

# PACCARB

Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria

## **Meeting Summary**

**14th Public Virtual Meeting of the  
Presidential Advisory Council on  
Combating Antibiotic-Resistant Bacteria  
September 9–10, 2020**

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# Meeting Proceedings

## Day 1

### Welcome, Overview, and Roll Call

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

Dr. Musmar called the meeting of the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) to order at noon and welcomed the participants. She explained that the Council was formed through an Executive Order in 2014 and has since been codified into legislation under the Pandemic and All-Hazards Preparedness and Advancing Innovation Act under the authority of the HHS Secretary. Dr. Musmar described the Council's charter and gave an overview of the agenda. She summarized the rules governing the Council under the Federal Advisory Committee Act and conflict-of-interest guidelines and called the roll. (See the appendix for the list of participants.)

### Opening Remarks and Swearing In of New Members

*ADM Brett P. Giroir, M.D., U.S. Public Health Service, Assistant Secretary for Health, HHS*

ADM Giroir extended sincere condolences to those who have suffered and those who have lost loved ones to COVID-19 (the disease caused by severe acute respiratory syndrome coronavirus - 2 [SARS-CoV-2]). He also expressed gratitude and respect for all the health care workers and first responders on the front lines of the pandemic. ADM Giroir related that as a pediatric physician, he witnessed the physical toll that antibiotic resistance takes on patients of all ages and its emotional toll on the health care workers treating them.

Antimicrobial resistance (AMR) is a slow, silent pandemic that has been smoldering for a long time and has flared up on the global level recently. ADM Giroir said 500 people die every day as a result of AMR, but sustaining efforts to battle AMR has been challenging. Data indicate that 72 percent of COVID-19 patients received antibiotics, but only 8 percent had a bacterial or fungal infection, so there is real potential for a surge in AMR as a result of the pandemic. Moreover, those admitted to hospitals are at increased risk of health-care-associated infections (HAIs), and some harbor organisms when they are admitted.

ADM Giroir identified three priorities for keeping pace with AMR:

- Use all antibiotics appropriately, as indicated, based on evidence, for humans and animals. A One Health approach is paramount.
- Implement systems and technologies to achieve the goals of antimicrobial stewardship, such as point-of-care diagnostics that can detect the presence or absence of infection and reveal an organism's susceptibility to treatment.
- Develop new antibiotics, therapeutics, and alternatives (e.g., vaccines) and create sustainable markets for new products.

The PACCARB plays a key role in identifying and evaluating information, said ADM Giroir. He looked forward to the discussion of the intersection of AMR and COVID-19.

ADM Giroir thanked the four liaison members retiring from the Council for their dedication and outstanding contributions to the topic of AMR and to the Council:

- Alice L. Johnson, D.V.M., National Turkey Federation
- Tiffany Lee, D.V.M., Ph.D., M.S., North American Meat Institute
- Kathryn L. Talkington, Pew Charitable Trusts
- Denise M. Toney, Ph.D., Association for Public Health Laboratories

ADM Giroir welcomed eight new liaison members to the Council and administered the oath of office:

- Elizabeth Dodds Ashley, Pharm.D., M.H.S., FCCP, BCPS, Society of Infectious Disease Pharmacists
- Greg Frank, Ph.D., Biotechnology Innovation Organization (BIO)
- Carla L. Huston, D.V.M., Ph.D., Dipl. ACVPM, American Association of Extension Veterinarians
- Timothy Jinks, Ph.D., Wellcome Trust
- Munr Kazmir, M.D., Direct Meds, Inc.
- Lisa Maragakis, M.D., M.P.H., Healthcare Infection Control Practices Advisory Committee
- Jason Newland, M.D., M.Ed., Pediatric Infectious Diseases Society
- Joni Scheftel, D.V.M., M.P.H., Dipl. ACVPM, American Veterinary Medical Association (AVMA)

## **Update on the National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB) 2020–2025**

*Amanda Cash, Dr.P.H., M.P.H., Director, Division of Evidence, Evaluation, and Data Policy, Office of the Assistant Secretary for Planning and Evaluation, HHS; Co-Chair, Federal CARB Task Force*

Dr. Cash outlined the growing problem of AMR, the development of the first National Strategy and National Action Plan for CARB, and the One Health approach. The Federal CARB Task Force brings together agencies across the federal government to promote collaboration and communication. The task force is made up of federal representatives only; while the PACCARB is primarily made up of external stakeholders. Among the major accomplishments since implementation of the first National Action Plan are the establishment of the Antibiotic Resistance Laboratory Network, the CARB-X research accelerator program, and the AMR Challenge prize; U.S. Department of Agriculture (USDA) support for agricultural research and development (R&D); and broad stakeholder commitment to global action.

While it is difficult to link activities with outcomes, Dr. Cash noted, from 2012 to 2017, U.S. deaths overall from resistant infections fell 18 percent, and such deaths in hospitals dropped 30 percent. More hospitals now have high-quality antibiotic stewardship programs, thanks in part to more federal support. Still, there are too many infections and deaths from resistant organisms,

Dr. Cash said, and new resistant pathogens are emerging all the time. Community-acquired resistant bacterial infections are increasing. Challenges persist with developing new antibiotics.

The National Action Plan for CARB 2020–2025 maintains the five goals of the original National Action Plan, adds some new objectives and targets, and identifies new challenges.

Implementation of the new plan depends on the resources available and capacity. The updated plan continues to prioritize the One Health approach, infection prevention and control, appropriate use of antibiotics, and support for innovative products. It incorporates an updated measurement and reporting strategy, with quantitative targets when possible. Targets will be updated as needed and described in annual reports. The new plan will be published in September 2020, followed by annual progress reports. A final annual report and a summary of progress toward the goals of the original plan are also expected.

## **How Life Has Changed: COVID-19 and AMR—Session I**

### **Overview of the COVID-19 and AMR Intersection**

*Arjun Srinivasan, M.D., CAPT, USPHS; National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention (CDC)*

Dr. Srinivasan summarized CDC's programs and investments in managing AMR. According to CDC data, COVID-19 patients experience bacterial and fungal infections at about the same frequency as patients with influenza-like illness (ILI). However, sporadic outbreaks of AMR infections are occurring in COVID units, along with higher rates of HAIs. Dr. Srinivasan explained that COVID-19 creates the perfect conditions for AMR infections in health care settings, given patients' length of stay, crowding, the presence of sick patients, antibiotic use, and infection control issues. Moreover, staff are overworked, some staff may not be fully trained in appropriate antibiotic use, and there are shortages of personal protective equipment (PPE).

Antibiotic use in hospitals spiked in early 2020 but flattened as the pandemic continued, although use remains too high, particularly use of antibiotics targeting respiratory infections. In outpatient settings and nursing homes, antibiotic use is down significantly compared with previous years, most likely as a result of overall declines in outpatient visits. Maintaining effective infection control and antibiotic stewardship programs is key to mitigating AMR, and such programs depend on a resilient health care system.

Dr. Srinivasan presented preliminary findings drawn from an assessment of CDC and commercial data sources. Compared with ILI patients from 2019, fewer COVID-19 patients had positive bacterial or fungal cultures within the first three days of hospitalization, and more COVID-19 patients had such infections after three days, suggesting that the length of hospital stay was more likely responsible for the infection than COVID-19. The most commonly seen community-onset infections in both were methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum beta lactamase (ESBL), with higher rates of MRSA in ILI patients and higher rates of ESBL in COVID-19 patients. COVID-19 patients had higher rates of hospital-acquired MRSA and ESBL infection than ILI patients. Dr. Srinivasan presented the early findings on the types of antibiotics used in hospitals, nursing homes, and outpatient visits—all of which reflected the changing understanding of how to treat COVID-19 via empiric and prophylactic antibiotic use, as well as steep declines in the number of people seeking health care.

The pandemic could have other impacts on antibiotic use and resistance. For example, most sexually transmitted infection (STI) clinics experienced some disruption in antibiotic supplies, and antibiotic shortages could be especially challenging for treatment of people with STIs or tuberculosis. The pandemic has hampered reporting on antibiotic use and resistance and decreased laboratory surveillance, which are vital to addressing AMR. The health care system has demonstrated that it can decrease infections through infection control procedures and antibiotic stewardship, but all such programs must be implemented fully and consistently, which is challenging during a pandemic. COVID-19 revealed that such efforts are underfunded and understaffed. Dr. Srinivasan called for serious discussion about building resiliency in the fields of infection prevention and antibiotic stewardship.

## **DISCUSSION**

Dr. Srinivasan noted that CDC aims to combine various datasets to better understand the drivers of infection and the impact of changes in antibiotic use patterns during the pandemic, such as the effect of increased prescribing of azithromycin on ESBL infection. Researchers are looking at data from outpatient and telemedicine visits to better understand the significant drop in antibiotic use among outpatients during the pandemic.

### **Adapting Antibiotic Stewardship Practices During a Public Health Emergency**

*Emily Heil, Pharm.D., BCIDP, Society of Infectious Diseases Pharmacists*

Among the challenges to antibiotic stewardship during the pandemic have been the uncertainty in diagnosing coinfections, the novelty of the disease, and staffing shifts required to address the pandemic, Dr. Heil observed. Her hospital experienced the same changes in antimicrobial use and the same rates and timing of bacterial infection as those described by Dr. Srinivasan.

Since the pandemic began, the pharmacy staff in Dr. Heil's hospital that usually advises on antibiotic stewardship pivoted to developing and updating COVID-19 guidelines, enrolling patients in clinical trials, and allocating therapeutics. To preserve PPE use, clinicians have been using more expensive antibiotics that require less contact with patients. As Dr. Srinivasan noted, much reporting of multidrug-resistant organisms (MDROs) and *Clostridioides difficile* has been suspended. Across the country, when pharmacy staff were reinstated after furloughs, excessive antibiotic use diminished.

Dr. Heil pointed out that clinicians and pharmacists specializing in infectious disease offer valuable leadership to antibiotic stewardship programs and have the ideal skills for dealing with a pandemic (including supply chain management), but more investment is needed in education to ensure such leaders are available when needed. In her hospital, Dr. Heil said, the infrastructure and guidelines put in place for antibiotic stewardship laid the foundation for timely creation and dissemination of COVID-19 guidance.

## **DISCUSSION**

Dr. Heil said her organization's data indicate that immunomodulators in particular added to the high risk of secondary infection in those who had a prolonged hospital stay. She confirmed that the increased use of ceftriaxone and azithromycin during the pandemic are likely to increase the risk of *C. difficile*. Dr. Heil said that healthcare systems that maintained their infectious disease staff during the pandemic should be able to restart antibiotic stewardship programs. However,

some organizations made permanent cuts to antibiotic stewardship programs and staff or decreased emphasis on antibiotic stewardship, which could have a big impact on antibiotic use and AMR moving forward.

### **Role of Diagnostic Stewardship During a Public Health Emergency**

*Kalvin Yu, M.D., Medical Director, Becton Dickinson & Co.*

Diagnostics provide clinicians with information on which to base decisions, said Dr. Yu. At the community level, diagnostics can reveal increases or decreases in COVID-19 in a given area, which can guide planning for resource allocation and stockpiling, for example. Data from 185,000 COVID-19 patients echo the CDC's findings of unnecessary antibiotic use, with the most used antibiotics being those likely to cause AMR. Use of diagnostics can minimize misuse and its consequences, such as resistance development, drug shortages, and adverse drug effects.

Among hospitalized patients tested for COVID-19, those who test positive are more likely than those who test negative to have *S. aureus*, *Pseudomonas*, or *Candida*—all of which have drug-resistant strains and are associated with poor outcomes. Diagnostic tests that identify these bacterial infections and their susceptibility can help clinicians minimize unnecessary use of antibiotics, particularly broad-spectrum antibiotics. The upcoming influenza and cold season will strain the health care system more than usual, affecting the turnaround time for diagnostic tests—which is already less than ideal for COVID-19 testing.

In addition to improving the turnaround time for COVID-19 testing, Dr. Yu called for investing in point-of-care diagnostics to improve patient care and mitigate AMR; stockpiling diagnostics for influenza and pandemic infections; educating clinicians about diagnostic use; and allocating resources for diagnostics, which is critical when health care needs surge.

### **DISCUSSION**

Dr. Yu observed that more health care entities are relying on in-house and local laboratories for diagnostic testing now than in the early stages of the pandemic, when many used specialty or state laboratories. However, hospitals that do not have access to local testing still depend on state laboratories, whose capacity and speed vary greatly across the country. In addition, during a health care surge, laboratories are often understaffed and under-resourced, further slowing down the turnaround time for results. Dr. Yu stressed the importance of educating clinicians about the importance of influenza vaccinations to minimize the burden on health care systems and to help with differential diagnosis when multiple respiratory infections are co-circulating.

Dr. Yu acknowledged the broad range of sensitivity and specificity of available COVID-19 diagnostic tests. The ideal timing and frequency of testing remain to be determined.

### **Looking Forward: Vaccine Uptake and Behavior**

*Sean O'Leary, M.D., M.P.H., FAAP, University of Colorado Anschutz Medical Campus*

Dr. O'Leary said investigators have been seeking to understand the likely uptake of a COVID-19 vaccine(s) when available. While there are limits to the reliability of survey findings about a vaccine that does not yet exist, responses indicate that Black people are the least likely to accept a COVID-19 vaccine—and they are also among those at highest risk of complications from the



virus. Many respondents expressed concern that the vaccine approval process is being driven by politics.

Efforts to increase vaccine acceptance have sought to understand how to improve messaging beyond sharing relevant facts. Behavioral scientists conclude that it is necessary, but not always sufficient, for communication to address, for example, vaccine ingredients and safety surveillance mechanisms. Conventional wisdom holds that simply providing the facts will ensure people make good decisions, but improving knowledge gaps is not enough, said Dr. O’Leary. He offered some key points from The Debunking Handbook to address myths and misinformation:

- Focus on the core facts rather than the myth to avoid making the myth more familiar (which can have the unintended effect of reinforcing the myth).
- Any mention of a myth should include an explicit warning that it is false.
- Give an alternative explanation that accounts for the original misinformation.

The Community Preventive Services Task Force’s Community Guide offers evidence-based strategies for increasing vaccine uptake that are grounded in behavioral science. Dr. O’Leary concluded that for COVID-19 vaccines, community engagement with vulnerable populations must begin early. Public health messages should be tested in advance, avoid perpetuating misinformation, and employ evidence-based strategies for improving vaccine acceptance.

## **DISCUSSION**

Dr. O’Leary described some of the reasons that childhood vaccination rates decreased early in the pandemic but expressed optimism that children will eventually catch up on their recommended vaccinations. He noted that mandating vaccines is controversial in general, and mandating the COVID-19 vaccine could lead to a backlash. However, health care settings have had some success requiring certain vaccines as a condition of employment.

Dr. O’Leary believes that the behavioral science on parental hesitation around childhood vaccines can be extrapolated to inform adult uptake to some extent, but there are many variables and unknowns around the COVID-19 vaccine that come into play. Whether seasonal influenza vaccine uptake will be affected by the availability or prospect of a COVID-19 vaccine remains to be seen.

Dr. Blaser pointed to the difficulty of overcoming mistrust of the vaccine. Dr. O’Leary reminded the participants that a strong, presumptive recommendation from a health care provider remains the best predictor of vaccine acceptance. Building trust among those within the health care system would trickle down, he said, but there is a lot of concern among providers about the process surrounding the approval of a COVID-19 vaccine. In addition, the H1N1 influenza pandemic demonstrated that there must be a vaccine available at the time that demand is high, and demand is fueled by the public perception that the vaccine is safe and the risk of disease high. State health departments and the Advisory Committee on Immunization Practices are currently considering how to roll out a vaccine in stages. Dr. O’Leary added that messaging must emphasize that safety is the top priority of those responsible for approving any vaccine.

Work is underway at the federal and state levels to develop effective communication and outreach strategies to vulnerable populations about a COVID-19 vaccine, said Dr. O’Leary. Public health leaders can build trust now in anticipation of a vaccine rollout, and they must take into account that Black people in the United States are already being targeted by vaccine disinformation campaigns.

## **How Life Has Changed: COVID-19 and AMR—Session II**

### **Data on COVID-19 Mortality Rate from Secondary Acquired Infections**

*Cornelius J. Clancy, M.D., University of Pittsburgh*

From 500 autopsy reports, Dr. Clancy observed that 37 percent of patients had evidence of secondary respiratory infection. Published reports often lack good microbiological information, so it can be difficult to discern the effects of COVID-19 from those of bacterial or fungal infection.

COVID-19 patients are at high risk for infections. Dr. Clancy suggested that any given health care system’s underlying patterns of AMR and susceptibility will be unmasked by COVID-19. About one third of COVID-19 patients in his facility (part of the Department of Veterans Affairs system) had a secondary infection, and those who did were more likely to have developed the infection during hospitalization than through community exposure, consistent with CDC findings.

The spread of COVID-19 to the area where Dr. Clancy practices was slow, and as a result, the system had time to institute its usual antibiotic stewardship strategies. Although there were increases in antibiotic use among inpatients, outpatient prescribing dropped (consistent with CDC findings in both settings). Dr. Clancy said that the relationship between COVID-19 and AMR is dynamic and varies by region and hospital. He called for better quality literature (including increased reporting by health care providers), use of more rigorous definitions of infections for postmortem studies, more surveillance data on antimicrobial use and resistance, and better education on when not to use antibiotics.

### **DISCUSSION**

Regarding reports of myocarditis following COVID-19 infection, especially in young people, Dr. Clancy noted that myocarditis is a complication of viral infection but is not usually a target of surveillance. He cautioned that without baseline data, the relevance of the correlation is not yet known. Dr. Clancy noted that his facility relies on infectious disease consultations to manage fever among COVID-19 patients, and he added that such consultation saves lives and saves money in the context of all kinds of infections. He stressed that the negative predictive value of some diagnostic tests is particularly helpful for decision making.

### **The Hot Zones: Implications of COVID-19 in Long-Term Care Facilities and the Role of Empiric Treatment**

*Patricia W. Stone, Ph.D., M.P.H., FAAN, CIC, Columbia University School of Nursing*

Dr. Stone explained that long-term care facilities (LTCFs) are hotspots for COVID-19 infection because of their design (e.g., open, shared spaces), population (mostly elderly people, many with advanced illness), and staffing (e.g., primarily nursing assistants and few infectious disease

specialists or advanced health care providers). Infection control has long been a persistent problem in LTCFs. Antibiotic use is high in such settings, and residents are at high risk for MDROs.

In response to requirements of the Centers for Medicare & Medicaid Services (CMS), more LTCFs are implementing infection prevention and control and antibiotic stewardship programs and policies, such as increased staff certification in infection prevention and more programs to address urinary tract infection and outbreak control. However, research demonstrates that antibiotic use in LTCFs overall has not changed substantially in the years since such efforts have been implemented, and Dr. Stone concluded that the policies are not yet working.

About 400,000 cases of COVID-19 have been diagnosed among LTCF residents, resulting in about 71,000 deaths, accounting for 42 percent of all deaths from COVID-19. Dr. Stone said it is not clear how many secondary infections are occurring in the setting. Despite the lack of impact of antibiotic stewardship programs so far, she was confident that the situation would eventually improve given increased scrutiny by CMS and others, new technology, more requirements for infection prevention training, dissemination of additional PPE and other equipment for LTCF staff, and increased infection surveillance.

## **DISCUSSION**

Dr. Stone emphasized that she believes a CMS mandate is needed to increase infection prevention training for LTCF staff. She pointed out that the staff who provide direct care to residents are usually certified nurse assistants who often lack training in infection prevention. Staff turnover is high at all levels in LTCFs, and infection control is further hampered by the fact that nursing aides sometimes work at more than one LTCF. Certified nursing assistants currently hold the most dangerous job in this country, Dr. Stone observed; better valuing such workers—for example, by providing better workplace benefits—could lead to a better trained workforce.

## **Disruptions in the U.S. Meat Supply and the Impact on Livestock Production and Antibiotic Use**

*Michael D. Apley, D.V.M., Ph.D., DACVCP, Kansas State University*

Using swine and beef production as examples, Dr. Apley described the steps taken to manage the food animal population when the pandemic hit. The pandemic led to a significant decrease in the number of animals slaughtered, which affected the supply of meat to consumers. For both swine and beef cattle, slaughter increased starting in May in response to summer barbecue season.

Humane management of the animal population was of paramount concern, and when depopulation was necessary, veterinarians, producers, and others worked together to ensure the welfare of the animals and to recognize the emotional toll on the workers who cared for them. In terms of antimicrobial use, swine and beef cattle were held longer than usual in either the earliest or latest phases of the production cycle. Typically, medically important antimicrobials are rarely used at the end of the production cycle. Transitions between production stages are associated with the highest risk of infectious disease, so producers delayed such transitions where possible.

Producers are particularly attentive to the withdrawal period required when antimicrobials are used because they must ensure the meat contains no residual drug, and that factors into drug

selection. Because the pace of production was uncertain, producers withheld drugs as much as possible. The disruption in production peaked in April and May, and the industry is working now to overcome backlogs. Dr. Apley said there is no evidence that the disruptions altered or increased antimicrobial use.

## **DISCUSSION**

Dr. Apley said the disruption demonstrated the importance of having some flexibility in the food production chain, because, for example, holding cattle at the endpoint of the production cycle is the least cost-effective time to do so. Locke Karriker, D.V.M., M.S., DACVPM, said the swine industry saw the need for more rapid engagement with employees at processing plants. A number of employees were absent because of illness or fear of infection, affecting plant capacity, which in turn affected animal management throughout the system.

Dr. Karriker noted that the U.S. food production system is larger and more centralized than that of other countries, which can more easily absorb disruptions in a given plant. Dr. Apley added that food exportation under COVID-19 was also initially challenged by transportation restrictions. Even if the industry had anticipated the pandemic, he did not think it could have predicted the impact of so many complex interactions.

Dr. Apley did not think that overall antibiotic increased when animals were held longer at the last stage of production. Dr. Karriker agreed, adding that depopulation in swine was carried out among the youngest, before they were likely to receive antibiotics, so it is possible the industry had an overall reduced use of antibiotics. Both felt their industries have learned lessons from the pandemic that will help manage future outbreaks.

## **Implications of Telehealth for Companion and Agriculture Animals on Antibiotic Stewardship**

*Gail Golab, Ph.D., D.V.M., MANZCVS, DACAW, AVMA*

Dr. Golab explained the application of telehealth to veterinary care for companion animals. The key components of telehealth—use of digital tools to identify concerns and pinpoint causes, access to consultants and specialists, initiation of early intervention, progress monitoring, and links to prescribers—can all support effective antibiotic stewardship. Telehealth has become especially useful for monitoring chronic conditions among companion animals. In food production, wearable technology and monitoring systems can identify common infections early and improve farm biosecurity.

In response to the pandemic, federal agencies and some states are applying discretion to enforcement of regulations about establishing the veterinarian-client-patient relationship for telehealth purposes. Dr. Golab said more work is needed to fully integrate telehealth into veterinary practices. She noted that an in-person, physical assessment can be critical for diagnosis. There are also concerns that the availability of prescription and over-the-counter treatments from online retailers could lead to inappropriate use.

Dr. Golab said telehealth has great potential for veterinary medicine, but veterinarians must consider and address a number of issues in determining when to use it. She pointed to the great

potential for using telehealth to increase veterinarians' access to specialists for consultations and to educate practitioners and clients.

## **DISCUSSION**

Dr. Golab acknowledged that veterinary health lacks the kind of comprehensive data that human health systems can provide, but with the increasing consolidation of practices, more data are available, and more data sharing is occurring. The AVMA gathers data from various sources.

Dr. Golab said veterinary practices have become less reliant on sales of antibiotics and other products as clients have had more access to products through other retailers. As in human medicine, client satisfaction may drive antibiotic use. Dr. Golab said veterinarians need good antibiotic stewardship resources and education about how to talk with clients to reduce the expectation of unnecessary drug prescriptions.

## **Final Comments and Adjournment for the Day**

*Lonnie J. King, D.V.M., M.S., M.P.A., ACVPM, Vice Chair*

Dr. King thanked the participants and presenters. He adjourned the meeting for the day at 3:30 p.m.

## **Day 2**

### **Welcome and Overview**

*Martin Blaser, M.D., Chair, and Lonnie J. King, D.V.M., M.S., M.P.A., ACVPM, Vice Chair*

Dr. Blaser and Dr. King welcomed the participants.

### **Roll Call**

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

Dr. Musmar welcomed the participants and called the roll.

### **Patient Story**

*Gabriella Balasa, Cystic Fibrosis Patient Advocate*

Ms. Balasa described her experience as a person living with cystic fibrosis (CF), which puts her among those particularly vulnerable to AMR infections and to complications from COVID-19. The safety precautions that have become familiar to everyone during the pandemic are ones she has long used daily to avoid bacterial infections that could be devastating to her health.

Despite recent medical advances to treat the underlying causes of CF, Ms. Balasa said, many with CF are still plagued by infections that require antibiotics, often intravenously in a hospital setting. For Ms. Balasa, the infections are becoming more difficult to treat, and only a few antibiotics are effective, illustrating the urgent need for new antibiotics. Even intravenous antibiotics are becoming ineffective. Last year, Ms. Balasa sought out experimental phage therapy for treatment of multiple resistant infections—and she is not the only one seeking therapies not yet approved by Food and Drug Administration (FDA).

AMR affects everyone and will remain a threat once the risk of COVID-19 is past. Ms. Balasa said resistant infections deserve at least as much attention and resource investment as COVID-19, especially given the risks of co-occurrence. She called for development of new antibiotics and innovative approaches through continued investment in R&D, particularly for smaller biotech companies. She highlighted the strong need for rapid diagnostic testing to minimize the development of resistance. A thorough examination of the process of getting new therapies to market is needed. The scope of the threat of AMR must be recognized; if another pandemic hits, the threat to vulnerable populations could be exponentially increased, Ms. Balasa observed. Combating AMR requires many stakeholders to work together, she concluded.

## **How Life Has Changed: COVID-19 and AMR—Session III**

### **International Perspective on COVID-19 and AMR**

*Hanan Balkhy, M.D., World Health Organization (WHO)*

The WHO established a division of AMR in 2019 and works closely with HHS and various U.S. public health agencies, said Dr. Balkhy. Although more member-states have developed AMR national action plans in the past few years, their governments have not provided sufficient funding for them, and many member-states lack clinical guidance on antimicrobial use. Since the pandemic, evidence shows low levels of bacterial coinfection with COVID-19 but high rates of empiric antimicrobial use, as in the United States. The WHO's guidance for clinical management of COVID-19, updated in May 2020, describes when to use antimicrobials.

To preserve access to antimicrobials, especially for low- and middle-income countries, the WHO created the AWaRe tool, which categorizes antibiotics according to availability, appropriate use, and risk of resistance (access, watch, and reserve). Member-states should strive to ensure that at least 60 percent of their antibiotic use falls into the access category: drugs that are widely available, affordable, and used empirically for common infections.

Dr. Balkhy said the WHO's antibiotic stewardship toolkit was delayed by the pandemic but will roll out soon. She stressed the global need to establish a career pathway in infection prevention and control and referenced several WHO training mechanisms, some of which are specific to COVID-19 but are broadly relevant. The WHO partnered with other international public health organizations to address problems with the supply chain for PPE, even in high-income countries. The WHO set up the AMR Multi-Partner Trust Fund to support innovative research, with the goal of bringing two to four novel antibiotics to market by 2030.

### **DISCUSSION**

Dr. Balkhy acknowledged the difficulty of coalescing global support for the AMR agenda but said she believes the effort is back on track. Ramanan Laxminarayan, Ph.D., M.P.H., hoped the pandemic would raise awareness about the effectiveness of PPE, hand hygiene, and other precautions to prevent the spread of disease. Dr. Balkhy said every disease outbreak draws attention, but that attention is difficult to sustain. She would like to see infection prevention and control recognized as a distinct discipline and more investment in education, such as a dedicated curriculum to build a pipeline of infection prevention and control leaders for health care settings. Sustaining the global AMR agenda will also require stronger support from governments and a

multisector response. She called on stakeholders to be more vocal about the risks of not addressing AMR.

### **The Pharmaceutical Industry Response to the Pandemic**

*Phyllis Arthur, Biotechnology Innovation Organization (BIO)*

Approximately 750 drugs and vaccines for COVID-19 were in development within eight months of the disease being recognized, Ms. Arthur observed. In a public health emergency, the partnership between the pharmaceutical industry and government is pivotal, as significant investment and cooperation are needed to advance products through development. Ms. Arthur said industry responded quickly to the pandemic, and companies worked collaboratively to leverage technologies, expertise, and other resources. The response was made possible in part by a U.S. government (USG) commitment to public-private partnerships (PPPs), and investments made before the pandemic (e.g., in rapid platform technologies) helped speed up the response.

In July, the industry started thinking about how to apply lessons learned so far from the pandemic to AMR product R&D. The AMR Action Fund was created to support antibiotic R&D through commercial development while efforts are underway to address the market barriers that hold back investment in antibiotics. Industry has invested \$1 billion in the effort, with the goal of bringing two to four novel antibiotics to market by 2030. Ms. Arthur said the AMR Action Fund seeks to catalyze the marketplace to make it possible for new antibiotics to thrive. It uses the venture capital model, in which an “engaged owner” contributes industry expertise to accelerate development. The Action Fund complements other PPPs and investments, buying time for new antibiotic development while seeking to create a more sustainable market for them.

### **DISCUSSION**

Dr. Blaser pointed out that pharmaceutical companies have stepped up efforts to make vaccines and other products for COVID-19 because the USG has guaranteed it will buy them, but the same cannot be said for antimicrobials. Ms. Arthur said the USG already has some mechanisms for underwriting the market that could be used. For example, the Biomedical Advanced Research and Development Authority (BARDA) could commit to purchase antibiotics for the Strategic National Stockpile and manage inventory, as it does for medical countermeasures.

Subscription-based models guarantee access to antimicrobials over the long-term by providing manufacturers a viable source of income to replace the profits that would have been gained from selling the product in a more traditional marketplace, Ms. Arthur noted. The approach compensates for the fact that antimicrobials offer a much lower return on investment than other products. Ms. Arthur said BIO believes subscription is a sustainable mechanism that prevents overuse of products. Stakeholders must consider models that value and pay for antimicrobials in novel ways to ensure they are available when needed over the long term, she observed.

### **The Intersection of AMR and Emergency Preparedness: The Need for New Antibiotics**

*Mark Albrecht, Ph.D., Biomedical Advanced Research and Development Authority (BARDA)*

Dr. Albrecht stressed that BARDA focuses on biothreats to security but recognizes that all such threats—chemical, biological, radiological and nuclear threats; pandemic influenza; and emerging infectious diseases—will require antimicrobials at some point. The impact of

infections is clear from past pandemics and amplified by AMR. BARDA views AMR as a public health threat that can impede response to public health emergencies, regardless of the cause.

Using the Emerging Infections Network, BARDA conducted a survey on infections secondary to COVID-19. As described in earlier presentations. Secondary infections are relatively rare, and the infections are consistent with those typically seen in hospitals.

Dr. Albrecht said COVID-19 has hampered antibiotic R&D in several ways. Some studies have been suspended as investigators and other staff turn their attention to the pandemic. Fewer people are seeking health care, and some subjects are dropping out of studies to avoid clinical settings. Manufacturing facilities closed in response to regional directives to prevent the spread of disease, which affected the production and availability of materials needed for research. However, BARDA continues to focus on strengthening the pipeline and supporting new technology for AMR. COVID-19 demonstrated that companies need more funding, Dr. Albrecht noted, so BARDA has provided more funding or shifted dollars within contracts to help them. He said that Project Bioshield's award for the development of omadacyline incorporates both push and pull market incentives. The award supports advanced R&D, and BARDA will purchase the resulting products for the Strategic National Stockpile once approved by FDA.

## **DISCUSSION**

Dr. Albrecht said BARDA has a division devoted to diagnostics, and it works with companies to use existing or new diagnostics to streamline enrollment of eligible subjects in studies. He noted that BARDA seeks to make another award in 2021 that would support R&D and also ensure product purchase for the Strategic National Stockpile. Dr. Newland pointed out that funding for the Emerging Infections Network is under threat, and Dr. Albrecht stated that the network has been invaluable to understanding the pandemic and day-to-day health care challenges.

Dr. Albrecht expressed that BARDA grapples constantly with where to focus its efforts; it has traditionally targeted new antibiotics and therapies but also recognizes the importance of better diagnostics. Dr. Blaser emphasized that diagnostics can inform treatment, allowing providers to select narrow-spectrum antibiotics that are less likely to select for resistance.

## **Environmental Impact of COVID-19 and Effects of Changing Behaviors**

*Andrew Singer, Ph.D., U.K. Centre for Ecology & Hydrology*

Dr. Singer summarized some of the indirect impacts of COVID-19 related to AMR. In the United Kingdom, as in the United States, antibiotic prescribing spiked early in the pandemic and then decreased, and shutdowns may have led to lower antibiotic use overall. Focusing on sewage release into waterways, Dr. Singer said the shutdowns reduced environmental surveillance, meaning that identification of potential compromises decreased, as did mitigation of sewage releases and enforcement of protections. At the same time, many people who chose not to travel for vacation also took advantage of local rivers during the hot summer months, and thus may have been exposed to potentially contaminated water.

Academic research on AMR has been paused during the pandemic, and many investigators have turned their attention to COVID-19, resulting in a brain drain and financial burdens. Dr. Singer



said the impact on environmental research and surveillance is substantial, and he advocated for restoring funding for AMR research to pre-pandemic levels.

The increased use of PPE, hand hygiene, and sanitation could have a positive effect on AMR. Although widespread use of alcohol-based hand sanitizers can reduce infections, the continued sale of non-alcohol-based sanitizers containing biocides will likely contribute to increased AMR.

## **DISCUSSION**

Paul Plummer, D.V.M., Ph.D., DACVIM, DECSRHM, wondered whether the use of field hospitals and other nontraditional settings to provide care to COVID-19 patients could lead to more environmental release of resistant organisms. Dr. Singer said most of the drivers of AMR come from wastewater, and he suspected that outdoor treatment settings were attentive to safety concerns. He said that behavioral changes that lead to less use of antiseptics that would eventually leach into the environment could ultimately result in a net decrease of environmental exposure. Dr. Singer said he anticipated the opposite would be true on the basis of events during the H1N1 influenza pandemic, but the COVID-19 pandemic response has been very different.

Dr. Singer clarified that any product that reduces the growth rate of bacteria will drive resistance, and biocides are particularly good at doing so. The mechanism by which resistance develops from use of biocides, pesticides, and many human drugs is complicated, he added.

## **AMR and COVID-19 Surveillance in Sewage**

*R. Sean Norman, Ph.D., University of South Carolina*

Dr. Norman explained that testing sewage samples coming in to a wastewater treatment plant provides a community-wide fecal sample that can be used to assess health at the community level. Dr. Norman's team has been studying AMR in wastewater and has found evidence of aerosolized antibiotic resistance genes downwind of treatment tanks, generated during the treatment process. The findings suggest that wastewater systems may be good indicators of potential community burden of AMR. That research was suspended when the pandemic hit, but the team has extensive baseline data on human antibiotic resistance gene abundance through December 2019.

Dr. Norman's laboratory is now working with CDC to monitor COVID-19 through sewage surveillance in South Carolina. The findings showed SARS-CoV-2 virus increasing in the state around Memorial Day and throughout the summer until masks were made mandatory, at which point the amount of virus in the wastewater decreased. Dr. Norman said the mask policy likely affects viral abundance. He also noted that samples from April through the summer showed an increased level of antibiotics. Dr. Norman plans to integrate the data from multiple studies to better understand the impact of COVID-19 on AMR in and across communities.

## **DISCUSSION**

Dr. Norman said wastewater surveillance has proven to be highly sensitive for SARS-CoV-2 virus, and he gave an example of its successful use on the University of South Carolina campus to identify students who ultimately tested positive for the virus. Dr. Norman said the technology could be scaled to any level. For example, investigators could sample areas identified by

vulnerability maps and break down the sewershed into small units for a more granular assessment. Dr. Norman said such an approach might be applicable to assess AMR.

## **Public Comment**

Dr. Musmar and Mark Kazmierczak, Ph.D., read aloud four written public comments submitted. Because of technical difficulties, the recorded public comments submitted were not played during the meeting. All public comments are available on the [PACCARB website](#).

**Jonathan Romanowsky of Inflammatrix, Inc.**, described his company’s molecular diagnostics tests, which he said could contribute to decreasing antibiotic resistance. Current reimbursement rules impose barriers to patient access to novel tests. He described the procedures by which CMS classifies diagnostic tests and the length of time it takes for products to qualify for CMS reimbursement, noting that it can take years for a product to become eligible for reimbursement, and the amount of reimbursement can be substantially lower than the cost of the product. Thus, instead of providers adopting potentially game-changing tests, they hesitate to order them given their reimbursement challenges. Additionally, investors shy away from funding potential high-impact diagnostic companies, given the incremental delays (and oftentimes uncertainty) in achieving a reasonable return on capital. As a result, patient access to some diagnostic tests is limited.

Mr. Romanowsky said that paths do exist for novel technologies to be adopted while providing assurance that their impact is positive and enduring. Inflammatrix encourages PACCARB to support a “coverage with evidence in development” program, including ensuring that the proposed Medicare Medical Coverage of Innovative Technology program includes novel diagnostic tests, advocating for a more timely and generous New Technology Add-On Payment program, and adding diagnostics coverage to the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms Act under consideration by Congress. These and other ideas should be implemented as temporary measures (e.g., four years), allowing time for new tests to clearly demonstrate clinical utility and patient safety when used in routine care. The tests that meet this high bar can then transition to permanent coverage status. In the interim, support for these programs allows patients to access clinically valuable tests that can also make strides to limiting antimicrobial resistance.

The **Center for Science in the Public Interest** said that usage of antimicrobials to combat secondary bacterial infections in the COVID-19 pandemic has further emphasized the importance of these drugs and that AMR remains a top public health threat. U.S. and international public health and regulatory agencies acknowledge that the usage of antimicrobials in agriculture increases the risk of resistance in bacteria that affect humans. As a result, the FDA has taken actions to curb inappropriate uses of antimicrobials in agriculture. These include implementing Guidance for Industry (GFI) #209, The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals, and GFI #213, New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209; ordering changes to the Veterinary Feed Directive; and issuing a draft GFI, #263, Recommendations for Sponsors of Medically Important Antimicrobial Drugs Approved for Use in Animals to Voluntarily Bring Under Veterinary Oversight All

Products That Continue to Be Available Over-the-Counter. Collectively, these steps eliminate the usage of antimicrobials for production and growth promotion purposes and bring all medically important antimicrobials under veterinary supervision. In addition, FDA published the plan, Supporting Antimicrobial Stewardship in Veterinary Settings, Goals for Fiscal Years 2019–2023. While the FDA Five-year plan sets many laudable overarching goals, PACCARB should request more concrete and timely actions, in addition to those outlined in the plan, be taken to ensure unnecessary antimicrobial use in agriculture is eliminated as soon as possible. These include:

- The elimination of other inappropriate uses of antimicrobials, such as regular or routine unnecessary mass treatments of animals that are otherwise healthy and unnecessary empiric treatments for certain conditions.
- The timely release of an integrated AMR report or reports containing individual components, which includes human and animal antimicrobial sales and usage data, biomass indicators, and human and animal AMR resistance and illness monitoring data, to provide needed evidence to drive further action where warranted.
- The establishment of policy to ensure that duration-of-use labeling on animal antimicrobial products are set with reference to risk-based principles outlined in GFI #152, Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern.

These actions will be crucial to ensuring antimicrobials remain effective for those critical situations when they are needed.

**Keep Antibiotics Working (KAW)** urged the Council to move away from creating lengthy documents that are never implemented and instead focus on making a limited number of concrete recommendations and then regularly following up with agencies to see what has been implemented. KAW asked what efforts have been made to update the National Strategy, issued September, 2014. In light of the COVID-19 pandemic, elements of the National Strategy should be revised to address pandemic preparedness and, more specifically, the threat of antimicrobial-resistant secondary infections associated with viral pandemic pathogens. The spread of AMR either to antiviral drugs or to antibiotics used to treat secondary infections greatly limits the ability to respond to pandemics and creates additional strains on the health system.

KAW said the 2015 National Action Plan for CARB failed to set targets for reducing antibiotic use in animals. KAW asked that the PACCARB recommend that the updated National Action Plan include specific targets for reducing inappropriate antibiotic use in livestock and specifically research and define “inappropriate use” in an animal context. The initial plan failed to prohibit the continuous use of antibiotics in food animals. Pointing to FDA GFI #213, KAW asked that the PACCARB ask FDA to require sufficiently short durations of antibiotic use consistent with existing FDA guidelines on labeling and that FDA require drug makers to provide data to support a request for longer duration of use along with evidence of safety with respect to antibiotic resistance. The initial plan also failed to consider antibiotic use in crops.

KAW asks that PACCARB make inquiries to federal agencies, including FDA and USDA, to determine the basis for delays in both releasing national reports and reporting data collection

from ongoing studies. FDA's Center for Veterinary Medicine (CVM) has yet to release its comprehensive report of available information about antimicrobial use and resistance in animal agriculture. In 2017, CVM sought comment on a proposed methodology for applying a biomass denominator to annual data, yet the adjusted biomass data has not been released. CVM is also very behind in updating the National Antimicrobial Resistance Monitoring System. At previous meetings, the PACCARB heard presentations from researchers collecting detailed voluntary antimicrobial use data in cattle and in swine under two FDA-funded cooperative agreements that started in 2016. Since 2016, there has been no public release of these data sets or an analysis of them. The PACCARB should evaluate where there have been delays in reporting on PACCARB-related activities, and it should not passively accept very long timelines set by agencies for CARB-related activities. CDC and HHS must more fully monitor and address antimicrobial use and resistance related to the COVID-19 pandemic.

**Kevin Kavanagh, M.D., of Health Watch USA** said we need to learn several lessons from the COVID-19 pandemic and apply them to all dangerous pathogens. First, "one size does not fit all" is an excuse for inaction. It did not work with MRSA, and it led to a disastrous, uncoordinated whack-a-mole approach with COVID-19. Second is the importance of surveillance and isolation. We have not universally adopted MRSA surveillance and isolation of carriers upon hospital admission. Similarly, we neglected the identification of SARS-CoV-2 community carriers with disastrous results, which led to early undetected spread of the pandemic throughout the State of Washington.

Strong federal coordination, along with surveillance and isolation strategies are needed. American Medical Association President Hunter McGuire stated, "A difficulty in dealing with infectious diseases in America was the rooted dislike to the curtailment of the personal liberty of the citizen for the benefit of the people at large." He stressed the need for a strong coordinated federal response. Tellingly, this appeal was in 1893. Things have not changed much. We are still stuck in the 1800s regarding our government's approach to pandemics.

Finally, of utmost importance is the implementation of a national reporting system for dangerous pathogens. Of the CDC's five urgent microbial threats, only one, *C. difficile*, is mandatorily reported on a national basis, but not for all types of health care facilities. Of the serious threats, only MRSA is mandatorily reportable on a national basis, but only for acute care hospitals. We need a national reporting system that is comprehensive for all dangerous pathogens; mandatory for all types of health care facilities and practices; and accessible in real time, having same-day or next-day public availability, Dr. Kavanagh concluded.

## **Council Discussion**

Dr. Blaser invited Council members to give brief statements in response to the presentations. He said that just as increasingly severe natural disasters have been linked to the underlying problem of climate change, he believes the increasing prevalence and severity of AMR, obesity, asthma, autoimmune disease, and now the COVID-19 pandemic might all be linked to selective pressure on the human microbiome. The current pandemic should be a wake-up call that common factors are driving all these health issues. Prioritizing development of new antibiotics will not be sufficient, Dr. Blaser said; efforts must turn to better aligning the ecology so that humans and animals are not subject to invading organisms. Until there is effective antibiotic stewardship,

AMR can only be kept at bay and may get worse. The silver lining of the pandemic may be the recognition of the importance of ecological considerations in gaining control of infectious disease.

Dr. King pointed to the similarities between COVID-19 and AMR. Both are pandemics (although AMR moves more slowly, with periodic acute episodes) that have been rising in the past two to three decades. They share similar drivers and are global in scale, with profound impacts on morbidity and mortality, with extreme negative economic and social consequences. Both should be viewed through a One Health lens, with systems thinking applied, and both have direct and indirect implications. COVID-19, for example, is likely to catalyze other epidemics, to have short- and long-term effects on mental health, and to lead to increased disease because of disruptions in childhood vaccinations. Both affect daily life, especially for vulnerable populations, and threaten national security. Both will be the most expensive pandemics in history.

Dr. King outlined some key actions that should be taken:

- Apply the principles of infection prevention and control broadly and extend them to the interface of nature and human civilization.
- Invest in prevention as well as medical care. The World Bank estimates that a global One Health infrastructure would cost \$3.5 billion annually—which seems like a bargain given the \$9 trillion price tag for the pandemic.
- Increase attention to emerging zoonotic diseases. COVID-19 is the third coronavirus to emerge in humans in the 21<sup>st</sup> century, and coronaviruses are common in animals.
- Use the lessons learned from this pandemic to inform a strategy for the next pandemic; be prepared for a new normal of emerging infectious disease.
- Support team collaborations, globally, bringing in a broad range of experts to address R&D and other efforts.
- Ensure leadership and governance are in place with the commitment, preparation, response, and resilience to withstand a global disaster. Rethink government organization and structure and the need for collective action to address national threats.
- Recognize that One Health problems are globally interconnected.

Dr. Plummer said the AVMA published a new report, [Antimicrobial-Resistant Pathogens Affecting Animal Health](#), a comprehensive review on treatment and management for major companion animal species. It builds on antibiotic stewardship resources provided by the AVMA and demonstrates the commitment of veterinarians to address AMR. The AVMA plans to update the report regularly.

Christine Ginocchio, Ph.D., MT, said that makers of diagnostics have demonstrated resilience and adaptability in the face of the pandemic, with more than 200 COVID-19 tests approved by FDA under emergency use authorization. Yet no single source can provide enough tests to meet the demands of testing during this pandemic. Consideration must be given to the complexity of regulatory compliance and manufacturing in anticipation of future needs. Supply chain constraints have led to competition among diagnostics makers; it is not clear whether sufficient

supplies will be available for manufacturers to scale up test production. The availability of facilities and personnel are also concerns.

Dr. Ginocchio called for more attention to equitable global distribution of tests as well as the need to produce diagnostics for other conditions. Manufacturers must consider competing demands in determining which diagnostics to produce and how much. Dr. Ginocchio applauded the PPPs that support diagnostics, but more focus is needed on sustainability and broad implementation. Antibiotic stewardship must be a high priority. To prepare for the future, a pathway must be created for laboratory-developed diagnostic tests, validated under CLIA, without FDA regulation, to be used for COVID-19 and other emerging pathogens.

Dr. Newland said the presentations underscored the importance of vaccines and public health infrastructure. Vaccines play a significant role in preventing the need for antibiotics, thus decreasing AMR. An effective COVID-19 vaccine is key to ending the pandemic. Yet infrastructure is lacking. Children, underserved populations, people of color, and others are likely to suffer unless the public health infrastructure is improved. Better mechanisms for data collection are also needed. Dr. Newland hoped the Council would focus on the need for vaccines and public health infrastructure worldwide to fight AMR.

Dr. Jinks said the significance of the AMR pandemic may not have been appreciated broadly, but COVID-19 has been a brutal, tragic wake-up call. AMR will persist, but preventing the spread of drug-resistant organisms is possible and should be a long-term goal. Intervention is needed to protect health and save lives. Research can provide details and solutions for sustainable success. Dr. Jinks proposed doubling efforts in three areas:

- Increase collection and sharing of actionable evidence.
- Accelerate work on tools and interventions for health care providers.
- Develop a sustainable market for useful products.

Dr. Jinks said work must progress in the United States and internationally. AMR cannot be defeated when there is insufficient political will for global cooperation. International collaboration is needed to foster implementation of solutions. The global AMR agenda should be reinvigorated, with international investment in sustained efforts.

Dr. Dodds Ashley said many of the lessons learned from COVID-19 can be applied to AMR. The National Institutes of Health guidelines for treating COVID-19 were crafted using a multidisciplinary approach that included infectious disease and critical care pharmacists. The guidelines offer practical treatment strategies for every setting, including settings where there are no infectious disease physicians or pharmacists. The approach can be adapted for other clinical guidelines. Dr. Dodds Ashley noted that the Infectious Diseases Society of America (IDSA) published treatment guidelines for MDROs, also using a multidisciplinary approach. She hoped that guidance would be updated as conditions change and new products emerge, so that facilities that lack internal expertise can use the guidance to deploy new therapies. (Helen W. Boucher, M.D., FIDSA, FACP, confirmed that IDSA's AMR guidelines will be updated as new data are available.) Dr. Dodds Ashley hoped the National Academy of Medicine and others would include physicians and others working on the front lines of the pandemic as they craft guidance

on remdesivir. Finally, she noted that pharmacists have been granted authority to administer routine and COVID-19 vaccinations to children, and she hoped that policy would continue, allowing more children to receive vaccines.

Michael Craig, M.P.P., of CDC emphasized the tremendous impact of the first National Action Plan for CARB. The investments that came about as a result of that plan helped during the pandemic in ways that were not predicted. Yet, the steps taken so far are not enough. As many presenters said, the number of people with infection prevention and control experience in health departments and hospitals is extremely limited. In the fall of 2019, CDC reported progress against some of the worst antimicrobial-resistant infections, but the pandemic could reverse those gains. The importance of data for understanding such changes cannot be overstated. In addition, robust infection prevention and control wherever health care is delivered helps everyone, around the world. As HHS updates the National Action Plan for CARB, the Council should think critically about the overlap between AMR and the COVID-19 pandemic.

Dr. Boucher highlighted the difficult pathway for diagnostics, including the challenges of low reimbursement for diagnostics and the need to create diagnostics in parallel with new drugs. She said these barriers must be addressed. Further, Dr. Boucher called for better pandemic preparedness. Workforce development, especially for the infectious disease workforce, must be considered. The next generation of health care providers needs training and education on infectious disease and on communicating effectively in times of fear and uncertainty. The lack of awareness of the AMR threat remains a persistent issue, and future advocacy efforts should take that into account.

Stephanie Black, M.D., M.Sc., said COVID-19 has exposed the lack of infection prevention and control in LTCFs, which amplifies AMR. She encouraged continued collaboration between CDC and CMS to go beyond requiring dedicated infection prevention and control staff in such settings. CMS should describe the specific training needed, and CDC should develop that training. Dr. Black called for incentives for infection prevention and control training, which could translate to monetary incentives for staff and decrease staff turnover in LTCFs. In addition, Dr. Black pointed out that COVID-19 highlighted racial and ethnic disparities in health care. She said all research on AMR should gather data on race and ethnicity to better understand disparities in the risks of infection and access to care.

Armando Nahum said the pandemic revealed the lack of education and exposure to misinformation at all levels—among patients and their families, in politics, in science, and in the media. The Council should educate the public at large about the use of antibiotics during the pandemic and beyond. The world sees the United States as a leader, but every day, there is evidence that the country is falling behind, said Mr. Nahum. If the people of the United States cannot unite all at once, perhaps education and awareness should be targeted to each state in an effort to build national unity state by state, over time.

## **Final Comments and Adjournment**

*Martin Blaser, M.D., Chair, and Lonnie J. King, D.V.M., M.S., M.P.A., ACVPM, Vice Chair*

Dr. Blaser thanked the presenters and participants. He appreciated the reflections of the Council members. He expressed thanks to Dr. Musmar and her colleagues for ensuring the success of the Council's first virtual meeting. Dr. Blaser adjourned the meeting at 2:57 p.m.



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

**September 9–10, 2020**

### **PACCARB Voting Members Present**

Martin J. Blaser, M.D., Chair  
Lonnie J. King, D.V.M., M.S., M.P.A., ACVPM, Vice Chair  
Michael D. Apley, D.V.M., Ph.D., DACVCP  
Stephanie Black, M.D., M.Sc.  
Helen W. Boucher, M.D., FIDSA, FACP  
Sara E. Cosgrove, M.D., M.S.  
Paula J. Fedorka Cray, Ph.D.  
Christine Ginocchio, Ph.D., MT  
Locke Karriker, D.V.M., M.S., DACVPM  
Kent E. Kester, M.D., FACP, FIDSA, FASTMH  
Elaine Larson, Ph.D., RN  
Ramanan Laxminarayan, Ph.D., M.P.H.  
Armando Nahum  
Paul Plummer, D.V.M., Ph.D., DACVIM, DECSRHM  
David White, M.S., Ph.D.

### **Organizational Liaisons Present**

*American Association of Extension Veterinarians*  
Carla L. Huston, D.V.M., Ph.D., DACVPM

*American Veterinary Medical Association*  
Joni Scheftel, D.V.M., M.P.H., DACVPM

*Biotechnology Innovation Organization*  
Greg Frank, Ph.D.

*Direct Meds, Inc.*  
Munir Kazmir, M.D.

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

*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*

Marjory Cannon, M.D. (for Shari Ling, M.D.), Centers for Medicare & Medicaid Services

Dennis M. Dixon, Ph.D., National Institute of Allergy and Infectious Diseases, National Institutes of Health

Lynn Filpi, Ph.D. (for Lawrence Kerr, Ph.D.), Office of Pandemics and Emerging Threats, Office of Global Affairs

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

Lawrence Kerr, Ph.D., Office of Pandemics and Emerging Threats, Office of Global Affairs

Rima Khabbaz, M.D., National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention

#### *U.S. Department of Agriculture*

Emilio Esteban, D.V.M., M.B.A., M.P.V.M., Ph.D., Food Safety and Inspection Service

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

#### *U.S. Department of Defense*

Paige Waterman, M.D., FACP, FIDSA, Walter Reed Army Institute of Research

### **Designated Federal Official**

Jomana F. Musmar, M.S., Ph.D., Advisory Council Committee Manager, Office of the Assistant Secretary for Health, Department of Health and Human Services

### **Advisory Council Staff**

Mark Kazmierczak, Ph.D., Gryphon Scientific

Taylor Simmons, M.P.H., ORISE Fellow, HHS

## Glossary of Abbreviations

AMR	antimicrobial resistance
AVMA	American Veterinary Medical Association
BARDA	Biomedical Advanced Research and Development Authority
BIO	Biotechnology Innovation Organization
CARB	combating antibiotic-resistant bacteria
CARB-X	Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator
CDC	Centers for Disease Control and Prevention
CF	cystic fibrosis
CLIA	Clinical Laboratory Improvement Amendments
CMS	Centers for Medicare & Medicaid Services
CoV	coronavirus
CVM	Center for Veterinary Medicine
ESBL	extended-spectrum beta lactamase
FDA	U.S. Food and Drug Administration
GFI	Guidance for Industry
HAI	health-care-associated infection
HHS	U.S. Department of Health and Human Services
IDSA	Infectious Diseases Society of America
ILI	influenza-like infection
KAW	Keep Antibiotics Working
LTCF	long-term care facility
MDRO	multidrug-resistant organism
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
OASH	Office of the Assistant Secretary for Health
PACCARB	Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria
PPE	personal protective equipment
PPP	public-private partnership
R&D	research and development
SARS	severe acute respiratory syndrome
USDA	U.S. Department of Agriculture
USG	U.S. government
WHO	World Health Organization