PACCARB

Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria

Meeting Summary

21st Public Meeting of the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria

Antimicrobial Resistance and Pandemic Preparedness Policy Workshop
September 12–13, 2022

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Meeting Proceedings

Welcome, Overview, and Roll Call

Martin Blaser, M.D., Council Chair; Michael D. Apley, D.V.M., Ph.D., DACVCP, Vice Chair; and Jomana F. Musmar, M.S., Ph.D., Designated Federal Official, Advisory Council Committee Manager, Office of the Assistant Secretary for Health (OASH), U.S. Department of Health and Human Services (HHS)

Dr. Blaser opened the meeting at 9 a.m. ET and welcomed the participants. Dr. Musmar described the Council's establishment and charter and summarized the rules governing the Council under the Federal Advisory Committee Act and conflict-of-interest guidelines. She then called the roll. (See Appendix A for the list of Council members and staff.)

Secretary Xavier Becerra tasked the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) with providing recommendations on how to strengthen defense against antimicrobial-resistant pathogens by revising current pandemic preparedness and response plans and policies. This PACCARB Antimicrobial Resistance (AMR) and Pandemic Preparedness Policy Workshop was designed to examine a hypothetical large-scale disease outbreak of a novel viral pathogen that causes significant antibiotic-resistant secondary bacterial infections in humans and swine (see Appendix B for the details on the mock scenario). This workshop aimed to provide PACCARB members the opportunity to discuss AMR in relation to pandemic preparedness and develop recommendations per the Secretary's charge.

Opening Remarks From the Assistant Secretary for Health

Rachel L. Levine, M.D., ADM, U.S. Public Health Service (USPHS), Assistant Secretary for Health, HHS

ADM Levine voiced her continued commitment to stopping the spread of AMR. The Centers for Disease Control and Prevention's (CDC's) report on the impact of COVID-19 on AMR was a sobering reminder that more action is critically needed, as well as better data. Global research similarly concluded that AMR is not only a leading cause of death worldwide, but there are major gaps in data. The lack of data limits understanding of the full scope of this public health crisis and complicates decision making. ADM Levine recognized the tireless work of colleagues across HHS to adapt diagnostic and surveillance systems to track the COVID-19 pandemic.

Pandemics provide an opportunity to do better. With the rapid dispersal of resources and funds, the United States can and should continue to address AMR hand-in-hand with pandemic preparedness and remain on the forefront of this fight, domestically and globally. Acknowledging the wide-reaching impact of the COVID-19 pandemic is a critical first step in understanding how to ensure the nation's continued resilience. The PACCARB's work at the intersection between human and animal health positions it to take a holistic approach to AMR and pandemic preparedness. This workshop is an opportunity for honest and hard conversations about whether the country is truly ready to meet the next challenge. It should highlight lessons learned as well as major barriers and gaps that still exist in human and animal health.

ADM Levine pointed out that public health is not only individual health, but also economic health, environmental health, and food and nutritional security. In the wake of the ongoing COVID-19 pandemic and monkeypox outbreak, policies must remain adaptable and resilient. ADM Levine thanked all of the participants for playing a critical part in ensuring that the nation becomes better prepared for future threats. She was encouraged that the PACCARB brought in experts from public health and pandemic preparedness for this workshop, because this complex effort deserves a coordinated and multidisciplinary approach. This workshop is a critical first step in creating more robust policy to meet the demand of the next great public health crisis.

Opening Remarks From the Assistant Secretary for Preparedness and Response (ASPR)

Dawn O'Connell, J.D., ASPR, HHS

Ms. O'Connell said antimicrobials are critical to national preparedness and the cornerstone of modern medicine. Following any public health emergency, effective antimicrobials are needed for treatment. AMR contributes to more deaths globally than HIV or malaria. In 2019, bacterial AMR infections caused 35,000 deaths in the United States and 1.27 million deaths globally. Rates of antibiotic-resistant health-care-associated infections (HAIs) increased 15 percent as the COVID-19 pandemic surged. New drug-resistant pathogens are emerging faster than new antibiotics can be developed to treat them. This silent pandemic of AMR poses significant resource and financial burdens on the country and its health care system.

The ASPR oversees the Biomedical Advanced Research and Development Authority (BARDA), which has invested $1.7 billion in public–private partnerships for research and development (R&D) of more than 120 antibacterial products. BARDA also manages Project BioShield, which aims to develop four new antibiotics by 2030. The Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), an international partnership between HHS and the Wellcome Trust to spark early-stage development, recently received continued funding for 10 more years. CARB-X has 18 products in its advanced R&D portfolio, five of which are in phase III clinical trials. It has brought three new antibiotics and one new diagnostic test to the market.

The Office of the ASPR is the lead federal agency for protecting Americans from health security threats. To foster interagency collaboration, the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE), a consortium of nine federal agencies, was relaunched to advise the Secretary on key issues such as AMR. Ms. O'Connell thanked the PACCARB members for their time, energy, and contributions to combating AMR.

Discussion

Ms. O'Connell acknowledged that recent years have highlighted the need for honest, clear communication. She recognized the importance of making decisions based on information and communicating the reasoning behind her decisions. As new information emerges, it is equally important to continue communication. The public should not be left behind as the government and its partners deal with an evolving situation. With AMR, there is much to learn, and it is necessary to help the public understand the need for new antimicrobials and how the federal government is supporting R&D.

Community Story

Armando Nahum, Council Member

The Council traditionally begins meetings with a personal testimony to put a face to the real-world impact of AMR. Chrissie Blackburn was scheduled to speak, but she died unexpectedly. Mr. Nahum, a close friend of Ms. Blackburn, spoke on her behalf. He explained that Ms. Blackburn planned to talk about her daughter, Lily, who was born prematurely with underdeveloped kidneys. Ms. Blackburn was told to expect Lily to die in infancy, but she fought for Lily's life. Lily received a kidney transplant and is now a teenager.

Mr. Nahum considered Ms. Blackburn a family member. She was described by many as a shining star who touched many people's lives and will be remembered as compassionate and deeply committed to her family, especially Lily. Ms. Blackburn was a persistent advocate for patient safety and the principal advisor for patient and family engagement at Cleveland's University Hospitals Case Medical Center. Inspired by Ms. Blackburn's passion, Mr. Nahum said he and others will continue to advocate for patients. He requested a moment of silence in memory of Ms. Blackburn.

Overview of the Mock Scenario and Meeting Objectives

Ramanan Laxminarayan, Ph.D., M.P.H., and Joni Scheftel, D.V.M., M.P.H., DACVPM, Co-Chairs, PACCARB AMR and Pandemic Preparedness Working Group

Workshop presenters were asked to describe how they anticipated their organizations would respond to the hypothetical scenario presented. Throughout the meeting, topics were introduced with mock "breaking news" video segments, created by the PACCARB staff, describing the impact of the mock scenario events on the country.

Dr. Laxminarayan reminded participants that the PACCARB was tasked with recommending how to augment existing pandemic preparedness policies to address AMR with the goal of being better prepared for large-scale events involving AMR pathogens. The One Health perspective that the PACCARB brings is vital to this task. All of the events outlined in the mock scenario (e.g., human pandemic, animal pandemic, and significant mortality secondary to respiratory infections) have occurred in some manner in the United States, so it is not hard to envision a situation where they happen simultaneously. However, Dr. Laxminarayan emphasized, the focus should not be on the past but rather on imagining how the future might be different and how to prepare for a new, different worst-case scenario that includes AMR.

Dr. Scheftel said that in a scenario affecting both humans and animals simultaneously, farms and food production facilities would be facing worker shortages, adding to the difficult task of maintaining safety of humans and animals in those settings. The workshop was divided into four modules:

- Surveillance
- Diagnostics
- Vaccines and Therapeutics
- Infection Prevention and Control (IPC) and Biosecurity

The main objectives of the workshop were (1) to identify gaps in existing pandemic preparedness guidance on prevention, detection, and treatment of AMR associated with a viral pandemic; and (2) to determine actions that federal agencies could take to improve response to AMR infection and maintain antibiotic stewardship throughout the response.

Pandemic Response From a Global Perspective

Jose Fernandez, Ph.D., Office of Global Affairs, HHS

In addition to the declaration of a public health emergency by the HHS Secretary, federal agencies also respond to international events identified by the World Health Organization's (WHO's) international health regulations (IHRs). The IHRs outline the reporting requirements for public health events and the criteria for determining a public health emergency of international concern (PHEIC), which may require an immediate, coordinated international response. The IHRs employ an algorithm to assess public health threats that takes into account the potential public health impact, the risk of international trade, and the risk of travel and trade restrictions, among other factors.

If WHO declares a PHEIC, it makes temporary recommendations regarding response, such as data sharing, contact tracing, response coordination, clinical management, IPC, travel and border restrictions, risk communication, community engagement, and immunization of populations at risk. The recommendations are not legally binding but offer guidance on how to control the spread of disease and trigger coordinated efforts. Since 2007, WHO has declared seven PHEICs, all of which involved viruses.

All U.S. federal agencies are currently discussing how to distinguish a pandemic from a PHEIC under IHRs, while also recognizing that multiple public health crises can occur at once. The U.S. government works closely with designated national and WHO contacts to share information. Global networks such as the Group of Seven, the Group of 20, the Global Health Security Agenda, and the Global Health Initiative facilitate rapid communication and coordination critical to emergency response. Some experts believe that AMR meets the criteria for a PHEIC. Dr. Fernandez recognized that any public health emergency response must be prepared to address infectious disease and AMR.

Discussion

Dr. Laxminarayan said the declaration of a PHEIC lacks a One Health perspective—for example, including travel and trade restrictions that do not adequately account for how animals travel freely. Dr. Fernandez acknowledged that implementation of IHRs focuses mostly on departments or ministries of health, and it remains a struggle to bring in other departments. Each sector needs to anticipate its role in emergency response and join the discussion around prevention. Dr. Fernandez said more stakeholders should come together to develop a holistic approach before an event occurs rather than focus on how to wedge AMR into the PHEIC model. Dr. Laxminarayan said improving surveillance is a key first step.

Module 1: Surveillance

Recognizing the Pandemic: Identifying the "AMR Pandemic" Within the Pandemic

Dawn Sievert, Ph.D., M.S., CDC

The Antimicrobial Resistance Laboratory Network (ARLN) works with regional and local health laboratories to identify pathogens, conduct susceptibility testing, perform advanced testing (including whole genome sequencing [WGS]), and identify infection and colonization. The network assesses threats across the One Health spectrum. During COVID-19, the ARLN enabled CDC to redirect specimens and share materials when laboratories faced shortages of staff and supplies. CDC's new Global Antimicrobial Resistance Laboratory and Response Network facilitates rapid detection of and response to resistant organisms across the One Health spectrum.

CDC's National Healthcare Safety Network (NHSN) is the leading surveillance platform for detecting infectious disease and patient safety threats and captures data from more than 37,000 U.S. health care facilities. The NHSN Antimicrobial Use and Resistance module can generate reports that identify the pathogens causing disease and their susceptibility profiles. It draws from electronic health records so that manual data collection is not required. CDC also monitors a short list of specific pathogens at 10 sites around the country to capture HAIs and community-associated disease. This system can evaluate the epidemiologic and public health impact of AMR and assess prevention and control strategies.

In response to COVID-19, researchers leveraged an existing CDC AMR project to create the National Wastewater Surveillance System (NWSS) to detect COVID-19 virus. As the NWSS expands, it will assess AMR with the goal of monitoring communities and facilities and developing capacity to create new assays to respond to emergencies. Dr. Sievert pointed out that all of the CDC programs described are currently subject to short-term funding set to expire in the next few years. Sustained funding is needed to support public health facilities, the health care workforce, laboratory supplies and equipment, IPC practices, and data tracking during emergencies and outbreaks.

Discussion

Michael Craig, M.P.P., noted that CDC is considering creating a panel of diseases for detection by the NWSS that includes resistant antibiotics; he will find out whether influenza detection is being considered. Helen Nguyen, Ph.D., of the University of Illinois said some published research covers detection of influenza in wastewater sampling.

Leveraging Current Human Antibiotic Use Monitoring for Antibiotic Resistance Pandemic Surveillance

Arjun Srinivasan, CAPT, USPHS, CDC

CAPT Srinivasan described how data from the NHSN Antimicrobial Use and Resistance module can be assessed to identify concerns quickly. By 2024, all hospitals will be required to report antibiotic use and resistance to NHSN as part of the Centers for Medicare & Medicaid Services (CMS) standard to promote interoperability. Recent NHSN data demonstrate surges in antibiotic use related to the COVID-19 pandemic. At the start of the pandemic, elective hospital admissions dropped; hospitals were populated with sicker inpatients who required longer hospital stays, and a higher proportion were prescribed broad-spectrum antibiotics—a recipe for AMR. NHSN data can reveal potential supply shortages, but as COVID-19 spread, authorities did not anticipate the mismatch in supply and demand. All of these findings have implications for future pandemic planning.

NHSN can be used to evaluate the use of new therapeutics as they are introduced. Real-time data can help direct supplies of new drugs to regions or even individual hospitals where they are most used. Data can trigger intervention if, for example, prescribing trends show antibiotic overuse or a mismatch with the target infection. As more health care facilities are required to report to NHSN, they need expanded and sustained investment to initiate and maintain reporting. Support is needed to expand surveillance capacity to other health care settings, including long-term care facilities. More investment is needed to ensure a robust workforce is available that can comply with new NHSN reporting requirements.

The Federal Strategy for Animal Surveillance, Information Sharing, and Disseminating Guidance

Michael Neafsey, D.V.M., Animal and Plant Health Inspection Service (APHIS), U.S. Department of Agriculture (USDA)

Dr. Neafsey said APHIS staff have well established relationships with the animal food industry at the national, regional, and local levels, so the agency relies on field operations staff to respond to outbreaks and emergencies. APHIS works closely with CDC and the Food Safety Inspection Service at the U.S. Food and Drug Administration (FDA) to exchange information. The National Veterinary Services Laboratory (NVSL) has a well-established framework for sharing information with CDC.

Surveillance for influenza and AMR in swine relies on cooperation among USDA, FDA, states, and industry. Surveillance seeks to monitor the genetic evolution of an influenza virus and identify and select isolates for use in developing diagnostics and vaccines. Surveillance is voluntary, so findings represent trends but cannot definitively show regional or national prevalence of disease. Samples from sick animals go the National Animal Health Laboratory Network (NAHLN), which enhances the capacity for early detection and response. In the mock scenario, APHIS' foreign animal disease investigations programs would also likely identify influenza (and later, AMR), and state animal health officials or APHIS area veterinarians in charge would be alerted. Samples would be duplicated and exchanged between the NVSL and the NAHLN and possibly sent to the CDC for further analysis. NVSL would perform WGS, communicate the findings to CDC, and deposit the results in GenBank for further analysis and modeling.

APHIS response would start at the local level, with swine veterinarians. As human cases are reported, field staff would work with state public health and animal health officials on capacity and response planning. Local laboratories would communicate with state laboratories and NAHLN. Communication would ramp up early around biosecurity to prevent disease spread. Messaging would address population density and potential methods of disease transmission within farms, emphasizing that symptomatic workers should get care and not come to work. Farms and processors are expected to have policies in place for personal protective equipment (PPE), cleaning, and disinfection. APHIS does not have authority over use of antimicrobials but could talk with local and national partners about appropriate use. NVSL and Food Safety Inspection Service laboratories regularly test for AMR. Dr. Neafsey proposed working with industry on common biosecurity techniques that would prevent the spread of influenza or AMR.

Recognizing, Characterizing, and Responding to an Influenza Pandemic in Swine

Daniel Linhares, D.V.M., Ph.D., M.B.A., Iowa State University College of Veterinary Medicine

Dr. Linhares described the Swine Disease Reporting System, a collaborative of five U.S. diagnostic laboratories that gathers and analyzes data to monitor pathogens. Its online dashboard is updated daily. The system can, for example, identify changes in swine virus and track activity by animal age, production phase, and state. The system has information on all known endemic diseases and the capacity to monitor for secondary bacterial or viral disease.

Most swine operations are adopting computer-based reporting that stores data in the cloud, allowing the Swine Disease Reporting System to track signs of infectious disease. Once a pathogen is identified, response includes vaccination and sanitization to limit the spread of disease among the herd and biocontainment to prevent spread to other farms. The same approaches can be applied regionally and also inform implementation of contingency plans.

Dr. Linhares said alert systems are in place to support early detection and control of swine disease. Expanding capacity would require agreements with laboratories and state and federal agencies as well as financial support to increase active surveillance. Systems are needed to track AMR industry-wide. At the farm level, tools are available to address influenza, but next-generation vaccines are needed. Regionally, investment is needed to improve infrastructure for surveillance, biosecurity, and tracking to ensure seamless implementation.

Sources of Environmental Contamination and the Potential for Surveillance

Rachel Whitaker, Ph.D., and Thanh (Helen) Nguyen, Ph.D., University of Illinois

Dr. Nguyen proposed community surveillance to target AMR directly, as most resistance emerges outside of health care settings. She advocated for expanding wastewater monitoring, an effective surveillance tool, but reminded participants that many people in rural areas do not have community wastewater management systems. Community-level surveillance can take into account social factors, health care access, and demographics. Drs. Whitaker and Nguyen proposed a microbial surveillance network of AMR transmission that includes environmental factors, based on a University of Illinois project that is collecting wastewater samples from a pork packing plant and from the surrounding community.

With state-of-the-art WGS technology, researchers can reveal genetic sequences at the plasmid level and compare them with samples from around the world to see how genes move around and resistance spreads geographically. Dr. Whitaker emphasized the importance of multi-scale networks to see how genes move among humans, animals, and bacteria to evolve quickly and spread. Understanding, identifying, and preventing carrier genes from disseminating can help prevent future pandemics.

Dr. Whitaker called for more access to advanced sequencing technology so that researchers could identify and target genes of concern before they spread, intervening at critical points where resistance spreads. She emphasized the continued need for an interdisciplinary, team science approach to One Health problems. The COVID-19 pandemic demonstrates that local dynamics can have global consequences, so local monitoring is needed to determine where evolution is happening.

Discussion

Dr. Sievert said some federal agencies communicate effectively with others, but much more work is needed to expand data sharing, upload information, and ensure the data are clear and detailed enough that users can understand the source of the data (e.g., humans or swine). Further, agencies must determine which data should be shared, including human demographic data. Globally, there are efforts to ensure that other countries collect data for internal use appropriately to inform response. Dr. Sievert said that, at the least, a global alert system that can share information is needed. Currently, such information is reported to WHO, which helps identify emerging pathogens, before research findings are published, but there is a lag.

CAPT Srinivasan said there is potential to capture outpatient antibiotic use data from proprietary systems (which have a lot of granular data), and many electronic systems at clinics and office practices are already connected to hospitals for reporting purposes. Major federal investment would be needed to improve surveillance outside of hospital reporting.

There was some debate about whether sharing the results publicly of required reporting on hospital infection rates is an incentive or disincentive to participation. There are also competing arguments about whether publicly reporting antibiotic use and resistance data is helpful. Better educating those responsible for reporting could help them make the case for better, more accurate reporting. Lack of enforcement of requirements is another barrier to reporting, although there are financial penalties for not reporting.

Barriers to mandatory reporting on the animal side include the wide array of systems used on site, the lack of a standardized approach to recordkeeping across veterinary practices, and the variations in data across species. Environmental surveillance can help, because it identifies pathogens regardless of the source. There is no AMR surveillance of companion animals, although some barriers to data standardization and collection might be addressed as more companion animal veterinarians take a corporate medicine approach to practice.

For animal food producers, data security and privacy are significant concerns that prevent data sharing. Dr. Linhares noted that his system started small and expanded as people saw how the data were managed and shared in a way that does not violate confidentiality and adds value to the industry by monitoring for early signs of disease. Currently, those data are only identifiable down to the state level, but states can use the information to increase awareness and knowledge.

CAPT Srinivasan said government agencies can build trust in data systems by ensuring that the academic community, patient advocates, and other stakeholders have an opportunity to contribute to system development and voice their concerns. Trust does not come from a one-time investment but from ongoing, transparent communication and mechanisms for people to weigh in. Julia E. Szymczak, Ph.D., said users must find the data to be meaningful and valuable to incentivize data collection and use.

Some surveillance techniques do not rely on intentional participation, such as wastewater sampling. Concerns about privacy remain, as wastewater surveillance results do identify communities. Expanding the accuracy of wastewater surveillance requires simultaneous data from health care facilities to determine whether the data match.

Scaling up existing systems quickly during a crisis requires technical capacity and personnel capacity. In addition to building the technology, facilities need individuals who understand how to report data. Shifting to more automated reporting helps, but training and engaging personnel remains vital. Dr. Sievert said that now is the time to build on lessons learned from COVID-19 about education, staffing, infrastructure, communication, and collaboration.

Mr. Craig pointed out that money is available when crises hit, but better preparedness and response demand sustained funding over time. Notably, the NWSS was based on a project funded 2 years before the pandemic that was rapidly adapted to respond to COVID-19. CDC was able to scale up the project with emergency funding. Similarly, NHSN was in place and scaled up to address pandemic concerns. Mr. Craig emphasized that public health needs resources all the time, because the current "boom and bust" funding approach is not working.

Dr. Scheftel pointed out that the animal health infrastructure is in even worse shape than the public health infrastructure. State funding for the land-grant universities that house much of the animal health infrastructure, including veterinary diagnostic laboratories, has been declining annually for almost 20 years. Across the board, there is a lack of human resources to address new problems and ongoing issues such as AMR. Worker burnout is a significant concern. Policies are needed to increase the workforce across the infectious disease field.

Consideration should be given to novel data sources—such as pharmacy purchasing and acquisition data and wearable technology (e.g., Apple watch). During a crisis, people are more willing to consent to broader data use.

Module 2: Diagnostics

Christine Ginocchio, Ph.D., MT, pointed out that the COVID-19 pandemic response has demonstrated that high-quality diagnostics can be developed quickly and that the FDA approval process can be streamlined, without threatening patient safety. But in the early days of the pandemic, there were no diagnostics to identify secondary infections, which contributed to misdiagnoses and overuse of antibiotics.

Understanding the Human Diagnostic Communication Network (Laboratories, Public Health Departments, and Providers)

Kimberly Musser, Ph.D., New York Department of Health Wadsworth Center

Dr. Musser noted that she represents a large laboratory with extensive capacity to conduct AMR testing at multiple levels, including some antimicrobial susceptibility testing (AST). While the laboratory can detect AMR in hours, expanded ASTs can take days, and new technology, such as WGS and bioinformatic analysis, can take weeks. When transmissible, resistant bacteria are identified, the laboratory provides health departments and health care facilities with materials to conduct colonization screening and test for AMR.

The Wadsworth Center is a hub for communication with the state's more than 250 microbiology laboratories, which conduct tests, report electronically, and send isolates or specimens to the Wadsworth Center. The Center tests samples and reports findings to the state Office of Public Health, CDC, the state health information exchange, and the National Institutes of Health's (NIH's) National Center for Biotechnology Information. When notable changes are identified,

the Center sends laboratory advisories, test updates, and new information to the microbiology laboratories.

State reporting policies vary, but mandatory reporting and isolate submission is key to detection and response. Among the new tools that improve AMR detection and infection control are advanced WGS and expanded AST (including use of three-dimensional printing). To ensure adequate response to the mock scenario, Dr. Musser said the existing entities would need the capacity to continue identifying and reporting AMR, incorporate new technology, integrate databases, and ensure communication. Dr. Musser estimated that about 20 percent of laboratories in the country have the staff and capacity to do complex testing.

Developing New Human Diagnostics in an Emergency Situation

Jean Patel, Ph.D., Beckman Coulter

Dr. Patel explained that current tests for diagnosing active infection take too long to be useful for decision making. New technology will help speed up the tests, but accuracy must improve. New tests are needed when new pathogens emerge.

Molecular tests of blood samples (that do not require incubation time) could have a big impact on antibiotic use if they were accurate and clinicians felt comfortable relying on them for decision making. However, identifying pathogens directly from blood is very challenging and would require breakthrough technology. Speeding up development of ASTs is possible but also requires innovation and investment. Uptake of new tests depends heavily on research that demonstrates impact. To make the case for investment, industry needs good data on how many people would likely be infected and tested. Currently, it takes less than 1 year to develop a molecular test to identify a new resistant gene, less than 2 years to develop a phenotypic AST for an existing drug, and more than 2 years to develop an AST for a novel drug. External funding (e.g., from BARDA) is needed to support risky R&D, and incentives for uptake are needed to ensure that tests are used in the field.

Preventive diagnostics would identify people at high risk for infection with or transmission of resistant bacteria. Dr. Patel outlined current thinking around assessing and restoring the microbiome to stop the spread of infections, which could have a significant impact on HAIs. Development of preventive diagnostics would require overcoming barriers to the use of tests, development of new interventions for mitigating risk of infection and transmission, and studies demonstrating the utility of the diagnostics.

Diagnosing Fungal Infections and AMR With Current Diagnostic Capacity

Tom Chiller, M.D., M.P.H.T.M., CDC

Dr. Chiller said the challenges for developing fungal diagnostics are even more daunting than for bacterial diagnostics. The few fungal diagnostic tests available need improvement. Very few sites test for resistant mold and *Aspergillus*.

Dr. Chiller described a case in which a healthy woman in the Netherlands died following influenza infection as a result of undiagnosed secondary infection with *Aspergillus*. Influenza-associated pulmonary aspergillosis was identified during the H1N1 influenza pandemic. COVID-19-associated pulmonary aspergillosis was first identified in Western Europe and has since

spread around the world; it may affect as many as 33 percent of COVID-19 patients. The COVID-19 pandemic has also coincided with a spike in U.S. *Candida auris* infections.

Antibody detection systems for diagnosing aspergillosis are not very good. Antigen detection systems are good for identifying invasive disease in immunocompromised people. Molecular DNA detection approaches have been approved and are working well in Europe but have not been approved in the United States. Some methods are available for antifungal susceptibility testing, but only one is commercially available for *Aspergillus*. Better automated systems are needed for antifungal susceptibility testing, as are more rapid tests and incentives to test. Within the next decade, the number of antifungal classes could double, and antifungal susceptibility tests are needed to ensure patients receive the best treatment. As others have noted, sustained funding is needed to tackle these challenges. Fungi are an important cause of AMR and should be considered alongside bacteria for the purposes of planning and investment.

The Role of Diagnostics in Herds: Availability, Challenges, and How They Are Used

Rodger Main, D.V.M., Ph.D., Iowa State University

Iowa State University's Veterinary Diagnostic Laboratory is a large, full-service laboratory, located within a land-grant university and is part of USDA's NAHLN. The laboratory links practicing veterinarians and state animal health officials in support of animal health. Clients—usually veterinarians who work with food animal producers—submit samples for assessment. In addition to providing diagnoses, the laboratory uses the findings to inform teaching and research programs.

In response to the mock scenario, the laboratory would apply the techniques it uses daily for diagnosis, including molecular diagnostics to identify the influenza virus and next-generation sequencing to assess secondary bacterial infection. Dr. Main pointed out that because it serves the food animal sector, much of the laboratory's bacteria and susceptibility testing uses tissue from sacrificed farm animals. Annually, the laboratory aggregates the results to reveal patterns of susceptibility to current antimicrobials that are reported back to clients.

In swine medicine, diagnostics are used extensively, primarily from a preventive perspective. The results drive population-level decision making for herd management and inform individual treatment. Dr. Main said the large veterinary diagnostic laboratories are part of an effective partnership among industry, state, and federal entities. Funding is needed to support disease surveillance, response, and recovery, particularly to ensure laboratories have sufficient infrastructure and capacity. Investment in NAHLN is bearing fruit, as evidenced by the current response to the highly pathogenic avian influenza outbreak. Dr. Main estimated that of the roughly 60 laboratories participating in the NAHLN, about 20 are full-service laboratories.

NAHLN Laboratory Response

Christina Loiacono, D.V.M., Ph.D., USDA

The NAHLN was created 20 years ago to support early detection of animal disease through surveillance; it also monitors recovery to demonstrate to trade partners the health of U.S. food animals. Detecting a secondary bacterial infection following an influenza outbreak, as described by the mock scenario, would be an opportunity to test out NAHLN's AMR surveillance program, which began as a pilot program 5 years ago. In the scenario, samples would be submitted to

NAHLN laboratories and analyzed, generating AMR profiles for animals that are ill. A centralized approach to data collection, reporting, and monitoring allows detection of trends and new or emerging resistance profiles. Testing associated with an outbreak would occur at laboratories around the country and combined with data from routine data collection to assess effects on the swine industry and also inform a One Health perspective.

Surveillance data come from regular reporting, and results are published on a public dashboard that state and federal animal health officials can use to get information directly, particularly during an outbreak. Data are reviewed routinely with internal and external stakeholders. Regular calls and contact with USDA agencies and CDC would help bring early findings to light. In an outbreak, NAHLN would ramp up communication with stakeholders. In response to the mock scenario, NAHLN would use the dashboard to communicate rapidly and focus on the pathogens of interest. Providing more real-time data would help with treatment in the field. The data are available for public use.

Discussion

There is strong interest in speeding up diagnostic testing to support decision making. Better technology is close to being realized, but the pressing question is how to ensure that laboratory testing translates to better care in the health care setting. Hospitals and clinics need rapid point-of-care testing to minimize empiric treatment, which results in inappropriate use of antibiotics. Current surveillance systems can highlight emerging resistance, but point-of-care testing is needed to respond to those findings. Animal medicine needs more diagnostic tests and more interpretive criteria that use up-to-date breakpoints. There is little gene-specific testing for AMR because of the inability to interpret the findings in a clinically relevant way, so testing defaults to phenotypic methods. There are insufficient outcome data to show breakpoints for antifungals, so epidemiological cutoffs are used, which are not very helpful for molds and other fungal infections. Some laboratories have advanced technology but not the trained laboratory staff to use it. Federal incentives are needed to support laboratory workforce development.

Paul Plummer, D.V.M., Ph.D., DACVIM, DECSRHM, summarized the financial barriers to using diagnostics by saying it is hard to get a clinician to order a $50 test when a $5 antibiotic is readily available. Consideration is needed on how to decouple those costs. Veterinary medicine faces a similar challenge.

The National Veterinary Stockpile primarily stocks materials for field use, although there has been some progress toward stocking diagnostics, especially those that do not require cold chain storage. Laboratories are expected to maintain their own local capacity. NAHLN works with vendors to maintain availability of testing materials during an outbreak. Veterinary laboratories have the technology to scale up high-throughput testing, and supply chain issues have improved, but susceptibility testing remains slow.

Significant collaboration between the federal government and the private sector would be needed to ensure that faster diagnostics, once available, are stored in the Strategic National Stockpile. Expanding and simplifying susceptibility tests for use in low- and middle-income countries and low-resource environments is achievable. However, the costs of testing and transport are major hurdles in such areas.

In an emergency, companies could speed up development of diagnostics quickly for existing drugs, but the process takes longer for new drugs. There is a path for co-development of ASTs and new antimicrobials. Working with pharmaceutical companies during drug creation helps diagnostic makers speed up development. Some laboratories develop their own tests quickly, which could help detect secondary AMR. New technology can also speed up the time to results. Diagnostic development could be accelerated by addressing regulations within jurisdictions that limit how laboratory-devised tests are used. There should be a clear articulation of what data users need from a diagnostic to inform their decision making, with confidence that the technology would follow.

Although diagnostics are inextricably connected with surveillance, some diagnostic use can bypass surveillance. COVID-19 infection may be as much as 10 times higher than estimated because diagnostics are not always linked to reporting. Decoupling diagnostics from surveillance is particularly concerning for food animal production, because trade partners must be confident that testing is proven and validated, which takes time. COVID-19 has demonstrated that manufacturers can move faster, but such speed would not be possible if trade partners pushed back, and federal agencies might not move as quickly as the private sector. CDC's NHSN and WHO capture data from hospital laboratories that use good diagnostics, which supports robust surveillance. Authorities might not be able to gather home-testing results but they can go after the diagnostic data already being gathered in laboratories every day.

The use of home diagnostic testing raises concerns about reporting results, providing patient counseling and follow-up advice, and conducting contact tracing. Some countries offer incentives to report COVID-19 results (e.g., access to treatment or clearance for participation in events). Home test kits could require the user to log on to a website to get the results, which would be sent to CDC at the same time, but such interactive applications could be costly to develop, pose barriers for people without internet access, and raise privacy concerns. On the other hand, de-identified results could be useful for research. More consideration is needed of how federal resources could be used to collect information from home tests.

The appropriate use of existing diagnostics in clinical settings remains an elusive goal. To prevent overuse of antibiotics, the ideal test would distinguish viral from bacterial infections. The best application of a diagnostic depends on the patient, the population, the test, and the cost. Diagnostic stewardship is needed to prevent overtreatment.

Focusing on the economic value of surveillance is one way to clarify and specify the investment needed. The PACCARB has repeatedly discussed the need to advance diagnostics and surveillance to support public health in general. The Council's report to the Secretary should explain the differences between the existing capacity and what would be needed to address an outbreak.

The PACCARB should consider creating a priority list of diagnostics for AMR in animals and humans, which could be the basis for federal R&D support. However, experts continue to overestimate the utility of diagnostics in real-world decision making. Much more education is

needed to ensure that diagnostics are appropriately integrated into practice. Simply developing more diagnostics will not be enough to overcome the barriers to use.

A priority goal should be to develop diagnostics that are simple, could be used internationally and at any time, and distinguish viral from bacterial infection. Such diagnostics would slow AMR, even in an emerging pandemic. Preparation should begin now by focusing on diagnostics that capture information that is currently missing and on the data, infrastructure, and people needed to respond to an emergency. The PACCARB's recommendations could address some current blind spots, such as AMR in the community (rather than hospitals), animals, and the environment. Better understanding is needed of the chain of transmission across the One Health spectrum.

To maintain diagnostic capacity for AMR and ensure equitable access during a pandemic, diagnostics could adopt the platform technology used for vaccinations, which sped up the development of vaccines for COVID-19. Currently, manufacturers must go through the entire approval process for diagnostics for every new gene. Novel technology might allow for approval without large, lengthy clinical trials. More automation and simpler processes would ease the demands on the workforce.

Public Comment

Steve Roach of the Food Animal Concerns Trust (FACT) appreciated the PACCARB's use of a One Health approach to address pandemic preparedness but is concerned that this meeting is focused too much on response and not enough on prevention. Prevention requires much more effort on monitoring for pandemic potential pathogens, including antimicrobial-resistant pathogens, on farms and feed lots. FACT calls on the PACCARB to support the development of a national monitoring program for pandemic potential organisms that includes both bacterial and viral threats, with the goal of preventing spillover from animals to people. FACT supports nonvoluntary monitoring programs. Antibiotic resistance also requires more focus on prevention and specifically on reducing the overuse of antibiotics that is driving resistance. Antimicrobial stewardship will not reduce resistance if it does not lead to reduced use. It is not clear whether all federal agencies support reducing antibiotic use as a tool to combat antibiotic resistance. Both FDA and USDA staff have opposed language supporting reductions in use in international settings. Mr. Roach said he received an email from a USDA staff member telling other staff that the U.S. government policy was to not refer to reducing use in agriculture. It is also not clear that the PACCARB supports reducing use. FACT calls on the PACCARB to be clear about the need to reduce antimicrobial use in agriculture, antifungal use in plant production, and antibiotic use in food animals; to ask federal agencies to support use reduction; and to call for national targets for reductions in use of antimicrobials in agricultural settings.

David Wallinga of the Natural Resources Defense Council said that, for decades, the United States did not recognize the public value of collecting data around antibiotic use. But the marketplace recognized a private value, and companies bought the data, or at least used sales from drug companies, and they are reselling those data to other drug companies and eventually back to government agencies. There is now acknowledgment of the enormous public value to tracking and reporting antibiotic use, but it is complicated, so it is still not done or not done robustly. The Natural Resources Defense Council's written comments to the PACCARB make

some recommendations intended to align the incentives to collect antibiotic use data with the public health benefits from collecting that use data. CDC's leadership has set a good example in terms of a national goal and a national action plan to curb the overuse in outpatient medicine of antibiotics by 50 percent. CDC has subsequently acknowledged that they need to do a better job to actually collect use data in those settings and identify ways to address overuse. Still, about two thirds or twice as many medically important antibiotics are sold for use in food animal production as for human medicine, but no systems track that use at all. The Natural Resources Defense Council recommends that HHS set a national goal of reducing antibiotic use by 50 percent in the food animal sector. It is hoped that would spur more collection of use data at the farm level to measure progress towards meeting that goal, just like it has in the CDC.

Amanda Jezek from the Infectious Diseases Society of America urged the Council to remember that, fundamentally, success in preparing for pandemics and addressing AMR relies upon people. The lifesaving potential of new tests and therapeutics can only be realized with an expert workforce able to optimally use these tools in all communities, and currently, the country does not have the workforce needed. Infectious disease physicians, clinical microbiologists, infection preventionists, and infectious disease pharmacists are all critical to pandemic preparedness and AMR, and they are all in short supply. Nearly 80 percent of U.S. counties do not have a single infectious disease physician. Year after year, only about 70 percent of infectious disease physician training programs are able to fill their slots. Patients with serious infections, including resistant infections, have better outcomes, shorter hospital stays, and lower health care costs when they are treated by an infectious disease physician. During the COVID-19 pandemic, some studies have shown that hospitals without infectious disease physicians have had far greater increases in HAIs. So, why aren't more physicians pursuing infectious disease? It is among the lowest paid subspecialties in medicine. The codes that infectious disease physicians use for billing, inpatient evaluation and management codes, are severely undervalued. The AMR community has long recognized that antibiotics are undervalued, so as a result, the antibiotic pipeline is in trouble. The same is true for our pipeline of infectious disease experts. The Infectious Diseases Society of America encourages the PACCARB to work with CMS to improve reimbursement for infectious disease physicians, to strengthen the workforce necessary for pandemic preparedness and AMR, and to ensure patients with or at risk of serious infections can access an infectious disease physician. Targeted, sustainable initiatives are needed that invest in the multidisciplinary infectious disease workforce, and the PACCARB should prioritize this important issue.

Bronwen Morgan of the Commonwealth Scientific and Industrial Research Organization of Australia said Australia's national science agency is looking to stand up a mission on AMR that takes a One Health approach and specifically focuses on prevention, management, and response, both in the sense of containment and treatment. Ms. Morgan recognized that the interventions and solutions for AMR are many and varied and that Australia needs to prioritize, particularly because it is a small country, and it needs to leverage initiatives in other countries. Although prevention is at the heart of the agency's efforts, and the mission to minimize AMR will be weighted toward prevention, the agency also knows it needs a robust framework for determining and evaluating what preventive measures will have the greatest impact on reducing AMR evolution and transmission. Ms. Morgan hoped that the PACCARB would describe which evaluation parameters and frameworks it recommends to prioritize interventions, products,

processes, or policies.

Henry Skinner of the AMR Action Fund said AMR is an issue during the current pandemic and will be for the next one. There has been a rise in AMR and a 15-percent increased use of antibiotics in treating COVID patients. The same is expected the next time as well with these co-infections. Holistic preparedness is needed. Improved surveillance, improved diagnostics, improved stewardship, and new antibiotics are absolutely needed. There is a need to be able to treat the resistance mechanisms that are emerging around the world and a growing crisis everywhere. The problem is, of course, that the pipeline is thin and also fragile. The absence of capital to invest in this field over the last 20 years is due to a number of bankruptcies, market failures, and, frankly, a market that does not reward new antibiotic development. The system should move to a value-based reward and away from a volume-based reward. Pull incentives are needed, in which the federal government has a critical role. The human capital is aging and fleeing this field. Without investment, there will not be enough scientists, entrepreneurs, and developers to move products forward, and there will not be enough capital to bring things to market or approval to have them available during the next pandemic.

Council Perspectives

Council members offered their key concerns and takeaways from the day's workshop. Their observations and recommendations are summarized here according to broad categories of interest.

Communication

- Building trust takes time.
- Appropriate communication with the public is needed to ensure uptake of new diagnostics and treatments.
- The concrete connection between AMR and pandemic preparedness should be articulated.
- Consider the outreach and education needed to reach people on the ground.
- Better communicate science to the lay population, including, e.g., state policymakers.
- Pair every AMR activity with communication plans for the public and for health professionals that use simple language to provide the rationale, discuss feasibility, outline the cost of not using the intervention, and describe the need for knowledge change, with an emphasis on public trust.

One Health

- Push the animal and human health sectors to work together, not in parallel.
- Bringing human and animal health representatives together reveals opportunities to work across the divide and fill gaps.
- Expand the animal focus to include companion animals and wildlife.
- Apply lessons learned from One Health efforts to the environment.
- Keep the global animal health perspective in mind.

Workforce Capacity/Training and Education

- Train the next generation of veterinarians on AMR.

- The insufficient workforce in health care and public health is an urgent, global problem.
- Attention to workers' well-being is key to recruitment and retention.
- Mobilize people to work together around a common goal despite scarce resources and multiple simultaneous threats.
- More clarity is needed on how to use data and diagnostics.
- Building the workforce takes time.
- The National Disaster Medical System could be expanded to increase the number of skilled laboratory technicians who can conduct testing during an emergency.

Surveillance

- Improve access to existing data across sectors.
- Develop data systems that provide real-time information but respect privacy and security concerns.
- Clarify how information collected is fed back to those who report.
- Stakeholders are drowning in data; data scientists are needed to pull out the best data for informed decision making.

New Product Development

- Encourage more brainstorming to come up with novel ideas.
- Keep the overall purpose of new diagnostics and surveillance in mind to avoid unintended consequences.
- Understanding what is working and what gaps remain helps clarify goals for new diagnostics.
- More research is needed on the proper targets for diagnostics.
- Consider how to maintain the pipeline.

Investment

- Stakeholders repeatedly illustrated the need for sustained and flexible funding.
- Response to the next emergency depends on investments now in public health, research, and the workforce.
- Public health needs access to reliable funding resources that can be tapped immediately in times of need rather than depending on emergency funding.
- CDC needs resources to meet high expectations.
- Create sustained federal investment in effective interventions.
- The PACCARB should prioritize the to-do list to focus investment.

Global Concerns

- Invest now to prevent the next pandemic from disrupting the global economy.
- Coordinated, collective action goes beyond domestic response.
- Determine how to translate effective antibiotic stewardship approaches internationally.

Other Comments

- Speed up the translation of knowledge and products to the pediatric population.
- Public health support for under-resourced facilities must center equity and access.

- Seek more creative solutions.
- Strive to be ambitious and quick, not perfect.

Recess for the Day

Martin Blaser, M.D., Council Chair, and Michael D. Apley, D.V.M., Ph.D., DACVCP, Vice Chair

Dr. Apley encouraged participants to think about steps the federal government can take to address AMR in the context of pandemic preparedness. The meeting recessed at 4:15 p.m.

Day 2

Welcome, Recap of Day 1, and Overview of Day 2

Martin Blaser, M.D., Council Chair, and Michael D. Apley, D.V.M., Ph.D., DACVCP, Vice Chair

Dr. Blaser welcomed the participants and said he was impressed by the innovative tools and methodologies being used for surveillance and diagnostics, as well as the continued commitment to combating AMR. Dr. Apley summarized some key points that struck him from day 1, including the need to prepare for the next emergency rather than continuing to go from crisis to crisis and the need for sustained funding for advances made during the COVID-19 pandemic.

Roll Call

Jomana F. Musmar, M.S., Ph.D., Designated Federal Official, Advisory Council Committee Manager, OASH, HHS

Dr. Musmar reiterated the rules governing the Council under the Federal Advisory Committee Act and conflict-of-interest guidelines. She then called the roll.

Overview of the Mock Scenario and Meeting Objectives

Ramanan Laxminarayan, Ph.D., M.P.H., and Joni Scheftel, D.V.M., M.P.H., DACVPM, Co-Chairs, AMR and Pandemic Preparedness Working Group

Dr. Scheftel reminded participants that the goal of this workshop was to gather insights on how to incorporate AMR prevention into pandemic planning and response, with particular focus on identifying gaps in existing guidance and suggesting potential federal actions. As the mock scenario illustrates, current public health challenges are more complicated than ever because they occur at the interface between human and animal health. The One Health approach is the only way to manage such challenges.

Module 3: Vaccines and Therapeutics

NIH Strategies for Developing Vaccines and Therapeutics in a Public Health Emergency

Kyung Moon, Ph.D., National Institute of Allergy and Infectious Diseases (NIAID), NIH

Dr. Moon pointed out that AMR poses a threat before and during a pandemic. AMR contributes to more deaths globally than HIV and malaria. It is important to consider nontraditional approaches to prevention and treatment during a pandemic because antibiotics to treat infections are already limited thanks to AMR, and AMR outbreaks are likely to occur in vulnerable

populations. NIAID's Antibiotic Resistance Research Framework supports basic, translational, and clinical research through funding, resources, and services to boost the vaccine and therapeutics pipeline.

The rapid creation of a COVID-19 vaccine occurred thanks to years of research undertaken to develop an mRNA vaccine platform. Funding should support continuous research to prime the pipeline for vaccines and therapeutics. Even when a candidate emerges, product development is slow. NIH and other agencies can expedite screening of high-probability candidates and advocate for repurposing existing therapeutics. During the COVID-19 pandemic, NIH has mobilized standing clinical trial networks to assess potential COVID-19 products, which has proven effective. Leveraging existing networks and expediting regulatory processes could help get products to the public quickly during an emergency. The COVID-19 pandemic brought about global supply chain shortages, so collaboration with federal and global partners is key to addressing anticipated challenges.

Ensuring Timely Access to Existing and Newly Developed AMR Therapeutics

Mark Albrecht, Ph.D., BARDA, Office of the ASPR

The ASPR leads the federal public health preparedness and emergency response effort, working across federal agencies and with state and local authorities to ensure appropriate coordination and preparation. BARDA leads product development by offering multiyear funding and expertise for R&D, facilitating partnerships, and promoting innovation. BARDA is also responsible for procuring products for the Strategic National Stockpile, primarily through Project BioShield.

Project BioShield establishes product characteristics and requirements based on a material threat determination (MTD). For public health emergencies that do not involve an MTD, Congress can provide supplemental funding for product procurement or a new MTD can be declared, as has been the case with the COVID-19 pandemic. Currently, MTDs exist for five bacteria but there is no MTD for AMR. While products are being created, BARDA uses the data generated by the product developers to file a preliminary emergency use authorization, which opens the door for regulatory discussions and speeds up the regulatory process. BARDA then develops a plan for procurement, stockpiling, and distribution.

Products in the stockpile can only be used as approved by FDA, as a condition of interstate distribution. Dr. Albrecht summarized two approaches to stockpiling:

- Traditional: Procuring products and storing them until they expire, then replacing them, which is costly.
- Vendor-managed inventory approach: Product sponsors hold the product at their facility until it nears expiration, at which point the vendor can sell the product on the commercial market. The vendor is required to restock the product at agreed-upon levels.

During a public health emergency, releasing products from the Strategic National Stockpile involves many steps, and partnerships are critical throughout.

Development of New Animal Vaccines and Understanding Federal Regulations

Michael Roof, Ph.D., Iowa State University

USDA regulates animal vaccines through the APHIS Center for Veterinary Biologics (CVB), and a typical development cycle ranges from 2 to 5 years. Most products used by veterinarians daily are fully licensed by USDA. However, CVB offers conditional licensing for emergencies, special circumstances, or local situations, as long as the product demonstrates reasonable efficacy and meets the same safety and purity standards as licensed products. Conditional licensing can take 12–18 months. CVB also recognizes autogenous products, such as farm-specific vaccines created from the farm's isolates in as little as 8–12 weeks. USDA makes no claims about the potency or efficacy of autogenous products, and farms use them at their own risk. The CVB prescription category recognizes new molecular technologies that can be used to standardize vector systems to introduce genes. To use prescription products, the treating veterinarian and client must have a relationship, and the vector must use a USDA-licensed nonreplicating platform. The prescription approach carriers safety and efficacy implications.

USDA has a strong partnerships with state laboratories to support diagnosis and surveillance, which in the case of the mock scenario would identify pathogens and epidemiological patterns to allow for vaccine target selection. Dr. Roof said that in the mock scenario, USDA would have licensed vaccine products for swine influenza but they might not be a perfect match. Autogenous vaccination would likely be the most useful tool for rapidly matching the isolates. Prescription products could be important; two commercially available prescription vaccine products use vector systems that could swap in a new gene. Addressing bacterial infection would be more difficult. Currently, most veterinarians use autogenous products so they can create broadly protective combinations. Veterinarians are also likely to use cheap, broad-spectrum antibiotics.

To improve emergency response, Dr. Roof said CVB could prioritize pandemic solutions over other products. It could eliminate or suspend enforcement of the farm-specific requirement for autogenous products and the veterinarian-client relationship requirement for prescription products. CVB could allow prescription products to be used across species without additional safety data. It could adopt a process for assessing safety and efficacy at the same time to speed up the timeline. Currently, there is no bacteria-specific platform for prescription licensing. Harmonizing USDA and FDA regulation through shared databases, cross-species approval, shared diagnostics, and regional control programs would accelerate emergency response.

Impact of a Public Health Emergency on Human Antibiotic Stewardship Practices

Emily Spivak, M.D., M.H.S., FIDSA, University of Utah

Dr. Spivak said the COVID-19 pandemic illustrates that the antibiotic stewardship team plays a role in all aspects of pandemic response, as it interacts with a wide range of health care and public health partners and stakeholders daily. In the mock scenario, Dr. Spivak said the antibiotic stewardship team would collaborate with stakeholders as follows:

- Laboratories: Develop testing guidance, plan for upfront susceptibility testing, and evaluate diagnostic supply chain issues. The antibiotic stewardship team could be a gatekeeper to limit testing, if needed.
- Informatics: Review surveillance reports, incorporate data from new diagnostics, upgrade surveillance of antibiotic use, and consider messaging to outpatients who test positive for

influenza to prevent hospitalization. Updated data are needed to justify restrictions if the supply of antimicrobials is strained.

- Infection prevention: Through daily collaboration, create diagnostic pathways, assess for and communicate about AMR, and explain how antibiotic use affects HAIs.
- Pharmacy: Assess supply chain shortages, stay up to date with FDA changes, and develop antibiotic restriction criteria, processes, and policies.
- Outpatient partners: Update treatment guidelines, monitor antibiotic use, and consider antiviral treatment for more outpatients or reaching out to people at high risk for severe disease (e.g., using automated messaging), keeping equity at the forefront.
- Stewardship team: Update treatment guidelines, restrict use of broad-spectrum agents, and regularly update staff and the community.
- Public health: Determine whether federal entities will allocate or manage therapeutics, whether inpatient treatment will differ from outpatient treatment, and how to coordinate with state entities on distribution, indications, and equitable access. (Utah developed an effective statewide partnership to create guidance for using remdesivir, but the group faced bureaucratic hurdles to its work.)

Implementing all of these steps requires significantly more personnel than currently available. In the mock scenario, with limited staff, Dr. Spivak predicted that stewardship teams would focus on the emergency response and stop conducting the routine activities required by CDC. Expanding the stewardship workforce is imperative to pandemic preparedness, as it touches every aspect of the human health response and plays a pivotal role in communication across groups. The current workforce is barely sufficient to meet today's needs, Dr. Spivak noted.

Role of Associations in Response and Information Dissemination During a Pandemic

Gail Golab, Ph.D., D.V.M., MANZCVS, DACAW, American Veterinary Medical Association (AVMA)

Dr. Golab explained that associations not only reach their own members but also allied professionals in the same field. They provide information and education to Congress and federal agencies and collaborate with academic institutions on research and training. Associations communicate with the public directly through traditional and social media. Global and regional associations reach international audiences.

During the COVID-19 pandemic—as it would during the mock scenario—AVMA has moved quickly to identify key contacts and schedule regular calls to coordinate and target a timely and practical response. It has provided guidance to veterinarians on treating patients and protecting against unnecessary exposure. AVMA has also created emergency guidance on biosecurity, population management, and antibiotic stewardship. It has helped identify alternative sources of supplies to overcome shortages. Notably, AVMA has worked to allow veterinary diagnostic laboratories to conduct some testing of human samples, filling a critical need. AVMA has a philanthropic arm that supports other activities. Its online resources were developed collaboratively and are updated frequently. The website includes a digital training program.

To support ongoing advocacy, Dr. Golab noted, associations develop relationships and build trust and credibility over time. These relationships with policymakers, agencies, industry, businesses, and other associations are critical during a crisis. During the COVID-19 pandemic,

veterinary practices have been designated as essential services to protect animal health. As a result of advocacy that highlighted veterinarians' training and skills, some veterinarians were called on to assist with human health care early in the pandemic.

Discussion

Mr. Craig observed that the mock scenario involves a concurrent viral and bacterial and fungal pandemic, which would involve different treatment issues and inter-related considerations. He said the United States is not in a position to deal with such a complicated situation.

Project BioShield and MTDs

The Department of Homeland Security makes MTDs with participation from PHEMCE, a consortium led by HHS and the Department of Defense that includes several federal agencies. Project BioShield recognizes AMR as a public health threat, but requires that funding for advanced R&D be used to address MTDs. Without an expansion of authority or designation of AMR as a material threat, BARDA will continue to be limited.

Guidelines

When the COVID-19 pandemic hit, many national guidelines emerged, which was confusing and overwhelming to staff. A more streamlined approach to guideline development around AMR would assist with decision making and enhance public trust. Infectious disease guidelines lack focus on antibiotic stewardship. Other countries rely on national guidelines, not products developed by professional societies that can be influenced by nonmembers. The U.S. model is unique and results in multiple guidelines for clinical practice that can conflict and are not comprehensive. It is not always feasible to wait for high-quality evidence to influence the delivery of public health services. However, there are some good examples demonstrating that investing early in collaboration between CDC and professional societies to create and disseminate emergency guidance is valuable. Front-line workers should have a role in guideline development so that the results are practical in the field. The AVMA worked with CDC to modify guidance to be more feasible for veterinary practice, demonstrating the value of connections and relationships.

Clinical Trials

Dr. Blaser suggested setting up a national, standing system for research review (e.g., a national institutional review board [IRB]), to speed up the initiation of human and animal research during an emergency. A national IRB could facilitate trials on care delivery, access, equity, and other topics. Mobilizing clinical trial units during an emergency response can be a bottleneck, but NIH succeeded during the COVID-19 pandemic by relying on an existing network of networks and embarking on a public–private partnership, Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), to ramp up trials rapidly. AVMA and others are seeking to foster more connections across facilities and to create standing institutional animal care and use committees (the animal counterpart to IRBs) to advance animal research, which could be leveraged during an emergency. Veterinarians treat many animal species in diverse locations, which affects antimicrobial stewardship and clinical research.

Another significant barrier to human clinical research during the COVID-19 pandemic has been patient recruitment. In addition, pediatric studies are always delayed; testing children and adults at the same time is one way to speed up the process.

Consideration should be given to creating an outpatient clinical trials network to support research that could prevent hospitalizations and deaths during a pandemic. (The ACTIV initiative incorporated some outpatient trials.) Infrastructure is needed to roll out treatment early in the disease course, not just for those with severe disease. To address antibiotic overuse in private practices, ambulatory settings could be required to have stewardship programs. However, real accountability requires high-quality measurement along with reimbursement consequences for failing to comply with guidelines.

Communication

The COVID-19 pandemic has threatened patient and community engagement efforts in hospitals. Better coordination within and across states could help align communication efforts. Communication should be streamlined to focus on facts. More attention is needed on how to build trust in the community in more creative ways.

Communicating about the effectiveness of vaccines for preventing disease is vital. Communication across animal and human health sectors needs attention. Messaging must also emphasize the value of preventive care, such as vaccines, as part of a viable business case for food animal production.

Veterinarians have been effective at disseminating vaccination information during the COVID-19 pandemic because of their client and community relationships. Furthermore, the AVMA is working on antimicrobial stewardship guidance for veterinarians and accompanying materials for clients to clarify the recommendations.

Workforce

Challenges persist in meeting human and animal health workforce demands during a surge. Some academic medical centers can call on physician and pharmacy trainees to respond to surges, but that approach is not sustainable. Clinical pharmacists who do not have specialty training in infectious diseases could be recruited. Nurse-led telemedicine in outpatient settings for issues that do not require physicians on the ground could be used to meet demand. Some institutions have deployed medical and nursing students during the pandemic, which has been helpful. Cross-training more people in the workforce is another option.

The Department of Defense activates reserves to respond to emergencies, but doing so takes people away from their local facilities. Some bureaucratic barriers to mobilizing qualified people to assist with emergencies should be easy to address at the state level.

The antibiotic stewardship team should not have to take on so much during an emergency, especially when the current staffing is not sufficient to meet routine stewardship needs. States should identify and remove barriers to surge staffing, recognizing that turf battles can pose barriers. Planning should take into account which professionals could participate in an emergency response and how to bring them up to speed quickly.

Development of Novel Therapeutics

There is potential for using decolonizing agents to address resistant pathogens during a pandemic to reduce AMR transmission in high-acuity settings, but a regulatory framework is needed to advance such approaches. BARDA is exploring some phage-based products and decolonizers. Animal health research is also looking at the microbiome, phages, and peptides.

More investment is needed in developing tools and programs to support animal health, because most of the current tools were created as rapid, short-term solutions to a pressing problem. A major barrier to vaccine development is getting the master seed to the manufacturer and then producing millions of doses. There could be a role for the NVSL to deliver seeds directly to manufacturers with CVB approval. Once a vaccine is available, it is estimated that most swine could be vaccinated within about 90 days. It is not clear that such rapidly developed vaccines would meet conditions required for food animals. In animal health, many therapeutic mechanisms are supported by the producers at their own expense.

Access to vaccines and therapeutics remains a persistent problem that should be addressed with alternative mechanisms. BARDA emphasizes development of antibiotics for pediatric patients.

Supply Chain Disruption

The supply chain is broken because the world has transitioned to a just-in-time manufacturing model that is built for efficiency, not resilience. As a result, there is no excess capacity. Contingency planning should consider public health needs. Dr. Laxminarayan said the health system prioritizes "extreme safety," and the effort to minimize risk to an extreme degree contributes to the high cost of drug development. A system is needed that functions well during and between pandemics. Project BioShield seeks to bring some manufacturing to the United States to increase security and minimize disruptions. Guidance should offer backup plans or alternatives when shortages occur.

Much antibiotic overuse occurs because of the focus on "extreme safety." It is unclear whether federal policies could support a willingness to take on more risk in an emergency situation.

Module 4: IPC and Biosecurity

IPC for Resistant Pathogens During a Medical Surge

Terri Rebmann, Ph.D., RN, CIC, FAPIC, Institute of Biosecurity, St. Louis University

Dr. Rebmann said strong federal support is needed to ensure that infection preventionists are involved in pandemic preparedness and response planning, including developing protocols that are evidence-based, clear, and coordinated around prevention and mitigation. Investment is needed to support IPC in all health care settings.

In the mock scenario, the workload for all health care staff would increase, but the current workforce already lacks sufficient expertise in infection prevention, a problem worsened by the COVID-19 pandemic. Dr. Rebmann proposed an academic pathway for IPC training paired with federally funded incentives to pursue and remain in the field. When workload increases during an emergency, some routine procedures are neglected. The Association for Professionals in

Infection Control and Epidemiology developed an IPC acuity scale to help with collaborative decision making about which duties to retain, delegate, or temporarily stop during a crisis. To mitigate likely PPE shortages, the federal government should invest now in products such as reusable or universal respiratory protection. Facilities should have evidence-based crisis protocols for using and maintaining PPE to prevent disease spread and occupational exposure. Facilities should have qualified infection preventionists who can take the lead during an emergency to maintain basic IPC practices and train staff accordingly. Public health facilities also need capacity to respond to AMR in the community setting.

Finally, Dr. Rebmann said many infection preventionists feel burned out and have left the field since the COVID-19 pandemic began. A survey of infection preventionists determined that resilience training, mental health counseling, and financial incentives would improve retention. Dr. Rebmann called for federal investment in the well-being of infection preventionists.

Preventing the Spread: Animal Producer Decision Making and Available Resources

Tiffany Lee, D.V.M., Ph.D., Clemens Food Group

Dr. Lee described the extensive biosecurity procedures at swine farms within her organization, such as requiring workers to take downtime (1–5 days) between visits to different sites (e.g., farms and slaughter facilities). Geofencing tracks workers' movements across sites and their downtime. At sow farms and swine nurseries, biosecurity practices are most strict. Workers must pass through locked doors and gates, shower in and out, don and doff designated shoes and clothing, and pass through fogging rooms for disinfection.

Under the mock scenario, companies like Clemens would rely on their veterinarians, who would use their clinical observations and experience to determine prevention and treatment approaches. If available, susceptibility profiles would inform decision making. Effectiveness and availability of treatment would be key factors. Influenza vaccination would be considered. Dr. Lee said many farms cross-train workers to maintain herd welfare. If the hypothetical pandemic resulted in compromised animal welfare, farms and processing plants might consider managing the market schedule, culling (targeted euthanasia), or depopulation—steps that are not taken lightly, Dr. Lee emphasized. She noted that Clemens has a crisis management team that fosters ongoing conversation across all departments to support decision making.

IPC and Biosecurity: The Agricultural Workforce

Jeff Bender, D.V.M., M.S., DACVPM, University of Minnesota

Dr. Bender said an analysis of the response to a 2015 avian influenza outbreak that devastated the domestic turkey population found that good working relationships were instrumental to cooperation on the ground. However, problems persisted around sharing information securely and quickly, mobilizing resources between federal and county emergency operations, training, and incident command systems. Concerns were raised about the safety of workers and emergency responders. Dr. Bender pointed out that workers often come from underserved communities and lack support. Another influenza outbreak study linked human cases to live animal markets, where viruses are easily exchanged among and across species.

Dr. Bender said pandemic preparedness planning for animal health should address worker protections against anticipated occupational issues—for example, exposure to animal euthanasia

agents, heat stress, and PPE misuse. More attention is needed to better communicating with various audiences and getting the right message to the right target. At the outset of the COVID-19 pandemic, guidelines were slow to emerge. In a crisis, guidelines should be developed quickly, even if they are imperfect, and should be translated into appropriate languages with cultural sensitivity. Planning should also anticipate the need for emotional and psychological support for the workforce, especially if depopulation becomes necessary. Planning should prioritize disease prevention. Dr. Bender also suggested taking into account the environmental concerns that can arise from response, such as mass disposal of euthanized animals.

Infection Control and Challenges Faced by Frontline Health Care Providers

Lillian Abbo, M.D., FIDSA, Jackson Health System

Dr. Abbo summarized numerous challenges her organization faced at the outset of the COVID-19 pandemic that exposed all the barriers to IPC. For example, the organization had stockpiled PPE, but some had expired or become unusable and some disappeared in the midst of shortages. With a scarcity of antimicrobials, staff placed more intravenous lines, resulting in more central-line-associated bloodstream infections. Staff had to be deployed to different areas of the hospital, and resources were diverted from the bedside. Hospitals had to choose between providing enough N95 masks or ensuring that environmental services had sufficient products to clean and disinfect rooms. Even nonclinical staff who had appropriate PPE were reluctant to serve patients in intensive care units, in part because they were not trained in how to don and doff PPE safely.

On the other hand, the pandemic allowed the organization to set up telemedicine resources in weeks, which it had not been trying to do for years. The system used laboratory-developed tests to speed up diagnosis. An inventory dashboard was used to manage critical medications.

The COVID-19 pandemic hit Dr. Abbo close to home, as she lost her uncle, a staff nurse, and a pediatric patient early on. She urged decision makers to approach policymaking as if it were their own loved ones in need of care. The tools that created the current problems will not help resolve those problems. Global solutions are needed that promote collaboration. Communication must be consistent. The United States should adopt the point-of-care tests being used in Europe. In silico trials could help expedite research on how to leverage the skills of the workforce and an educated public to respond to emergencies.

IPC During a Pandemic Outbreak

Arjun Srinivasan, CAPT, USPHS, CDC

CAPT Srinivasan emphasized that prevention is crucial, as AMR is inevitable. For a decade, CDC has been funding state programs to help prevent infections and address AMR, and it expanded capacity in response to the COVID-19 pandemic, strengthening the IPC infrastructure, particularly in nursing homes. CDC increased data collection by using pandemic resources to expand the NHSN within weeks of the identification of COVID-19. Data were used to direct supplies to areas of most need and assess the effectiveness of recommendations, vaccines, and treatment.

Given the new infrastructure, workers needed training on using PPE and implementing new protocols, but infection prevention staff were overwhelmed with other responsibilities. CDC launched Project Firstline, a tailored, on-demand training program for every U.S. health care

provider, developed with health equity in mind. CAPT Srinivasan emphasized that there is no funding designated for maintaining the infrastructure created. Staff shortages were already a problem before the pandemic and require broad, novel solutions.

Current vaccines can prevent against viral infection and eliminate the need for antimicrobials for secondary infections. CAPT Srinivasan called for investment in vaccines that target resistant pathogens such as *Escherichia coli* and *Clostridioides difficile*. Innovation is needed to increase vaccine acceptance. Promising research suggests that decolonizing agents can be used to eliminate resistant pathogens from the gastrointestinal tract, which could prevent transmission. All infection control procedures depend exclusively on human behavior; in emergencies, staff shortages and other challenges make infection control more difficult to maintain. Better technology, such as devices that are more resistant to contamination or easier to clean, would help. The expansion of telemedicine was a huge step forward in addressing disparities and increasing access to care. Other novel strategies could support better health care delivery.

CAPT Srinivasan concluded that regardless of the question, the answer is money. Sustained funding is needed to maintain advancements and infrastructure. Innovation requires investment across the spectrum.

Discussion

Protocols and Guidelines

Guidelines should highlight activities—such as antibiotic stewardship and use monitoring—that should occur all the time, even during a pandemic response. Guideline development should not be micromanaged. Opportunities must be available for innovation on the fly that meets local and context-specific challenges.

Guidelines must be updated regularly. They should be evidence-based and good enough that the intended audience feels comfortable implementing them. On the agricultural side, at the outset of the COVID-19 pandemic, government experts struggled to develop workforce guidance that applied to the wide range of agriculture settings. By the time the guidance went through review by multiple agencies, industry associations had already jumped in to produce their own guidance. At the same time, frequently changing the message as more evidence emerges can cause confusion. Federal agencies are trusted authorities that should offer guidance but need to improve timeliness. New communication strategies are needed for guidelines; in agriculture, for example, the extension workforce has diminished, and many agents no longer work directly with employees.

Recognizing the need to balance economic viability with individual safety is key to developing local government policies on how to keep businesses open during the pandemic. For future pandemics, attention should be paid to determining the right type of PPE needed to avoid wasting supplies.

Communication

Dr. Abbo said that 2 weeks before the COVID-19 pandemic hit New York City, she and her colleagues met via Zoom with an Italian interventionist who described what to expect. That collaboration was critical to her organization’s response. Information should be consistent and

communicated simply, using infographics and taking advantage of digital platforms. Communication should be informed by design thinking and take readability into account.

Messaging to the workforce is critical so that people understand best practices to reduce harm to themselves, their patients, and animals in their care. In a rapidly changing environment, organizations could have designated communicators who provide a consistent message. Federal entities should communicate to stakeholders about big changes in policies before they are publicly disseminated, so that stakeholders are better prepared to implement and explain changes. Federal entities are also in a position to think through all the aspects of crisis communication.

The federal government could create information materials, targeted to various audiences and translated into multiple languages to reach as many people as possible, related to human and animal health. Messages should be short and targeted, simple and concrete. Messaging should be flexible to allow for changing science.

It is possible that some of the workforce burnout and turnover in health care relates to the lack of public education about how science works. Community engagement is one way to increase understanding and build trust in the health care system. The country should unite around health, with a focus on evidence and what is good for all. COVID-19 vaccination efforts were hampered by mixed messages even after education efforts.

Education and Training

Previous federal efforts to support advanced degree programs for infection preventionists have been unable to draw enough applicants, either because of low pay or lack of awareness of the field. Curricula already exist that describe what infection preventionists need to know, but it is not clear how to get people trained quickly so they can be deployed in an emergency. The academic path could be a graduate certificate, an undergraduate program, or a short-term education program that includes hands-on experience so participants can transition into the field rapidly. Some education could start in high school. A campaign to raise awareness about IPC as a career could help. CMS has recognized the need for infection prevention in long-term care facilities and created a certification process, which is one step forward. Currently, the field draws on nurses, microbiologists, and people with academic public health degrees. The field needs retention strategies and pathways for advancement.

The infection prevention field has expanded during the COVID-19 pandemic, but it is difficult to quantify the ongoing workforce shortage. Dr. Blaser said more concrete data are needed about the scale of the infection prevention workforce shortage for the next 5–10 years on which to base recommendations.

Protecting Workers' Health

Better engineering of food processing facilities to enhance IPC would protect workers. Increased automation in food production could help address labor shortages. Notably, the budget for the National Institute for Occupational Safety and Health has been slashed, preventing it from researching workforce issues. Interdisciplinary approaches could bring together industrial hygienists and extension staff, among others, to identify occupational health needs in food

production and translate them to the field. Public buildings, such as health care facilities, schools, and churches, would also benefit from attention to better ventilation, so there are opportunities for synergistic learning.

The animal food industry is looking toward automation but also recognizes the value of humans; the more people caring for animals, the lower the mortality rates. In all sectors, humans cannot be replaced completely, but cost-effective technology can support human effort.

Community health workers can serve as liaisons between labor and management to improve worker health and safety. In health care, trust between labor and management must be rebuilt; workers feel that systems are focused on cost without regard for employee health. In agriculture, many teams are multinational, and trust comes from understanding individual cultures. In all cases, managers must demonstrate that they care about workers.

Innovation

Discussion turned to novel products for preserving the microbiome. There is no pathway for FDA to approve a product that restores microbiome as a means of preventing the spread of resistant pathogens. Research on using virtual reality for training and modeling to increase patient safety should be considered, but funding should require that the research address measurable, meaningful outcomes.

Public Comment: Innovation Spotlight

The Innovation Spotlight is an opportunity for public comment open to all individuals with relevant new and emerging technologies they wish to present to the Council. The Council does not endorse or sponsor any of the companies or products described.

Mark Stibich, Ph.D., of Xenex described LightStrike, a "germ-zapping robot" that uses powerful ultraviolet light to disinfect surfaces. Data indicate that during a hospital stay, about 50 percent of surfaces are high-touch surfaces that come into contact with patients, health care workers, and others. Conventional housekeeping techniques correctly disinfect about 60 percent of those high-touch surfaces. The LightStrike is easily implemented by housekeeping staff in the context of their workflow and does not damage surfaces. The cleaning effects are persistent. LightStrike is being used by more than 1,000 hospitals, which have found them cost-effective and beneficial. The device gives the environmental services staff a good tool to achieve their demanding goals. It offers an aggressive approach to eliminate germs and prevent infections.

Carl Genberg, J.D., of N8 Biosciences said that any strategy to combat AMR that fails to address biofilm is missing half the problem. His company's CeraShield biofilm coating system prevents biofilm on nearly all indwelling medical devices. Biofilms are inherently resistant to conventional antibiotics. Ceragenins are a novel class of synthetic compounds that mimic antimicrobial peptides. They are safe, broad-spectrum, fast-acting agents that works against bacteria, fungi, and lipid-enveloped viruses and do not induce mutational resistance. Ceragenins can eradicate and prevent biofilms. They are active against a range of AMR pathogens. At very low concentrations, they have no drug-like activity but rather act as anti-fouling agents when coated onto or incorporated into indwelling medical devices. A first-in-humans study of CeraShield endotracheal tubes in Canada showed a 97-percent reduction in colonization of

patients' endotracheal tubes. FDA has designated CeraShield as a breakthrough device, and it was recently approved for use in Canada and Brazil.

Rebecca Li of Vivli described the AMR Register (available at amr.vivli.org), an innovative platform for sharing industry surveillance data. The database, initiated with Wellcome Trust support, includes postmarket susceptibility surveillance data from more than 81 countries (of which about 40 are low- and middle-income countries). The data come from more than 925,000 isolates and represents testing of approximately 69 antimicrobials. Since the AMR Register launched in July 2022, a number of researchers have used it to access susceptibility surveillance data and conduct analyses. Vivli hopes to make the AMR Register data as widely and broadly available as possible to researchers and policymakers as a universal, free, and easily searchable platform for public access, a significant step forward for advancing antimicrobial stewardship.

Greg Merril of Adaptive Phage Therapeutics (APT) explained that every new antibiotic becomes less effective over time as bacteria evolve resistance. It takes about 15 years to develop a new antibiotic, and resistance develops in about 2 years. Bacteriophages (or phages) are narrow-spectrum, natural bactericidal agents. The APT Phage Bank covers all bacteria within CDC's most serious and urgent biological threat categories. Specimens in the APT Phage Bank are paired with a phage susceptibility test that matches a bacterial isolate to a lytic phage within the collection, analogous to an AST for matching antibiotics. In relation to overcoming AMR, as inevitable resistance to a phage is identified, additional phages can be found; the Phage Bank can be rapidly expanded to cover any resistant pathogen. Identification of new phages to address resistance can be accomplished in less than 120 days, including regulatory review. APT's Phage Bank will be the first antimicrobial ever developed for which coverage does not decrease over time. The Phage Bank has been used in over 50 compassionate use cases in which standard of care antibiotics have failed, and it is currently in phase II clinical trials.

Council Perspectives

Council members offered their key concerns and takeaways, which are summarized here according to broad categories of interest.

Workforce Development

- All four modules highlighted workforce challenges, the need for cross-training, and the need for incentives (whether for product development or workforce retention).
- Could the federal government identify where and what types of surge staffing are needed?
- The federal government should engage stakeholder organizations in boosting the workforce.
- Train high school and college students to assist with simple tasks during an emergency response.
- Create national training programs that states and localities could adapt to meet community needs.

Guidelines

- Guidelines must be nimble to respond to emergencies, which requires trust between health care providers and management.
- Current guidelines are not user-friendly and do not fit into the workflow. Look for international models of effective guideline development.
- Local universities, health departments, and communities are key to disseminating guidelines and ensuring their uptake.
- It is difficult to create guidelines that are seen as applicable across medical fields or across animal species.
- Guidelines should help people at the point of care address AMR.

Investment

- Invest today to prepare for the future; federal investment is critical.
- The federal government can provide incentives and funding to address all kinds of gaps, including workforce development.
- Consistent and stable funding is needed for AMR research.

Animal Health Response

- More emphasis is needed on planning and response for pandemics involving animals.
- Better integrate AMR work into animal health emergency response.
- Recognize that animal health care does not involve third-party payers and does not have coding or management rules that drive standardization of care.

Communication and Messaging

- Simplify the messaging around AMR. See Project Firstline as a model of effective, adaptable communication.
- Better mechanisms are needed to share information among federal agencies, with key stakeholders, and with the public.
- Better use technology to communicate more effectively.
- Bring science back to the forefront of messaging by focusing on patient safety.
- Sometimes the science does not keep pace with the demand for public messaging.
- The PACCARB should dedicate time to understanding the theories and approaches to effective, purposeful communication, addressing content and tone, diversity of messages and messengers, behavior, delivery methods, and implementation science.

Behavioral and Social Issues

- Human behavior affects pandemic response; the PACCARB's report should acknowledge the challenge of building response networks that take into account the many human dimensions.
- Behavioral and social barriers to effective care may be worse now than before the COVID-19 pandemic.

Considerations for Recommendations on Pandemic Response

- The federal government sets the tone for the response on the ground.

- Leverage systems outside the federal government, such as the cooperative extension programs, which are trusted in many rural communities.
- Develop a unified command approach to pandemic response that unites animal and human health priorities.
- Enable a more agile response.
- Repurpose animal disease response mechanisms to assist with human health response.
- During a pandemic, focus on prevention to stop the spread of disease,
- There is a disproportionate emphasis on vaccines at the expense of other interventions that benefit patients and serve public health objectives.
- Recommended actions must be easy for individuals to implement during a response.
- Prioritize the recommendations to the federal government to prevent overinvestment in products that are not highly needed.
- Keep in mind the role of pull incentives to stabilize the pipeline of products to respond to current and future threats.
- The COVID-19 pandemic changed thinking, and recommendations must advocate for changes that acknowledge the new context.
- The PACCARB should keep in mind opportunities to make high-level recommendations at the next United Nations meeting on AMR.
- The PACCARB should consider recommendations that go beyond traditional incentives to bridge the gaps between technology and humans.

Other Comments

- Rapid, point-of-care diagnostics are needed.
- Lay the groundwork to prevent AMR before a pandemic occurs; it is not realistic to create response systems during a pandemic.
- Access to clinical trials, testing, and treatments remains a persistent problem for pediatric populations.
- Schools look to CDC for guidance during a pandemic.
- Feedback and outcomes data should come from the point of care.
- Recognition of AMR across all health contexts has increased.

Final Comments and Adjournment

Martin Blaser, M.D., Council Chair, and Michael D. Apley, D.V.M., Ph.D., DACVCP, Vice Chair

Dr. Blaser thanked the participants, presenters, staff, and audience for a productive meeting. The next public meeting will take place virtually on January 24–25, 2023, and focus on communication issues. The PACCARB aims to meet in March to finalize its report to the Secretary. Dr. Blaser adjourned the meeting at 4:09 p.m.

Appendix A: Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) Members

September 12–13, 2022

PACCARB Voting Members Present
Martin J. Blaser, M.D., Chair
Michael D. Apley, D.V.M., Ph.D., DACVCP
Stephanie Black, M.D., M.Sc.
Virginia R. Fajt, D.V.M., Ph.D., DACVCP
Christine Ginocchio, Ph.D., MT
Elaine Larson, Ph.D., RN
Ramanan Laxminarayan, Ph.D., M.P.H.
Armando Nahum
Payal K. Patel, M.D., M.P.H.
Paul Plummer, D.V.M., Ph.D., DACVIM, DECSRHM
Julia E. Szymczak, Ph.D.
David White, M.S., Ph.D.

Organizational Liaisons Present
American Association of Extension Veterinarians
Carla L. Huston, D.V.M., Ph.D., Dipl. ACVPM

American Veterinary Medical Association
Joni Scheftel, D.V.M., M.P.H., Dipl. ACVPM

Biotechnology Innovation Organization
Emily Wheeler

Healthcare Infection Control Practices Advisory Committee
Lisa Maragakis, M.D., M.P.H.

Minor Crop Farmers Alliance
James Adaskaveg, Ph.D. (*by phone, day 2 only*)

Pediatric Infectious Diseases Society
Jason Newland, M.D., M.Ed.

Society of Infectious Disease Pharmacists
Elizabeth Dodds Ashley, Pharm.D., M.H.S., FCCP, BCPS

Wellcome Trust
Timothy Jinks, Ph.D.

Regular Government Employees Present
U.S. Department of Health and Human Services

Michael Craig, M.P.P., Antibiotic Resistance Coordination and Strategy Unit, Centers for Disease Control and Prevention
Jasmine Dhindsa, M.D. (for Shari Ling, M.D.), Centers for Medicare & Medicaid Services
Lynn Filpi, Ph.D., Office of Pandemics and Emerging Threats, Office of Global Affairs *(day 1 and day 2 morning only)*
William Flynn, D.V.M., Center for Veterinary Medicine, Food and Drug Administration
Christopher Houchens, Ph.D., Biomedical Advanced Research and Development Authority, Office of the Assistant Secretary for Preparedness and Response
Natalie LaHood (for Lynn Filpi, Ph.D.), Office of Pandemics and Emerging Threats, Office of Global Affairs *(day 2 afternoon only)*
Melissa Miller, M.D., M.S., FCCM, Agency for Healthcare Research and Quality
Kyung Moon, Ph.D., (for Dennis M. Dixon, Ph.D.), National Institute of Allergy and Infectious Diseases, National Institutes of Health

U.S. Department of Agriculture
Neena Anandaram (for Emilio Esteban, D.V.M., M.BA., M.P.V.M., Ph.D.), Food Safety and Inspection Service *(day 2 only)*
Roxann Motroni, D.V.M., Ph.D. (for Jeffrey Silverstein, Ph.D.), Agricultural Research Service *(day 2 only)*
Chelsey Shivley, D.V.M., Ph.D., DACAW (for Sarah Tomlinson, D.V.M.), Animal and Plant Health Inspection Service
Jeffrey Silverstein, Ph.D., Agricultural Research Service *(day 1 only)*

U.S. Department of Defense
Paige Waterman, M.D., FACP, FIDSA, Walter Reed Army Institute of Research

U.S. Environmental Protection Agency
Jay Garland, Ph.D., Center for Environmental Solutions and Emergency Response *(by phone, day 2 only)*

Designated Federal Official
Jomana F. Musmar, M.S., Ph.D., Advisory Council Committee Manager, Office of the Assistant Secretary for Health (OASH), Department of Health and Human Services (HHS)

Advisory Council Staff
Mark Kazmierczak, Ph.D., Gryphon Scientific
Haley Krem, Committee Management Officer, OASH, HHS
Chloe Loving, M.P.H., CHES, CPH, ORISE Fellow, HHS
Sarah McClelland, M.P.H., Public Health Advisor, OASH, HHS
Katharyn Kryda, D.V.M., M.P.H., Gryphon Scientific
Lauren Plaine, Gryphon Scientific
Taylor Simmons, M.P.H., ORISE Fellow, HHS
Jennifer Adona, Rose Li Associates

Appendix B: TBD

Base Scenario

In the summer of 2022, a rapidly expanding influenza outbreak was identified in several countries. The virus was confirmed as a novel reassortant influenza A virus, although the origin is unclear. Epidemiological data indicates that the virus is highly transmissible. The outbreak continued to spread globally and was declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO) in early July. By mid-July, cases were identified and rapidly rising in multiple U.S. cities, and the Secretary of Health and Human Services declared a public health emergency as our nation's healthcare system became increasingly overwhelmed. Around the same time, the Director General of WHO and world leaders begin to refer to the outbreak as a pandemic.

The influenza pandemic is characterized by a high frequency of severe disease requiring hospitalization, with frequent bacterial superinfection at presentation or developed during hospitalization.[1] In late August, infections increased to over 250,000 new cases daily, nationwide, with a daily average of 120,000 inpatients and a 30% increase in ICU admissions over pre-pandemic levels. As a result, many hospitals are running out of space to admit new patients. Due to the broad sweeping impacts of the pandemic, the President declares a major disaster under the Robert T. Stafford Relief and Emergency Assistance Act of 1988.[2] The public health emergency and major disaster declarations provide a broad range of funding and resources to strengthen response efforts in hopes of mitigating the impacts of the pandemic.

The influenza pandemic is complicated by a significantly higher than normal rate of secondary bacterial community-acquired pneumonia (CAP) in patients of all ages. The severe viral disease is also leading to increased ventilator use among patients not presenting with CAP, and subsequently, higher than normal ventilator-associated pneumonia (VAP) rates. Many of the secondary bacterial infections are resistant to antimicrobials, leading to a second, underlying AMR pandemic that is responsible for much of the observed mortality; admitted influenza patients contracting a healthcare associated infection (HAI) face a mortality rate of 56%. Moreover, the secondary bacterial infections are increasing length of stay in hospitals, and further exacerbating bed shortages. Case fatality proportions of patients with viral infections who are not admitted to a facility are twice that of those receiving inpatient care, and the numbers of patients who have to be treated outside regular facilities is climbing rapidly. Therefore, the secondary AMR epidemic is vastly increasing the health and economic toll of the viral pandemic.

[1] The Public Health Emergency Fund is a no-year fund at the U.S. Treasury to provide funding in the event of a public health emergency. This is the only immediate and flexible no-year funding source available to ensure a timely response to an urgent event that is declared a public health emergency. More information may be found at https://www.phe.gov/Preparedness/legal/Pages/phedeclaration.aspx.

[2] The Robert T. Stafford Relief and Emergency Assistance Act of 1988 (Stafford Act) authorizes the President to provide financial and other assistance to support response, recovery, and mitigation efforts following Presidential emergency or major disaster declaration. More information may be found at https://www.fema.gov/disaster/how-declared or in the Biological Incident Annex to the Response and Recovery Federal Interagency Operational Plans.

The bacterial agents associated with the observed VAP are similar to those observed prior to the outbreak. Although some local and regional variation exists, these pathogens include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), carbapenem-resistant *Acinetobacter baumannii* (CRAB), multidrug-resistant *Pseudomonas aeruginosa*, and azole-resistant *Aspergillus fumigatus.* Similarly, the pathogens typically associated with CAP patients are seen in this outbreak as well, including *Streptococcus pneumoniae* and *Staphylococcus aureus*, which are commonly seen as secondary bacterial pneumoniae associated with seasonal and pandemic influenza, as well as *Haemophilus influenzae, Klebsiella pneumoniae,* and *Legionella.* Due to the high incidence and significant attributable mortality of VAP, inpatient prescribers are empirically treating these patients with cefepime, piperacillin-tazobactam or carbapenems (for antipseudomonal activity), vancomycin or linezolid (if risk factors for MRSA are present), ciprofloxacin or colistin. Typically, intravenous ceftriaxone and oral azithromycin are used initially for CAP. Increased demand has strained local supplies of antimicrobials. Other HAIs, in particular resistant *Candida auris* infections, have been observed due to challenges to infection prevention and control (IPC) efforts caused by the high patient loads, longer hospital stays, and staffing shortages experienced by many hospitals.

Meanwhile, the same pandemic influenza A virus strain is spreading rapidly among a susceptible animal population. A high incidence of moderate to severe clinical influenza cases among swine populations leads to increased use of antibiotics to treat secondary bacterial infections. Veterinarians are most concerned about bacterial *Pasteurella multocida, Streptococcus suis, Bordetella bronchiseptica,* and *Glaesserella parasuis* infections, which frequently demonstrate resistance to several antibiotics. Considering the known resistance to tetracyclines among common bacterial pathogens affecting swine, veterinarians are treating herds at finishing barns with tiamulin, lincomycin, or florfenicol added to water. At nursery barns, veterinarians are treating severely ill individual animals with injectable ceftiofur, tulathromycin, or penicillin. When clinically ill pigs are refractory to empirical treatment, they are being treated with injectable enrofloxacin. While susceptibility profiles exist in some regions of the country for certain antimicrobials, these patterns are not necessarily consistent across all routes of administration (e.g., oral administration of a medication may be less bioavailable than injectable administration). Furthermore, susceptibility profiles may differ by geographic region, making accurate and quick determination of the most effective antibiotic regimen difficult.

In addition to the direct effects of influenza virus infections in pigs, farms are seeing a general decline in husbandry and swine health due to a production workforce that has been depleted by human illness from the pandemic, resulting in fewer onsite workers to care for animals, monitor clinical signs, and treat disease. Slaughter facilities are having difficulty keeping up with processing of animals due to workforce shortages, exacerbating challenges at the farm level as pigs have nowhere to move when they reach market weight. Further management challenges, including mixing pigs from different sources, an inability to maintain all-in/all-out management, and increased environmental stress are also contributing to a rise in secondary infections in pigs.

In the resource-constrained healthcare and animal agriculture environments, decisions must be made about the use and allocation of resources, including diagnostics and medical countermeasures, and on IPC and biosecurity measures. In both settings, the effectiveness of

standard outbreak response operations is being challenged in this highly antibiotic-resistant environment.

Glossary of Abbreviations

ACTIV	Accelerating COVID-19 Therapeutic Interventions and Vaccines (initiative)
APHIS	Animal and Plant Health Inspection Service
AMR	antimicrobial resistance
ARLN	Antibiotic Resistance Laboratory Network (CDC)
ASPR	Assistant Secretary for Preparedness and Response
AST	antimicrobial susceptibility test
AVMA	American Veterinary Medical Association
BARDA	Biomedical Advanced Research and Development Authority
CARB-X	Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare & Medicaid Services
COVID-19	coronavirus disease 2019
CVB	Center for Veterinary Biologics
FACT	Food Animal Concerns Trust
FDA	U.S. Food and Drug Administration
HAI	health-care-associated infection
HHS	U.S. Department of Health and Human Services
IHR	international health regulation
IPC	infection prevention and control
IRB	institutional review board
MTD	material threat determination
NAHLN	National Animal Health Laboratory Network
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NHSN	National Healthcare Safety Network
NVSL	National Veterinary Services Laboratory
NWSS	National Wastewater Surveillance System
OASH	Office of the Assistant Secretary for Health
PACCARB	Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria
PHEIC	public health emergency of international concern
PPE	personal protective equipment
R&D	research and development
USDA	U.S. Department of Agriculture
WGS	whole genome sequencing
WHO	World Health Organization