Witness: Beth Bell, MD, MPH

Testimony: House Energy and Commerce Committee, Subcommittee on Oversight and Investigations

Good morning Chairman Murphy, Ranking Member DeGette, and members of the Subcommittee. Thank you for the opportunity to testify before you today on the Centers for Disease Control and Prevention's (CDC's) continued efforts to combat antibiotic resistance, which threatens the United States and modern medicine itself.

CDC is the nation's premier health protection agency, working 24-7 to save lives and protect people against the threat of untreatable infections. We know that, although much effort is being expended to develop new antibiotics, we also must work right now to slow the spread of these resistant bacteria and improve how we use the antibiotics we have.

Threat of Antibiotic Resistance

Antibiotic resistance is perhaps the single most important infectious disease threat of our time.

Every year, more than two million people in the United States get infections that are resistant to antibiotics, and at least 23,000 people die as a result. In addition, *Clostridium difficile* (*C. difficile*), a serious diarrheal infection associated with antibiotic use, causes at least 15,000 deaths every year in the United States.

Modern medicine is at stake. If we lose antibiotics, we lose the ability to effectively treat sepsis and to provide care to cancer patients, organ transplant recipients, and burn or trauma victims. Losing antibiotics would devastate our medical system. In 2014, the President issued an Executive Order directing the development of the National Action Plan for Combating Antibiotic Resistant Bacteria to identify steps Departments across the Federal Government could take to combat antibiotic resistance.

CDC's Antibiotic Resistance Solutions Initiative

In fiscal year (FY) 2016, Congress recognized the large and growing threat of antibiotic resistance (AR) and appropriated $160 million to CDC to implement the National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB) activities: To detect and respond to resistant pathogens; prevent the spread of resistant infections; and collaborate with partners to

encourage innovation for new prevention strategies. These resources are transforming how our nation tackles and slows antibiotic resistance comprehensively, efficiently, and systematically.

With support from Congress, CDC is working with Federal, state, and local public health, academic, healthcare, and veterinary partners to: improve capacity to detect and respond to AR threats in healthcare and communities, protect patients, and save lives. CDC will invest the largest extramural portion of this funding in the 50 state health departments, the six largest local health departments, and Puerto Rico. This Antibiotic Resistance Solutions Initiative will support comprehensive and coordinated public health action to minimize the spread of antibiotic resistance across states, counties, and cities.

DETECT AND RESPOND

This public health investment opens a new chapter against antibiotic resistance, improving state health department healthcare-associated infection (HAI) and AR detection capacity so they can better detect resistance and respond to outbreaks faster. Beginning this fall, CDC's Antibiotic Resistance Lab Network will provide infrastructure and lab capacity through as many as eight regional labs across the country. These labs will be able to detect resistant organisms recovered from human samples and new forms of antibiotic resistance—including mutations that allow bacteria to withstand last-resort drugs like colistin—and report these findings to CDC as well as back to facilities and states. These efforts will generate better data for stronger infection control to contain current threats and prevent future resistance threats.

CDC is particularly concerned about *carbapenem-resistant Enterobacteriaceae* (CRE)—often referred to as the nightmare bacteria—and emerging multidrug-resistant organisms. In addition to building on existing HAI/AR state programs, CDC will provide support for labs in all states to test for CRE and support regional labs for additional testing in outbreak response (e.g., screening colonized patients). The Emerging Infections Program (EIP), a national resource for surveillance, prevention, and control of emerging infectious diseases, will also build on population-based detection of all invasive *Staphylococcus aureus* (including MRSA), *carbapenem-resistant Pseudomonas*, and ESBL-producing *Enterobacteriaceae*.

CDC's advanced molecular detection (AMD) initiative is another important tool in our efforts to identify and address antibiotic resistance. The expansion of whole genome sequencing into public health surveillance activities represents a paradigm shift that has already saved lives by identifying and solving more outbreaks, faster. For example, CDC is using AMD to better characterize *Listeria* bacteria in foodborne disease outbreaks. Earlier this year, whole genome

sequencing was used in a multi-state *Listeria* outbreak associated with packaged salads; this technology confirmed that cases identified in Canada were closely related. CDC will scale up whole genome sequencing of multiple foodborne pathogens—including *Salmonella*, *Shigella*, and *Campylobacter*—to better understand foodborne AR patterns. CDC will also use the National Antimicrobial Resistance Monitoring System (NARMS) and work with the Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA) to sequence foodborne pathogens to identify new ways of preventing human infection associated with resistant bacteria in food animals. Finally, CDC will provide states with additional epidemiologic support for foodborne investigations to ensure rapid response to new illness reports and outbreaks of resistant infections identified through this new testing.

PREVENT

CDC's Antibiotic Resistance Solutions Initiative will help slow resistance and protect the antibiotics we have today with active coordination of care across communities, data collection, and stewardship program implementation. State HAI/AR Prevention Programs will work with healthcare facilities in up to 25 states to scale up this coordinated approach to prevent the transmission of multidrug-resistant organisms and *C. difficile* across communities.

Our ability to reduce antibiotic resistance will depend in part on improving antibiotic use, and we are working toward that through better measurement of antibiotic use, expansion of stewardship programs, and support for educational campaigns. CDC is working with large healthcare systems to demonstrate best practices in stewardship programs using CDC's Core Elements of Antibiotic Stewardship and measure antibiotic use outcomes. Using electronic data through the National Healthcare Safety Network's (NHSN's) antibiotic use module, we can assess appropriate use and target interventions in and across healthcare settings. These data will inform how facilities can improve antibiotic use and reduce resistance. CDC is collaborating with partners including the Centers for Medicare & Medicaid Services (CMS), Quality Improvement Networks (QINs), and CMS's Center for Medicare and Medicaid Innovation (CMMI) to implement effective stewardship programs.

Much of this work in turn responds to the threat of sepsis, often a sign of severe infection that can include resistant infections. CDC is committed to preventing infections that lead to sepsis and promoting early recognition of sepsis across medical care.

Finally, CDC will also work with FDA and USDA to ensure that practicing veterinarians have the tools, information, and training to prevent drug resistance by promoting responsible use of antibiotics in animals, including those animals consumed by humans.

INNOVATE

CDC's Antibiotic Resistance Solutions Initiative will accelerate prevention innovation, giving us new tools to slow the threat of resistance. Through the Prevention Epi-Centers and other innovation partners, CDC is able to address questions and gaps in knowledge related to resistant infections. CDC is also performing intramural studies and supporting extramural studies to better understand the microbiome and how its disruption influences an individual's risk for developing an antibiotic resistant infection. This work could help in tailoring prevention and antibiotic stewardship programs and uncovering new therapies that restore the healthy microbiome, reducing the risk of AR infections.

COLLABORATE

CDC is working with state, Federal, and international partners to align AR activities and maximize the effectiveness of funding. For example, CDC's efforts in whole genome sequencing for foodborne AR infections will involve collaborations with the FDA, USDA, and the National Institutes of Health (NIH) to track how antibiotic resistant genes in pathogenic and commensal bacteria that may be impacting humans, food, and animals. CDC, NIH, and the Department of Defense (DoD) are working together on when and how to best use whole genome sequencing to solve CRE outbreaks. CDC is collaborating with FDA on supporting and expanding use of the AR Isolate Bank, including coordinating efforts to generate genomic sequence data for all isolates in the AR Isolate Bank, which supports industry and academic partners working to develop new treatments and diagnostics.

Additional Investments

The Administration's budget request for FY 2017 includes an increase of $40 million for year two of CDC's Antibiotic Resistance Solutions Initiative. This increase will build on AR capacities started in FY 2016, allowing CDC to expand the nation's ability to detect, respond to, and prevent AR infections across healthcare settings and in the community.

In FY 2017, in addition to sustaining AR capacities started in FY 2016, CDC will expand the State HAI/AR Prevention Programs in up to 50 states, six large cities, and Puerto Rico to better respond to outbreaks, improve prescribing, and prevent AR infections across all healthcare

settings (e.g., inpatient, outpatient, and long-term care settings). CDC will also further expand state public health laboratory capacity in up to 50 states, six large cities, and Puerto Rico to rapidly screen enteric bacteria for resistance and ensure the nation's ability to rapidly detect and investigate AR threats across the country and in more enteric pathogens, specifically *Campylobacter* and Shiga toxin-producing *E. coli*.

These collective investments have a direct impact on the public health response to the AR threat, including our continued response to new threats, such as the emergence of the *mcr-1* gene, reported in November of 2015 in China.

Public Health Response to Discovery of *mcr-1*

The antibiotic colistin is used as a last-resort drug to treat patients with multidrug-resistant infections, including CRE. The *mcr-1* gene makes bacteria resistant to colistin. The gene exists on a plasmid, a small piece of DNA that is capable of moving from one bacterium to another, spreading antibiotic resistance among bacterial species. CDC and Federal partners have been hunting for this gene in the U.S. since its emergence in China was reported in 2015.

Following the identification of *mcr-1* in China, CDC, FDA and USDA began searching for *mcr*-1 in bacterial samples taken from human, retail meat, and food animal sources. This work is facilitated by the National Antimicrobial Resistance Monitoring System (NARMS), which has detected emerging resistance to clinically important antibiotics for the past 20 years. NARMS is a partnership among FDA, USDA, CDC, and state and local public health departments that tracks changes in the antimicrobial susceptibility of intestinal bacteria. Through NARMS, the USDA discovered *mcr-1* in an *E. coli* isolate collected from a pig intestine. The DNA sequence of that isolate revealed that the strain contained the *mcr-1* gene on a plasmid. USDA scientists also determined that the *mcr-1* carrying colistin-resistant *E. coli* from intestinal content of a pig was resistant to other antibiotics, including ampicillin, streptomycin, sulfisoxazole, and tetracycline. The resistance to these other antibiotics was not on the plasmid carrying the *mcr-1* gene. Preliminary analysis by USDA's Agricultural Research service indicates that the bacterial strain is *E. coli* 0160:H40. An isolate from a second pig is undergoing analysis. As of April 2016, more than 55,000 genome sequences of several types of bacteria from humans, retail meat, and food animals have been screened through NARMS. All were negative for the *mcr-1* gene. NARMS continues to look for this gene.

In addition, CDC investigated bacterial genomes and used a highly sensitive testing method known as polymerase chain reaction, or PCR-screening, to look for the *mcr-1* gene among

healthcare-associated pathogens. In this effort, CDC screened 735 genomes, including 690 Enterobacteriaceae (e.g., carbapenem-susceptible Enterobacteriaceae (CSE) and carbapenem-resistant Enterobacteriaceae (CRE)) and 45 non-Enterobacteriaceae (e.g., *Pseudomonas* and *Acinetobacter*) from the surveillance, outbreak, and special study and reference collections. All these human isolates were negative for *mcr-1* using this PCR screening method.

In May 2016, DoD scientists announced the first discovery of the *mcr-1* gene in bacteria isolated from a person in the United States. CDC is currently part of the coordinated public health response to DoD's identification of the gene in *E. coli* bacteria in a urine sample from a Pennsylvania woman with no recent travel outside of the country. The isolates identified from the 1st pig is different from the isolate identified in the human case; the isolate from the 2nd pig is currently undergoing analysis.

The DoD finding of the *mcr-1* gene in bacteria from a person started an ongoing public health investigation led by CDC and the Pennsylvania Department of Health. Although only one human isolate has been recovered in the United States to date, CDC takes this finding very seriously and is working with DoD, the Pennsylvania Department of Health, local health departments, and others to identify people who have had contact with the Pennsylvania patient. The investigation is currently focused on identifying and screening close contacts, including household and healthcare contacts of the Pennsylvania patient to determine whether any of them might carry bacteria containing the *mcr-1* gene.

Despite some media reports, the Pennsylvania Department of Health investigation has determined that the woman did not have CRE, and the bacteria identified is not resistant to all antibiotics (referred to as a pan-resistant infection). The presence of the *mcr-1* gene, however, and its ability to share its colistin resistance with other bacteria, such as CRE, raises the possibility that pan-resistant bacteria could develop.

The transformative improvements being implemented across the country through CDC's Antibiotic Resistance Solutions Initiative will greatly expand and strengthen national efforts to identify and respond to this gene if it is circulating.

Conclusion

The emergence and reemergence of health threats, including those caused by antibiotic resistant bacteria, is something we can expect to continue to see in the future. Consistent with the *National Action Plan for Combating Antibiotic-Resistant Bacteria*, CDC and other government agencies continue to track the emergence of antibiotic resistance. CDC is working

to strengthen the nation's ability to respond rapidly and effectively, protecting Americans and the precious antibiotics we need to fight deadly bacteria.

Thank you again for the opportunity to appear before you today. I appreciate your attention to the antibiotic resistance threat, and I look forward to answering your questions.