emergency, help to deliver a clear and obvious signal to the public about the desired protective behavior in the context of a specific threat and recommended MCM(s), if any.

While FDA has specific regulatory responsibilities in an emergency, the agency nonetheless is part of the larger public health response system that has the paramount goal of reducing illness and saving lives. Past emergencies suggest that even if FDA is not a prime responder, the agency should embrace a supportive role in assuring that members of the public have the information they need for self-protective behavior. This supportive role can involve disseminating science-based messages that provide greater legitimacy to the public information and directives of other agencies regarding a health threat and appropriate protective actions.

3. Put Communication “Best Practices” into Action: Act on evidence-informed advice regarding how to communicate when knowledge is uncertain and rapidly evolving in an emergency,¹⁹ when outrage causes the public’s appraisals of risks/benefits to be non-aligned with that of authorities,⁴⁷ and when the goal is to adequately inform health decision-making by the public.⁴⁸
 - a. Uncertainty: Admit limits to the ability of FDA to determine all aspects of the emergency due to missing, complex, or rapidly evolving information. Share in your audience’s distress and describe how FDA will get more answers. When policy positions shift, alert your audience, explain why what you are saying is different from before, and acknowledge any emotive responses to the change.⁴⁷
 - b. Outrage: Recognize variables known to provoke public outrage including dreaded hazards and perceived unfairness, moral indifference, and impacts on vulnerable groups. When these elements are present, do not dismiss them as mere misperception; use values-based language with supporting evidence to enhance public understanding and to diminish impassioned critiques of the agency (see Tables 3-4 for examples).⁴⁷
 - c. Adequacy: Test the adequacy of a communication (eg, on MCM risk/benefit) by checking if it equips a person with information essential to making an effective health decision (ie, it is material), if it reaches a person via their normal information channels and gathering practices (ie, it is accessible), AND if it is readily digestible so that a person can apply it to make a sound choice (ie, it is comprehensible).⁴⁸
4. Show Agility as a Communicator: Communicate knowing the crises are time-sensitive. Strive for minimal time lags in connection with internal FDA clearance procedures for MCM emergency communication to keep up with growing public demands for prompt sharing of information.

Promptly communicating and staying ahead of the issues are critical, because for members of the public, the first source of information often becomes the preferred source.²³ FDA should actively seek out opportunities to communicate with the media and the public in order to ensure key messages are provided frequently and are readily accessible in the memories of target audiences.

After the Emergency

1. Share “After Action” Results and the Path Forward: Publicly share what FDA and its partners learned from MCM use in the health emergency, including response missteps and successes; communicate how the agency plans to address concerns on the basis of that information.¹⁹

In the aftermath of an emergency, it will be important to acknowledge any blunders and outline how systematic changes are being implemented to improve MCM stewardship in the future. The inclusion of external stakeholders in preparation of after-action reports regarding the overall MCM campaign can help increase trust and provide viewpoints that are more representative of public concerns. Recommendations resulting from after-action reviews should be quickly implemented.

2. Plan for Recovery-Themed Communication: Develop crisis resolution and recovery messages in earlier phases of the emergency to address anticipated issues, especially high intensity dilemmas such as MCM scarcity and MCM adverse effects.

Recovery, like response, requires deliberate planning and execution to assure the best outcomes for a community. Recovery narratives that confer meaning on the experience of mass tragedy and that are forward looking can help lessen people’s distress. For instance, messages about the plans to apply any newly acquired data about MCM safety and efficacy to improve future situations will be important for helping to renew a sense of wellbeing.

3. Reassess Overall Communication System Performance: Conduct an “after action” analysis of the agency’s performance as an MCM emergency communicator and incorporate improvements.

Potential issues to consider are: how well did spokespersons perform and is more training in crisis and risk communication necessary; was the clearance process efficient; did unforeseen topics arise that deserve further audience research to be ready for next time; were there any groups to whom the agency could have reached out harder to get them information or to understand their information needs better; what were the successes and how can they be repeated?

Casebook Methods

A project team of analysts at the UPMC Center for Health Security conducted 4 in-depth case studies of select public health emergencies involving MCMs, with input from the Expert Working Group (EWG) on MCM Emergency Communication Strategies (Table 2). This expert panel included top scholars in risk and crisis communication; seasoned MCM developers, producers, and regulators; leading practitioners in medicine, public health, and pharmacy science; and decision makers experienced in public health emergency management. Moreover, the EWG had strong interagency representation (eg, CDC, NIH, HHS/ASPR, and former FDA staff). The purpose of the casebook was to characterize recent communication challenges for FDA, with implications for public behavior around MCMs, and based on leading literature and professional judgment concerning risk and crisis communication, to develop suggestions on how to mitigate similar problems in the future. Tables 3-6 summarize the communication dilemmas and recommendations from chapters 2 through 5.

Casebook development entailed a recursive process of research and analysis by the UPMC team, review and feedback from EWG members and agency sponsors, and external review by authorities on risk communication and medical countermeasures.^a Initially, the project team identified a preliminary

^a External reviewers were Brad Smith, PhD, Policy Director, FasterCures, Milken Institute; Ji Sun Lee, JD, Director, Security and Resilience Program, Survey Research Division, RTI International; Kunal Rambhia, MS, Health Team Lead, Zell Lurie Commercialization Fund, and Doctoral Candidate, University of Michigan; and Rita Obey,

list of potential cases to pursue through a review of LexisNexis, the scholarly literature, and government reports. They later refined the list, based on interviews with the EWG and sponsors to ascertain which issues were priorities. The EWG provided virtual feedback on the final plan to guide casebook research and organization. The 4 selected cases presented a broad range of health threats; MCMs with variable testing, availability, and risk/benefit profiles; social media influences; and trust issues.

Analysts relied primarily upon secondary sources when constructing their case studies, and where noted in individual chapters, also incorporated content from key informant interviews. In general, analysts performed a web-based review of the available scholarly literature using an array of search engines (eg, PubMed, Google Scholar). Using other databases (eg, LexisNexis, Google), they also identified NGO and government reports, news articles, and blogs that provided further details, especially in the case of the urgent and rapidly evolving Ebola outbreak. Initiating research in the fall of 2014, the project team submitted draft cases for review by the EWG, the sponsor, and 4 external referees a year later. FDA offered written and verbal feedback on October 22, 2015. EWG members proposed revisions via individual written comments and group discussion at a meeting on October 26, 2015 at the Center's Baltimore offices. External reviewers provided in-depth written comments during the fall of 2015.

After discussing a revision plan with the sponsor, the project team conducted an additional round of data gathering, including follow-up FDA interviews, and they completed a second draft of the casebook in March 2016. In April 2016, 4 EWG members, with expertise in risk and crisis communication reviewed the case chapters, and the project team incorporated their suggestions to produce the penultimate draft. The sponsor performed a final review in May 2016, to which the project team responded with further refinements, producing the final draft represented here. Any errors and omissions that remain in the casebook are those of the project team.

The case studies manifest certain limitations: they do not constitute a comprehensive assessment of every public message or communication activity undertaken by FDA during the incidents examined; the project team was limited to publicly available information and did not have access to internal FDA communication information; and, the use of older examples like anthrax predate the establishment of FDA's MCMi and the PHEMCE, two important initiatives that evolved to help address some of the challenges and "lessons learned" noted in specific cases.

The individual case studies that follow provide a brief overview of the emergency, depictions of significant communication issues for FDA and its partners, and an outline of implications including specific actions for the FDA to manage similar or analogous challenges better in the future. Though they span a period of 15 years, the highlighted dilemmas and mitigation strategies have direct relevance to today's practice. That is, they reflect persistent and significant concerns, involve high-stakes lessons

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whose continued application by FDA is critical, and/or illustrate foundational “best practices” that individuals new to MCM emergency communication should adopt.

Table 4. MCM Communication Dilemmas and Mitigation Strategies for FDA –
Case #1: Recent West Africa Ebola Epidemic

- **Dilemma:** The FDA stance on the best way to enable access to investigational MCMs (ie, clinical trials versus broad availability) met opposition from diverse quarters including other experts, Congress, and the public.
 - **Finding:** To communicate most convincingly about clinical trials during emergencies, the FDA can approach this topic as one where technical and normative issues are inextricably linked, values about the public good can be perceived to be in competition (eg, scientifically defensible data versus hope amidst mass tragedy), and the merits of the opposition’s arguments are acknowledged.
 - **Action Items:** In advance of any future crisis, commission research that would elicit public views and values about the appropriate use and clinical study of unproven MCMs during emergencies, and on this basis, be prepared to embed any technical claims about the advantages of clinical studies in a larger values-based narrative.

- **Dilemma:** The FDA legal requirement to protect confidential commercial information triggered accusations of government secrecy and perceptions of privileging agency/industry relations over human health.
 - **Finding:** While protecting confidential commercial information (CCI), FDA can work concurrently to strengthen communication channels with non-industry stakeholders (ie, Congress, providers, consumers, the media), offsetting perceptions that the agency is obstructionist.
 - **Action Items:** To mitigate against public outrage, acknowledge people’s concern in FDA communication about protecting CCI; engage with industry partners developing emergency MCMs to underscore the public health value of disclosing CCI (eg, clinical trial data) during a crisis; and work with sister agencies bound by less-restrictive confidentiality laws to describe to Congress regulatory challenges around CCI.

- **Dilemma:** Initial authorization of investigational MCMs for use by Americans and Europeans outside of clinical trials fueled concern over inequities experienced by West Africans affected by the epidemic.
 - **Finding:** To reverse unfounded perceptions that certain people are given preferential access to investigational MCMs, particularly over historically disadvantaged groups, FDA can acknowledge people’s concerns about fairness and relate to them in a way that helps abates frustration.
 - **Action Items:** Train FDA spokespersons to recognize variables known by risk communications to provoke public outrage including perceived unfairness, moral indifference, and impacts on vulnerable groups. When these elements are present, do not dismiss them as mere misperception; use values-based language with supporting evidence to diminish impassioned critiques.

Table 5. MCM Communication Dilemmas and Mitigation Strategies for FDA –
Case #2: Fukushima Nuclear Accident of 2011

- **Dilemma:** Despite the vast distance between the US and the Fukushima accident, Americans still had a strong interest in self-protection against the dread-inducing threat of radiation.
 - **Finding:** Fulfilling its regulatory duties may be the primary role for FDA in certain emergencies, but the agency is still part of the larger public health emergency response system that has a priority interest in appropriate public use of MCMs. Although not legally required, FDA may be expected to communicate the science-based messages that provide greater legitimacy to directives put out by other agencies.
 - **Action Items:** To deter the public from using unnecessary and/or possibly harmful MCMs, coordinate at the interagency level to draft and deliver common warnings, based on evidence regarding content and style (see chapter 3), that will motivate people to take appropriate actions.
- **Dilemma:** Amidst an information void and inadequate government coordination, people actively sought out a countermeasure (KI) that held no benefits and posed some risks.
 - **Finding:** To help counter inappropriate MCM-seeking behaviors, as in the case of KI for an unfounded radiological risk, FDA can along with its partners empathize with people’s desire for self-protection when faced with a dreaded hazard, specify the impacts of potentially ineffective or unsafe products, and redirect the personal impetus to act in a more positive direction.
 - **Action Items:** During an emergency, help to deliver a clear and obvious signal to the public about the desired protective behavior in the context of a specific threat and recommended MCM(s), if any. During an acute health crisis, help be responsive to top public information demands. Make public information about the risk and proper protective actions more prominent, for instance, on the FDA website.
- **Dilemma:** With limited KI access, some people turned to substitutes such as home remedies, fake KI, and other fraudulent products, prompting the need for another critical line of public health messages.
 - **Finding:** During the US response to Fukushima, FDA played a critical role in educating consumers about how to spot and avoid buying suspicious products, a role that can be further strengthened by making FDA statements on fraudulent products the headline news that people readily access on the web.
 - **Action Items:** Design the FDA website based on user experience principles. Optimize message accessibility through search engine providers and “debunking” websites to ensure that agency messages are high ranking in internet search results and that opposing messages do not go unchallenged. Consider purchasing placement with leading search engines when the public safety issue is immense.

Table 6. MCM Communication Dilemmas and Mitigation Strategies for FDA –
Case #3: H1N1 Influenza Pandemic of 2009-2010

- **Dilemma:** Perceptions of the H1N1 vaccines as “risky,” “rushed” through production, and/or “untested” motivated some people to shun vaccination.
 - **Finding:** FDA can strengthen its ongoing communication efforts to demonstrate the ways in which the agency ensures the safety of vaccines in the US, pre- and post-licensure.
 - **Action Items:** Enhance public resources on FDA’s role in assuring safety over the lifecycle of a vaccine: eg, continue using the FDA Basics Webinar series to represent the agency’s commitment to, and procedures for assuring vaccine safety; link to CDC materials, benefiting from the trust people hold in this agency; and supplement “text heavy” FDA communications with more readily consumable graphic representations.

- **Dilemma:** Unmet public expectations about when and how a newly manufactured vaccine would become available during the pandemic had an adverse impact on its uptake.
 - **Finding:** FDA can work with partners to help demystify the vaccine production process that is, to most people, a black box operation, and better align public expectations with the actual timetable for when the product can realistically be available in an emergency.
 - **Action Items:** In cases where MCMs are developed during an emergency, provide either generic details on the manufacturing process (within the confines of CCI) or work with manufacturers to develop and share MCM production details, as these are relevant to the public. If delays are possible, then be prepared to explain why production may be slower than anticipated and share in your audience’s distress at the wait.

- **Dilemma:** In the absence of trustworthy and culturally appropriate information, certain groups were less likely to seek out vaccination against the H1N1 virus.
 - **Finding:** FDA can help mitigate against differential rates of morbidity and mortality in future health emergencies by helping assure that the entire US public, including specific subgroups, have access to credible, accessible, and meaningful information that enables them to make appropriate use of potentially lifesaving MCMs.
 - **Action Items:** Strengthen the Office of Minority Health’s (OMH) role in the Medical Countermeasures Initiative (MCMi) to uncover, understand, and meet the communication needs of a diverse US populace, in particular, historically underserved communities.

- **Dilemma:** Difficult-to-access and hard-to-understand information undermined efforts to make antivirals available to the public.
 - **Finding:** To avoid inadequate emergency MCM communication (eg, antivirals authorized for emergency use), FDA and its partners can aim to use information channels on which people normally rely, provide information that users see as relevant to key decisions about their health (and/or that of their patients or dependents), and deliver information that is readily consumed and integrated into a person’s decision making.
 - **Action Items:** Assess any FDA communication about new MCMs or new uses of MCMs in terms of the 3 standards of accessibility, materiality, and comprehensibility. For instance, survey intended audiences about their routine information gathering behaviors, and test written materials for salience and understandability with end-users before these are disseminated.

Table 7. MCM Communication Dilemmas and Mitigation Strategies for FDA –
Case #4: Anthrax Letter Attacks of 2001

- **Dilemma:** An evolving health crisis with a high degree of uncertainty generated acute demands for timely information, including that regarding MCMs, which leaders were not prepared to meet.
 - **Finding:** During periods of uncertainty, FDA can preserve the agency’s credibility and remain responsive to information demands by the public, media, and health practitioners, by adopting crisis communication strategies and language.
 - **Action Items:** Admit limits to the ability to determine all aspects of the emergency due to missing, complex, or rapidly evolving information. Share in your audience’s distress and describe how FDA will get more answers. When policy positions shift, alert your audience, explain why what you are saying is different from before, and acknowledge any emotive responses to the change.

- **Dilemma:** Contradictory messages and inadequate coordination of risk communication across multiple governmental jurisdictions and the private sector impeded response efforts and generated public mistrust.
 - **Finding:** Between crises, FDA can extend the reach and impact of its emergency MCM communication by strengthening relationships with other agencies and stakeholders, maintaining familiarity with its partners’ priorities and capabilities, and creating a cooperative environment that allows for ready exchange of information.
 - **Action Items:** Re-commit to PHEMCE coordination and collaboration, including that needed to get “credible, understandable, and actionable information” to responders and the public before and during health crises.⁴⁹ Maintain FDA’s frequent contact with public health NGOs and state/local health officials to support their MCM preparedness and response capabilities, and ensure coordinated communications.

- **Dilemma:** Inconsistent public health interventions coupled with historic disparities nurtured perceptions that health authorities delivered substandard care to, and even experimented on certain populations.
 - **Finding:** Sensitive to the historical conflicts between public health and minority communities, FDA can take steps prior to, and during an emergency to address any public anxiety around discrimination and human experimentation in the context of MCM clinical trials.
 - **Action Items:** Seek OMH’s strategic help in framing and conveying communications, namely those involving clinical trials and investigational products, to reassure affected groups that equal consideration is given to all. Enlist PHEMCE partners in developing, testing, and delivering MCM messages that are culturally appropriate, respond to community concerns, and help reestablish trust within historically underserved communities.

Table 8. Foreseeable MCM Emergency Communication Dilemmas – A Typology

Uncomfortable MCM Qualities

- MCM attributes induce dread (eg, GMO or irradiated component), suggest product is not fully tested (eg, in clinical trial, “sped up surge production,” accelerated approval, animal rule), or raise fears of adulteration (eg, adjuvanted, compounded).
- Unfamiliar technical jargon spurs misunderstanding and hesitation (eg, killed versus live vaccine, egg versus cell-based production).
- Regulatory mechanisms under which a MCM is being made available are unfamiliar (eg, EUA, IND); regulatory terms may have divergent popular meanings (eg, “approved,” “authorized”).
- Administration of the MCM may contradict everyday norms and personal experiences (eg, “expired” SNS stock, unfamiliar use of familiar drug, administration by non-traditional provider).

Unequal Supply and Demand

- A novel and/or highly lethal threat prompts unwarranted demand among low-risk groups.
- Unaware high-risk individuals and groups do not seek out beneficial MCMs.
- High-risk groups and infected persons facing a highly-lethal disease strongly desire access to unproven MCMs that are very early in development.
- A system of designated priority groups determines access to scarce MCMs.
- Too few MCMs exist to meet genuine needs in an emergency.
- Empty-handed or out of misplaced belief or misinformation, people turn to unsafe, ineffective, or fraudulent alternatives.

Discordant Authoritative Voices

- Different health officials issue divergent guidance on MCM allocation and administration.
- Health professional guidance competes with advice from other trusted sources (eg, media, political, religious, community).
- Information on benefits/risks may change as MCMs are used and clinical information is reviewed, which could alter their recommended use.
- Opinions differ on using randomized controlled trials to test efficacy of MCMs in an emergency
- Authorities are split on the MCM risk/benefit balance.
- Public health authorities overseas promote or prohibit a MCM contrary to US practice.

Under-Represented Groups Poorly Served by Status Quo

- Prior grievances with biomedicine or public health erode trust in MCM recommendations.
- Individuals do not access critical MCM information because major health institutions remain unschooled in how language, culture, and citizenship status can throw up barriers.
- MCM guidance for pregnant women, children, and other at-risk groups must be issued despite limited data on safety, efficacy and dosing.

Endnotes

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Chapter Two: West Africa Ebola Epidemic

Author's Note: The analysis and comments regarding the communication efforts described in this case study are solely those of the authors; this analysis does not represent the official position of the FDA. This case was selected, because it is a highly relevant and recent example of the challenges of communicating about medical countermeasures (MCMs). The West Africa Ebola epidemic posed unique challenges in that the only available MCM options were still in development, requiring special messaging to address the relevant authorization and approval processes and uncertainty regarding the products' safety and efficacy. This case study does not provide a comprehensive assessment of all communication efforts. The authors intend to use this case study as a means of highlighting communication challenges strictly within the context of this incident, not to evaluate the success or merit of individual investigational products or any changes made as a result of these events.

Abstract

In late 2013, an Ebola outbreak began in Guinea, quickly growing to become the largest Ebola epidemic on record. Widespread transmission occurred in Guinea, Liberia, and Sierra Leone with imported cases and limited transmission occurring in other countries, including the United States. The absence of approved medical countermeasures (MCMs) and a severely limited supply of investigational drugs—in early stages of development and with limited production capacity—compounded delays in the global response to the epidemic. Several of the major communications challenges for the West Africa Ebola epidemic concerned the development, testing, and use of investigational MCMs. Questions arose in the media, public, government, and even the scientific community regarding the status of individual—often highly publicized—MCMs, specifically calling for increased transparency for the testing, approval, and production processes; challenging traditional requirements for testing; and questioning allocation of limited supplies of these products in the context of the growing Ebola epidemic.

Background

In December 2013, an Ebola outbreak began in Guinea,¹ and three months later, it was officially reported by the World Health Organization (WHO).² The epidemic peaked in late 2014, and cases continued through 2015 and into 2016, resulting the largest epidemic of Ebola virus disease (EVD) in history.³ By March 2016, the epidemic had resulted more than 28,000 cases, including more than 11,000 deaths, in the West African countries of Guinea, Liberia, and Sierra Leone. Additional cases were identified in Italy, Mali, Nigeria, Senegal, Spain, the United Kingdom, and the United States.⁴ In contrast to past Ebola outbreaks, which typically occurred in small, remote villages in Central Africa, the outbreak quickly took root in densely populated urban areas in West Africa, where the disease had not been seen before. A context of uncertainty, fear, and public mistrust of both local and international interventions resulted in difficulty identifying and isolating patients and facilitated rapid spread of the disease.⁵ Without effective MCMs to combat the outbreak, efforts to control the epidemic were based largely on the ability to improve supportive care for Ebola patients and deliver—and engage the public to accept—non-pharmaceutical interventions. In addition to these efforts, considerable resources in the United

States were dedicated to the rapid development, production, testing, and approval of investigational MCMs to support response activities in West Africa, including international coordination to navigate complex regulatory requirements, implement clinical trials, and facilitate access to these investigational products.

Widespread transmission of EVD occurred in Guinea, Liberia, and Sierra Leone, with imported cases also arising in the United States and elsewhere.

The index case of Ebola Zaire for the West Africa Ebola epidemic was a two-year-old child who acquired the disease in early December 2013 in a Guinean village near the border between Sierra Leone and Liberia. The disease spread from there to nearby villages and towns in all three countries over the next several weeks.¹ The WHO reported the outbreak on March 23, 2014, and by mid-July, the epidemic had reached the capital cities of Sierra Leone, Liberia, and Guinea.^{2,6,7} On August 8, 2014, the WHO declared the Ebola outbreak in West Africa to be a Public Health Emergency of International Concern (PHEIC).⁸ The epidemic peaked in all three countries in December 2014 and January 2015. As of March 27, 2016, a total of 28,646 cases and 11,323 deaths had been reported across all affected countries,⁴ dwarfing the next largest Ebola outbreak by a factor of more than 67.⁹ While the epidemic has not yet been declared over—as of this writing—only sporadic cases have been identified since late in 2015.

In West Africa, implementing public health interventions and tracking patients and exposed persons proved to be extremely difficult, especially amid reports of attacks on aid workers and clinics.^{10,11,12,13} Additionally, there were numerous reports of communities hiding sick friends and family members as well as reports of ill persons fleeing to evade medical care, fearing doctors as the source of the infection or hospital admission as a death sentence.^{14,15,16,17,18,19} At the time of death, Ebola victims have extremely high viral load, and the severe hemorrhaging that often accompanies the disease leaves victims' bodies highly contagious. As a result, local burial practices that involve intimate contact with the deceased accelerated the spread of the epidemic.^{20,21,22} In an effort to prevent the infection from spreading beyond the affected countries, several other nations issued border closures and travel bans to West Africa, even as far away as Australia. Border closures led to concerns that canceled flights would impede transportation of aid to the region and that those crossing the borders would simply avoid security checkpoints.^{23,24,25,26}

In addition to Guinea, Liberia, and Sierra Leone, there were a number of cases of EVD diagnosed in other countries. Nearly thirty cases, including 14 deaths, and localized transmission were reported in Nigeria and Mali, and an imported case was identified in Senegal; however, intervention efforts were able to prevent further spread of the disease.^{27,28} A nurse in Spain contracted the disease in October 2014 while caring for an infected missionary who had returned from West Africa for treatment, the first transmission of the Ebola virus outside of Africa.²⁹ The first patient diagnosed with EVD in the United States was a Liberian national visiting family in Dallas, Texas, where he became symptomatic in September 2014 and was admitted to Texas Health Presbyterian Hospital. The patient ultimately died, and two healthcare workers were infected during his treatment. One healthcare worker was transported to Emory University Hospital in Atlanta, Georgia for treatment, and the other was treated at

the National Institutes of Health (NIH) Clinical Center in Bethesda, Maryland. Both of these patients recovered and were discharged in October 2014. The final case of Ebola diagnosed in the United States to date was a doctor from Médecins Sans Frontières (MSF) who had recently returned from Guinea. He was diagnosed in October 2014 and successfully treated at Bellevue Hospital Center in New York.³⁰ The United Kingdom's first Ebola patient, a Scottish nurse returning from work in Sierra Leone in December 2014, was successfully treated in London.^{31,32} Finally, a healthcare worker who had recently returned to Italy from Sierra Leone was diagnosed with EVD in May 2015 and recovered a month later.^{33,34}

At the outset, health authorities were hamstrung by a lack of approved Ebola drugs and vaccines and turned to the limited options available in the MCM development pipeline.

Readily available prophylactic or therapeutic MCMs could have mitigated the impact of the West Africa Ebola epidemic by preventing new infections, reducing patients' infectiousness, or decreasing morbidity and mortality. When the outbreak struck, however, the only available drugs and vaccines for Ebola were still in early, preclinical stages of development and had yet to be tested in humans. Multiple factors contributed to a lack of approved Ebola drugs and vaccines at the start of the West Africa outbreak. First, previous Ebola outbreaks were infrequent, small-scale events that occurred primarily in isolated rural settings. The paucity of cases—along with a lack of infrastructure in West Africa for recruiting, treating, and testing human patients—meant that randomized controlled trials (RCTs)—beyond Phase 1 safety trials—were not feasible. As a result, the efficacy and safety of investigational Ebola MCMs in human subjects remained uncertain, although several products had shown promising results in animal testing.^{35,36,37,38} Additionally, the low number of Ebola cases prior to the West Africa epidemic provided little incentive to invest significant resources in the development of Ebola treatments and vaccines for pharmaceutical companies seeking to turn a profit.³⁹ Due to a combination of inadequate funding support, inefficient research and development cultures, and cumbersome procurement and contracting processes, responsible federal entities had also failed to sufficiently spur the private sector to develop investigational Ebola MCMs in the years leading up to the West Africa epidemic.⁴⁰

Though there were no Ebola MCMs at the time that had been shown to be both safe and effective in humans, several investigational drugs existed in various early stages of the development pipeline. Notable among these drugs were ZMapp, a combination of monoclonal antibodies;⁴¹ TKM-Ebola, an RNA interference therapeutic;⁴² brincidofovir, an antiviral drug being assessed for the treatment of smallpox, cytomegalovirus, and adenovirus;⁴³ and favipiravir, an antiviral under investigation as a treatment of influenza.⁴⁴ Investigational vaccines against Ebola included a single-dose vaccine from the Public Health Association of Canada/NewLink/Merck,³⁶ a recombinant vector vaccine derived from a chimpanzee adenovirus developed by NIAID/GlaxoSmithKline,⁴⁵ a multivalent immunization against filoviruses from Janssen/Johnson & Johnson,⁴⁶ and a glycoprotein recombinant nanoparticle vaccine from Novavax.⁴⁷ At the time the West Africa epidemic rose to global attention, none of the vaccines had yet demonstrated efficacy in human trials, and while several of the investigational therapeutics showed promise in animal models, only a very limited supply was available for use in humans,^{48,49,50,51} let alone sufficient volume to conduct clinical trials.

A common desire to help those most affected by the epidemic nonetheless led to split opinions and controversy over how best to make use of scarce investigational Ebola MCMs.

As vaccines and therapeutics were explored for activity in animal studies and for preliminary safety and tolerability in early-phase human trials, many experts and vocal members of the public called for widespread compassionate use of these products in affected communities in West Africa, arguing that it was unethical to withhold potentially life-saving MCMs. Many others, including the FDA, countered that it was, in fact, unethical to provide widespread access to MCMs without knowing whether the products would help, do nothing, or even harm those who took it. Additionally, they argued that widespread use of investigational products outside of RCTs would not provide usable data for determining their effect, positive or negative, and that this posed an additional risk of perpetuating the use of these drugs in future outbreaks without knowing whether they helped or harmed patients.⁵² Compounding the ethical questions surrounding RCTs and compassionate use was the provision of the initial limited supply of ZMapp to treat two American aid workers, three Liberian medical doctors, a British nurse, and a Spanish priest.⁵³ The decision to allocate a scarce drug in this manner fueled perceptions that wealthy American and European aid workers were being prioritized over poorer West African patients, thereby leaving fewer drugs available for communities struck hardest by the outbreak.^{54,55} Additionally, cases of Ebola treated in the United States received a variety of investigational treatments; however, because initial patients were not part of clinical trials, they yielded no usable efficacy data.^{52,56,57} To some critics, the fact that Westerners could access investigational products outside of clinical trials while West Africans could not was indicative of prevailing inequities between Africa and the West.⁵⁸ While the FDA is only responsible for responding to requests for compassionate use, not for identifying or selecting who receives the investigational products, they received a significant portion of the criticism by virtue of their presumed role in the authorization process.

Product developers resorted to various approaches when testing MCMs, owing to complex circumstances surrounding the West Africa Ebola epidemic. The desire to provide help to a desperate population was complicated initially by insufficient supplies of investigational MCMs, and by the time clinical trials were ready to commence, the epidemic was waning, providing progressively fewer opportunities to gather data on MCM safety and efficacy. This variegated approach to testing led to a wide range of outcomes. For instance, TKM-Ebola was evaluated in Sierra Leone in a non-randomized controlled trial, but the trial ended after enrolling only 14 patients due to early indications that the drug was not beneficial. A trial of brincidofovir in Liberia, designed in conjunction with the University of Oxford and MSF, ended after enrolling only four patients, owing in large part to the overall low numbers of Ebola patients.^{59,60} A trial of favipiravir in Guinea yielded seemingly “encouraging” preliminary indications of efficacy; however, the trial was not a randomized controlled design, so many experts questioned the quality of the results. The recovery of several infected healthcare workers treated with ZMapp provided highly publicized anecdotal evidence of its efficacy, despite the fact that it was impossible to separate the drug’s effect from that of the intensive supportive care that the initial recipients received. By the time the RCT for ZMapp began in Liberia, however, there were few patients available to enroll in the study. The study was expanded to Sierra Leone and Guinea to increase the data

pool; however, all patients in Guinea also received favipiravir, complicating the study's ability to identify the independent effect of ZMapp.⁶⁰

Investigational vaccine products faced similar challenges in their trial designs. The GlaxoSmithKline vaccine trial began just as the epidemic in Liberia was winding down, and low enrollment relegated the Phase 3 trial to Phase 2; as of December 31, 2015, the trial was still ongoing and collecting data. The Merck vaccine was assessed utilizing a ring vaccination trial design—vaccinating close contacts of identified cases—that used a control group consisting of similar populations that received the vaccine several weeks later. Results indicate that the vaccine was 100% effective in preventing new cases of Ebola (zero cases within ten days of receiving the vaccine compared to 16 in the control group over the same time period); however, due to concerns with the innovative trial design, it remains to be seen whether this effort yields sufficient data to support product approval.⁶¹ In a Phase 1 clinical trial of a prime-boost vaccine combination from Johnson & Johnson and Bavarian Nordic, the vaccine combination demonstrated safety in humans and provided evidence of both initial and sustained immune response.⁶² Despite many efforts to evaluate investigational Ebola MCMs, tragically little progress has been made in determining their effect.⁶⁰

Dilemma #1: Given a strong desire to combat the outbreak, tension developed around the best way to enable access to investigational MCMs: clinical trials versus broad availability.

As anecdotal evidence seemed to show that the investigational vaccines and therapeutics appeared safe to use in humans, the debate began regarding how to best utilize them as they became available. Although there were many nuances of argument and proposed trial designs, various viewpoints emphasized differences in how and when the MCMs should be distributed. Some felt that, due to the severity of the disease and the outbreak, the investigational products should be made available as widely as possible to provide the greatest potential benefit to those populations ravaged by the Ebola virus. Others maintained that, in order to determine safety and efficacy, RCTs should be conducted. Further complicating MCM use for the epidemic, making the investigational products available to affected populations in West Africa required adhering to regulatory authorities in the affected countries. FDA regulations would apply if the product was provided under a US Investigational New Drug protocol (IND);^{63,i} however, not all products were being developed under a US IND.

ⁱ Some regulations also apply if the product is manufactured in the United States, even if not being developed under a US IND.

Under specific circumstances, the FDA can authorize use of unapproved products, including MCMs, for an individual (or use of an approved product in an unapproved manner) under a provision called expanded access, commonly known as “compassionate use.” Similarly, use in small groups or wider populations is designated as “under treatment protocol.” In all cases, the patients must be affected by a “serious or immediately life-threatening disease or condition” for which there is “no comparable or satisfactory alternative therapy.” Additionally, there must be some evidence that the product will provide benefit without unreasonable risk “in the context of the disease.”⁶⁴ Specifically with respect to vaccines, the expanded access provision does allow for the use of unapproved vaccines even though the condition is not technically present in those who receive it as prophylaxis.⁶⁵ Although West Africa is outside of FDA jurisdiction, those in favor of compassionate use cited the sheer volume of cases and deaths in the West Africa region and the high case fatality rate as justification for providing the experimental vaccines and therapeutics broadly to the affected populations.^{58,66} They made the argument that clinical trials were unnecessary, because historical data from Ebola outbreaks would be sufficient to serve as a control group to assess the efficacy of the new vaccines.⁶⁷ Proponents of widespread compassionate use viewed the broad distribution of vaccines and therapeutics as the best way to provide the most benefit to the most people and address widespread suffering in West Africa.

On the opposite side of the argument were those calling for RCTs for all new vaccines and therapeutics. The placebo-controlled, randomized trial is widely accepted as the “gold standard for determining the efficacy of a new treatment,” although several additional trial designs were debated.⁶⁸ While compassionate use advocates claimed that it would be unethical to give someone a placebo, delay treatment, or withhold treatment during an epidemic such as Ebola, others, such as FDA Office of Counterterrorism and Emerging Treatments Director Dr. Luciana Borio, asserted that a trial using unreliable historical controls would be an invalid study design and that, by definition, invalid trials cannot be ethical.⁵² The use of historical data would not necessarily provide a legitimate control group, as differences in population demographics, treatment regimens, and virus virulence or lethality would significantly impact the ability to assess the efficacy of vaccines or treatments.⁶⁷ Moreover, without a proper placebo control group, it would be difficult to gather sufficient evidence regarding the safety and efficacy of these products.⁶⁸ Further, Dr. Borio noted that random allocation would provide a fair means of deciding who could access limited quantities of investigational MCMs, which could still cause more harm than benefit. And due to low inventory of investigational MCMs, not everyone would be able to receive a vaccine or treatment anyway, so conducting a placebo-controlled trial would not actually deprive anyone of a product.⁶⁷ In a region where the outside medical community is treated, at best, with skepticism, conducting trials in the most ethical manner possible is vital to earning and maintaining the trust of the West African people.¹²

In July 2014, two American aid workers in Liberia who contracted Ebola were treated with the investigational product ZMapp and transported to specialized medical facilities at Emory University Hospital in Atlanta, Georgia, where they later made full recoveries. Because they received high levels of supportive care at the same time, there was unfortunately no way to determine how much, if any, benefit the ZMapp provided.^{69,70,71} Initial supplies of ZMapp yielded only enough doses to treat a handful of patients, and it would take months to produce more.^{57,72,73} Without enough ZMapp or human

subjects to conduct a randomized trial, scientists remained uncertain about the MCM's true efficacy in treating Ebola.

Despite the lack of scientific evidence needed to justify broad use of ZMapp and other investigational Ebola MCMs, the media, the healthcare and public health communities, and the general public continued to criticize what they perceived to be inefficient, ineffective institutional responses to the escalating outbreak. For example, access to ZMapp was arranged by the drug's manufacturer to treat Ebola patients prior to the establishment of clinical trials, when clinical circumstances warranted its use. It was widely reported that the FDA authorized the use of ZMapp for these patients under the "compassionate use" provision due to the severity of the disease and the lack of other viable treatment options;^{74,75,76} however, some reported that initial use of ZMapp was outside of the FDA's jurisdiction due to it being administered in West Africa before the patients returned to the United States.⁷⁷ While the FDA is legally prohibited from discussing IND applications or commenting on whether individual patients receive products under IND protocols, a FDA representative did acknowledge that the initial patients treated at Emory University received investigational products under emergency IND (eIND) protocols and that all Ebola patients treated in the United Statesⁱⁱ received at least one investigational product.^{78,79} Some questioned why these few ZMapp doses were initially provided to Americans and not to those in West Africa.^{80,81,82} Specific concerns arose around the perceived disparity between Americans being given the investigational ZMapp serum outside of a controlled trial while mandating trials for investigational treatments and vaccines in West Africa.⁵⁸ Once clinical trials were established, both Americans and Africans were afforded access to investigational products in accordance with trial protocols,⁸³ but without the ability to comment directly on specific instances of compassionate use, the FDA was unable to deflect criticism from the media and public over early use of investigational MCMs outside of clinical trials.

The FDA faced the challenge of conveying its message that RCTs are the best, fastest, and most ethical means of rapidly evaluating the safety and efficacy of investigational MCMs and ultimately providing products that work to patients in need. The perception of disparity in access and pushback from many respected experts made these communication efforts even more difficult.

Implications for the Future:

Recent experience with the Ebola epidemic revealed a range of expert and public views about the appropriate use and clinical study of unproven therapies during a major infectious disease emergency. Whether investigational MCMs should be provided via RCTs that would require some

ⁱⁱ As of October 16, 2014.

patients be administered placebos is a debate likely to be repeated in future health emergencies, especially because US government investments in MCM development are now expanding the pipeline of candidate therapies. The FDA will confront an ongoing challenge of communicating persuasively about the value of RCTs during a health emergency. To communicate most convincingly about clinical trials—and to a range of audiences that include the media, Congress, and the general public—the FDA should approach this topic as one where technical and normative issues are inextricably linked, competing values about the public good are in play, and the merits of the opposition’s arguments deserve to be acknowledged.⁸⁴

From a risk communication perspective, when and how to provide potentially life-saving MCMs to affected populations is a public health question that has a strong moral component (eg, the duty to address mass suffering) and one that elicits public desire for a compassionate, humanistic response rather than a dispassionate, technocratic one.⁸⁴ In the context of Ebola, the FDA produced two notable resources outlining its rationale for RCTs: a strong science-based article by FDA leadership in *The New England Journal of Medicine*⁶⁷ and a compelling TEDx talk delivered by Dr. Luciana Borio to a broader audience.⁸³ Arguments in each case were heavily weighted toward the technical merits afforded by RCTs in efficiently producing critical knowledge about the safety and efficacy of investigational MCMs, specifically contrasting them against historically controlled trials, while the larger social and moral aspects of MCM access went largely unaddressed. Commentators on the RCT debate regarding experimental Ebola drugs help illustrate two different ways of framing the case:

“It sounds inhumane to give sick and dying people placebos when testing experimental treatments, but it is tragic on a different scale to conduct a study that doesn’t tell us clearly where, or how well, a new treatment works.”⁸⁵

Versus

“The blinded randomized control trial is the most robust study design for testing the efficacy of a treatment.”⁸⁶

While the complex debate over RCTs during the Ebola epidemic touched on an array of scientific and practical matters, differing values and understanding attached to the placebo seemed to underpin much of the controversy. For instance, regulators and investigators may see a placebo as strengthening the reliability of data on whether a therapy helps, harms, or does nothing, while patients and the larger community may perceive a placebo as missing out on a treatment that offers hope and that could possibly extend life or lessen pain, regardless of the slim odds of it doing so or the chances of it causing an adverse reaction instead.⁸⁷ The value of scientifically defensible data and the value of hope amidst mass tragedy may involve competing ideas about the public good. During the Ebola response, an important value for those who rejected the RCT approach was a desire to reduce suffering. By acknowledging this objective and, more importantly, highlighting how this and other values are reflected in FDA policy, the FDA could greatly improve the impact of its messages.

To speak credibly and meaningfully on the topic of RCTs to a broad audience requires that a science-driven agency like FDA be responsive to opposing arguments grounded in cultural norms, social values, and a moral perspective. In the Ebola case, effective communicators outside of the FDA were promoting a strategy counter to that promoted by the FDA. A rich body of literature on competing message frames highlights the importance of effective communication through framing issues, such as the need for clinical trials, using language that is salient (ie, relevant) to potential audiences and using strong messages that tap the power of emotion.⁸⁸ In addition, the frequency and timing of these messages also play a role.^{89,90} From a risk communication standpoint, it is sensible to work the opposition's strongest points (eg, facts, arguments, emotions) into one's own statements.⁸⁴ Speaking in ways that show genuine appreciation for alternate viewpoints and for a range of deeply held values, particularly how those underlying values are already incorporated into existing policy, can enhance the legitimacy of FDA positions. Framing current policy in terms of the opposition's values provides the audience context in which to evaluate, understand, and appreciate these positions. It is important that communication efforts be made in the midst of the debate, rather than after attention has drifted from the issue, since many audiences will no longer be primed to receive information. In this case, Dr. Borio's TEDx talk—one of the FDA's principal efforts to communicate with the broader public—did not take place until October 2015, more than a year after the RCT debate began.⁸³ The use of familiar language and arguments in well-timed and regular communications can help effectively overcome competing message frames and improve overall communication efforts.

Action Items for FDA

1. In advance of future crises, commission research that would elicit public views and values about the appropriate use and clinical study of unproven therapies, and on this basis, develop informational materials designed to help broaden support for the use of RCTs during health emergencies.
2. Embed any technical claims about the advantages of placebo-controlled clinical studies in the context of a larger values-based narrative that reflects the common, overarching desire to provide assistance to affected populations. In this case, express the moral convictions that sick and dying people deserve appropriate care and that populations under duress deserve society's best efforts at support, both for current and future epidemics.
3. During periods of active debate, listen to opposing arguments to discern the cultural norms, social values, and moral perspectives relevant to the audience, and craft messages that incorporate and reflect these important underlying priorities. Use opposing views as important data points to understand where empathy and reflection of values are important in producing a message that resonates with the target audience.
4. Deliver these messages early and frequently in order to compete effectively with opposing message frames. Late messaging occurring after the period of active debate is not as effective as messaging that is applied when audiences are paying attention to the issue.

Dilemma #2: The need to protect confidential commercial information relating to emergency MCMs against Ebola created communication barriers between FDA and members of Congress, industry, and the general public.

In addition to the challenges that emerged during the Ebola MCM development process, the FDA also fielded concerns around potential disclosures of confidential commercial information (CCI), some of which stemmed directly from ongoing communication dilemmas around perceived inequities in MCM distribution. For example, following news that two American clinicians working in West Africa received ZMapp after contracting Ebola, the Goldwater Institute (a public policy think tank) sent the FDA a Freedom of Information Act (FOIA) request in August 2014, seeking information about the agency's process for approving use of ZMapp.⁹¹ Concerned about potential disclosures of industry trade secrets or CCI, the FDA denied the FOIA request. After unsuccessfully appealing the decision to the US Department of Health and Human Services, the Goldwater Institute filed a lawsuit against the FDA in June 2015, citing the importance of ensuring equitable access to potentially life-saving drugs.⁹² The FDA also encountered blowback from Congress over CCI during the clinical trials process for investigational Ebola MCMs. For instance, during a hearing before the US House Committee on Foreign Affairs in September 2014, members of Congress asked witnesses representing the FDA and the NIH why certain investigational MCMs were placed on clinical hold.⁹³ However, the FDA could not acknowledge the existence of the investigational applications for the MCMs in question. Though in each of these instances, the FDA was complying with legal requirements to protect CCI, the agency's actions were perceived as being obstructionist and privileging industry needs over those of other stakeholders—namely, Congress and the general public.

Given the tension between the FDA's legal obligation to protect CCI submitted by pharmaceutical developers and a public that demands transparency, the FDA faces considerable challenges around publicly sharing information about MCMs that could result in competitive harm to industry. Under Title 21 of the Code of Federal Regulations (CFR), the FDA is prohibited from disclosing CCI without written authorization from a product sponsor. The regulations, in 21 CFR §20.88, do allow the FDA Commissioner (or his or her designee) under certain conditions to authorize disclosure of CCI to state government officials without sponsor permission if doing so is in the interest of the public's health.^{94,95} However, it remains unclear as to whether state officials invoked this regulation during the Ebola outbreak.

The FDA does employ other mechanisms for facilitating non-public information sharing with foreign government officials in the midst of an international public health emergency, as authorized by CFR 21 §20.89, for example. In September 2014, for instance the International Coalition of Medicines Regulatory Authorities (of which the FDA is a member) affirmed its commitment to cooperate with the World Health Organization (WHO) and regulatory agencies "to encourage submission of regulatory dossiers and evaluation of the submitted information on potential new medicines...to accelerate access to investigational treatments for patients most in need during the current outbreak," as well as to ensure that affected communities could access safe, efficacious medicines in the event of future outbreaks.⁹⁶ Furthermore, the FDA made a mutual confidentiality agreement with the WHO in 2014 to

facilitate interagency exchanges of CCI while ensuring public non-disclosure of such information.⁹⁷ The FDA made similar commitments to protecting CCI with the Ministry of Health and Public Hygiene of Guinea, the Pharmacy Board of Sierra Leone, and the Liberian Medicines and Health Products Regulatory Authority during the West Africa Ebola epidemic.^{98,99,100}

Implications for the Future:

The FDA's dual role as both a regulatory body and a protector of the public's health confers the agency with the difficult tasks of handling industry considerations, ensuring the safety of emergency MCMs, and responding to the needs and concerns of its partners in government, healthcare, and the general public. The FDA has already taken important regulatory steps to ensure that select partners are privy to certain types of CCI during a public health crisis, but without concurrently strengthening channels of communications with other, non-industry stakeholders—namely, members of Congress, healthcare providers, and consumers—the agency will likely continue facing the repercussions of perceived non-transparency as it strives to satisfy its public health mission.

The disclosure of CCI could certainly discourage pharmaceutical companies from pursuing development of MCMs for critical public health threats. However, the perception that the FDA's legal obligation to protect CCI is obstructionist could fuel distrust among the aforementioned stakeholders, and potentially result in future lawsuits, low uptake of MCMs among consumers, frustration among healthcare providers and public health officials contributing to emergency response efforts, and ongoing Congressional pressure to divulge proprietary information—consequences that would require the FDA to continue depleting its already limited pool of resources. The FDA could mitigate some of these challenges by including acknowledgements of public anxiety and concern in its communications about the importance of protecting CCI, as well as by hiring personnel with the expertise necessary to craft messages about MCM risks for its various audiences. Finally, it is critical for the FDA to assume a more proactive approach to setting public expectations around the scope of its legal and regulatory powers during public health crises. During such events, misperceptions of obstructionism could exacerbate existing anxieties around the health threat in question; the public, in turn, might be less receptive to explanations of the FDA's legal constraints in the midst of an ongoing threat. Therefore, in advance of a public health emergency, the FDA might consider collaborating with sister agencies and industry partners to increase awareness of its legal obligations and other CCI challenges among members of Congress, Congressional staffers, and consumers.

Action Items for FDA

1. Engage with industry partners developing emergency MCMs to explain the FDA's challenges in protecting CCI and underscore the immense public health value of disclosing relevant CCI (eg, clinical trial data) during a crisis. Collaborating with industry partners to develop prepositioned messages for Congress, healthcare providers, and consumers about MCM safety to deploy during crises could also further facilitate emergency communication.

2. Reach out to relevant members of Congress to explain the legal restrictions that prohibit the FDA from publicizing certain details about investigational MCMs. Partnering with sister agencies/offices bound by less-restrictive confidentiality laws—eg, the NIH, the CDC, and the ASPR Biomedical Advanced Research and Development Authority—to describe regulatory challenges around CCI could help provide context and details that the FDA may be unable to disclose.

Dilemma #3: Initial authorization of investigational Ebola MCMs for use by Americans and Europeans outside of clinical trials fueled concerns over inequities experienced by West Africans affected by the Ebola epidemic.

One of the largest controversies involving Ebola MCMs was the act of providing limited quantities of investigational products to American and European responders rather than the affected West African population. On one hand, the extremely limited supply of investigational Ebola MCMs would likely have little impact on the growing Ebola epidemic, and many felt an obligation to help those who had voluntarily placed themselves in harm's way to respond to the outbreak. Health officials also feared that if West Africans were administered an investigational MCM that turned out to be harmful, it would be perceived that "Africans [were] used as guinea pigs" for the American pharmaceutical industry.⁵⁴ Opponents, including medical experts, argued that it was unethical to deprive the affected population of a potentially life-saving drug, even if it had not been previously tested in humans.^{58,101} Additionally, they argued that the lives of West African volunteers who contracted Ebola were equally as valuable as those who received the drugs, so the investigational products should be distributed accordingly, not just to white Westerners.¹⁰² A variety of challenges came into play in a debate that grew well beyond the act of authorizing the use of investigational MCMs to encompass larger perceptions of health inequities associated with the West African Ebola epidemic.

ZMapp provides a prime example of the controversy over the ethics involved in allocating scarce Ebola MCMs in the midst of the West Africa epidemic. The world first learned about ZMapp in early August 2014 when reports surfaced about the first use of the investigational drug in humans, two American missionaries fighting the Ebola outbreak in Liberia.⁷⁶ Use of the drug was presumed by many to have been authorized under the FDA's compassionate use (expanded access) protocol, because the drug was not yet approved for use in humans;^{74,75,76} however, the exact process by which early Ebola patients in the United States accessed investigational products and the extent to which the FDA was involved remains unclear.^{77,92} The survival of both of these patients, in conjunction with promising animal trial results, provided support for ZMapp's efficacy, if only anecdotal. ZMapp's subsequent and rapid rise to "miracle" drug status in the media sparked immediate demand for the product to be sent to West Africa.^{75,103,104} Unfortunately, the supply of ZMapp at the time was limited to only a handful of doses, all of which were distributed by August 11.¹⁰⁵ In total, ZMapp was administered to seven people, five of whom survived. Among these were two patients from the United States, one from Britain, and one from Spain;¹⁰⁶ the remaining doses were used to treat three healthcare workers in Liberia.¹⁰⁷ In the context of the unprecedented and growing epidemic in West Africa, many questioned providing the limited supply of the miracle drug to wealthy, white Americans and Europeans while thousands of poorer West Africans suffered and died.⁷⁵ Many others countered that the severely limited inventory of

ZMapp, in and of itself, precluded its use among the affected West African population, but some countered by questioning why Dr. Sheik Umar Khan—one of Sierra Leone’s leading Ebola physicians and a “national hero” who contracted Ebola and died the day before Americans Dr. Kent Brantly and Nancy Writebol received doses of ZMapp—was not given the drug or even informed of its existence.^{81,82,108} As the federal agency responsible for approving MCMs, the FDA bore the brunt of the public and media contempt, but there were many mitigating factors beyond their control.

Fueling the debate was a lack of transparency regarding the availability and distribution of investigational Ebola MCMs like ZMapp.¹⁰⁹ As previously mentioned, the existence of drugs like ZMapp was largely unknown in the general public at the time, prompting demand from the media, the public, and government officials for more information on the products and their respective status in the FDA approval process. Legal constraints on the FDA, however, prohibited officials from discussing confidential information about these products, including approval status. FDA officials were not even permitted to acknowledge if compassionate use authorization had been requested, let alone discuss the process by which a product’s use was authorized or how the allocation was determined.⁷⁴ The FDA did acknowledge that the eIND protocol was used to provide investigational drugs to Ebola patients, but further details were not provided.⁷⁸ An NIH representative described in general the process by which ZMapp was obtained for the initial patients, in that Samaritan’s Purse, the organization that Dr. Kent Brantly worked for, contacted ZMapp’s manufacturer directly, via the Centers for Disease Control and Prevention (CDC) and NIH;¹¹⁰ however, explicit details—including how many requests were submitted and approved, which patients received which products, and the extent to which FDA regulated the use of products outside the United States—have not been made public due to confidentiality restrictions.⁹² The opacity of this process led to questions regarding how the patients who received ZMapp were selected, and the perceived inequity in resource allocation—specifically providing Westerners, authorizing the limited supply of investigational products for use in Westerners outside of clinical trials while requiring placebo-controlled trials in West Africa—resulted in intense media scrutiny around the ethics of MCM distribution.^{111,112}

Superficially, the initial allotment of ZMapp appeared to perpetuate health disparities between America/Europe and Africa; however, a number of factors played into its authorization and allocation. These factors were highlighted with the arrival of the United States’ first diagnosis of Ebola in Thomas Eric Duncan in Dallas, Texas. In the wake of his death, accusations of racism and classism surrounded Duncan’s treatment, ranging from the hospital sending him home from his initial visit to his clinical treatment once admitted. Many, including Duncan’s friends and family and Reverend Jesse Jackson, decried withholding ZMapp from Duncan after its earlier use with Dr. Kent Brantly and Nancy Writebol,^{113,114} despite the fact that the limited supply of ZMapp had been exhausted months prior.¹⁰⁵ Other considerations—such as Duncan’s current health condition and blood type—also factored heavily into the treatment options available to him.^{115,116} Similarly, the authorization of ZMapp and other investigational products for individual patients depended on a number of considerations. First, compassionate use requests are submitted by treating physicians, not offered by the FDA. The FDA can only respond to those requests based on their merit, and allocation of the product is subject to availability from the manufacturer.¹¹⁷ Additionally, FDA has no standing international authority, and use

of investigational products abroad must be coordinated through the appropriate national governments to ensure they are used safely and ethically. While providing investigational products to patients in need seems, on the surface, like a straightforward process, there are many factors—information for many of which remains confidential—that must be considered before this can occur.

Implications for the Future:

Many aspects of the West Africa Ebola response prompted concerns over ethical treatment and health inequities between West Africa and Western nations. In this case, the high-profile use of limited supplies of investigational treatments in white Americans and Europeans that had not been made available to West Africans was complicated by limitations on the FDA's ability to discuss specifics of the compassionate use requests. This instance is similar to historical examples involving health inequities and medical research. Unlike other scenarios, however, this case involves the perception that an investigational drug was being withheld from the affected population rather than being forced on a vulnerable population to test a new product, resulting in nuanced communications challenges. As discussed previously, the FDA is legally obligated to protect confidential information for investigational products. Under these restrictions, it was difficult to address questions regarding how and why the initial supply of investigational MCMs like ZMapp were provided to white Americans and Europeans. While federal agencies—including the NIH and the State Department—did an effective job at publicizing the process by which Samaritan's Purse obtained ZMapp for Dr. Kent Brantly, Nancy Writebol, and others,^{118,119,120} health officials did not effectively acknowledge the public's ethical concerns nor relate to them in a way that could help abate their frustration.

In situations such as this—where the media and public could perceive that certain people were given preferential treatment, particularly over a historically disadvantaged population—health officials need to address these concerns explicitly. Simply stating the inability to comment due to legal restraints or lack of information leaves a void that the media and public can fill with speculation and information—as well as misinformation—from unofficial sources.¹²¹ The first step is to provide the information that *is* available. As mentioned above, the process by which the initial doses of ZMapp were obtained was discussed in general terms by several federal sources, and this message was carried by numerous media outlets. Secondly, and most importantly, health officials need to acknowledge the public's grievance—in this case, that white Westerners received preferential treatment—and provide concrete support to clarify the situation. By specifically addressing concerns regarding fairness, health officials give themselves the opportunity to demonstrate why the actions taken were morally sound and in keeping with ethical principles and established protocols. Communications should also address any factors that are beyond the control of the applicable agencies and limitations on their scope of authority. In this case, for example, communications should have highlighted that the FDA can only respond to requests for compassionate use, not proactively issue them. Additionally, statements should have emphasized that the requesting organizations approached the CDC and FDA rather than these agencies working to actively identify Americans for whom investigational treatment options could be supplied.

Action Item for FDA

Train agency spokespersons to recognize variables known by risk communicators to provoke public outrage including perceived unfairness, moral indifference, and impacts on vulnerable populations. When these elements are present in a situation, recognize that they are central to public health objectives rather than dismiss them as mere misperceptions.⁸⁴ Instead, openly acknowledge these concerns and use values-based language with supporting evidence to diminish impassioned critiques, direct or indirect, of agency policies and actions.

Conclusion

While there were countless problems with the global response to the West Africa Ebola epidemic, much of the conflict focused on the availability of MCMs. With few products in development and none with demonstrated safety and efficacy in humans, traditional development and approval processes were called into question by the public, media, and government as well as public health and bioethics experts. The desire to provide much-needed aid to a population facing a devastating epidemic with limited medical and public health resources drove many to question the necessity of clinical trials, including RCTs, when they felt that more good could be done with widespread use of investigational products. These ethical concerns were bolstered by highly publicized reports of the use of some of these investigational products outside of clinical trials, increasing concern that Americans and Europeans were being prioritized over the struggling West African population. In addition to ethical challenges, there were also calls for increased transparency in product development and testing, challenging legal responsibilities to maintain confidentiality for products currently in development. These complex issues would be difficult to address even under ideal circumstances, but the rapidly expanding Ebola epidemic and rising global anxiety applied increased pressure to provide rapid solutions.

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Chapter Three: The Fukushima Nuclear Accident of 2011

Author's Note: The analysis and comments regarding the communication efforts described in this case study are solely those of the authors. This analysis does not represent the official position of the FDA. This case was selected because it illustrates communication around an unneeded medical countermeasure and provides additional insight into the important supportive role FDA may play even if the US government is not the primary responder to the event. This case study does not provide a comprehensive assessment of all FDA communication efforts. The authors intend to use this case study as a means of highlighting communication challenges strictly within the context of this incident, not to evaluate the success or merit of any changes made as a result of these events.

Abstract

The Tohoku earthquake in Japan caused a series of tragic and cascading disasters in Japan, including the release of radiological materials from the Fukushima Daiichi Nuclear Power Plant. The vast majority of the nuclear release affected only Japan, and as a result, no medical countermeasures were recommended in the US. However, despite messages to the public by health authorities not to purchase, stockpile, or administer potassium iodide (KI), some consumers still sought out the radiation countermeasure. Additionally, when KI was not available, some consumers attempted to acquire potassium from other sources even though these sources were ineffective and/or not approved by the FDA. The adverse effects of such behaviors were the potential occurrence of negative side effects from taking unnecessary or unapproved products. Additionally, in the event of a future emergency requiring KI for a limited proportion of the population, demand for KI by those who would receive no benefit may prevent those who need KI from accessing it.

To improve public response, a more rapid federal response was necessary in coordination with state and local officials to fill an information vacuum. Specifically, the FDA could have improved its supportive role in this disaster by more actively promoting the messages it was producing about KI. Salient information points included acknowledging people's reasonable desire to protect themselves and outlining the negative impacts of seeking out unwarranted and potentially ineffective or unsafe countermeasures. Additionally, the public required hard data about radiation levels to improve trust of messages about safety.

Background

On March 11, 2011, a 9.0 magnitude earthquake occurred off the Pacific Coast of Japan. Known as the Tohoku earthquake or the Great East Japan Earthquake, this earthquake created 15-meter tsunami waves that quickly reached the Tohoku region of Japan. The waves overwhelmed the protective seawalls of the region and caused one of the worst natural disasters in Japan's history, killing 15,889 people with an additional 2,594 still missing, and injuring 6,152.¹

When the earthquake struck, 6 nuclear power units were located at the Fukushima Daiichi Nuclear Power Plant, in the Fukushima prefecture of the Tohoku region. Of the 6 reactors located at the

site, 3 were in operation. These reactors initiated an emergency shutdown process and external power to the reactors was lost. A short time later, the tsunami breached protective sea walls and flooded the back-up power units at the nuclear power plant. This caused the reactors, as well as spent fuel pools, to lose their cooling capabilities. The next day, on March 12, explosions caused by pressure from hydrogen released from damaged nuclear cores occurred at 3 reactors.²

The radiation released by the disaster at the Fukushima Daiichi Nuclear Power Plant was about 5.5% of that of the Chernobyl accident.^{3,4} At the time of the accident, prevailing winds blew much of the radiation eastward and out to sea.² This event marked the world's most significant radiological accident in 25 years, rating 7 on the International Nuclear Event Scale.⁵ While the amount of radiation predicted to reach the United States was small, there was a perceived risk, especially in West Coast communities, that radiological poisoning might occur in the US as a result of the incident. However, during the first few days of the disaster, there was a marked lack of communication from the federal government.⁶

Potassium Iodide (KI) can block absorption of a radioactive isotope of iodine (I-131), which may be absorbed and concentrated in the thyroid in the event of an environmental release. Following the Chernobyl accident, approximately 5,000 cases of thyroid cancer in children were attributed to exposure to I-131.⁷ However, the use of KI can decrease the risk of developing thyroid cancer in those exposed to an environmental release of I-131.⁸ For this reason, KI is considered a medical countermeasure in the event of nuclear power plant accident. KI is stockpiled and has been distributed to the public in the Emergency Planning Zones (EPZ) around nuclear power plants in some states, which has likely increased public awareness of this countermeasure.⁹

Although KI can be used as an effective medical countermeasure against I-131, its role is limited. It must be ingested within a few hours of exposure, and its protective abilities are reduced as the time since exposure increases. KI is also ineffective if given more than 48 hours before exposure. Side effects can include nausea, vomiting, diarrhea, and rash. It may also cause short-term underactive thyroid function, especially in infants. Additionally, persons with iodine sensitivity and certain conditions such as dermatitis herpetiformis, hypocomplementemic vasculitis, Graves' disease, and autoimmune thyroiditis should avoid KI or take it with caution.¹⁰ These negative side effects highlight the fact that KI should not be taken if not needed. This balance of risks and benefits is true for other MCMs as well.

In short, using KI carries potential risks that should be avoided in the absence of any potential benefit from the drug. Furthermore, in the event of a future emergency requiring KI for a limited proportion of the population, demand for KI by those who would receive no benefit may prevent those who need KI from accessing it.^{11,12}

Dilemma #1: Despite the vast distance between the US and the Fukushima accident, Americans still had strong interest in self-protection against the dread-inducing threat of radiation.

Because of KI's limited role as a medical countermeasure in this instance, due to low levels of exposure, it was not recommended for use in the US following the accident in Japan.^{13,14} However, some

US consumers chose to ignore these recommendations and US KI consumption increased.¹¹ For example, one online company was receiving a new order every 30 seconds.^{15,16} Much of this demand for KI was concentrated in western parts of the country, although similar concerns were echoed across the nation on a smaller scale (informant interview completed for this project, public health official). Many consumers attempted to acquire KI from KI manufacturers and pharmacies, which quickly sold out or never stocked it in the first place.

Between March 11 and April 16, 2011, poison control centers in the United States captured 340 requests for information and 60 potential exposures to KI, iodine or iodide product ingestions, or radiological exposures related to the nuclear power plant incident in Japan. There were 38 reported exposures specifically related to KI, iodine or iodide products.¹⁷ These incidents likely represent only a portion of actual exposures since not all were reported to poison control centers.

Implications for the Future:

Individuals will actively search out information on self-protection when they perceive risks, even if their heightened sense of risk is unfounded from a professional viewpoint. Radiation is one of several hazards that evoke an increased perception of risk from the public. Other hazards that often trigger more pronounced reactions are those that are not directly observable, unknown to those exposed, new or unknown to science, uncontrollable, catastrophic, fatal, not equitable, risky to future generations, not easily reduced, increasing in risk, or involuntary, or those that have delayed effects.¹⁸ In the context of these dread hazards, the FDA should be prepared for intense reactions as well as enhanced public demand for information and potential MCMs. Officials, including those at the FDA, can most effectively counter inappropriate MCM-seeking behaviors by acknowledging the desire of individuals to protect themselves, reframing personal health concerns in proportion to objective risk, specifying the negative impacts of using potentially ineffective or unsafe products, and redirecting the impetus to take protective action in a more positive direction.

Action Items for FDA

1. Be prepared to communicate about potential MCMs even if the USG has a limited or non-existent role in an international incident, especially one involving a dread hazard like radiation. The public does not limit its concerns or questions because the USG is not an official responder to an incident.
2. Pre-emergency, engage radiation-related groups [eg, National Alliance for Radiation Readiness (NARR) and Conference of Radiation Control Program Directors (CRCPD)] to build up working relationships and familiarity with FDA's emergency roles and responsibilities. These entities can help communicate in a radiological incident about the risks/benefits of specific MCMs and/or redirect inquiries to FDA.
3. To deter the public from using unnecessary and/or potentially harmful countermeasures, coordinate at interagency level to draft and deliver common warning messages that motivate people to take appropriate actions, based on evidence regarding content and style (see Table 1).

Table 1: Sample Public Warning about Potassium Iodide in the Fukushima Context:
Content and Style Tips

NOTE: The following public statement illustrates communication best practices, using a specific example to demonstrate in concrete fashion the more general content and style principles recommended. It is not intended to represent an actual public warning issued by the FDA. In actuality, any FDA and/or interagency statement would have to be adjusted for different threats, MCMs, and the specific communication goals of the FDA and its interagency collaborators.

CONTENT

- Specify who is issuing the warning, invoking a chorus of credible sources.
- Describe exactly what action people should take and explain why.
- Note the timeframe for when to engage in the behavior.
- Single out who should take action and explain why.
- Outline the consequences of taking the action.
- Indicate if the recommendations have changed or may change in the future.
- Channel concerns about potential risk to productive behaviors.

STYLE

- Aim for clarity, by using simply worded messages and avoiding technical jargon.
- Be as concrete as possible and use familiar landmarks when telling people what to do.
- Project confidence and certainty, while preparing people for dynamic conditions.
- Employ accurate information; avoid any misunderstanding.
- Maintain consistency; avoid “mixed messages.” Explain when advice differs or evolves.

This is a public advisory from the US government informed by experts from the Centers for Disease Control, the Environmental Protection Agency, the Department of Health and Human Services, the Food and Drug Administration, and the Nuclear Regulatory Commission.

The Tohoku earthquake in Japan damaged the Fukushima Daiichi nuclear power plant, causing a release of radiological materials that began March 12, 2011.

According to the US Nuclear Regulatory Commission, harmful levels of radioactivity are not expected in Hawaii, Alaska, the US Territories, the US West Coast, or the rest of the country, based on data that is regularly updated.

If you are in Alaska, Hawaii, a US territory, or the continental US, there is no reason for you to take any protective actions at this time. You will be notified if conditions should change, but experts agree that this is not likely.

Do not take potassium iodide, even as a preventative measure. Harmful levels of radioactivity are not expected, so potassium iodide is not needed. Potassium iodide has potential negative side effects, and it should not be taken if not needed.

Table 1: Sample Public Warning about Potassium Iodide in the Fukushima Context:
Content and Style Tips, continued

Side effects can include nausea, vomiting, diarrhea, and rash. Potassium iodide may also temporarily interfere with the thyroid's functioning. People at higher risk of these side negative effects are infants and persons with iodine sensitivity and certain medical conditions involving the thyroid and heart.

Do not seek out substitutes for potassium iodide, as they are not needed and may cause you harm. Be wary of internet sites and stores that promote products falsely claiming to prevent or treat the effects of radiation. Avoid products that are not FDA-approved. Fraudulent products come in all shapes such as dietary supplements, food items, or products said to be drugs, devices or vaccines.

Actions that you can take include the following:

1. Go the FDA website to learn more about potassium iodide and when this drug is and is not useful to protect against the effects of radiation.
2. Go to the EPA Rad Net website to track up-to-date monitoring of radiation levels associated with the recent events in Japan.
3. Learn how to make smarter choices when buying medical products on line. Visit the webpage [Buying Medicines and Medical Products Online](#), and check [The Orange Book](#) or [Drugs@FDA](#) to confirm if a particular drug is FDA approved.

Dilemma #2: Amidst an information void and inadequate government coordination, people actively sought out a countermeasure (KI) that held no benefits and posed some risks.

Given that radiation levels in the US were very low and there was little potential for the public to benefit from KI, official recommendations advised against purchasing, stockpiling, and administering KI. Despite this public messaging, there was significant demand for KI.¹⁹ The desire to take personal protective measures, a perception that the Japanese government was not being transparent about the disaster, confusion about what “low” meant, and delays in guidance from trusted officials in the US negatively affected public perception of the disaster and likely spurred interest in KI.^{20,21} The mismatch between US government recommendations and rising demand for KI suggests that some people did not receive the government messaging, did not trust these recommendations, or were ignoring these messages in favor of other information sources.

A several day delay in the overall US government communication response coupled with an acute demand for knowledge about personal protective measures created an information vacuum. Unfortunately, this information vacuum was filled by people, such as “experts” used in news media reports or internet bloggers, who provided inaccurate information.²² Social media allowed for rapid and widespread dissemination of information but this platform allowed inaccurate information to go “viral” quickly.²³ Although most eventual public messages regarding potential countermeasures noted that no countermeasures were necessary, mixed messaging from the federal government also complicated the issue. When asked about the demand for KI in an interview, Surgeon General Regina Benjamin supported KI purchases as a worthy “precaution.”²⁴ Health officials needed to maintain unified health messaging across multiple agencies, which did not occur until after public concerns had already grown.

Members of the public were eager to know radiation levels to put their perceived risk and need for self-protection in context, but this data was slow to emerge, unevenly available, and difficult to interpret. The Federal Radiological Monitoring and Assessment Center (FRMAC), which is typically activated for an event occurring in the US, was not activated (although a limited deployment to Japan occurred); a centralized source for radiation monitoring data was thus absent.¹² The EPA did develop a website to provide public data from EPA’s RadNet monitors.²⁵ Nonetheless, state health officials still felt that they were left to answer the public’s questions and concerns with little data to support the idea that there was no need to take protective actions against radiation from Japan, including taking a countermeasure like KI.^{6,19} Federal release of radiological readings occasionally occurred before state and local officials were aware of them (informant interview, public health official), which led to confusion when concerned citizens called local public health officials. This situation was particularly difficult because health officials needed to “prove a negative” (informant interview for this project, public health official). Furthermore, no official public health definition of a safe radiation dose existed.²⁶ Moreover, when hard data was available, it was often difficult for the public to interpret due to the different units of measurement used for radiation.¹²

Some states were able to generate their own radiation readings, but these data releases often got stuck in wordsmithing cycles with higher level but less radiation-informed officials (informant interview for this project, public health official). Without hard data, it was easy for the public to dismiss claims that there were no public health effects of concern. The ability of frontline health officials to refer to specific readings and put them in context for the public was important in persuading concerned citizens that KI was not necessary. Experts noted the importance of creating effective public messages around the fact that KI was not necessary but also that KI could cause negative health impacts for certain subpopulations. For example, California's Department of Public Health and Emergency Management Agency on Risk of Radiation Exposure issued a statement urging Californians not to take KI, stating that it was unnecessary and could present a danger to some people, especially if taken inappropriately.²⁷ States also attempted to address the unwarranted public desire to access KI by engaging pharmacies and healthcare providers as spokespersons on the issue.

In the Fukushima disaster, the FDA played a supportive role, utilizing its expertise to advise other agencies and provide relevant information to the public. To disseminate information to the public, the agency relied heavily on the internet and developed its own website. Using a "frequently asked questions" (FAQ) format, the agency addressed issues about the Fukushima disaster relevant to the agency's mission. Topics included the safety of Japanese drug and food imports (eg, dairy products, seafood) and information regarding medical products to treat internal contamination with radioactive materials.¹⁴

Implications for the Future:

In general, public health officials should be prepared to support claims about a lack of threat (and thus, the lack of need for a MCM) with concrete evidence. However, in the case of the Fukushima disaster, not all of the necessary information for the disaster fell under the purview of one organization. A more rapid, visible, and unified federal response to public concerns about radiation and demand for KI, was needed and would likely have reduced early fears, increased the credibility of messaging, and buttressed the communication efforts at the state and local level. Due to the international nature of the event, interagency coordination and information sharing with locals was a challenge. Since the Fukushima accident occurred, work has been done to improve coordination of the federal and local response to such events including pre-developed messages for radiological incidents and joint message development between the National Alliance for Radiation Readiness and the Centers for Disease Control and Prevention.¹²

During the Fukushima emergency, the FDA played a critical supportive role in helping to assure that the public was accurately informed about the potential threat of radiation (i.e., negligible) and any need for protective actions (i.e., none, including potassium iodide). While FDA's regulatory responsibilities may be broader during an event like Fukushima, as in safety screening of drugs from Japan, the agency is nonetheless part of the larger public health emergency response system that has a priority interest in appropriate public use of medical countermeasures. The agency has an essential supportive role in communicating the science behind the need or lack of need for KI and other radiation

MCMs, and it remains a key information source for the public on MCMs even when MCMs are not necessary.

Action Items for FDA

1. In the health emergency context, embrace the supportive role in helping to deliver a clear and obvious signal to the public about the desired protective behavior in the context of a specific threat and recommended MCM(s), if any. Even when the FDA is not a primary responder, it can still provide important, science based messages that provide greater legitimacy to information and directives put out by other agencies.
2. Improve the ability of internet users to find FDA's webpage easily, which is the central archive for its key messages and to which the agency drives consumers via twitter and other social media. During an emergency, FDA should work to ensure that the rank of its website in internet search engines is high so that it is a "go-to" site for information on risks and benefits of KI and other radiological MCMs.
3. When publishing resources for the public on the web during an emergency, take steps to enhance the prominence of information about the health risk and appropriate protective actions (including MCM use). Take steps to call out this information, for example, by sharing it first or layering information in ways that make this kind of information readily accessible.

Dilemma #3: With limited access to KI, some people sought out substitutes such as home remedies, fake potassium iodide, and other fraudulent products, prompting the need for another critical line of public health messages.

As KI stocks dwindled, home remedies or alternative sources of potassium iodide were also in high demand. Further complicating the issue, fake KI and other products claiming to protect against radiation were being marketed and sold in the US following the disaster in Japan.²⁸ In the US and around the world, salt and other dietary supplements were used as potential remedies for perceived risks from the radiation from the nuclear power plant accident in Japan.^{28,29,30} Even if a countermeasure for radiation exposure had been necessary in the US following the accident, these alternative sources of KI would not have been able to provide protection.

While their wares were unnecessary, online retailers still promoted a wide array of products and practices to counter supposed radiation exposure. These included foods that supposedly supported detoxification, supplements and natural products purported to protect against free radicals created during radiation exposure, and topical treatments to treat potential effects of radiation sickness. Several companies received warning letters from the FDA about marketing and labeling violations, highlighting the possibility of regulatory action.¹⁴ In addition, several fraudulent products were noted on the FDA webpage dedicated to Fukushima, along with detailed instructions to consumers on how to spot and avoid buying suspicious products.

Via its website, the FDA provided helpful information about the lack of need for KI and about fraudulent products. Nonetheless, certain design and content elements potentially reduced the accessibility and salience of the information for the user:

- Critical information about MCMs was relegated to the end of a long, scrolling, text-heavy webpage that lacked hyperlinked questions at the top of the page to improve interactivity and navigability;
- Details about radiation contamination MCMs were mixed in with information about imported drug safety, under the heading of “questions about medical products.” This generic title failed to signal the public’s dominant concern – protection against the effects of radiation.
- Prior to noting the lack of need for any countermeasure (ie, “Does FDA recommend that consumers purchase potassium iodide as a protective step?”), the website first discussed radiation countermeasures (ie, “Hypothetically, if they were needed, what are the FDA-approved products for treatment of internal contamination with radioactive iodine?”). This created a potential inconsistency for those reading these messages, undermining the bottom-line that no countermeasure was necessary due to Fukushima for people on American soil.³¹
- Finally, the website failed to link to FDA’s more detailed FAQ webpage regarding potassium iodide.¹⁰

Implications for the Future:

The agency could have strengthened its messages by more explicitly acknowledging and prioritizing potential concerns about radiation, the dominant issue for the public as evidenced by their demands for this information from local public health officials and less trustworthy sources. Communicating about unnecessary and ineffective countermeasures requires that communicators acknowledge potential concerns and then provide consistent and transparent messages about the lack of any health benefit from these products. Additionally, as occurred in the case of the Fukushima disaster, actions should be undertaken directly with the companies advertising these products.

Action Items for FDA

1. Design webpages from the viewpoint of the target audience, using state-of-the-art virtual design principles. For instance, users should be able to easily access important information through navigational tools and hotlinks, without having to scroll through and search a long, text-heavy webpage.
2. Use social media such as Twitter, Facebook and YouTube rapidly and repeatedly to support the response to public concerns and preempt dissemination of inaccurate information. Employ plain and consistent language, convey accurate and up-to-date

information, and maintain transparency.

3. Extend beyond traditional messaging allies and optimize message accessibility through search engine providers and “debunking” websites to ensure that FDA messages are high ranking in internet search results and that opposing messages do not go unchallenged. A sufficiently important public safety issue may require the FDA to purchase placement with leading internet search engines.

Conclusions

The dilemmas highlighted in this case study focus around public demand for a countermeasure that is unnecessary but also in limited quantity. Although much attention is paid to convincing the public to use or accept a medical countermeasure during an emergency situation, it is equally important to ensure good communication when the appropriate public action requires the public to forgo a potential medical countermeasure. In this case, more rapid and visible communication, data to back up messages informing the public that countermeasures were unnecessary, and united messaging were strategies that could have reduced public concerns and resolved these dilemmas.

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Chapter Four: The H1N1 Influenza Pandemic of 2009-2010

Author's Note: The analysis and comments regarding the communication efforts described in this case study are solely those of the authors. This analysis does not represent the official position of the FDA. This case was selected because it illustrates MCM communication challenges in the context of an influenza pandemic, including vaccine safety themes. This case study does not provide a comprehensive assessment of all FDA and USG communication efforts. The authors intend to use this case study as a means of highlighting communication challenges strictly within the context of this incident, not to evaluate the success or merit of any changes made as a result of these events. Intensive after-action reports and lessons-learned concerning the H1N1 pandemic influenza response served as the basis for systemic changes, such as the FDA's MCMi.

Abstract

The H1N1 outbreak of 2009-2010 was the result of a novel flu strain. The response to H1N1 was multifaceted and involved multiple governmental organizations. In particular, at the beginning of the outbreak FDA instituted an H1N1 management system to coordinate a response, which included creating seven teams to address specific public health needs related to H1N1. While FDA's response to H1N1 was thus far-reaching, in relation to communication several components of FDA's response could have been enhanced: communicating about vaccine production including responding to concerns that the vaccine was risky, rushed through production, or untested; being more transparent about the vaccine manufacturing process generally including reasons why vaccine production might be delayed; strengthening collaboration with other health entities to overcome disparities in MCM uptake; and finally, in conjunction with CDC, clarifying the use of new MCMs/new uses of approved MCMs to both healthcare providers and the public.

Background

In early April 2009, reports surfaced of an influenza outbreak in rural Mexico.^{1,2} On April 15, a novel flu virus was detected in a child living in southern California.³ Additional cases of the disease were identified in California and Texas within a week.⁴ Subsequent testing indicated the earlier outbreak in Mexico was due to the same virus.⁴ By June, the disease, classified as 2009 H1N1, was found in all 50 US states and across the world.⁴ The World Health Organization subsequently declared a pandemic.⁵

By the end of the outbreak in April 2010, it is estimated that there were as many as 60.8 million cases of H1N1 in the US, resulting in 274,304 hospitalizations and 12,469 deaths.⁶ Compared to the average seasonal flu virus, H1N1 was typical in regards to morbidity and mortality.^{7,8} Unlike typical seasonal flu viruses, however, H1N1 appeared to pose the greatest risk to adults (aged of 25-64 years) with underlying medical conditions.^{9,10} Greater rates of morbidity and mortality were also seen among pregnant women, who had compromised immune systems due to pregnancy, and minority populations, who were at greater risk for both underlying medical conditions and a lack of access to healthcare.¹¹⁻¹⁴

The Food and Drug Administration (FDA) responded to public health needs throughout the pandemic. At the beginning of the outbreak FDA instituted an H1N1 incident management system to coordinate a response. As a component of this, FDA created seven teams to address public health needs related to H1N1: the vaccine team, the antiviral team, the in vitro diagnostics team, the personal protective equipment team, the blood team, the drug shortage team and the consumer protection team.¹³ While FDA's response to H1N1 was thus multifaceted and far-reaching, in regards to communication several components of FDA's response are of particular importance to future communication efforts: vaccine development, vaccine availability, health disparities, and communication of emergency use authorizations (EUAs). This chapter will focus primarily on these issues.

Dilemma #1: Perceptions of the H1N1 vaccine as “risky,” “rushed” through production, and/or “untested” motivated some people to shun vaccination.

Vaccine development began in earnest in June 2009.⁴ Although lab tests had revealed the H1N1 virus did not have the 1918-like markers associated with severe disease nor the markers associated with the high death rates seen in H5N1 flu strains, H1N1 was still seen as a health concern that warranted a response.⁴

The first doses of H1N1 vaccine were administered in the US on October 5, 2009. Due to production issues, however, vaccine supplies were limited until the end of December.⁴ Despite the fact that the H1N1 vaccine was a safe and effective way to prevent the spread of the disease, vaccine uptake in the US was lower than expected; only 24-27% of Americans were vaccinated and tens of millions of doses of vaccine went unused.^{14,15} A significant reason for this was perceptions that the H1N1 vaccine was “risky,” “rushed” through production and/or “untested.” Moreover, by the time that vaccines became widely available, public perception that the pandemic was mild or that there was limited risk also curtailed demand for the vaccine.¹⁶

Typical of vaccination in the US today, concerns about vaccine additives such as thimerosal and adjuvants were present during the 2009-10 H1N1 pandemic.¹⁷⁻¹⁹ Despite the fact that thimerosal, a organomercury preservative, was only used in one formulation of the H1N1 vaccine (multi-dose vials) and the fact that adjuvants were not used in any of the H1N1 formulations administered in the US, internet reports, primarily from anti-vaccination blogs and news sources, raised concerns about the possible link between these vaccine components and autism, Gulf War Syndrome and other neurological and developmental disorders.¹⁷⁻¹⁹ Consequently, these sources suggested that the public refrain from receiving the H1N1 vaccine.

The related issue of the novelty of the H1N1 vaccine was also raised by the anti-vaccination blogs and news sources, but unlike the additive issue, this topic was reported in the mainstream media as well.²⁰⁻²¹ The underlying perception related to this concern was that the production of the H1N1 vaccine was “rushed;” that because of its accelerated production it was somehow unsafe. Additionally, some sources suggested that the vaccine had not been sufficiently tested for safety. In reality, the H1N1

vaccine was produced by the same manufacturers and using the same methods as the seasonal flu vaccine and, unlike the 2009 seasonal flu vaccine, the H1N1 vaccine had been tested for safety in clinical trials conducted over the summer.⁴ However, confusion about how vaccines are produced and tested persisted, leading to claims that the vaccine was unsafe.

Concerns about vaccine safety were more common in certain subpopulations. Pregnant women, for example, were more likely than women in general to have concerns about the vaccine and to resist vaccination, in spite of the fact that they were more at risk for complications from H1N1 infections.^{11,18,19} Particular concerns of pregnant women centered on the health of their fetuses including the possibilities of miscarriage or autism and other developmental issues. Healthcare providers in some areas were also reluctant about receiving the live attenuated vaccine (LAIV) formulation of the H1N1 vaccine.²² Their concern was that the live virus in the vaccine could be spread to patients in healthcare settings. While all of these concerns were unfounded, messaging about the safety of vaccines generally, the H1N1 vaccine specifically, and even different formulations of the H1N1 vaccine was not sufficient to overcome doubt. Many pregnant women and healthcare providers remained unvaccinated.

FDA's communication about the H1N1 vaccine included news releases;²³ information for consumers posted on FDA's website,²⁴ including a Q&A page targeted toward pregnant women;²⁵ and an update for healthcare providers.²⁶ Information provided in these sources contained statements that FDA had approved different formulations of the vaccines, the names of the manufacturers of the vaccines, warnings of potential side effects, and specifically for providers: dosage recommendations and contraindications. In all of this communication, however, FDA did little to explain the oversight that went into the manufacturing processes to ensure vaccine safety. An FDA press release from September 15, 2009,²³ for example, provided only the following information on this topic:

"The H1N1 vaccines approved today undergo the same rigorous FDA manufacturing oversight, product quality testing and lot release procedures that apply to seasonal influenza vaccines," said Jesse Goodman, M.D., FDA acting chief scientist.

Based on preliminary data from adults participating in multiple clinical studies, the 2009 H1N1 vaccines induce a robust immune response in most healthy adults eight to 10 days after a single dose, as occurs with the seasonal influenza vaccine.

Clinical studies under way will provide additional information about the optimal dose in children. The recommendations for dosing will be updated if indicated by findings from those studies. The findings are expected in the near future.

While FDA is limited by confidential commercial information (CCI) protocol from sharing specific information on manufacturing processes, additional information comparing the production of seasonal flu vaccines to H1N1 vaccine production and specific details on steps FDA took to ensure "safe" H1N1 vaccines could have stemmed consumer fears.

Implications for the Future:

To address future lack of interest in medical countermeasures due to unwarranted concerns about safety, including production issues, various strategic and practical communication approaches are necessary. First, FDA should gauge its public credibility periodically as a "safety" gatekeeper for MCMs

(ie, within its role to assess product safety), capitalizing upon this reputation when it is strong and relying more heavily on communication partners (who have more sway among certain key audiences) when it is weak. Second, FDA should provide clear explanations about countermeasure components and testing and to do so as early as possible. In fact, pre-disaster preventative messaging, such as regularly communicating the universal and routine steps FDA takes to ensure product safety, including safe vaccine production, could mitigate the need for intensive messaging during a disaster. Third, depending on the nature of the emergency, including the size of subpopulations affected and the nature of the risks they face, it may be necessary to tailor messages for particular groups. In the case of H1N1 vaccines, FDA did this type of tailoring for both pregnant women and healthcare providers. Finally, it is necessary to disseminate messages in such a way that they will be accessible to members of the targeted groups. In the case of H1N1 vaccines FDA's communication strategies could have been improved in this regard; for example, messages about the safety of the LAIV formulation for health care providers were disseminated through the FDA website and other sources including the American Medical Association. The fact that some healthcare providers remained concerned about the LAIV formulation²² suggests that these efforts could have been more successful.

Action Items for FDA

1. Conduct an initial baseline survey regarding the FDA's standing in the public domain, followed by periodic assessments of the agency's credibility and reputation as gatekeeper for MCM safety. To have credence when speaking about MCM safety in an emergency, the agency must already have public opinion on its side. Between emergencies, the agency can take measures to strengthen its public standing.
2. Develop additional public resources on FDA's role in assuring safety over the lifecycle of a vaccine. In particular, continue to use the FDA Basics Webinar series to represent the agency's commitment to, and specific procedures for assuring vaccine safety; link to CDC materials on influenza vaccine safety, benefiting from the trust people hold in this agency; and supplement "text heavy" public communications about vaccine safety with more readily consumable graphic representations.
3. Tailor FDA's communication strategies to match the information consumption patterns and behaviors of subpopulations of interest:
 - a. Use surveys to investigate how particular groups (eg, HCWs, pregnant women) receive and consume messages pre-emergency, and build outreach mechanisms accordingly; poll subgroups of interest during an emergency to check whether or not FDA messages have been received, and if not, the mechanisms necessary to make them accessible.
 - b. Enlist strategic communication partners to convey FDA messages, including those about vaccine safety, to key subgroups. Maternity care providers and childbirth educators (reachable through their respective professional societies), for instance, are the top 2 sources pregnant women consult for information about pregnancy, with government agency websites following in sixth place.²⁷

Dilemma #2: Unmet public expectations about when and how a newly manufactured vaccine would become available during the H1N1 pandemic had an adverse impact on its uptake.

To maximize the amount of available vaccine, the US government contracted with 5 pharmaceutical companies.²² Four of these companies were contracted to produce different formulations of inactivated vaccine that would be administered via injection, while the fifth company was contracted to develop a LAIV formulation that would be administered via nasal inhalation. Early production estimates suggested that approximately 45 million doses of vaccine would be available in early to mid-October.¹⁵

While the H1N1 vaccine was being prepared, the CDC developed plans to distribute it across the country. The CDC contracted with a logistics company to establish a centralized distribution network that would distribute the vaccine to state and local health departments based on population estimates.¹⁴ State health departments, in turn, worked with local health departments to develop plans to distribute and administer the vaccine.²⁸ Many of these state and local efforts were covered by state and local media.

The first doses of the H1N1 vaccine were administered in early October 2009.⁴ Due to various manufacturing issues, however, the amount of vaccine available by the end of October, 23.2 million doses, was less than anticipated (CDC 4, CDC 5).^{14,29} As a consequence, many healthcare providers, including hospitals and clinics, received less vaccine than expected.^{22,30,31} In addition, vaccine deliveries were sporadic. Often healthcare providers were given only a few days' notice that a vaccine shipment was arriving.²² Both of these conditions made it difficult for healthcare providers to schedule vaccination appointments with their patients and to give answers to the patients who were calling their offices asking when they could come in to be vaccinated.³¹

The situation was further complicated by the availability, or lack of availability, of the different vaccine formulations and the co-messaging about the seasonal flu vaccine. The LAIV nasal spray, for example, was the first vaccine available, but it was contraindicated for both pregnant women and persons with underlying medical conditions like asthma.²⁹ For members of these groups, this meant that even though they had repeatedly been told they were in a priority group for vaccination, and even though they had planned on being vaccinated as soon as possible, that they had to wait until the correct formulation was available. This situation and related communication dilemmas including how vaccination distribution programs were implemented in different areas (discussed below) led to reduced vaccine uptake across the country.

Due to the limited supply of vaccine, the availability of different formulations, and on-the-ground exigencies, local public health departments and organizations opted to implement the vaccination guidelines in different ways.^{16,22} Some, like Group Health Cooperative in Seattle, used a strict interpretation of the CDC Advisory Committee on Immunization Practice (ACIP) guidelines and only gave vaccines to people in the priority groups.¹⁶ Others like the Chicago Department of Health, focused

vaccination efforts on people in the priority groups but did not turn away anyone who came to mass vaccination clinics.¹⁶ Such differences, especially when they occurred in close geographic proximity, led to some people to wonder why one jurisdiction was vaccinating a certain subset of its population and another was not.

Some of the distribution programs themselves became controversial. In New York City (NYC), for example, the local public health department opted to provide H1N1 vaccine to occupational clinics, including clinics for Wall Street firms such as Goldman Sachs and Citibank.³¹⁻³⁴ While vaccine distribution through occupational clinics was a well-established practice for the NYC health department, under the particular conditions of H1N1 vaccine scarcity, it was widely interpreted as a form of favoritism and prompted public outcry.^{31,32,35} Amidst these and other complexities of vaccine supply and demand, many people became discouraged in their search for vaccination.

Implications for the Future:

While FDA's role in vaccine distribution was limited – the majority of decisions about distribution and communication about these decisions came from the CDC and state/local public health – there is one aspect in which greater transparency from FDA may have made a difference: clearer communication about vaccine manufacturing generally, including reasons that vaccine manufacturing may take longer than anticipated. While CCI laws may limit the amount of specific detail FDA can provide, FDA could either provide a generic overview of a manufacturing process, or work with countermeasure manufacturers to develop and disseminate specific details of manufacturing processes of relevance to the public. Along with this information, FDA can continue to reassure the public about the role FDA plays in ensuring the production of safe countermeasures.

Action Item for FDA

In cases where countermeasures are developed during an emergency, FDA should provide either generic details on the countermeasure manufacturing process or work with the countermeasure manufacturers to develop and disseminate specific details of their manufacturing processes as this is relevant to the public. If delays in the manufacturing process are possible, then these messages should also include reasons production may be slower than anticipated.

Dilemma #3: In the absence of trustworthy and culturally appropriate information, certain groups were less likely to seek out vaccination against the H1N1 virus.

Disparities in vaccine uptake particularly among different subpopulations in the US represented another communication dilemma of the H1N1 pandemic.³⁶⁻⁴⁰ In some cases, these disparities were the result of how people within the subpopulations accessed available information. In others, they were the result of community beliefs about such things as healthcare, the significance of particular vaccine components, and the trustworthiness of the US government.

In general, marginalized subpopulations, like many poor, racial/ethnic minorities in the US, have less access to authoritative public health information than non-marginalized populations.^{20,41} For example, post-pandemic research has suggested that, for H1N1 and the H1N1 vaccine, higher educated people relied primarily on the internet (a primary platform for FDA's public communication); in contrast, for that same information, lower educated individuals were more likely to rely on television.⁴¹⁻⁴³ In addition, in some poorer communities, personal and community social networks, including faith-based organizations and radio stations, were key sources of information during the H1N1 pandemic.^{20,41} When misinformation was spread through these social networks, additional communication from public health agencies and others was needed.

Among poor, African American subpopulations in Los Angeles County, CA, for example, longstanding distrust in the US government stemming from the Tuskegee experiment led local faith-based leaders to urge their congregants not to accept the H1N1 vaccine, local disc jockeys from stations with predominantly African American audiences to advise their listeners to not be vaccinated, and community members to forward chain emails and like Facebook posts with anti-vaccination messages.²⁰ Subsequently, vaccination rates for African Americans in Los Angeles County were lower than rates for all other racial/ethnic groups in that area.

To address this issue during the pandemic, the Los Angeles County Public Health Department expanded their outreach to the African American community and actively sought to develop partnerships with faith-based leaders.²⁰ The public health department also sought to provide consistent messaging through community leaders focusing on increasing understanding of the health risks of H1N1 for African Americans. Combined with increasing the number of public vaccination clinics, these steps were somewhat successful in addressing disparities in H1N1 vaccine uptake among African Americans living in Los Angeles County.

Public Health-Seattle & King County took a similar approach to address concerns within the county's Somali population. In addition to varying understandings of preventative medicine and vaccines, many in the Somali community in Seattle had concerns about porcine gelatin as a vaccine component.⁴⁴ As Muslims, members of this community believed that taking any pork-related products into their bodies was a violation of their faith. To address this issue, Public Health-Seattle & King County attempted to work with local Somali leaders during the H1N1 pandemic with varying degrees of success (informant interview, public health official).

Implications for the Future:

To help mitigate against differential rates of morbidity and mortality in future health emergencies, it is critical that the entire US public, including specific subgroups, have access to credible, accessible, and meaningful information that enables them to make appropriate use of potentially life-saving MCMs. Local public health agencies are well-positioned to understand the populations they serve, to develop close relationships with faith-based leaders and other trusted intermediaries to reach specific communities, and to elicit greater understanding as to the health knowledge-needs of diverse constituent groups.⁴⁵ Through its own Office of Minority Health, the FDA can reach out to state offices of

minority health to solicit ideas about how the agency can better support those on the frontlines of MCM administration and communication. In addition, prior to any emergency, the FDA can establish ties with national non-governmental organizations that represent the health interests of minority populations to have them serve as potential conduits for targeted messages that the regulatory agency may need to disseminate about MCMs in an emergency.

Action Items for FDA

1. Strengthen the Office of Minority Health's role in the Medical Countermeasures Initiative (MCMi) to uncover, understand, and meet the communication needs of a diverse US populace, particularly underserved communities.
2. In the pre-crisis period, build working relationships with national non-governmental organizations that represent the health interests of minority populations. Rely on these partners to help disseminate any targeted MCM-related messages in an emergency.

Dilemma #4: Difficult-to-access and hard-to-understand information undermined efforts to make non-vaccine MCMs, including antivirals and N95 respirators, available to healthcare workers and the public.

Efforts to contain the H1N1 virus were not limited to the development, production and dissemination of the H1N1 vaccine. In fact, the first lines of defense centered on providing antivirals to affected individuals and personal protective equipment (PPE) to healthcare workers and other front line responders.

Shortly after the first case of H1N1 in the US was confirmed through laboratory testing, the Secretary of Health and Human Services determined that a public health emergency existed. As a result of this, FDA issued a series of emergency use authorizations (EUA). On April 27, 2009, FDA issued an EUA for oseltamivir (Tamiflu) and zanamivir (Relenza) to expand the age and patient populations these previously approved antivirals could be used to treat.⁴⁶ Four days later FDA issued an EUA for certain disposable respirators, known collectively as N95 respirators, in order to permit the distribution of these products to the general public, and particularly people performing work-related duties who were not under OSHA regulations.⁴⁷⁻⁴⁹ Over the course of the pandemic FDA would issue additional EUAs including one for an unapproved IV antiviral (Peramivir) and eighteen for different diagnostic tests.^{50,51}

Since the H1N1 pandemic, reviews of EUA protocols have led to a series of changes in policy, and along with other factors, influenced the passage of the Pandemic and All-Hazards Preparedness Reauthorization Act (PAHPRA) in 2013.⁵²⁻⁵³ These statutory changes have had a direct impact on how FDA responds to future public health emergencies. In particular, FDA now has the authority to authorize the emergency use of certain approved MCMs without issuing a EUA. Regardless of the procedural changes (ie, PAHPRA's MCM emergency use authorities for approved MCMs) since the 2009 H1N1

experience, the issue of what constitutes an adequate MCM communication, according to known standards, is still relevant. A communication is considered adequate if it equips a person with information essential to making an effective health decision (ie, it is material), it reaches a person via their normal information channels and gathering practices (ie, it is accessible), and it is readily digestible so that a person can apply it to make a sound choice (ie, it is comprehensible).⁵⁴ Inadequacies with respect to these standards were evident in relation to EUAs issued for antivirals during the H1N1 pandemic.

On April 27, 2009, FDA issued an EUA expanding the use of Tamiflu and Relenza, at the request of CDC; the issuance was timely as a result of enhanced FDA-CDC coordination afforded by earlier pandemic planning.⁵⁵ Under this EUA, Tamiflu was allowed in for use in children under one year of age (previously it was limited to patients one year of age and older) and both Tamiflu and Relenza were allowed to treat patients beyond two days of symptom onset (which was the previous requirement).⁵⁵ FDA, in concert with other governmental organizations including the CDC, released this EUA through traditional channels including FDA's website. While the EUA had a direct impact on healthcare providers and pharmacists, the information was not communicated effectively, resulting in delayed distribution of these drugs.⁵⁶ Specifically, on local levels some healthcare providers and pharmacists did not receive information about the EUA (a break down in accessibility), and in other cases when they did, they did not understand the language of the message being provided (a breakdown in comprehensibility).⁵⁶ Implementation of the EUA provisions would have been more timely and effective, if information on the expanded use of Tamiflu and Relenza had been clearer and more concise, and if it had been communicated through mechanisms routinely used by healthcare providers and pharmacists, such as an official federal letter to state pharmacy boards.⁵⁶ Confusion resulting from a lack of clear communication was also seen in relation to information on compounding oral suspensions of Tamiflu capsules for pediatric use; the information provided was complicated and difficult for many pharmacists to understand.⁵⁶ A consequence of the confusion was an insufficient supply of pediatric doses of the medication during the pandemic.

In addition to being accessible and comprehensible, MCM communications must also provide end users (such as healthcare providers, pharmacists, and consumers) with relevant information that enables them to make quality decisions. Some evidence suggests that this may not have been the case with antivirals during the H1N1 pandemic. A national study conducted during the pandemic,³⁸ for example, showed that given the information provided on the EUA Fact Sheet for Tamiflu that only 54.4% of respondents were willing to take the drug and only 48.8% would allow their children to take the drug. Moreover, 29.9% of respondents stated that they were moderately concerned about taking Tamiflu based on the information provided on the Fact Sheet and 21.0% stated that they were worried or extremely worried about taking the drug based on the information they received. This overabundance of caution with regard to Tamiflu use, despite the fact that the antiviral had undergone extensive testing and was already approved by the FDA, suggests that the Fact Sheet may not have successfully delivered the information that many people required to meet their own goal of personal health protection during the pandemic.

Implications for the Future:

EUA requesters – like CDC in the case of Tamiflu and Relenza – bear the major share of responsibility for MCM communication (eg, Fact Sheets) during an emergency. Nonetheless, the FDA can draw important “best practice” inferences from the overall H1N1 experience with antiviral EUAs and enhance its own communication practice in the future accordingly. In particular, it is important that MCM communication to end users (ie, healthcare providers, pharmacists, and the public) meet the 3 standards of adequacy: communicating through means that ensure populations of interest are being reached, providing users with information they consider material to making quality decisions about their health (and/or that of their patients or dependents), and delivering information that is readily comprehended and integrated into a person’s decision making. Each of these qualities is amenable to research that takes into account the user’s perspective and needs.

While FDA is not the only organization charged with communicating about topics that during H1N1 were EUA-related issues, FDA has a unique opportunity to reassure the public in regards to government oversight and product safety. In the future, FDA should leverage this role in their communication with the public, for example, by providing explanations of the steps FDA has taken to assure public safety in regards to particular MCMs.

Action Items for FDA

1. Leverage the agency’s role as ‘guardian of the public’s interests’ to increase the public’s confidence in MCMs during an emergency. As part of this communicate, in a general sense, how FDA approves and authorizes MCMs and consequently how MCMs can be trusted, in a general sense, in the current crisis.
2. Assess the adequacy of FDA communication concerning an MCM in terms of the 3 standards of materiality, accessibility, and comprehensibility. For instance, survey intended audiences regarding their routine information gathering behaviors (including sources on which they rely) and materials for salience and understandability with end-users before these are disseminated.

Conclusion

The H1N1 outbreak of 2009-2010 exemplified significant public health accomplishments. In less than a year a novel pathogen was identified and an effective countermeasure was developed, produced and delivered to 81 million people in the US alone. At the same time, the public health outcome was less than optimal. Less than half of the US population was vaccinated and vaccination rates were significantly lower in certain subpopulations including some racial/ethnic minorities and pregnant women.

The cause of this poor public health outcome was multifaceted and due in part to the actions of multiple governmental agencies. In regards to FDA, several communication-related issues were of particular importance: concerns about the safety of the H1N1 vaccine, confusion about countermeasure

availability, unevenness in uptake, and a lack of understanding about new MCMs/new uses of approved MCMs. To address these issues we recommend: tailoring messages for particular groups and disseminating these messages in such ways that they will be seen/read by members of these groups; providing more transparent explanations of how MCMs are tested to assure public safety; and leveraging FDA's role as 'guardians of the public interest' in order to reassure the public about MCM use.

All of these steps can be done during a public health emergency, but we also suggest that FDA preemptively take the following steps: provide pre-disaster preventative messaging relating to common MCMs, such as routinely communicating the steps FDA takes to ensure product safety in regards to vaccine and drug production; investigate how commonly communicated with groups, like healthcare providers and pharmacists, receive messages and, based on the information received, modify FDA communication methods as necessary; and finally improve the comprehensibility of existing communications, from which future communications can be modeled, by either testing messages for understandability with end users, including the general public, and/or working more closely with social scientists and other communication experts to refine old messages and develop new ones.

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Chapter Five: 2001 Anthrax Letters

Author's Note: The analysis and comments regarding the communication efforts described in this case study are solely those of the authors; this analysis does not represent the official position of the FDA. This case was selected because it is one of the few major federal efforts to distribute medical countermeasures in response to an acute biological incident. These events occurred more than a decade ago and represent the early stages of US biosecurity preparedness and response; however, this incident serves as an excellent illustration of the types of communication challenges expected in these scenarios. Due in part to the extended time since these events and the limited accessibility of individual communications and messages, this case study does not provide a comprehensive assessment of all communication efforts. In contrast to the previous case studies in this casebook, the FDA's role in the 2001 anthrax response was relatively small, and as such, this analysis focuses principally on the communication efforts of the CDC and state and local public health agencies. The 2001 anthrax attacks have been studied extensively, and the myriad of internal and external assessments led to numerous changes to response and communications policies and protocols. The authors intend to use this case study as a means of highlighting communication challenges strictly within the context of this incident, not to evaluate the success or merit of changes made as a result of these events.

Abstract

The dissemination of *Bacillus anthracis* via the US Postal Service (USPS) in 2001 represented a new public health threat, the first intentional exposure to anthrax in the United States. The attacks resulted in 22 cases of anthrax—eleven inhalational and eleven cutaneous—five of which were fatal.¹ Public health officials faced the challenge of communicating risk during rapidly evolving circumstances in response to terrorist attacks that affected numerous states and Washington, DC. A total of 21 USPS facilities were contaminated in the attacks, and 32,000 potentially exposed persons initiated post-exposure prophylaxis.² These attacks followed closely after those of September 11th, further complicating the challenge of addressing a new threat in a nation still recovering from a traumatic event.^{3,4,5} Conflicting public health guidance across different government jurisdictions and changing directives about prophylaxis undermined public confidence in health authorities' handling of the crisis and in the recommended personal protective actions, particularly among affected minority populations.

Background

Florida

On October 2, 2001 the index patient was taken to an emergency department in Palm Beach County, Florida. After an examination and further testing, clinicians suspected inhalational anthrax and contacted the Palm Beach County Health Department. On October 4, Florida State Department of Health and Centers for Disease Control and Prevention (CDC) laboratories confirmed the presence of *B. anthracis* in samples from the index patient. The index case was a photo editor for a media company,

and coworkers reported that he had opened and scrutinized a suspicious letter containing a white powder on September 19.⁶ Despite receiving antibiotic treatment, the index patient died three days after seeking care.^{7,8} This was the first case of inhalational anthrax in the United States since 1978 and would later be determined to be the first known use of anthrax in the United States as an agent of biological terrorism.⁶ A coworker of the index patient was admitted to the hospital on October 1 for what was initially misdiagnosed as pneumonia and later also determined to be inhalational anthrax. This second patient also received antibiotic treatment and ultimately survived.⁹

The epidemiological investigation identified *B. anthracis* in the mail and package area of the patients' workplace.^{8,10} Environmental samples from local and regional postal centers that processed mail sent to the office also tested positive for *B. anthracis*.¹⁰ Nearly 1,100 people in Florida began post-exposure prophylaxis (PEP) for suspected anthrax exposure.¹¹

New York City

On October 9, the New York City Department of Health and Mental Hygiene notified the CDC of a suspected case of cutaneous anthrax, prompting a second, parallel epidemiological investigation. The first identified New York anthrax patient had opened a letter containing a suspicious powder at her workplace, and she sought medical care for a skin lesion on October 1.⁸ In total, seven people in New York acquired cutaneous anthrax and one individual acquired and died from inhalational anthrax. With the exception of an infant who visited his mother's workplace, all of the cutaneous cases handled mail at work. All of the patients with cutaneous anthrax in New York were treated with ciprofloxacin—at the time only available as name-brand Cipro—and all survived.^{1,2,8,10,12} In total, more than 2,200 exposed persons were prescribed a full sixty-day course of antibiotic PEP in connection with the New York incidents.¹¹

New Jersey

On October 1, a USPS mail carrier in West Trenton, New Jersey sought treatment at a local hospital for a skin lesion on her arm.¹⁰ Ultimately, six individuals in New Jersey—five of whom worked in postal facilities—developed anthrax.ⁱ Two of the individuals developed inhalational anthrax, while the remaining four cases were cutaneous anthrax.^{2,12} Environmental testing confirmed the presence of *B. anthracis* spores at the Trenton Processing and Distribution Center—where four of the cases worked and contaminated letters transited en route to New York and Washington, DC.¹³ While most of the earlier cases in other jurisdictions were exposed through handling contaminated letters, the anthrax cases at the postal distribution facility suggested that automated, high-speed sorting machines could cause the release of anthrax spores into the environment. More than 1,400 persons in New Jersey received sixty-day courses of PEP as a result of suspected anthrax exposure.¹¹

ⁱ One of the postal workers lived in Pennsylvania but worked in New Jersey.

Washington, DC

On October 15, a staff member for Senate Majority Leader Tom Daschle opened a letter in the Hart Senate Office Building, releasing a white powder. Preliminary tests indicated the presence of *B. anthracis* spores, and the immediate area was evacuated. Based on environmental sampling, nasal swabs, and tracing of the envelope's delivery, investigators determined that 625 persons who worked at the Hart Senate Office Building, a nearby mail sorting facility, and mail rooms in two other Congressional office buildings were at risk of exposure. These at-risk persons were provided with a full sixty-day course of antibiotics.¹⁴ On October 19, an employee of the Brentwood USPS distribution facility in Washington, DC was admitted to a Virginia hospital and diagnosed with inhalational anthrax. Ultimately, five DC-area individuals were infected with inhalational anthrax, two of whom died. Four of the patients worked at the Brentwood facility, which had processed the letter mailed to Senator Daschle's office.¹⁵

The USPS closed the Brentwood facility on October 21, 2001, and it remained closed until December 2003.^{10,16} Officials initially recommended PEP only for employees working near the worksite of the first case, but this quickly expanded to include all postal workers in DC-area facilities served by the Brentwood distribution center.¹⁰ The Washington, DC; Virginia; and Maryland health departments provided full sixty-day courses of PEP directly to nearly 1,900 of 2,400 Brentwood employees, and more than 800 additional persons throughout the Washington, DC area were provided prophylaxis in connection with the Daschle letter.^{11,15}

Connecticut

On November 16, a Connecticut woman was hospitalized with inhalational anthrax and died four days later. The victim was homebound and lived alone in a rural area of Connecticut. Although the source of this victim's exposure to *B. anthracis* was never identified, genetic testing linked her case to the bioterror attacks. Despite no positive environmental samples or nasal swabs, officials offered PEP to the victim's family and friends as well as postal workers from two Connecticut facilities.¹⁷ More than 1,200 persons in Connecticut were ultimately prescribed full sixty-day courses of antibiotics.¹¹

Communication Milieu

In 2001, most Americans were unfamiliar with anthrax or its symptoms and treatment regimens. As a result, they relied heavily on public health officials for information and guidance. With little practical experience with anthrax experience, federal, state, and local officials were forced to develop key information and response recommendations in real time.⁵ Additionally, the speed with which events unfolded required officials to address questions and implement response procedures with an incomplete and evolving grasp of the situation. Due to the considerable uncertainty surrounding the attacks, official guidance changed dramatically as the incident progressed. Finally, due to the sheer number of jurisdictions involved, there were many instances of state and local policies conflicting with federal recommendations as well as various organizations presenting contradictory information. These missteps instilled a sense of mistrust among Americans, particularly those directly affected by the attacks.

Dilemma #1: An evolving health crisis with a high degree of uncertainty generated acute demands for timely information, which leaders were not prepared to meet.

The CDC and other clinical and public health experts struggled to effectively communicate risk to the public and healthcare professionals in the absence of complete information about the situation. This challenge was exacerbated by their limited experience dealing with anthrax, particularly on such a large scale and in the context of bioterrorism.^{5,18,19,20} As new information became available, public messaging evolved, at times significantly changing or contradicting previous communications.^{21,22} Risk assessments, environmental and clinical sampling techniques, and PEP recommendations all underwent substantial changes over the course of the response. When federal agencies were unable to effectively justify these changes, they were met with resistance. Additionally, health officials at the federal, state, and local level found it difficult to dedicate resources to addressing the media, making it difficult to control the public message. The absence of established procedures to respond to inquiries forced the public and media to seek out other, often unofficial, sources of information, resulting in contradictory messaging and further confusion.^{5,19,23}

At the time of the 2001 anthrax attacks, little anthrax expertise existed in federal, state, or local health agencies, resulting in inconsistencies in messaging as information was gathered. The CDC's experience with anthrax at that point largely dealt with naturally occurring outbreaks rather than intentional releases, which combined with the sheer scale of the response, forced many health officials to operate outside their area of expertise. The public and media perceived this lack of expertise as an attempt to conceal information about ongoing response efforts and the threat posed by the disease.^{18,24} For example, the CDC initially believed that sealed envelopes did not release anthrax spores and assured Brentwood postal employees that they faced minimal risk of contracting the disease. Once their fellow employees fell ill, however, the workers questioned the effectiveness of the CDC's response.^{18,23,25}

Federal officials also faced communication challenges surrounding PEP recommendations. In 2000, the FDA approved labeling for the drug ciprofloxacin—at the time of the anthrax attacks, only available as name-brand Cipro—that included PEP for inhalational anthrax as an indication, and this remained the only product specifically labeled as such until October 2001. In the midst of the anthrax response, the FDA clarified that the approved indications for doxycycline and penicillin—both available in a number of generic forms—included prophylaxis for inhalational anthrax exposure and provided corresponding dosing information. They encouraged manufacturers of these products to submit applications for corresponding label supplements.²⁶ While both drugs were already FDA-approved for both PEP and treatment for anthrax—the new label merely clarified the indications²⁶—the label change was widely reported as new approvals for doxycycline and penicillin as PEP for inhalational anthrax.^{21,27,28} Subsequent to the FDA announcement—and upon determination that the strain of anthrax used in the attacks was susceptible to doxycycline—the CDC updated its PEP drug of choice from ciprofloxacin to doxycycline. Doxycycline was equally effective as PEP, cheaper, resulted in fewer side effects, and was more widely available than Cipro.^{21,29,30} Additionally, there were concerns that widespread use of ciprofloxacin could result in anthrax (and potentially other bacteria) developing resistance to a powerful antibiotic.²¹ Because the initial anthrax patients and exposure populations were

provided Cipro, the name-brand product was already widely publicized in the media as the best option to combat anthrax.^{31,32,33} Regardless of the fact that CDC recommended the drug itself, ciprofloxacin, and not specifically the name-brand product,⁸ Cipro was the only version of ciprofloxacin available at the time, making it difficult to distinguish between guidance and endorsement. Without strong, consistent communication from officials at the FDA, CDC, and other federal agencies with respect to the new labeling and updated MCM guidance, particularly in the face of significant media publicity for Cipro, many were confused by the shift to doxycycline, including public health and healthcare professionals.⁵

At the completion of the initially prescribed sixty-day course of antibiotics, the CDC offered another forty days of antibiotics and vaccination to individuals with high exposure levels and those who had not completed the initial course of antibiotics in order to reduce the risk due to *B. anthracis* spores still remaining in the lungs after sixty days.³⁴ This change led to concerns over the efficacy of Cipro and doxycycline and revisited questions regarding anthrax vaccine safety. Prior reports of negative side effects during the military's vaccination program led many to question the vaccine's use in civilians.³⁵ Furthermore, while military service members were given six doses of the vaccine over an 18-month period,³⁶ the civilian victims of the anthrax attacks were only offered three doses over four weeks.³⁷ The vaccine was not FDA-approved for PEP, so the government required a signed informed consent form—which many believed waived their rights to compensation for adverse side effects—as well as consent to follow-up observation under Investigational New Drug (IND) policies.^{37,38} The vast majority of those offered the vaccine refused it, some believing that the government was simply taking advantage of the attacks as an opportunity to test the vaccine in human subjects. Of those who were offered the vaccine that had already completed a sixty-day course of antibiotics, many perceived their continuing risk as low and were reluctant to take additional drugs with potential adverse side effects.³⁵ The failure of health authorities to effectively communicate justification for these policy changes and the informed consent and follow-up requirements under the IND protocol led many to doubt the competence and authenticity of the local and federal officials leading the response efforts.

At times, communication problems began with a misinterpretation of information, and without effective communication mechanisms in place to respond, small mistakes quickly became national issues. In one example, a state health representative was called to an emergency meeting with the Governor, leaving a local health official to lead a meeting with New Jersey postal workers. In addressing the postal workers, the local official misspoke about two local “suspect” anthrax cases—both individuals, in fact, had positive nasal swabs but no positive diagnostic test or symptoms. The situation grew worse when state health officials were unavailable to confirm or clarify the statement for the media. Subsequently, a local paper ran the story on the suspect cases, which was then picked up nationally by CNN. This incident underscores the challenges of sharing accurate information in an uncertain environment and the absence of well-informed response authorities and communication protocols.^{20,39}

Healthcare providers also struggled to obtain timely, consistent guidance from health officials.⁴ When federal officials *did* have pertinent information to share with the medical community, they did so through inadequate mechanisms. For example, CDC officials published updates in their *Morbidity and*

Mortality Weekly Report (MMWR). Though these reports are freely available, their weekly periodicity was insufficient for keeping pace with a rapidly evolving incident. The CDC also utilized two fledgling technologies, Epi-X and the Health Alert Network (HAN), to share updates; however, access to these in 2001 was limited, particularly for healthcare providers. The CDC did publish updates to its public website, but the site crashed multiple times during the response, due in part to high traffic.^{5,23} The CDC's inability to provide timely, accurate, and easily accessible information resulted in inconsistent messaging and created an information void that unofficial, less reliable sources were left to fill.^{4,23}

Implications for the Future:

All disasters, including acts of bioterrorism, are inherently replete with uncertainty; however, training agency representatives in the following steps can help ensure effective emergency communication with the public: acknowledge the uncertainty; explain efforts to gather and analyze information; explicitly respond to requests for information, even if only to state openly that the answer is currently not known; and offer situational updates as the crisis progresses.^{18,22,24,35,39,40} These efforts will promote transparency and garner a sense of trust in the response. Advance preparation to deal with a rapidly evolving and ambiguous situation includes establishing streamlined protocols for message dissemination in order to reduce delays in communication.⁴⁰ Federal agencies also need to ensure that clinicians receive accurate updates. Increased access to technology—including HAN and Epi-X—provides means to rapidly disseminate technical information;⁴¹ equipping clinicians with key messages will better enable them to engage their patients.^{23,42} Efforts are required, however, to ensure that key audiences have access to these new technologies in advance of an event. Even under ideal circumstances, the public will predictably seek out alternate information sources, so it is vital for official representatives to protect their credibility as authoritative sources of information by communicating early, openly, and often.⁴³ Still, mistakes will inevitably be made during any emergency. Acknowledging errors, directly addressing policy changes, and updating public messaging accordingly will help maintain agency transparency and credibility throughout the response.^{18,39}

Action Items for FDA

1. Employ crisis communication strategies and language that can help the FDA preserve its credibility and remain responsive to information demands by the public, media, and healthcare providers during periods of uncertainty:
 - a. Acknowledge limits on the ability to determine or predict all aspects of the emergency and response due to missing, complex, or rapidly evolving information.⁴⁴ Do this apologetically and self-critically, and share in the audience's distress at having incomplete knowledge—eg, “It must be difficult for people to hear how tentative we must be, because there is still so much we don't know...”⁴⁵

- b. Describe the process being used to obtain additional information about the evolving situation—eg, “I can’t tell you today whether investigational drug ‘X’ is effective in humans against the current outbreak of disease, because we only have results from laboratory and animal studies. But I can tell you what we’re doing to find out...”⁴⁶
 - c. When policy positions shift in a crisis, alert the audience, explain how and why the message is different from before, and acknowledge the emotive response(s) that the change may evoke—eg, “More evidence has come to light during the outbreak, indicating that investigational drug ‘X’ is not safe and has no benefits in humans. We have, therefore, halted its use in patients. We share your grief at this disappointing development.”⁴⁷
2. Coordinate with federal partners to increase the reach of vital messaging:
- a. In this case, the CDC utilized technologies such as HAN and Epi-X to help ensure that the medical community was updated regarding recent developments in the anthrax response, including PEP recommendations. Coordinating with the CDC and other partners to leverage existing communication networks could provide additional means of informing clinicians, the public, and other audiences of the status of investigational products, product recalls, fraudulent products, and other vital information.
 - i. New communications technologies require planning, implementation, and testing—prior to an event—to ensure that desired audiences are being reached. In this case, HAN and Epi-X were utilized by the CDC, but they were not yet widely accessed by the intended audience, reducing their effectiveness.
 - b. Similar approaches should be utilized to expand the reach of social media communications. Coordinating with public information staff in other agencies can enable widespread sharing (eg, “retweeting” a message on Twitter) through and between expanded social networks to reach a broader audience.
3. Streamline social media communication approval processes to enable the FDA to respond rapidly to the public, media, and government officials. Monitoring and publicly replying to inquiries and comments on various social media platforms provides insight into how the public is receiving existing communications, helps identify topics that require additional effort or updated communication approaches, and facilitates responsive engagement with influential members of the media and public.

Dilemma #2: Contradictory messages and inadequate coordination of risk communication across multiple governmental jurisdictions and the private sector impeded response efforts and generated public mistrust.

Public health authority and responsibility resides largely at the state level, so response policies can vary significantly across states.⁵ In addition to the three states (Florida, New York, and New Jersey) and Washington, DC where the initial cases were exposed, several other states were also involved in response activities. As previously mentioned, one of the infected postal workers from the New Jersey

USPS facilities lived in Pennsylvania. Additionally, the letters sent to Washington, DC affected a number of people who lived in Maryland and Virginia but worked in the District. Initial recommendations in these three jurisdictions varied, and there was considerable confusion in the public over which to follow, those from where they worked or those from where they lived. For instance, prophylaxis recommendations in Maryland and Virginia followed CDC guidelines while Washington, DC had its own policy. Some jurisdictions made prophylaxis recommendations before the CDC issued guidance, and others waited for the CDC policy. In some cases the guidance issued by jurisdictions directly conflicted with CDC-issued recommendations. Furthermore, state and federal agencies used different criteria for identifying at-risk populations. Some definitions of “at-risk” were limited to those who handled contaminated envelopes, while other definitions encompassed service staff and visitors at affected facilities.^{5,48}

The inherent tension regarding the scope of the CDC’s authority compared to state and local health departments further complicated risk assessment and communication efforts. In one instance, New Jersey recommended that postal workers at facilities where two cases of anthrax were identified receive PEP; however, because this contradicted CDC guidance at the time, the federal government did not make National Pharmaceutical Stockpile (now the Strategic National Stockpile) resources available. As a result, local governments, responders, and physicians made treatment and prophylaxis decisions on a case-by-case basis, often determining eligibility based solely on the patient’s own perceived risk.^{5,43} The inconsistencies in public health recommendations between state/local jurisdictions and the federal government impeded rapid, effective response to potential cases and planted seeds of doubt and mistrust of public officials in affected populations.

Two significant policy contradictions regarding nasal swabs and the anthrax vaccine highlight the complexities associated with coordinating responses across multiple agencies and jurisdictions. First, nasal swabs can help identify the scope of exposure in and around areas known or suspected to be contaminated with *B. anthracis*; however, they are inadequate for use as a diagnostic or in determining individual-level exposure. Health officials immediately conducted nasal swabs to determine potential exposures for the Florida, New York, and Capitol Hill incidents.²⁰ Because the postal distribution centers in New Jersey and Washington, DC were not initially identified as contaminated, ten days passed between when the letters passed through the facilities and when health officials conducted nasal swabs at these locations.^{1,13,15} Official federal and state guidance indicated that nasal swabs were not to be used as diagnostic tools for anthrax, but some hospitals and other facilities offered them at the demand of the local population and reported the results to local health departments. Nasal swabs routinely result in false positives and false negatives, which officials worried could give those tested an unwarranted sense of risk or safety, based solely on the swab results.^{20,22,43,49} To reduce this risk, many of those persons swabbed by official responders were not provided the results of their test. Because the explanation for this was insufficient, it increased feelings that they were the subject of experimentation.^{22,43} The general misunderstanding, in the public and medical community, of the purpose and reliability of the nasal swab tests and the local deviation from state and federal guidance led to further public mistrust of health officials. Additionally, the CDC’s delay in conducting nasal swabs

at the Brentwood facility was viewed by many, especially the Brentwood employees, as substandard care for poor, minority populations compared to the exposed population on Capitol Hill.^{24,43}

In December 2001, CDC and other Department of Health and Human Services officials announced that they would offer the anthrax vaccine to certain subsets of the exposed population, a decision met with opposition from the public as well as state and local governments. The initial justification for the change indicated that those with high levels of exposure to anthrax spores and those who did not complete their initial sixty-day course of antibiotics could still be at risk for developing anthrax after sixty days.^{34,37} Despite offering the vaccine, federal health officials remained uncertain about how the vaccine's potential benefits weighed against possible side effects. Consequently, they neglected to take a definitive stance on whether exposed populations *should* be vaccinated.⁵⁰ This perceived lack of conviction, combined with the investigational nature of the vaccine and the perception that the government offering the vaccine was motivated by political rather than medical factors, left many questioning whether vaccination was the right decision.^{25,35} Compounding the public mistrust, the vaccination plan received considerable pushback from the postal worker union and the health departments in New Jersey and Washington, DC.^{35,50} Finally, while federal health officials discussed the vaccination directly with affected Senate staffers, they coordinated with state officials, the USPS, and the postal worker union to disseminate information to the rest of the exposed population. The vetting process in each of these organizations resulted in delays in the information reaching the affected populations and intensified fears that these organizations, particularly the USPS, were weighing the benefits to their constituents against their own interests. The effect of inconsistent messaging is evident in the vaccination rate for the Senate staff (38%) compared to the affected media and postal workers (2%).⁵⁰

The public's mistrust in federal, state, and local leadership was attributable, in part, to unfamiliarity with the agencies responsible for responding to health emergencies. Without having any prior relationship or interactions with the CDC, for example, many found it difficult to trust the messages that the CDC disseminated, particularly when those messages changed or conflicted with information coming from other agencies. As a result, most of the affected population sought out local health officials, friends and family, the internet, and/or the media as information sources.^{18,42} Some also assumed that the federal agencies and state and local public health agencies worked closely together and collaborated to rapidly share information, which was not always the case.¹⁸ In fact, reports indicate that state and local governments vetted risk communications from senior governmental sources before presenting them to the public, often resulting in delays and changes to the message content.³⁹

Implications for the Future:

One key to effective risk communication during a disaster is coordination between relevant agencies and stakeholders prior to the incident.^{4,19,51} Pre-established relationships enable responders and organization representatives to learn about other entities' respective priorities and capabilities, thereby facilitating greater coordination during an emergency. Utilizing multidisciplinary task forces for daily operations and preparedness planning breeds familiarity between agencies and promotes

collaboration across jurisdictional and agency lines.^{25,52,53} When stakeholders cooperate and maintain the same operational picture, communication can be decentralized, decreasing delays and promoting proactive—as opposed to reactive—communication.^{19,20,39} Risk communication recommendations often include the principle of “speaking with one voice.” Even so, stakeholders may evaluate circumstances differently and reach conflicting conclusions. Directly addressing the basis and rationale for these differences will engage the public, allow them to make informed decisions, and promote trust within the community.^{35,39} Additionally, engaging journalists in preparedness efforts helps ensure that media understands the rationale for these changes or differences in MCM and emergency response policies and accounts for them in their coverage of health emergencies.⁴⁰ Finally, pre-event coordination between responders, the media, and other stakeholders—such as informational workshops and exercises—should include risk communication development and dissemination protocols to facilitate rapid, accurate transmission of vital messaging during an incident to a variety of audiences.⁵

Even with ideal pre-event planning and coordination, certain aspects of incident responses may remain foreign to the public. Illustrated here by the public’s unfamiliarity with the CDC, this issue can also pertain to lesser known programs or policies within well-known agencies as well as novel diseases or prophylaxis or treatment options. Even with increased public access to governmental agencies and representatives today—via increased traditional and social media presence and agency websites—some aspects of incident response may remain largely unknown to the public. This places the burden on agencies to raise their individual and collective response profiles prior to an emergency and be proactive and responsive to demands for information on unfamiliar aspects and issues in ways that garner broad understanding in order to counter competing messages before they can take root.

Action Items for FDA

1. Continue to strengthen PHEMCE interagency coordination and collaboration, including concerted efforts to “ensure effective communications with both responders and the public through the timely release of credible, understandable, and actionable information both prior to and during public health emergencies.”⁵⁴ Maintain the FDA’s frequent contact with state/local public health authorities and responders and public health non-governmental organizations to support their MCM preparedness and response capabilities,⁵⁵ and engender coordinated communications.
2. Enlist PHEMCE partners in a joint communication effort to develop, test, and promulgate an accessible narrative, supported by graphics, about the Strategic National Stockpile that projects a unified governmental effort to facilitate prompt, appropriate access to safe and effective MCMs in an emergency (from development to distribution to monitoring). Use this storyline in diverse public communications and single out FDA contributions, disseminating broadly, including at www.phe.gov.

3. Reinforce the FDA’s public reputation as an agile emergency responder and credible information source on MCM safety and efficacy. Actively deliver information using, in particular, channels already integral to people’s daily lives (eg, existing and emerging social media platforms, daily news or talk show programs on television or radio). Develop a network of respected and popular social media personalities to help deliver messages to people not currently monitoring FDA social media efforts.

Dilemma #3: Inconsistent public health interventions coupled with historic health disparities nurtured perceptions that health authorities delivered substandard care to, and even experimented on, certain populations.

Members of some affected populations believed that variations in public health recommendations reflected existing racial and socioeconomic disparities. In Washington, DC, for example, this perception was highly prevalent among the postal service employees at the Brentwood facility. USPS workers felt that the CDC should have recognized earlier that they were a high-risk population and provided care prior to the first identified Brentwood anthrax patient. Additionally, they were concerned not only that the treatment they received was inferior to that of the affected Senate staff, but also that the CDC and other health officials were more concerned with gathering data from them than addressing their individual concerns and fears.¹⁸

The CDC initially, and incorrectly, assumed that sealed envelopes did not allow for the aerosolization of anthrax spores and that exposure to anthrax required direct exposure to the open envelopes, and early indications otherwise did not prompt environmental sampling at postal distribution facilities.^{5,24,56,57} In fact, testing and PEP did not begin at the Brentwood facility until October 21, two days after the first case was admitted to the hospital.^{15,24} Workers at the Brentwood facility knew from the beginning that the sorting machines routinely damaged envelopes and that cleaning the machines required blowing significant quantities of dust into the air, potentially exposing workers far beyond the immediate area, but the CDC did not immediately reach the same conclusion. To many, the CDC’s failure to identify the Brentwood employees as a high-risk group represented a significant disparity in the level of attention and care devoted to the Senate staff versus the Brentwood staff, many of whom belonged to racial minorities or came from lower socioeconomic backgrounds.^{5,18,43}

In addition to the delay in initiating the investigation at the Brentwood facility, there were also differences between the prophylaxis options offered to the Senate and Brentwood staffs. When the Daschle letter was identified, the Senate staff were prescribed name-brand Cipro, in accordance with the initial CDC guidance.ⁱⁱ As discussed previously, clarified indications and updated labeling for doxycycline during the response led to revised CDC guidance, changing the preferred PEP from ciprofloxacin to doxycycline.²¹ While doxycycline offered several significant benefits over ciprofloxacin,^{21,29,30} the name-brand Cipro product was already widely portrayed in the media as the drug of choice.^{31,32,33} When the postal workers at the Brentwood facility were provided with doxycycline

ⁱⁱ CDC guidance recommended ciprofloxacin, not specifically Cipro; however, name-brand Cipro was the only ciprofloxacin product available in the United States at the time.

as PEP, the fact that they received a generic drug resulted in the perception that they, being minorities and of low socioeconomic status, were being offered a substandard option compared to the name-brand product provided to wealthier, white Senate staffers.^{5,31,32} Given the timing of the PEP policy change, postal workers viewed the difference between the response on Capitol Hill and at the Brentwood facility as disparities in care due to differences in socioeconomic status rather than as a necessary policy update based on new information.⁵

Brentwood employees also felt that federal health officials ignored the health and concerns of individual workers, reporting that CDC investigators merely gathered data instead of answering questions or mitigating public anxiety. For example, CDC teams arrived at the Brentwood facility to collect environmental samples while wearing biohazard suits, despite the fact that there were employees still working at the site.^{18,43} Additionally, health officials were seen as working closely with the USPS leadership, who were viewed by the workers as prioritizing mail delivery and profits over employee health and safety.^{18,35} Many of these concerns stemmed from historical examples of ethics violations such as the Tuskegee syphilis study, leading some postal workers to believe that the CDC was using the anthrax attacks as an opportunity to conduct human testing instead of helping them.^{18,24,35} Reports from the Senate staff and the Brentwood employees also indicate significant differences in the level of attention they received from health professionals. The Senate staff had direct contact with the Office of the Attending Physician as well as consistent access to a single Navy physician. In contrast, postal workers reported that they met with many different federal health representatives who were rarely, if ever, available to address their questions and concerns.²⁴ By failing to effectively empathize with the Brentwood workers and address their individual fears, federal health officials alienated the postal workers and propagated feelings of socioeconomic and racial discrimination.

Implications for the Future:

In this case, feelings of discrimination were tied to delays in the CDC identifying the risk to postal workers and a failure to communicate justification for changes in PEP policy. During the initial phases of response, the CDC failed to identify postal workers as a primary risk communication audience. Had the CDC identified these workers as priority populations, their attention would have fostered a stronger sense of trust. Furthermore, by engaging these populations early on, the CDC may have better understood the risks faced by postal workers and potentially initiated PEP prior to identifying the first anthrax cases were identified in postal workers.^{18,39} Additionally, health officials need to be able to address the individual concerns of affected populations. While public health traditionally focuses on population-level health, individual fears and questions are most important to those directly impacted by an incident. Such concerns must be acknowledged with empathy to foster trust among affected individuals, assure them that their health and safety is a priority, and encourage compliance with official guidance.^{4,18}

Empathizing with minority and other marginalized groups inherently involves understanding historical conflicts between these groups and the healthcare community. It is essential that health professionals are able to recognize public anxiety around the possibility of human experimentation and

address concerns about clinical trials and epidemiological studies in the context of historical incidents.^{18,35} To facilitate this, directed research to identify specific concerns within intended target audiences would provide context for framing complex ideas in emergency communications. Finally, leaders must ensure two-way communication throughout the response period, perhaps by assigning dedicated communications personnel or identifying and enlisting established advocates within affected populations.^{3,4,18,52} Such advocates must be able to elucidate complex issues for the population in question—such as informed consent, the difference between treatment and prophylaxis, or the purpose of collecting follow-up data—and provide responses to specific concerns.^{4,24} By ensuring that all affected populations are properly informed of updated recommendations, risk communicators can empower the public to make informed decisions about their health and decrease feelings of discrimination and disparity.

Action Items for FDA

1. Strengthen the Office of Minority Health's role in the Medical Countermeasures Initiative (MCMi) to better acknowledge, understand, and address special communications challenges involved with audiences that have historical mistrust in health officials. This added insight can help frame MCM communications, namely those involving clinical trials and investigational products, to reassure affected populations that equal treatment and consideration is given to all, regardless of race, religion, socioeconomic status, education, or other factors.
2. In conjunction with PHEMCE partners, and their respective experts in health equity and disparity, develop, test, and disseminate MCM messages that are culturally appropriate, respond to community concerns, and help foster a greater sense of trust within historically underserved and vulnerable communities. These messages can support enhanced accessibility to life-preserving MCMs in emergencies.

Conclusions

During the 2001 anthrax attacks, public health officials faced significant challenges in communicating risk during a rapidly evolving public health crisis that spanned numerous states. Conflicting messages across jurisdictions and changing or inconsistent recommendations about treatment and prophylaxis undermined public confidence in health officials and led many to perceive significant disparities in care based on race and socioeconomic status. Public health officials can improve future emergency communication efforts by incorporating communication into preparedness planning and acknowledging uncertainty during incident response. Officials need to inform the public from the outset that guidance will evolve, acknowledge errors when they occur, and provide continuous updates throughout the course of an emergency to maintain transparency and enable the public to make informed decisions. Finally, health officials need to engage with the affected population to understand, acknowledge, and empathize with their individual concerns. Reassuring the affected population that health officials have their best interest in mind will build trust and encourage adherence to recommended actions.

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