

# PACCARB

Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria

## **Meeting Summary**

### **Seventh Public Meeting of the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria September 13–14, 2017**

**Department of Health and Human Services  
Great Hall, Hubert H. Humphrey Building  
200 Independence Avenue, SW  
Washington, DC 20201**

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# Meeting Proceedings

## Day One

### 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 called the meeting to order at 9:00 a.m. and welcomed the participants.

### Call to Order, Roll Call, and Rules of Engagement

*Jomana F. Musmar, M.S., Ph.D.c, Designated Federal Officer (Acting)*

Ms. Musmar explained the rules governing the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) under the Federal Advisory Committee Act and conflict-of-interest guidelines. She then called the roll. (See Appendix A for the list of participants.)

### Opening Remarks

*Garrett Grigsby, Director, Office of Global Affairs (OGA), U.S. Department of Health and Human Services (HHS)*

Mr. Grigsby thanked the PACCARB members for their time, expertise, and hard work, noting that the Council's advice to the Secretary and the administration on key priorities is highly regarded and very useful. He described the OGA's role in combating antibiotic resistance, particularly in concert with the Department of State and the U.S. Department of Agriculture (USDA) around Goal 5 of the *Combating Antibiotic-Resistant Bacteria National Action Plan*, which focuses on improving international collaboration and capacity.

Over the past 3 years, global attention to antimicrobial resistance (AMR) has grown remarkably. This year, the World Health Organization (WHO) and the Group of Seven (G7) countries have elevated the issue to a high priority. The OGA represents HHS in such efforts and supports HHS Secretary Tom Price, M.D., in this work. Mr. Grigsby said Sec. Price has prioritized combating AMR, noting that a threat anywhere is a threat everywhere. Efforts are underway to ensure that U.S. Government (USG) agencies work seamlessly with each other and engage with other countries. International organizations must treat AMR as a priority, while taking into account the wisdom and clear advice of the private sector. Mr. Grigsby said the OGA looks forward to working with domestic and international partners.

### Patient Story

*Christian Lillis, Peggy Lillis Foundation*

Mr. Lillis movingly described how his mother, Peggy, became infected with antibiotic resistant *Clostridium difficile* and died within days of diagnosis. He depicted his bewilderment that a healthy woman in her mid-50s could suddenly become ill and die from an infection that he had never heard of. Mr. Lillis painted a picture of his mother

and her impact not just on his family but on her whole community. “She was the best person I’ve ever known,” he said, as he outlined her perseverance and compassion. Mr. Lillis applied his experience in advocating for the rights of lesbian, gay, bisexual, and transgender people in health care to raising awareness about antibiotic-resistant infections, founding the Peggy Lillis Foundation. He has shared Peggy’s story nationally and heard thousands of stories like hers.

Mr. Lillis recalled the words of wisdom his mother imparted to him and his brother when they fought as children. “All you have in this world is each other,” she stressed. Mr. Lillis emphasized the importance of taking care of one another, no matter what, and especially in the face of a dysfunctional health care system. Despite education and some clearly effective methods to prevent infection—prescribing fewer antibiotics, getting health care workers to wash their hands regularly, sanitizing hospital rooms—the moral thing to do, the right thing to do, is often lost, said Mr. Lillis, as profits, ideology, and the needs of oneself are prioritized over the needs of the community.

In closing, Mr. Lillis noted that the cause of his mother’s death was not reported to any public health authority, as individual cases are not tracked. The lack of urgency disturbs him, he said, and it should disturb all Americans, he said. Every day, 300 people die from *C. difficile*, and hundreds more die from other infections. Mr. Lillis asked the Council members to consider that urgency as they make recommendations.

“Our country deserves a health care system where resistant infections are rare, treatable, and survivable,” said Mr. Lillis. “We must prove that my mother and every other person lost to an antibiotic-resistant infection matters. We have a moral duty to make sure they count.” Dr. Blaser thanked Mr. Lillis for sharing his mother’s story and for highlighting the moral imperative to combat AMR.

## ***National Action Plan Goal 1: Stewardship***

### **Prevention and Antibiotic Stewardship: Progress and Opportunities to Improve Antibiotic Use in Human Health—Hospitals, Outpatient Settings, and Nursing Homes**

*Arjun Srinivasan, M.D., CAPT, U.S. Public Health Service, Centers for Disease Control and Prevention (CDC), HHS*

To address stewardship goals, CDC created a set of Core Elements of effective programs (adopted by The Joint Commission and others) and worked with the National Quality Forum (NQF) on an implementation guide. It is assessing implementation through the National Healthcare Safety Network (NHSN) and supports state efforts around stewardship. The federal Office of Rural Health Policy aims to encourage small, critical access hospitals to implement stewardship by making adoption of the Core Elements a criterion for certain federally funded programs.

CDC launched the NHSN Antimicrobial Use option to capture data electronically and developed the standardized antimicrobial administration ratio (SAAR), which compares observed to predicted use for high-priority antibiotics. The measure was adopted by NQF

and is used by Centers for Medicare and Medicaid Services (CMS), among others, to assess antibiotic use policies.

Dr. Srinivasan stressed the importance of addressing unnecessary antibiotic use in the outpatient setting, such as urgent care clinics. CDC is collaborating with states on data collection and partnering with various stakeholders to identify targets for antibiotic stewardship. To link payment with stewardship, CDC is working with CMS to incorporate antibiotic use measures in performance improvement and with private payers to improve antibiotic use. On the regulatory side, CDC is focused on stewardship and data collection in nursing homes.

### **CMS Progress Update**

*Shari Ling, M.D., CMS, HHS*

CMS' quality improvement efforts include the Hospital Improvement Innovation Networks (HIINs), which provide technical assistance and data to help organizations at the national, state, and hospital system level reduce health-care-associated infections (HAIs), AMR, and other patient harms. The Quality Improvement Network–Quality Improvement Organizations (QIN–QIOs) partner at the community level to promote quality improvement principles and engage patients and families.

QIN–QIOs recruited more than 2,000 nursing homes to report *C. difficile* data to NHSN and trained more than 12,000 in stewardship and infection control through the National Quality Care Collaborative. Dr. Ling pointed out that nursing homes are complex settings because they are both residences and care facilities. QIN–QIOs have also engaged 7,600 other outpatient care settings in antibiotic stewardship efforts, with education and tools tailored for the setting.

Federal laws and regulations allow CMS to include antibiotic use in merit-based payment systems and integrate antibiotic stewardship into alternative payment models. CMS is phasing antibiotic stewardship program requirements into its Conditions of Participation (CoPs) for long-term care facilities. Similar requirements for hospitals are in the rulemaking process. Dr. Ling said CMS is committed to enabling safe, high-quality care and remains mindful of the burden on facilities of reporting.

### **Update on Agency for Healthcare Research and Quality (AHRQ) Antibiotic Stewardship Activities**

*Melissa A. Miller, M.D., M.S., AHRQ, HHS*

AHRQ's efforts to address antibiotic resistance fall under its HAI activities and range from research to implementation. AHRQ announced two new funding opportunities in 2016 to stimulate research in all settings. Several funded projects are addressing antibiotic use and stewardship, including appropriate use in dental practices. AHRQ translates research findings into tools, such as the Nursing Home Antimicrobial Stewardship Guide, which it disseminates widely.

The agency's most powerful mechanism for implementation is its Comprehensive Unit-Based Safety Program (CUSP). The Antibiotic Stewardship CUSP launched in 2016,

recruiting acute-care settings, and will expand to long-term and ambulatory care settings in coming years. A nationwide CUSP project in long-term care significantly reduced catheter-associated urinary tract infections (CAUTIs). It also yielded a toolkit that facilities can use to improve antibiotic and diagnostic stewardship and reduce CAUTIs.

Dr. Miller described AHRQ efforts to implement PACCARB recommendations, including more coordination across agencies (e.g., working with CMS and CDC) and strengthening partnerships (including working with integrated delivery systems to learn more from the private sector). AHRQ aims to promote a culture of antibiotic stewardship through its CUSP programs. Its research initiatives support the development of evidence-based stewardship programs. The agency's work also reflects PACCARB recommendations to address stewardship in outpatient settings.

### **The Joint Commission's Antimicrobial Stewardship Standard**

*David Baker, M.D., M.P.H., FACP, The Joint Commission*

Dr. Baker said The Joint Commission is well positioned to move antibiotic stewardship forward. Its stewardship standard went into effect in 2017 for hospitals and nursing homes. The key elements of the standard are leadership (as demonstrated by organizational prioritization of stewardship), a multidisciplinary team approach, education (including patients and their families), multidisciplinary protocols, data monitoring, and performance improvement.

Among the challenges that organizations face in meeting the standard is are the lack of generally accepted performance measures, bringing into question the value of performance improvement data; difficulty finding infectious disease (ID) expertise to inform programs; barriers to engaging pharmacy and physician champions; difficulty tracking data efficiently; and problems disseminating information.

Dr. Baker noted that nursing home face challenges to implementing stewardship programs fully. They often have limited resources and high staff turnover, and the clinical status of residents is often uncertain (e.g., residents may have cognitive impairment or difficulty communicating). The Joint Commission has not yet applied its standard to ambulatory care settings because they vary so much. An alternative model is needed for such settings, and The Joint Commission is working on a new standard.

### **Stewardship in Veterinary Settings: Food and Drug Administration (FDA) Update**

*William "Bill" Flynn, D.V.M., M.S., Center for Veterinary Medicine (CVM), FDA, HHS*

Effective January 2107, FDA Guidance #213 eliminated the use of antibiotics in animals for growth promotion and required veterinary oversight for therapeutic use of medically important antibiotics. In response to PACCARB recommendations to assess the impact and progress of the effort, FDA is engaging stakeholders in determining metrics and defining the core principles of stewardship and appropriate use. To improve interpretation of metrics, FDA proposed a biomass denominator that would assist with evaluating sales data when accompanied with species estimates (now required). The agency is working with USDA's Center for Epidemiology and Animal Health (CEAH) on a framework for

reporting data and assessing progress. The two entities are also partnering to address concerns about data collection and confidentiality.

To foster stewardship, FDA has focused efforts on implementing Guidance #213 and the Veterinary Feed Directive, reaching out through various education channels. Dr. Flynn observed that direct funding to address AMR in veterinary settings has been limited, but FDA seeks to engage in public-private partnerships to further the goals of combating resistance. While FDA is primarily focused on food animals, in January, the agency published the *CVM Key Initiatives for Antimicrobial Stewardship*, which includes an objective of developing a stewardship strategy for companion animals.

Dr. Flynn said FDA will assess what additional measures it can take to ensure antibiotic use and labeling are consistent with the current thinking around stewardship. The agency remains aware of other medically important antibiotics that are available over the counter. It will continue assessing the impact of strategies around stewardship.

### **U.S. Department of Veterans Affairs (VA) Update on Goal 1**

*Gary A. Roselle, M.D., FACP, VA (by phone)*

Dr. Roselle said the VA has longstanding antibiotic stewardship programs, going back to the initiative to screen for methicillin-resistant *Staphylococcus aureus* (MRSA) that began in 2007. He presented data demonstrating sustained improvement in MRSA and *C. difficile* infections following targeted approaches. Resources and educational offerings from the Veterans Health Administration's (VHA's) National Antibiotic Stewardship Taskforce are recognized as standard references for ID treatment, and tools available online for providers and hospitals include sample policies that can be adapted for local settings. A pilot project is exploring mechanisms for reporting data to the NHSN Antibiotic Use module.

The VA plans to continue developing targeted guidance for addressing multidrug-resistant organisms (MDROs). It will expand antimicrobial stewardship programs into its long-term care and outpatient settings. It will also expand its capabilities to share VHA data with key stakeholders.

### **U.S. Department of Defense (DoD) Antimicrobial Stewardship**

*Paige Waterman, M.D., FACP, FIDSA, DoD*

Dr. Waterman said DoD expects to approve a formal stewardship policy this year and an accompanying implementation plan in 2018. Its Antimicrobial Resistance Monitoring and Research (ARMoR) Program brings together data from the Multidrug-Resistant Organism Repository and Surveillance Network (MRSN) at the Walter Reed Army Institute of Research (a confirmatory laboratory for isolates), the Army Pharmacovigilance Center (which inputs data into the NHSN), and the Navy and Marine Corps Public Health Center's EpiData Center (which provides DoD-wide surveillance and epidemiological analysis), painting a picture of laboratory results and prescribing practices throughout DoD. Through medical treatment and research sites around the world, DoD has longstanding partnerships with overseas partners and broad reach.

The Army Pharmacovigilance Center provides access to a lot of data that can provide insight on specific needs and goals. While DoD is a contained system, it provides care to more than 9.4 million beneficiaries. Patterns identified through the data can guide stewardship priorities and interventions in all the DoD hospitals in the country. DoD continues to work with federal partners such as the VA and AHRQ, as well as nonfederal partners.

### **Promoting and Prioritizing Stewardship**

*Lynn Filpi, Ph.D., OGA, HHS*

Dr. Filpi said the USG champions antibiotic stewardship in international gatherings but met resistance in some cases because of a translation barrier. Some international partners consider “stewardship” to mean limiting access to antibiotics, so USG representatives learned to clarify the goal of judicious and appropriate use of antibiotics, emphasizing that stewardship programs seek to assist with decision-making. International progress includes the WHO’s Global Action Plan, which emphasizes conservation, stewardship, investment in research and development (R&D), and a public health framework of stewardship. Dr. Filpi cited several other examples of high-level attention to AMR on the global stage (e.g., in the G7 and Group of 20 [G20]). In September 2016, the United States hosted a United Nations (UN) General Assembly meeting dedicated to stewardship and infection prevention and control, highlighting its commitment to advancing stewardship.

### **Animal and Plant Health Inspection Service (APHIS) Report**

*Brian McCluskey, D.V.M., Ph.D., APHIS, United States Department of Agriculture (USDA)*

Dr. McCluskey said APHIS’ three major investments relevant to antibiotic stewardship are the National Animal Health Monitoring System (NAHMS), the National Veterinary Services Laboratories (working with the National Animal Health Laboratory Network), and the National Veterinary Accreditation Program. Of note, USDA also provides insight and expertise into international efforts with the World Organisation for Animal Health, the Food and Agriculture Organization, the WHO, and the Transatlantic Task Force on Antimicrobial Resistance (TATFAR).

Dr. McCluskey described on-site livestock surveys underway using NAHMS to assess antimicrobial use, which will inform stewardship efforts. APHIS is establishing a pilot project in which laboratories within the National Animal Health Laboratory Network will submit antimicrobial susceptibility test (AST) data on key bacteria in numerous animal species. Practitioners who submit samples will receive reports on findings, which may influence prescribing practices.

USDA accredits veterinarians to perform certain regulatory activities (e.g., sign health certificates for animals moved overseas) following completion of specified education modules. In 2012, USDA added an online module on antibiotics in animals that has become internationally recognized as a best practice for combating AMR. The module was significantly revised this year. A module on the Veterinary Feed Directive, created with FDA’s CVM, is the most-viewed module in the system this year and has been used

by many in the agricultural sector beyond veterinarians. Dr. McCluskey said the modules exemplify how USDA has been able to educate veterinarians and others on the proper uses of antibiotics.

### **National Institute of Food Agriculture (NIFA)**

*Mervalin Morant, Ph.D., NIFA, USDA*

NIFA funds extramural grants in basic and applied research and integrated projects. Grantees for integrated projects must incorporate two of three areas: research, education, and cooperative extension. Fiscal year 2017 will be the final year for NIFA competitive grants on AMR. Funded programs often involve collaborations among researchers, federal agencies, state agencies, and private-sector entities and may involve multiple states.

Dr. Morant cited some examples of research projects underway around antimicrobial stewardship, which can be found [online](#). For public access to all NIFA awards and impacts, see <http://www.nifa.usda.gov>.

### **Council Discussion**

Dr. Blaser asked whether CDC is evaluating the appropriate duration of use of antibiotics prescribed in inpatient and outpatient settings. Dr. Srinivasan noted that every study comparing short and long courses finds that short courses of antibiotics are as effective and less toxic, but more research is needed. He added that the National Institutes of Health's (NIH's) Antibiotic Resistance Leadership Group (ARLG) is funding such research. CDC is working to better align practice guidelines with current recommendations and best practices.

Kent E. Kester, M.D., FACP, FIDSA, FASTMH, asked how research findings and best practices are disseminated and translated into practice. Dr. Miller said AHRQ invests in translating findings into toolkits and also funds dissemination. Its implementation projects incorporate the evidence produced by funded research. Dr. Srinivasan said CDC seeks to incorporate lessons from federal partners—for example, reflecting the VA's experience in the Core Elements of antibiotic stewardship.

Helen W. Boucher, M.D., FIDSA, FACP, asked what role diagnostics play in stewardship. Dr. Srinivasan said new and better ways to more accurately and quickly detect disease and AMR are critical. A lot of existing diagnostics are underused, misused, or misinterpreted.

Jay C. Butler, M.D., noted that the SAAR is useful for gathering data and creating benchmarks, but it is not clear how CDC works with state and local public health agencies or state hospital associations to address high SAAR measures. Dr. Srinivasan said the consent agreement for NHSN in 2018 will expand CDC's ability to share data with states and QIN-QIOs, which is critical for local action.

Elizabeth Jungman, J.D., M.P.H., asked what can be done to encourage more participation in the NHSN antibiotic module. Dr. Srinivasan said hospitals recognize the

value of the data but face technology barriers. If more electronic health record (EHR) vendors incorporated the ability to report to NHSN into their software updates, more facilities would enroll. Dr. Srinivasan said CDC is open to suggestions on how to facilitate reporting.

Alicia Cole noted that many speakers discussed challenges to stewardship in nursing homes. She asked whether any agencies are addressing language barriers that arise among staff who are not native English speakers and are not trained nurses. Ms. Cole also noted that many antibiotic prescriptions for nursing homes are made over the phone. She proposed educating staff on how to communicate a resident's condition so that the most appropriate antibiotic can be selected. Dr. Ling said language and other communication barriers are critical and could be addressed through training and tools, such as AHRQ's Team Strategies and Tools to Enhance Performance and Patient Safety (TeamSTEPPS).

Dr. Ling also noted that CMS now has authority to collect staff data from payroll records and to include that information on the Nursing Home Compare website. Such data would not identify language barriers but could help CMS determine where tools are needed. Dr. Baker said effective communication about antibiotic use could be a topic for development of a standardized communication tool.

Lonnie J. King, D.V.M., M.S., M.P.A., ACVPM, pointed out that the popularity of the USDA education modules for veterinarians indicates an obvious need for more education tools across the field. He asked how cooperative extension services are integrated into the education efforts around stewardship. Neena Anandaraman responded that USDA cannot dictate what extension services do, but it can state the Secretary's priorities and encourage education through grants. Also, some NIFA integrative projects involve extension services.

Peter Robert Davies, B.V.Sc., Ph.D., asked how efforts to improve stewardship in human health could inform the animal side, specifically defining success and measuring the impact of efforts on antibiotic resistance and infection rates. Dr. Srinivasan acknowledged the difficulty of measuring appropriate antibiotic use in humans or animals. However, efforts are underway to bring experts on the human and animal sides together to discuss issues. Dr. Ling stressed the need to recognize that requiring reporting sometimes results in an increase in reported events, which should not be seen as a failure of the reporting mechanisms.

Thomas R. Shryock, Ph.D., suggested drawing lessons from other countries' animal stewardship programs. Dr. Filpi said such approaches are just beginning. For example, as part of the G20, Germany is hosting a meeting of experts in public health and animal medicine in which CDC and FDA representatives are taking part. Michael Craig said global stewardship is a priority for CDC, which recognizes that different approaches are needed in different settings and among different countries.

Randall Singer, D.V.M., M.P.V.M., Ph.D., asked how experts would determine predicted antibiotic use in animals based on actual antibiotic use data currently being collected. Dr. Srinivasan said modeling used on the human side might be possible for animals.

## **Influencing Stewardship Behavior**

### **Overview of Behavioral Science Research**

*Elana Safran, M.P.P., Office of Evaluation Sciences*

The Office of Evaluation Sciences gathers research findings and expertise from psychology, economics, public health, and statistics to identify what works and how to implement programs effectively. Ms. Safran explained that individual behavior is guided by “system 1” thinking—automatic, easy actions that require little planning—and “system 2” thinking—slow, deliberative actions that involve a lot of thought and effort. Behavioral science recognizes that interventions can be designed to target system 1 thinking so that individuals are more likely to perform the desired action.

Behavior is also governed by various forms of bias:

- **Limited attention and memory:** Higher-priority goals (e.g., patient assessment) are likely to occupy more attention than secondary goals (e.g., handwashing). Checklists and implementation prompts can ensure that secondary goals are met.
- **Status quo bias:** Changing the default behavior (e.g., automatic enrollment in a program) can override the status quo bias.
- **Present bias:** Individuals tend to overvalue immediate costs over future, distant benefits. In the case of antibiotics, overcoming present bias may involve adding costs or effort (e.g., requiring a justification for a prescription).

Projects that are amenable to a behavioral approach share some common characteristics:

- A clear touchpoint between the program and the individual
- An outcome that depends on the actions of people in the program
- An outcome that can be measured by data currently being collected
- A population size that is statistically relevant and policy-relevant
- The capacity to assess different versions of an intervention to compare outcomes
- A collaborator to champion the project

Ms. Safran described one study in which letters identifying “high prescribers” among peers did not affect prescribers’ behavior. However, variations of this approach (timing, language, consequences) may be worth exploring further. Taking into account how individuals make decisions and act can be a power tool, Ms. Safran concluded.

### **Influencing Behavior in Different Settings**

*Julia Szymczak, Ph.D., University of Pennsylvania*

Dr. Szymczak emphasized that in health care settings, as in other settings, humans are constantly navigating conflict, seeking to maintain status, managing emotions, saving face, making decisions based on identity, and being aware of the role of hierarchy. On top

of that, the field of health care has its own culture, and institutions have their own cultures and even microcultures.

Prescribing antibiotics is a highly social interaction between providers and patients that involves social norms, behavioral expectations, and beliefs that may not be related to treating infection. It follows unspoken rules of etiquette that prevent providers from questioning others' prescribing behavior. (In some hospitals, residents appreciate that a strong antibiotic stewardship program can provide cover for such questioning.)

These social interactions involve risk, fear, and anxiety. Prescribers tend to have far more concern about undertreating than overprescribing. Potential adverse effects of antibiotics are not a significant part of the equation, while the fear of harm from undertreatment is substantial. In addition, health care providers sometimes perceive others as the cause of the problem (not themselves) or believe their unique experience or patient population is not subject to traditional guidelines. Faced with evidence about their own prescribing practices, they may pick apart the data and raise doubts.

Dr. Szymczak pointed to the role of competing priorities in health care settings. Time pressures may push providers to treat rather than watch and wait. Assuaging patients' concerns by prescribing medication leads to better patient satisfaction scores, which play a big part in an institution's success and profits. Providers are also subject to "decision fatigue"—the ability to make good decisions erodes as one becomes tired or hungry.

Direct education does not have a lot of long-term impact on stewardship goals, said Dr. Szymczak. Dysfunctional behavior can thwart stewardship efforts (e.g., providers find ways to game the system). Notably, judicious use of antibiotics is not yet a social or group norm, and antibiotics are still perceived as benign. Dr. Szymczak described a successful intervention in The Netherlands that increased appropriate antibiotic prescribing by implementing a participatory research approach. It drew on three behavioral principles: preserving prescribing autonomy, engaging providers in policymaking, and requiring providers to make a public commitment.

Future research should address the factors that shape antibiotic prescribing, recognizing that targets may vary by clinical area and provider type. Research is also needed on implementing stewardship programs, better communicating best practices and recommendations, and designing and framing incentives. Dr. Szymczak said the following concepts should guide research:

- How to develop interventions that modify the culture to change norms
- How to design interventions that target the emotional dimensions of antibiotic prescribing
- What sociobehavioral dynamics characterize optimal stewardship

### **Long-Term Care Setting**

*Ghinwa Dumyati, M.D., University of Rochester Medical Center*

Dr. Dumyati said 25 to 75 percent of antibiotics prescriptions in nursing homes are inappropriate or unnecessary. While CMS requires long-term care facilities to develop stewardship programs and protocols for treatment of infections, nursing homes have difficulty implementing the requirements, because so many factors affect antibiotic use:

- Patients' clinical conditions (e.g., dementia) make it difficult to assess or confirm infection.
- Staff assessing the patients are poorly trained.
- Even when a registered nurse examines the patient, the findings are usually communicated to a medical provider by phone.
- The decision to treat is often made on the basis of an inadequate assessment.
- Decisions are often made without the benefit of laboratory test results.
- If diagnostic tests are ordered, they are likely to be inadequate or inconclusive.
- When conducted, laboratory test results may never reach the patient, so unnecessary treatment may continue.
- Frail, elderly people facing an infection may deteriorate more quickly than healthy, younger people, so providers are reluctant to delay treatment.
- Concerned family members may push for testing and treatment.
- Resources for educating nursing home care providers are limited, and staff turnover is very high, so it is difficult to sustain programs and protocols.

Dr. Dumyati recommended educating staff, nurses, physicians, and families about appropriate testing and use of antibiotics and improving communication across nursing home staff and medical providers. Some organizations use decision support tools (e.g., posters, pocket cards) to bolster appropriate diagnostic testing and antibiotic use. Asking staff to fill out assessment forms before calling the medical provider has proven burdensome and unhelpful. Nursing homes usually do not have effective EHRs in place to gather and communicate information. External consultants can help improve processes, but many nursing homes lack the resources to hire them. Dr. Dumyati offered some other recommendations:

- Incorporate tools into EHRs to help nursing home staff assess patients.
- Explore telemedicine options to improve patient evaluation.
- Increase turnaround time of diagnostic laboratory and imaging studies.
- Develop evidence-based treatment guidelines specifically for elderly patients in nursing homes.
- Include decision support tools for antibiotic prescribing in EHRs.
- Improve EHR capacity to track antibiotic use, provide feedback, and collect data from dispensing pharmacies.
- Provide resources and expertise to help nursing homes establish stewardship programs and protocols (e.g., consultants, ID experts, and pharmacists).

### **Pediatric Setting**

*Rita Mangione-Smith, M.D., M.P.H., University of Washington*

Dr. Mangione-Smith described findings of her research project, Dialogue Around Respiratory Illness Treatment (DART), which aims to improve communication between pediatric care providers and parents of patients. How parents communicate during visits for their child’s acute respiratory infection strongly influences whether providers perceive them as wanting antibiotics. When they perceive that parents want antibiotics, providers are significantly more likely to prescribe them, even if they know the illness is viral.

Parents communicate their expectations indirectly—for example, by proposing a candidate diagnosis when describing the child’s condition (e.g., describing symptoms that correlate specifically with a diagnosis). Parents who offer a candidate diagnosis are 25 percent more likely than others to expect antibiotics.

Dr. Mangione-Smith summarized four steps providers can use to manage parents’ expectations and avoid prescribing unnecessary antibiotics:

1. Make the case for the diagnosis by reviewing the findings of the physical examination.
2. Deliver a clear diagnosis.
3. Use a two-part, “negative/positive” treatment recommendation. The negative recommendation explicitly rules out the need for antibiotics. The positive recommendations include steps the parent can take to relieve symptoms. Deliver the two-part recommendation using the framework, “on the one hand, [negative treatment recommendation]/but on the other hand, [positive treatment recommendation]” so that parents are not tempted to respond to the negative before they hear the positive.
4. Provide a contingency plan (i.e., what to do if symptoms do not improve over a specified time).

Giving negative treatment recommendations alone is frustrating to parents and increases the likelihood that the parent will question the treatment plan. It also can shift provider decision-making into provider–parent negotiation. Using the two-part negative/positive treatment recommendation structure results in less unwarranted prescribing, higher parent satisfaction levels, and shorter visits lengths than other approaches. Providing a contingency plan also significantly increases parents’ satisfaction. Dr. Mangione-Smith said the DART approach not only decreases unnecessary prescriptions but also shortens visits and improves parents’ satisfaction—making it a mutually beneficial approach.

### **Council Discussion**

Dr. Blaser observed that CMS data show big geographical differences in prescribing patterns that point to cultural differences, and he wondered how to address them. Dr. Szymczak said the data demonstrate that overprescribing is a cultural problem affected by social beliefs and norms. She said more research is needed to understand how prescribers and patients think about antibiotics, health, and disease. Dr. Mangione-Smith said she and her colleagues are conducting a national trial of the DART intervention, and she anticipated that culture and context will affect the results.

Lauri Hicks, D.O., of the CDC said she has looked at reasons for the geographic variability and identified population-level differences around health that drive some of the differences. A combined investigation of sociological issues and population-level health factors is needed, she added.

Angela Caliendo, M.D., Ph.D., FIDSA, asked what fears providers face regarding the decision not to prescribe antibiotics. Dr. Szymczak said that providers fear bad patient outcomes, and “preventing disaster” is a strong motivation. Some fears can be addressed through education and by having peers and colleagues who act as “ambassadors” for eliminating unnecessary prescribing. Ms. Safran said information asymmetry can be tackled with literature or posters in the provider’s office or waiting room that ensure that patients and providers have the same information and similar expectations.

Ms. Safran added that, when it comes to weighing risks and benefits, individuals often do not have a balanced perception of future risks/benefits and current risks/benefits. Presenter Jeffrey Linder, M.D., M.P.H., FACP, pointed out that prescribers tend to see antibiotics as harmless, while prescribing could prevent a dangerous outcome. He aims to educate residents that antibiotics can cause harm to patients and that avoiding overuse can prevent societal harm. Michael D. Apley, D.V.M., Ph.D., DACVCP, confirmed that physicians are highly concerned about avoiding the possible danger that could result from not prescribing antibiotics, even if that danger is very rare. Dr. Szymczak agreed, saying immediate patient care overrides bigger-picture concerns. Dr. Linder said these instances exemplify why diagnostics may not be useful in addressing overprescribing; providers remember and fear the worst, so they do not accept the results of diagnostic tests. Dr. Mangione-Smith added that the negative effects of antibiotics are more common and more devastating than the rare problems that arise from not treating with antibiotics.

Ms. Cole pointed out a consistent theme of presentations is the need for better communication and better interpersonal skills at the point of care. She asked how researchers are disseminating their findings in medical schools and other training opportunities. Dr. Mangione-Smith said that if the intervention trial confirms that the DART approach is effective, implementation tools will be made available—for example, as part of education recertification for prescribing offered by the American Academy of Pediatrics. There is strong interest in bringing the DART intervention to medical schools. Mr. Craig said CDC is working with CMS on making stewardship tools part of physician training for the Merit-Based Incentive Payment System.

Dr. Boucher said some providers claim to have higher-risk populations that require more treatment, and they feel a duty to do all they can. In contrast, in the United Kingdom, providers and the public are more comfortable with accepting some individual risk in the name of protecting the larger population. Dr. Linder said providers often do not consider that overtreatment could be harming their patients. Dr. Blaser said the variation in prescribing practices indicates that some providers can resist pressure to prescribe antibiotics. Dr. Linder noted that comparisons between the United States and Sweden demonstrate that American providers are clearly overprescribing.

Dr. Butler said patient satisfaction surveys ask, for example, whether a provider has done everything possible to control the patient's pain. He asked whether providers have incentives for inappropriate prescribing that should be addressed. Dr. Szymczak said the question bears more study, but clearly a social incentive is needed to reframe the issue.

### **Outpatient Setting**

*Jeffrey Linder, M.D., M.P.H., FACP, Northwestern University*

Clinical decision support tools and education-based interventions to prevent health care providers from prescribing antibiotics unnecessarily have had limited success because they do not take behavior into account. To influence behavior, interventions could leverage biases toward rapid, automatic decision-making; appeal to clinicians' self-image; and factor in social motivations. The factors driving antibiotic prescribing are immediate and emotionally salient (fear, habit, perception that a patient wants antibiotics, and reluctance to spend time explaining why they are not needed), while deterrents are remote and less emotional (risks, need for stewardship, desire to decrease unnecessary spending and follow guidelines). As Dr. Szymczak mentioned, providers also suffer from decision fatigue.

Dr. Linder described an intervention in which providers' prescribing varied depending on how choices about treatment ("aggressive" vs. over-the-counter) were organized and presented. Incorporating this approach, known as "choice architecture," may be effective in driving down unnecessary use. EHRs already structure choices, and current approaches to care facilitate doing the wrong thing. In another intervention, providers posted a personalized, signed poster in their office describing their commitment to avoid prescribing unnecessary antibiotics. Making this type of public commitment in advance essentially "short-circuits" the automatic prescribing behavior and minimizes providers' discomfort, because patients are aware of the issue going into the visit. Dr. Linder believes personalizing the poster (with a photo and signature) increases the impact over generic informational materials.

Other approaches involved leveraging EHRs and data to limit inappropriate prescribing. The most successful were 1) requiring providers to write some sort of justification before the EHR system would allow an antibiotic prescription for an indication that did not appear to require it and 2) monthly emails describing the provider as a "top performer" or "not a top performer" depending on the number of unnecessary antibiotic prescriptions in comparison with peers. Dr. Linder noted that the control groups in both of these interventions substantially decreased unnecessary prescription rates just by virtue of taking part in the study.

More or better diagnostic testing is unlikely to decrease unnecessary prescribing, Dr. Linder maintained. As previous interventions have shown, information and education are not enough to change behavior.

### **Consumer Messaging**

*Jasmin Malone, Truth Initiative*

Ms. Malone described the methodology the Truth Initiative uses to develop consumer messaging around reducing smoking, particularly preventing young people from starting smoking. She noted that its approach has changed since the early 2000s, when it focused on publicizing information revealed in the master settlement agreement involving tobacco companies. In 2014, the Truth Initiative began to focus on encouraging young people to become the generation to end smoking. Not only does this generation have plenty of access to information, it also faces different kinds of tobacco use (hookah bars and e-cigarettes) and different perceptions about what it means to be a “real” smoker. Data also showed that by 2014, young people started smoking later, around age 18.

The current campaign appeals to the desire to have a positive impact on the world; it factors in how social media shines a light on individual choices and actions. The Truth Initiative seeks out ways that its message can intersect with the interests of its target audience. All messages must align with the tenets of the Truth Initiative brand, which include being rooted in fact (not fear), inclusiveness, provocativeness, and being “for” non-smoking (not anti-smoking).

Some themes of the Truth Initiative align with the goals of reducing antibiotic prescribing. For example, because it is difficult to convince people to consider the long-term, potential consequences of their actions, messaging must appeal to current self-perception, highlight the unintended harm to others, and demonstrate the immediate effects. Ms. Malone said every message from the Truth Initiative aims to resonate with the individual by answering the questions “Why should I care?” and “What can I do about it?” Moreover, the Truth Initiative reveals unexpected findings related to smoking—such as the negative impact of smoking on dating, pet health, and the environment—that affect things the target audience cares about. Ms. Malone concluded by showing two Truth Initiative commercials that highlight how the tobacco industry targets vulnerable populations.

### **Veterinary Setting**

*Michael D. Apley, D.V.M., Ph.D., DACVCP, PACCARB Member*

Dr. Apley noted that there are common themes across animal and human health around antibiotic stewardship and prescribing behavior. For example, the veterinary field has studied where veterinarians get information, their prescribing patterns, their behaviors, and what influences them. The field is interested in monitoring and using data to inform practice. Understanding the culture around antibiotic use in animals is also a significant issue. Dr. Apley said that while this meeting was focused on stewardship on the human side, a subsequent PACCARB meeting will address it on the animal and veterinary side.

### **Council Discussion**

Sara E. Cosgrove, M.D., M.S., asked whether nursing homes’ problems stem from behavior or lack of resources. Dr. Dumyati said both issues play a role. Nursing homes lack the expertise to address their stewardship problems; they need ID prevention specialists to guide staff in collecting and interpreting data, as well as medical practitioners to champion such efforts. Nursing homes also need adequate staffing and

education that takes into account high staff turnover rates. They need expertise from hospitals and dispensing pharmacies and sufficient review and feedback procedures.

Marjory Cannon, M.D., of CMS said CDC and CMS collaborate through the QIN–QIOs to help nursing homes report *C. difficile* rates to the NHSN, and the task is incredibly difficult, requiring a lot of basic, hands-on education (e.g., how to use an EHR). Also, CDC and CMS are collaborating on interpretive guidelines and a pilot project to help nursing homes implement stewardship programs. Dr. Cannon recommended combining regulations to spur action with expertise to help nursing homes better use their existing resources.

Dr. Cannon pointed out that the goal of requiring nursing homes to implement stewardship is to start seeing what works and how federal agencies can apply resources to fill gaps and respond to issues. Dr. Dumyati stressed that nursing home resources are extremely limited. Dr. Cannon observed that just drawing attention to the problem is valuable in itself and sets the stage for collaboration at multiple levels. Some local organizations work with state and regional partners to get resources, she noted. Dr. Cosgrove said a marketing strategy is needed to encourage ID physicians to think about their role in helping people in nursing homes.

Dr. Blaser asked how to convey the fact that antibiotics are neither neutral nor free but in fact can cause harm and increase the costs of care. A growing body of evidence suggests that antibiotic use early in life is linked with diabetes, obesity, asthma, and inflammatory bowel disease. Dr. Blaser said people are more worried about their own children than the nebulous concept of antibiotic resistance. Dr. Linder and Dr. Mangione-Smith both suggested portraying the risk in a way that is more salient and immediate, as the Truth Initiative did.

Ms. Malone agreed that the message must be crafted and disseminated in compelling ways. The Truth Initiative relies on a lot of in-depth quantitative and qualitative research to determine what people care about and which messages resonate, reevaluating and reworking messages constantly.

Dr. King asked for input on how to overcome self-interest to benefit the common good. Dr. Linder stressed the need to eliminate unnecessary prescribing of antibiotics for conditions for which they have no benefit. He also recommended finding a way to change the default thinking, so that individuals start to tell their providers that they only want an antibiotic if they really need one. Dr. Szymczak said individual motivations must be better understood; she said interventions should address issues closer to the surface.

Dr. Caliendo wondered whether risk-averse behavior is hardwired. Dr. Szymczak replied that more research is needed to better understand different types of prescribers, similar to the research that pharmaceutical companies conduct to create prescriber profiles and target their product promotion accordingly. Dr. Mangione-Smith agreed, noting that better interventions will recognize that different approaches work for different people. Ms. Safran noted that the Defense Health Agency may have data to inform predictors of

prescribing or what interventions work for different groups. Elizabeth Allen Wagstrom, D.V.M., M.S., added that the pork industry studied “barn culture,” which may provide some insights into antibiotic prescribing for animal health.

Dr. Wagstrom asked whether social media reviews of health care providers can drive behavior. Dr. Linder replied that retail clinics tell their nurse practitioners that they will not be “dinged” by the system if they do the right thing for the patient and get a negative patient satisfaction survey score. Retail clinics compete on quality, he said, whereas urgent care clinics compete on patient satisfaction and repeat business.

Dr. Apley asked for more input about situations in which diagnostics could be helpful. Dr. Mangione-Smith said a sensitive, easy-to-use diagnostic test for streptococcal infection was available to provider offices for many years yet had no effect on antibiotic prescribing, nor do diagnostic test panels in hospital settings.

Dr. Apley further asked about how to persuade prescribers to follow guidelines. Dr. Szymczak said that countering the norm of noninterference (i.e., not questioning a provider’s prescribing decisions) will require a culture shift across the whole domain of patient safety. There is growing acceptance of giving and getting feedback and empowering people to speak up for safety, she noted. Prescribers may need to hear the message from external peers within their professional groups; the credibility and legitimacy of the person delivering the message is important in changing behavior.

Dr. Apley observed that including high prescribers in professional efforts to craft guidelines and protocols will increase their buy-in. Dr. Szymczak suggested emphasizing how interventions can improve the provider’s life, e.g., by shortening visits.

Mr. Craig said CDC is revamping its campaign around antibiotic use. He asked for insight on how to balance messaging about the risks of antibiotic use while acknowledging that antibiotics can be lifesaving medicines that should be used when needed. Ms. Malone said education may help, particularly a clear explanation from the health care provider about what will or will not work. She added that young people want to know the facts, risks, and benefits, but they do not want to be told what to do.

Regarding how to segment audiences, Ms. Malone said a multipronged approach may be needed that identifies the target audiences and what they care about, tailoring the message to each. She recommended a willingness to take risks and to refine messaging as needed. Dr. Linder said one simple message could spell out common, appropriate uses for antibiotics. Dr. Mangione-Smith pointed out that fear-based campaigns can backfire among people who go to extremes (e.g., they may refuse antibiotics when needed).

Dr. Blaser said urgent care centers are disproportionately high prescribers of antibiotics. He wondered if the structure of the medical visit predisposes providers to overprescribe. Dr. Linder said the high number of ambulatory visits can lead to waste, errors, and potentially dangerous events; some type of triage might prevent unnecessary events.

In terms of quality improvement, Dr. Mangione-Smith said, it is much easier to persuade someone to adopt a new practice than to stop a current practice. In countries with socialized medicine, providers have an incentive not to do certain things, but providers in the United States have a history of doing too much. Dr. Linder pointed out that limited access to health care may drive providers to prescribe because they think they may not see the patient again, and patients may demand antibiotics because they do not think they will have another chance to see the provider.

## **Public Comment**

**Kevin Kavanagh of HealthWatch USA** said recent NHSN data suggest MRSA bloodstream infections may be rising, and we are not on track to meet the HHS goal of a 50-percent reduction. We need a paradigm shift in our thinking from the management of outbreaks to how to deal with resistant bacteria, he said. Better data are needed. The definition of an outbreak should be quantified and standardized. In the context of drug-resistant bacteria, hand hygiene should be a backup measure; the presence of infectious organisms on workers' hands indicates a problem in containment and control. In the future, documenting an individual's microbiome may become part of maintaining a healthy lifestyle, said Mr. Kavanagh, and may even become part of the annual physical examination. In the meantime, it is crucial to start screening for dangerous pathogens and multidrug-resistant bacteria in both patients and health care workers.

**Steven Roach of the Food Animal Concerns Trust** said stewardship is key to making sure antibiotics will continue to be effective in the future, but changing people's behavior is very challenging. He referred the Council to the report [\*Combating Antibiotic Resistance: A Policy Roadmap to Reduce Use of Medically Important Antibiotics in Livestock\*](#). It was developed by a group of physicians, veterinarians, and other U.S. health experts (with input from some European countries) to identify gaps in the response to antibiotic resistance as it relates to animal agriculture. The key policy recommendations with respect to stewardship are to

- set targets for reducing antibiotic use (which already exist for human health);
- phase out routine or programmed use of medically important antibiotics (which FDA is addressing, but it does not go nearly far enough);
- reduce the need for antibiotics by adopting nonantibiotic best practices;
- eliminate antibiotic use where efficacy can no longer be shown;
- prioritize the use in veterinary practice of antibiotics that are not considered critically important by WHO; and
- bolster veterinary oversight of antibiotic use.

Mr. Roach hoped PACCARB would take the report into consideration when developing its recommendations. He emphasized that antibiotic stewardship is an urgent matter involving people's lives. He urged the Council members to demand needed change.

**Amanda Jezek of the Infectious Diseases Society of America (IDSA)** said she was heartened to hear about the great progress made in stewardship, although there is much more to be done. IDSA has been advocating for full funding for all of the federal agency

efforts for stewardship and all the activities to combat AMR. IDSA continues to develop educational resources for ID physicians and trainees, and members are leading stewardship programs. Increasingly, ID physicians are using innovative means like telehealth and flexible contracting agreements to expand the reach of ID expertise into smaller facilities, rural areas, and other underserved areas.

IDSA remains very concerned about the decline in young physicians pursuing ID training, and compensation is a key driver of this problem. Ms. Jezek asked that stewardship efforts be appropriately compensated and, more broadly, that payment disparities between ID physicians and other specialties who provide more procedure-based care be addressed, so that there is a level playing field. Such efforts will also ensure we have the future workforce needed not only to lead stewardship programs but to care for patients who have resistant infections and to drive the research needed for new antibiotics, diagnostics, and vaccines. IDSA encourages PACCARB to keep workforce issues in mind.

**Tharini Sathiamoorthy of AdvaMedDX** said diagnostics can and must be a critical component of any approach to reduce the threat of antibiotic resistance. Diagnostic tests are currently underutilized. Barriers to the access and uptake of currently available diagnostic tests as well as the development of next-generation technologies must be removed. One way to improve access is through the recognition of the true value of a diagnostic test. The cost of utilizing diagnostic tests is very small compared to the cost of infection, hospitalization, readmission, and the long-term negative impact of antibiotic resistance.

AdvaMedDX agrees with the Council's draft incentives report finding that there is a lack of clinical and economic outcome studies showing that a diagnostic test can prevent the emergence of antibiotic-resistant bacteria and can be cost-effective. The company further believes that more funding for clinical and economic outcome studies will have the most positive impact of all the recommendations in the draft report. Ms. Sathiamoorthy also appreciated the acknowledgment of the need for a reimbursement methodology for diagnostic tests that aligns with the value of the test. Failure to appreciate the true value limits effective adoption and appropriate reimbursement.

**Sarah Sorscher of the Center for Science in the Public Interest** said her organization is part of a coalition of consumer and environmental groups that have pressed major restaurant chains to reduce the use of antibiotics in their food supply. The food industry has made enormous changes in response to these efforts over the past few years. Major mainstream U.S. chains have adopted public policies to phase out the routine use of antibiotics in some or all their food supply, and major producers now have policies focused on reducing antibiotics use.

In some ways, the *National Action Plan* is now tailing changes that have been made by mainstream sections of industry, said Ms. Sorscher. She urged the Council to consider how to update the goals. In particular, the *National Action Plan* could benefit from setting concrete targets and metrics for reducing animal antibiotics use, as some members of

industry have done already. In addition, industry has made strides towards phasing out the routine use of antibiotics in healthy animals—for disease prevention as well as growth promotion—and also limiting the use of antibiotics that are critically important in human medicine, but these goals are not reflected in the *National Action Plan*.

Finally, Ms. Sorscher urged the council to consider stewardship in the discussions that will be happening tomorrow around the development of new drugs to ensure that the effectiveness of these new treatments are preserved. This includes preventing antibiotics that are critically important in human medicine from being approved for new animal uses that will encourage resistance.

**Lisa McGiffert of Consumers Union** emphasized that the only way to achieve the kinds of changes in prescribing practices and reductions of antibiotic-resistant infections illustrated by the VA and DoD is through a national mandate. These agencies had success because they can require their providers to do certain things. Ms. McGiffert begged the Council to make antibiotic stewardship at the hospital and outpatient level a measurable mandate. She noted that Council members are in positions to speak up about the urgency of addressing this problem now. Voluntary collaboration with hospital associations will not achieve the goal, but mandated stewardship can begin to change the culture, along with public transparency so the communities that these providers serve can see a visible reduction in the inappropriate use of antibiotics.

Ms. McGiffert made the analogy that if a car mechanic recommended changing your oil when it was not needed or would not help resolve a problem, we would call it fraud. Hospitals in Missouri are working with CDC on tracking antibiotic use because Missouri passed a law that requires it. Again hospitals and physicians will seek solutions when mandates are in place to require them to do it.

Consumers Union spent about 6 years going from state to state to get hospital infection reporting in place before a national mandate was established. The organization also worked in Missouri on a bill to monitor antibiotic use that took about 3 years to get passed. Patients cannot wait, said Ms. McGiffert. We do not have the luxury and time to wait 10 years for a national policy that requires judicious use of antibiotics. Changing the prescribing culture will take incentives and disincentives. It takes a multidisciplinary approach, and timely cultural change will not come without a looming mandate that includes consequences. Reaching the goals of such a mandate can take many forms, like public transparency or financial consequences—which have worked to reduce hospital infections—but only a mandate will prod the desired result, Ms. McGiffert concluded.

**Carole Moss of Nile's Project** reminded the Council that she had previously shared the story of her son (Nile), who died at age 15 when he entered a top children's hospital for an imaging exam and contracted MRSA. He died about 72 hours after the first signs of influenza because two pediatric doctors did not take the signs of sepsis seriously. At a visit with Tom Frieden at the CDC, Ms. Moss talked about the importance of rapid testing. Later, she saw an inscription: "History is written by those who make the wake, not by those who ride on it nor by those who watch safely by at the shore."

Ms. Moss asked who on the Council will make the wake? Who is going to stand with consumers and solve the problem? It is time to empower consumers with low-cost, at-home tests, similar to pregnancy tests, that can distinguish bacterial from viral infections. Ms. Moss expressed confidence that the CDC could put together such a product “in a week.” Such a test would help families and drive a change in the use of antibiotics, because it would prompt providers to dig further before prescribing. She concluded, “We need to be empowered consumers.”

## **Closing Remarks and Reflections**

Robert A. Weinstein, M.D., said he was struck by regional differences in antibiotic prescribing. He said providers order tests on the basis of their training, and most providers practice within 100 miles of the facility where they trained, so the problem is self-perpetuating. Such information could be used to target education efforts, he said. Aileen M. Marty, M.D., FACP, observed that much centers on the issue of trust. Cultural issues have a huge impact on antibiotic use, she added, and the Council must grapple with that issue among others.

Dr. Blaser adjourned the meeting for the day at 4:35 p.m.

## **Day Two**

### **Welcome**

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

Dr. Blaser opened the meeting at 9:05 a.m. and welcomed the participants.

### **Roll Call**

*Jomana F. Musmar, M.S., Ph.D.c, Designated Federal Officer (Acting)*

Ms. Musmar called the roll.

## **Agency Updates on *National Action Plan Infection Prevention and Goals 2–5***

### **Prevention and Antibiotic Stewardship: Implementing a Comprehensive Public Health Approach to Prevent and Control Antibiotic Resistance**

*Michael Craig, CDC, HHS*

Traditional approaches to improving HAIs within single hospitals or systems are not sufficient to protect whole communities. A regional approach incorporates infrastructure to detect pathogens and respond to emerging threats. CDC has invested at the state and local level to expand infrastructure, supported by the Antibiotic Resistance Laboratory Network. The first national Tuberculosis (TB) Molecular Surveillance Center will be rolled out in Michigan and will sequence every TB case in the United States.

Improved detection contributes to rapid and effective response, preventing new infections, and containing the spread of disease. The CDC containment strategy aims to identify emerging threats, such as *Candida auris*. CDC is working with the State Department on policies to expand screening for TB among visitors to the United States and with international partners on making TB treatment less burdensome for patients and potentially more effective. The United States established a stockpile of drugs to treat TB.

CDC and FDA jointly operate the CDC-FDA Antimicrobial Resistance Isolate Bank, which provides thousands of isolates that can be used to assess new diagnostic tests and therapeutics. CDC has invested in capacity for whole genome sequencing in every state to detect foodborne disease outbreaks. The resulting data will provide more granular information about resistance and transmission dynamics, especially when combined with whole genome sequencing by FDA and USDA. CDC has also bolstered local and regional laboratories' capacity to detect resistant gonorrhea strains.

Internationally, CDC has partnered with ministries of health to establish the first national TB program in China and to establish or strengthen HAI prevention programs and antibiotic resistance surveillance in Vietnam and India, among other efforts.

### **Antibiotic Data Collection in Food-Producing Animals**

*William "Bill" Flynn, D.V.M., M.S., CVM, FDA, HHS*

To expand laboratory capacity, FDA has invested in whole genome sequencing equipment for two Veterinary Laboratory Investigation and Response Network (Vet-LIRN) facilities. Twenty Vet-LIRN laboratories are collaborating to obtain AMR data from clinical isolates. FDA has limited resources to enhance monitoring. However, enhancements to the NARMS system include increasing the amount of retail meat samples tested and the number of sites testing for *Enterococcus* and *Escherichia coli*, subjecting more bacteria to whole genome sequencing, and creating interactive data dashboards.

As of 2016, FDA established reporting requirements for antimicrobials sold for use in food-producing animals, including sales estimates for major food animal species. FDA is seeking public comment on the use of a biomass denominator to adjust the data collected. To monitor use, FDA funded two pilot programs to collect detailed information about on-farm antibiotic use. The agency also works with USDA's CEAH to collect use data.

### **Drug and Diagnostic Update**

*Steven Gitterman, M.D., Office of In Vitro Diagnostics and Radiological Health, FDA, HHS*

Tremendous progress on antimicrobial drug development includes publishing numerous guidance documents on unmet need and public meetings that informed that guidance. FDA is working with international counterparts in Europe and Japan on recommended trial designs. Of the substantial number of antibacterial and antifungal products that have qualified for expedited review, eight have been approved, and several of those used streamlined approaches to address unmet medical needs. FDA is implementing

provisions of the 21st Century Cures Act around AST criteria and the limited population pathway for antibacterial and antifungal drugs.

Mr. Gitterman described some devices that have cleared their first hurdles toward approval. FDA continues to develop its Database for Reference-Grade Microbial Sequences. The agency is supporting efforts to standardize coding of microbiology laboratory diagnostic tests, which could eventually facilitate real-time epidemiology.

FDA guidance on the need to make AST devices available should be finalized soon. FDA has nine such products in the presubmission phase. Mr. Gitterman noted that within a month of the approval of delafloxacin, three correlating AST devices were available. He said the coordinated pathway approach is an effective process for moving devices through FDA review rapidly.

### **CMS Update on Goals 2–5**

*Shari Ling, M.D., CMS, HHS*

To expand infrastructure for public health surveillance, CMS has incorporated *C. difficile* infection, two HAIs, and MRSA into quality reporting and performance measures that will become effective in 2018. CMS is adopting quality measures that use the NHSN for reporting by hospitals and other care settings to contribute to a systemic approach to surveillance. Under the hospital value-based purchasing program, which aims to incentivize high-quality care, safety is worth one-fourth of the total score for payment adjustments, equal to the scoring of clinical care measures, efficiency and cost reduction, and person and community engagement. All of the quality measures are endorsed by NQF. Moreover, all the measures have been demonstrated to be useful and feasible.

Dr. Ling added that in times of disasters or public health emergencies, CMS grants exemptions from quality reporting so that hospitals and other care settings can focus on disaster response and recovery. CMS will provide updates about the exemptions.

### **Update on AHRQ's Activities for Preventing HAIs**

*James Cleeman, M.D., AHRQ, HHS*

AHRQ's recent research funding announcements highlight the link between HAIs and AMR. Every HAI prevented is an episode of antibiotic use avoided, slowing the development of resistance. Currently funded HAI prevention research address various care settings and households. For example, Project Protect is examining universal decolonization with chlorhexidine body wash and nasal ionophore to reduce infections with MDROs in nursing homes. Another study is implementing chlorhexidine bathing in care settings using a systems engineering approach that takes a holistic view of patient safety. It will yield an implementation toolkit. Yet another aims to create a toolkit of effective management strategies to prevent HAIs.

AHRQ's CUSP approach combines behavioral elements (safety culture, teamwork, and communication) with clinical elements (e.g., implementing a checklist of proven practices) to create a powerful tool for accelerating the adoption of evidence-based practices to prevent HAIs. A CUSP project in nursing homes yielded a 54% reduction in

CAUTIs and culminated in a toolkit for others to use. The project reflects PACCARB's recommendations to increase collaboration among federal agencies, disseminate tools for improvement, and partner with nonfederal stakeholders. Dr. Cleeman described several other CUSP projects that address behavior, tackle site-specific concerns, take advantage of partnerships, and result in broadly disseminated toolkits.

### **NIH Update on *National Action Plan* Goals 2–5**

*Jane Knisely, Ph.D., NIH, HHS*

Dr. Knisely said the National Institute of Allergy and Infectious Diseases' (NIAID's) 2014 antibacterial resistance research strategy outlines a comprehensive approach that includes basic research, translational research and product development, and clinical research, all with an eye toward better ways to diagnose, prevent, and treat antibacterial-resistant infections. In recent years, NIAID has explored new therapeutic approaches, emphasized diagnostic technologies, and focused on ways to better use existing drugs.

In addition to its support for sequencing isolates housed in the CDC-FDA Antimicrobial Resistance Isolate Bank, NIH's National Library of Medicine contributes to surveillance and detection by providing access to sequenced bacterial genomes and the NIH National Database of Resistant Pathogens. The Pathosystems Resource and Integration Center develops bioinformatic tools to assist with analysis. A number of NIH and NIAID initiatives emphasize new diagnostics, including the \$20-million challenge established by NIH and the Biomedical Advanced Research and Development Authority (BARDA), which is underway. The ARLG supports diagnostic research and provides access to a virtual viral repository that complements the isolate banks.

NIH has had three targeted funding opportunities for antimicrobial-resistant vaccines since 2015. Dr. Knisely described numerous services NIH provides to assist researchers, including trial networks, manufacturing capacity, and animal models. Over the past decade, NIH has sponsored several clinic trials to evaluate the optimal dose and duration of antibiotics, with mixed results. On the international stage, NIH works with counterparts in other countries, particularly through TATFAR.

### **BARDA Progress Update**

*Joe Larsen, Ph.D., BARDA, HHS*

BARDA has partnered with several large manufacturers to further development of therapeutics and diagnostics. A number of programs have reached phase-III clinical development, and some are on track to submit applications to FDA. Internationally, BARDA collaborates with TATFAR and partners with the Innovative Medicines Initiative's New Drugs for Bad Bugs program to leverage its clinical trial networks.

In addition to the NIH-BARDA challenge prize for new diagnostics, BARDA has three new partnerships looking at different approaches to rapid AST, rapid genotypic and phenotypic determinations of resistance markers, and rapid pathogen identification. BARDA's Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program, co-sponsored by NIAID and the Wellcome Trust, seeks to

incentivize innovative treatments for drug-resistant infections at the preclinical stage of development. It is up and running ahead of schedule, with numerous companies already engaged, and aims to get products into human testing over the next 5 years, building up the antibiotic pipeline. Dr. Larsen said the number of applications for CARB-X was far higher than anticipated, and the applications come from around the world, underscoring the need for business and entrepreneurial support as a means of nurturing good ideas and translating them effectively into products.

Recently, Vabomere (for complicated urinary tract infections) became the first BARDA-supported antibiotic to win FDA approval, and supporting studies indicate it may be effective for treating carbapenem-resistant Enterobacteriaceae (CRE). Other BARDA-supported antibiotics are close to approval. BARDA continues to initiate new partnerships, with promising products on the horizon. In coming years, BARDA aims to expand the scope of technologies supported by its portfolio.

Dr. Larsen said incentives must also address return on investment (ROI), because manufacturers will not continue to produce a product if it makes no money. He called for more “pull” incentives to complement the existing “push” incentives. BARDA continues to engage stakeholders in discussion about the need for an alternative market model to reward innovation and support companies. He noted that Project BioShield (directing the USG to purchase products for use against bioterrorism attacks) worked as a pull incentive but lacked a corresponding push incentive to support development. Recent studies suggest market entry rewards may be an effective mechanism for reducing the uncertainty of the first 5 years of a launch of a new antibiotic. Dr. Larsen stressed that BARDA has a lot of experience with push and pull incentives and believes both must work effectively and in tandem to mobilize the industry successfully.

## **OGA Update**

*Lynn Filpi, Ph.D., OGA, HHS*

Through global health diplomacy—the intersection of public health and foreign affairs—OGA fosters critical global relationships, coordinates international engagement across HHS and the USG, and provides leadership and expertise in global health. OGA works with the State Department and USDA to coordinate an interagency working group on AMR with a One Health approach that includes representation from numerous federal departments and agencies. The working group’s efforts inform international engagement and ensure that the USG presents a consistent message in international negotiations. Dr. Filpi gave an example illustrating how the USG’s One Health approach contributed to better understanding and agreement of terms in G7 talks about AMR in agriculture.

This year, a G7 call to action around AMR led to creation of UN interagency coordination group headed by a WHO representative and made up of experts on AMR and representatives from UN organizations. The call to action urged G7 countries to participate in WHO’s Global Antimicrobial Resistance Surveillance System and to complete their national action plans. Dr. Filpi described other international efforts in the past year to decrease antibiotic use in agriculture, expand R&D, and increase laboratory

and surveillance capacity. The USG is also harmonizing surveillance practices with other countries and collaborating on how to approach incentives for product development.

On the horizon, WHO is drafting a roadmap for the creation of a global framework on development and stewardship. It is meant to support the development, control, distribution, and appropriate use of new antimicrobial medicines, diagnostic tools, vaccines, and other interventions, while preserving existing drugs and promoting affordable access. In addition, the United Kingdom is proposing an international meeting that will highlight the work of governments, multilateral institutions, civil society, philanthropic organizations, and others to coordinate global effort and accelerate action.

### **U.S. Department of State Update on Goals 2–5**

*Jessica Petrillo, Ph.D., U.S. Department of State*

International engagement over time has led to high-level recognition of AMR as a key threat, acknowledgement of the need to mobilize multistakeholder action, and efforts to convert political commitments into action. High-level commitment is insufficient, however; immediate and lasting change also requires the world's 7 billion-plus people to take action for change.

One example of the State Department's efforts on the ground was a meeting in Rome, focused on enhancing the ability of faith-based organizations to identify their own roles and responsibilities in addressing drug-resistant disease and to mobilize. In some countries, faith-based communities can provide up to 70 percent of health care. The meeting led to call to action among faith-based communities and a report that can serve as a template that other stakeholder groups can use to mobilize.

To address the lack of understanding of the environmental component of drug-resistant disease, the State Department hosted a meeting in Southeast Asia to map the lifecycle of antibiotic resistance. The initiative invited citizen scientists to give input into interventions. A key outcome of this meeting was the ability to demonstrate all the steps in the process, from the production of an antibiotic to its eventual decomposition.

The State Department also reached out to science fiction fans for help describing a future without antibiotics, which can be used in community outreach to explain the urgency of AMR. With the UN General Assembly, it launched a social network campaign to engage people in different sectors. The department also works through its embassies to raise awareness in other countries about resistance.

### **VA Goal 2 Update**

*Gary Roselle, VA, (by phone)*

Under the VA's Antimicrobial Stewardship Initiative, more than half of all acute-care VA medical facilities are enrolling in or have submitted data to the NHSN Antimicrobial Use option. With such reporting, local stewardship champions can monitor antibiotic use over time and make comparisons across facilities.

The VA has made great strides in preventing the emergence and spread of resistant

infections. Of note, the VA's long-term care facilities submit antibiotic data to the NHSN the same way that its acute-care facilities do. When the CDC is prepared to enroll long-term care facilities in the NHSN Antibiotic Use option, VA is well-prepared to support submission of that data. The VA continues to explore the feasibility and capability of submitting antimicrobial resistance data to the NHSN Antibiotic Resistance option.

## **DoD Update**

*Paige Waterman, M.D., FACP, FIDSA, DoD*

The cornerstone of DoD's extensive surveillance system is the MRSN, which was established for quality control within military hospitals but benefits the entire hospital system. Data are exchanged with the Navy and Marine Corps EpiData Center, the Pharmacovigilance Center, and, if appropriate, with CDC's Antibiotic Resistant Regional Laboratory Network, among others. MRSN collects clinically relevant pathogens, including all carbapenem-resistant and colistin-resistant organisms, and recently added *C. difficile* and some resistant fungal organisms to its portfolio. It has isolates collected since the early 2000s. The MRSN also partners with the Global Emerging Infectious Disease network (GEIS, which recently expanded its geographic footprint). A new EpiData Center resource will allow users to compare antibiotic resistance patterns across states or regions.

Building on AMR data compiled by WHO from 129 member states, researchers from GEIS partnered with Georgetown University's Center on Medical Product Access Safety and Stewardship, which brings experts and decision-makers together around state-of-the-art technologies. They created a "living" global map of CRE, expanding understanding of resistance. Another collaborative effort, the Infectious Disease Clinical Research Program, formed in 2005 as an interagency agreement between the Uniformed Services University and NIAID. It operates a clinical research network to reduce the impact of infectious diseases in the military population. The program is supporting development of a vaccine for *S. aureus* that is set to begin human trials shortly.

The Walter Reed Army Institute of Research is using its expertise in malaria drug development to inform work on antibiotics and has several promising candidates in early research stages. Navy researchers working to battle antibiotic-resistant *Acinetobacter* have seen some early anecdotal success. On the international front, the global surveillance enabled by the MRSN enabled military laboratories in Thailand and Peru to begin identifying resistant pathogens.

## **Agricultural Research Service (ARS) Update on *National Action Plan* Goals 1–5**

*Lisa Durso, Ph.D., M.S., ARS, USDA*

Dr. Durso focused her comments on the environmental dimensions of antibiotic resistance. ARS' research portfolio includes efforts to identify and track organisms harboring the genes associated with resistance in animals, soil, water, and crops; develop and evaluate best management practices to reduce resistance; and collect on-farm data to inform modeling and risk assessment studies. ARS supports a variety of manure

management projects aimed at reducing the transport of bacteria and genes in soil, water, and air. Other projects focus on antibiotic resistance in plants.

ARS provides research support to the NARMS efforts. For example, ARS screened hundreds of NARMS isolates and discovered a plasmid-borne colistin-resistance gene in the swine isolate. Diagnostics can play an important role in animal and environmental antibiotic resistance. One ARS-supported researcher is developing a low-cost, high-throughput tool using polymerase chain reaction (PCR) and sequencing to detect hundreds of genes in environmental and manure samples, and it is being tested in a large-scale watershed project.

ARS also has a well-established alternatives to antibiotic research program, which is key to reducing medical antibiotic use in agriculture. Efforts are underway around vaccines, phages, phytochemicals, prebiotics, immune-derived products, and other chemicals and enzymes. Dr. Durso gave several examples of research to enhance understanding of environmental factors and the nature of microbial communities.

Internationally, ARS is coordinating research on agricultural wastewater with European surveillance efforts and seeking to harmonize methods. ARS has a database on antibiotic-resistance field data that will soon be publicly available. Finally, the Agricultural Antibiotic Resistance network encourages ARS-supported researchers to address ARM goals in their individual research.

### **Council Discussion**

Ramanan Laxminarayan, Ph.D., M.P.H., asked when antibiotic use would become part of value-based purchasing metrics and Medicare CoPs. Dr. Cannon explained that the issue is making its way through the federal rulemaking process, but she could not offer a specific timeline.

Dr. Laxminarayan asked how AHRQ encourages stewardship. Dr. Cleeman said AHRQ issued a new funding announcement last year that supports a lot of research on methods to improve stewardship in various settings. AHRQ offers many tools to improve stewardship and has also implemented a major CUSP project on antibiotic use in all settings.

Dr. Laxminarayan asked what NIH program was equivalent to DoD's ARMoR. Dr. Knisely said ARLG's virtual repository is an online catalogue of isolates housed in individual laboratories, and NIH is seeking to make the system more user-friendly.

Dr. Laxminarayan asked Dr. Larsen what size pull incentive he thought would be effective. Dr. Larsen said the numbers can be eye-popping, but the aim is to remove the uncertainty around the first 5 years on the market. He proposed that incentives of \$400 million to \$500 million per candidate, spread over 5 years, might cover about 60 percent of the costs, and other regions of the world should contribute the rest.

Dr. Blaser asked what CDC can do to limit the spread of emerging infectious diseases, especially where stewardship is weak. Mr. Craig responded that CDC is currently focusing on building an infrastructure to address the problem. He noted that a deadly *C. auris* infection in Oklahoma was quickly identified and contained, while cases in New York and New Jersey were not identified and spread through long-term care facilities. With imported diseases and a mobile population, stopping the spread is hard.

Dr. Butler expressed concern about a phrase from Dr. Larsen's slide set indicating that market entry rewards could be supported by using public health policy to dictate consumption of products. He said such an approach could be interpreted as meaning that policy would be driven by the goal of ensuring ROI for private companies. Dr. Larsen said incentives provide an opportunity for companies to agree to provisions that take into account stewardship and conservation of products, but he did not think policy would be dictated by ROI.

John H. Rex, M.D., asked how to boost or change the approach to diagnostics. Dr. Knisely said the NIH-BARDA challenge is a test case, and it has already brought forth some ideas. Also, NIAID has moved toward more broad funding announcements that allow for more innovation around specific needs.

Dr. Kester said presenters gave some evidence of breaking down silos, increasing collaboration, and reducing redundancy. Still, he wondered how the VA and DoD hospitals could be used more to test approaches and identify best practices and how the major repositories could leverage each other's capacities. Dr. Cleeman gave examples of AHRQ partnerships with the VA and DoD, adding that private-sector partnerships are also important. Mr. Craig said CDC has several agreements in place with the VA, whose integrated EHR system makes it a great test bed. Regarding the repositories, Mr. Craig said the two gather data from different populations and are not in competition. Dr. Waterman said both repositories have plenty of demand. She pointed out that CDC provides lots of technical support for DoD to ensure information reaches the NHSN.

Dr. Shryock asked presenters to comment on a report by the FDA Science Board evaluating NARMS. Dr. Flynn said the board provided a detailed analysis along with some opportunities to enhance the database. An upcoming public meeting about NARMS will address several topics, such as the use of whole genome sequencing in surveillance and how to expand the database. Dr. King hoped that NARMS could be expanded to address animal health by including animal pathogens and resistant organisms.

Dr. Marty asked for Dr. Flynn's opinion on which FDA surveillance programs most need to be funded. He said he is particularly concerned that on-farm data be gathered and reported, although not necessarily collected by FDA, and FDA is talking with USDA about the matter. The USDA received some funding to support it, but FDA did not.

Ms. Cole said advocates are finding that local policies are creating barriers to putting federal programs in place. For example, hospitals across the country collect and report data to the NHSN, but states have firewalls that prohibit sharing data with infection

preventionists. Despite receiving millions of dollars for programs, California continues to see rising infections and death rates. Ms. Cole asked what can be done to ensure that federal funding is used as intended. Mr. Craig responded that CDC is just beginning to provide resources to states for stewardship. Recognizing that the complexity of state laws can hinder program implementation, CDC is asking laboratories, through cooperative agreements, to identify policies or other barriers that might limit implementation so that CDC can better understand the problem.

## **Incentives for the Development of Therapeutics, Diagnostics, and Vaccines to Combat Antibiotic Resistance**

### **Overview of Working Group Activity**

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

Dr. Blaser said PACCARB was tasked by the HHS Secretary with addressing the best way to incentivize the development of therapeutics and anti-infectives (including alternatives to antibiotics), rapid diagnostics, and vaccines for both humans and animals. The Council set up three working groups (one for each category of development) with Council members and invited subject matter experts. The working groups held multiple meetings, including two public meetings, and ultimately organized its recommendations in the following categories:

- **Economic:** Issues that influence the ROI to companies or food animal producers regarding product development or use
- **R&D:** Issues related to discovery research and the development process
- **Regulatory:** Issues related to the federal regulatory processes that influence the development or modification of a product, ranging from basic research through studies that meet approval criteria
- **Behavioral:** Issues related to the behavior of consumers, providers, end-users, or companies relative to product use or development

The final report identified 45 critical issues and offered 64 recommendations. The top 10 recommendations are summarized in the report's executive summary. Council members who led the working group discussions outlined the issues and recommendations in the final draft.

### **Council Discussion and Vote**

Dr. Blaser praised the thoroughness of the report and thanked the PACCARB staff for making the process and the report possible. He hoped that the continued development and refinement of narrow-spectrum antibiotics (described in subsections 3.2 and 3.3 of the section, "Incentives for Therapeutics for Human Use") would be considered a high priority. Dr. Blaser said narrow-spectrum antibiotics might decrease the ecological damage that antibiotics cause to individuals' microbiomes.

Dr. Laxminarayan said the report appears to request a lot of money, but some of the recommendations could be accomplished in the short term without very large

investments, such as creating clinical trials networks to lower the cost of R&D. In addition, the USG can take a stepwise approach to adopting and funding the recommendations. Dr. Laxminarayan commended the report for being the first in the world to address the problem of antibiotic resistance in humans and animals side by side. He hoped the recommendations would be treated as equal priorities and that they would be adopted quickly.

Ms. Cole suggested and Dr. Blaser agreed that the VA may have mechanisms in place to test ideas and products on a large scale.

Ms. Jungman said that full funding of the recommendations is unlikely given the current fiscal environment. She noted that the report requests taxpayer dollars to fund private company activities, which is significant and should be taken seriously. The report describes a menu of incentives and their goals at a high level, but it is important to clearly identify what the recommendations seek to incentivize, why the Council believes incentives work, and the rationale explaining why investing in incentives will have more impact than other mechanisms to spur development. The next step will be to provide more detail on what is needed and how to achieve the goals.

*Vote:* The Council voted unanimously to approve as written the report *Recommendations for Incentivizing the Development of Therapeutics, Diagnostics, and Vaccines for Humans and Animals.*

## **Public Comment**

**Louis Mendelson of AllerQuest LLC** said his company brought back to market a skin test to identify people who are allergic to penicillin. He explained that 30 million people are labeled as allergic to penicillin, but 90 percent or more of them can take penicillin without risk of severe reaction. Without penicillin allergy skin testing, millions of patients are needlessly diverted to broad-spectrum alternatives, such as vancomycin, which are associated with a higher degree of infectious disease and a higher risk of clinical complications.

Recognizing these costs, the CDC in 2016 issued a fact sheet encouraging penicillin skin testing as a reliable and useful method for evaluating penicillin allergy. Other public health authorities have joined the CDC in recognizing the important role that a thorough penicillin evaluation can play in antibiotic stewardship.

The American Academy of Allergy, Asthma, and Immunology issued its first position statement in 10 years to address the topic, strongly encouraging, when indicated, widespread and routine penicillin allergy skin testing to reduce the costs of care, enhance patient safety, and improve outcomes of care. Penicillin allergy evaluation has been supported by the American Board of Internal Medicine; the Infectious Diseases Society of America; the American College of Allergy, Asthma, and Immunology; and the Society of Healthcare and Immunology. Mr. Mendelson asked the Council and its partners to promote awareness of penicillin allergy testing as potential way to stem antibiotic resistance.

**Steven Roach from Food Animal Concerns Trust** said infection prevention in animal agriculture is primarily related to farm management practices that lead to disease. In both cattle and swine production, comingling animals from different sources is still a problem that is often addressed with routine antibiotics. Most feedlot cattle receive macrolide antibiotics to address health problems created by inappropriate diet. Weaning practices are associated with illnesses in both cattle and swine. The poultry industry has made some changes and no longer needs to routinely use antibiotics in the hatchery. In many cases, economics drive these choices. Many of these practices are based on access to inexpensive antibiotics. Prevention should take into account economics in animal agriculture.

Mr. Roach asked the Council to take into consideration several issues. First, there is no federal authority for on-farm food safety for meat and poultry. FDA has authority over feed and drugs, but there is no authority for addressing human pathogens on farms, either resistant or not. So even if an MDRO outbreak associated with animal products is traced back to the farm, there is no authority to require farms to take steps to control risks or even allow public health officials access. Also, there is no system to collect actionable data on antibiotic use on farms. Several Council members are funded by FDA to develop systems to collect antibiotic use data, but it is unclear whether these efforts will be sustained over the long run. USDA has some data collection programs. Mr. Roach asked the Council to explore whether the quality of data collected by USDA programs is adequate to identify problems and solutions.

Mr. Roach said that CDC has efforts to create a system to detect, respond, prevent, and innovate in human medicine, but in animal agriculture, detection is rudimentary, and the other three are nonexistent. He also said that while Dr. Flynn mentioned the lack of resources, the FDA did not ask for new resources in its budget request. If resources are not requested, it is much harder to get Congress to provide them.

**Kevin Kavanagh of Health Watch USA** said FDA's embrace of efforts to increase the speed of approval for device-drug hybrids raises significant safety concerns. In addition, he had concerns about AHRQ's promotion of chlorhexidine, especially in light of the integrity issues identified regarding the Randomized Evaluation of Decolonization versus Universal Clearance to Eliminate MRSA (REDUCE MRSA) study. Investigative reports and FDA warnings raise serious questions about chlorhexidine use.

The Health Watch USA web site features a video about research integrity problems that includes the recent meta-analysis performed by WHO for its current recommendations regarding surgical antisepsis using chlorhexidine. Mr. Kavanagh reminded the Council of another chlorhexidine-related debacle, saying he feels there is a pattern of significant concern that needs careful evaluation.

Finally, Mr. Kavanagh said it would be very interesting to determine what percentage of the world's population currently can obtain an antibiotic without a prescription and where.

**Lisa McGiffert of Consumer's Union** echoed the concerns of Ms. Jungman, saying Consumer's Union is concerned about the use of taxpayer money for private enterprise as envisioned by the Council's report on incentives.

In addition, numerous recommendations have been made to speed through FDA approval of devices and diagnostic tests by relying on postmarket studies. These studies often do not start for years after a device is approved, and it can take 3–5 years before results are reported, which could lead to many patients being harmed or misdiagnosed without coming to the attention of the FDA. Ms. McGiffert recommended that the Council look into specifying that such studies begin immediately after approval. That is, in exchange for putting untested products on the market because of logistical problems, like responding to a rare bacteria, the companies and health care providers using these untested products should be required to sign an agreement to submit data regarding their use and results as soon as the products are available. Ms. McGiffert also suggested that the data submitted be evaluated on an ongoing basis, so that authorities can determine whether the products are actually working and ensure that patients are not harmed.

### **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 announced that the next public PACCARB meeting is scheduled for January 24–25, 2018. He adjourned the meeting at 3:09 p.m.

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

**September 13–14, 2017**

### **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 (in person day one, by phone day two)

Helen W. Boucher, M.D., FIDSA, FACP

Angela Caliendo, M.D., Ph.D., FIDSA

Alicia Cole (by phone)

Sara E. Cosgrove, M.D., M.S.

Peter Robert Davies, B.V.Sc., Ph.D.

Kent E. Kester, M.D., FACP, FIDSA, FASTMH

Ramanan Laxminarayan, Ph.D., M.P.H. (day two)

Aileen M. Marty, M.D., FACP

John H. Rex, M.D. (day two)

Thomas R. Shryock, Ph.D.

Randall Singer, D.V.M., M.P.V.M., Ph.D.

Robert A. Weinstein, M.D.

### **Organizational Liaisons Present**

#### *Animal Health Institute*

Richard Carnevale, V.M.D. (by phone)

#### *Association of State and Territorial Health Officials*

Jay C. Butler, M.D.

#### *National Association of Directors of Nursing Administration in Long-Term Care*

Sherrie Dornberger, R.N., CDONA, GDCN, CDP, CADDCT, FACDONA (by phone)

#### *National Pork Producers Council*

Elizabeth Allen Wagstrom, D.V.M., M.S.

#### *The Pew Charitable Trusts*

Elizabeth Jungman, J.D., M.P.H.

### **Ex Officiis Present**

#### *U.S. Department of Health and Human Services*

Marjory Cannon, M.D. (for Shari Ling, M.D.), Centers for Medicare and Medicaid Services (day two)

Michael Craig, Senior Advisor for Antibiotic Resistance Coordination and Strategy, Centers for Disease Control and Prevention

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

Jane Knisely (for Dennis M. Dixon, Ph.D.), National Institute of Allergy and Infectious Diseases, National Institutes of Health  
Joe Larsen, Ph.D., Director, Division of Chemical, Biological, Radiological, and Nuclear Medical Countermeasures, Biomedical Advanced Research and Development Authority (day two)  
Shari Ling, M.D., Deputy Chief Medical Officer, Centers for Medicare and Medicaid Services (day one)  
Daniel W. Sigelman, J.D., Senior Advisor, Office of Public Health Strategy and Analysis, Office of the Commissioner, Food and Drug Administration

*U.S. Department of Defense*

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

*U.S. Department of Agriculture*

Neena Anandaraman (for Jeffrey Silverstein, Ph.D.), Agricultural Research Service  
David Goldman, M.D., Chief Medical Officer and Assistant Administrator, Office of Public Health Science, Food Safety and Inspection Service (day one)  
Brian McCluskey, D.V.M., Ph.D., Chief Veterinary Officer and Deputy Administrator for Veterinary Services, Animal and Plant Health Inspection Service

**Designated Federal Officer (Acting)**

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

**Advisory Council Staff**

Laura Gottschalk, Ph.D., HHS Fellow  
MacKenzie Robertson, Committee Management Officer, Office of the Assistant Secretary for Health, Department of Health and Human Services  
Ayah O. Wali, M.P.H., Committee Management Officer, Office of the Assistant Secretary for Health, Department of Health and Human Services

## Glossary of Abbreviations

AHRQ	Agency for Healthcare Research and Quality
AMR	antimicrobial resistance
APHIS	Animal and Plant Health Inspection Service
ARLG	Antibacterial Resistance Leadership Group
ARMoR	Antimicrobial Resistance Monitoring and Research [Program]
ARS	Agricultural Research Service
AST	antimicrobial susceptibility test
BARDA	Biomedical Advanced Research and Development Authority
CARB-X	Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator
CAUTI	catheter-associated urinary tract infection
CDC	Centers for Disease Control and Prevention
CEAH	Center for Epidemiology and Animal Health
CMS	Centers for Medicare and Medicaid Services
CoPs	Conditions of Participation
CRE	carbapenem-resistant Enterobacteriaceae
CUSP	Comprehensive Unit-Based Safety Program
CVM	Center for Veterinary Medicine
DART	Dialogue Around Respiratory Illness Treatment
DoD	U.S. Department of Defense
EHR	electronic health record
FDA	Food and Drug Administration
G7	Group of 7
G20	Group of 20
GEIS	Global Emerging Infectious Disease [network]
HAI	health-care-associated infection
HHS	Department of Health and Human Services
HIINs	Hospital Improvement Innovation Networks
ID	infectious disease
IDSA	Infectious Diseases Society of America
MDRO	multidrug-resistant organism
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
MRSN	Multidrug-Resistant Organism Repository and Surveillance Network
NAHMS	National Animal Health Monitoring System
NARMS	National Antimicrobial Resistance Monitoring System
NIAID	National Institute of Allergy and Infectious Diseases
NIFA	National Institute of Food Agriculture
NIH	National Institutes of Health
NHSN	National Healthcare Safety Network
NQF	National Quality Forum
OGA	Office of Global Affairs
PACCARB	Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria
PCR	polymerase chain reaction

QIN–QIOs	Quality Improvement Network–Quality Improvement Organizations
R&D	research and development
REDUCE MRSA	Randomized Evaluation of Decolonization versus Universal Clearance to Eliminate MRSA
ROI	return on investment
SAAR	standardized antimicrobial administration ratio
TATFAR	Transatlantic Task Force on Antimicrobial Resistance
TB	tuberculosis
TeamSTEPPS	Team Strategies and Tools to Enhance Performance and Patient Safety
UN	United Nations
USDA	U.S. Department of Agriculture
USG	U.S. Government
VA	U.S. Department of Veterans Affairs
Vet-LIRN	Veterinary Laboratory Investigation and Response Network
VHA	Veterans Health Administration
WG	working group
WHO	World Health Organization