Overview of Written Testimony: American Society of Microbiology

“Antimicrobial Resistance: Examining an Emerging Public Health Threat”

Energy & Commerce Committee, Oversight and Investigations Subcommittee April 28, 2023

American Society for Microbiology (ASM), one of the largest life science societies with more than 30,000 members in the U.S. and around the globe focused on advancing the microbial sciences. We are here today because antimicrobial resistance (AMR) is one of the most daunting public health challenges facing the United States and the world and ASM has been focused on understanding the needs to address this issue.

Basic and translational research is foundational to addressing AMR as there are large knowledge gaps in our understanding of the emergence and transmission of AMR. Resources devoted to understanding the contributors and locations of antimicrobial resistance are needed to target interventions and slow or even reverse the emergence of antimicrobial resistance bacteria and fungi. Improved antimicrobial resistance surveillance both in the US and globally will be critical in addressing some of these gaps. Recent funding of public health-academic partnerships to adopt novel genomic technologies and improved use of the data through the Centers for Disease Control and Prevention Pathogen Genomic Centers of Excellence Network will be hugely helpful if funding is sustained. Funding in this area will also allow the research and public health community to explore the utility of wastewater surveillance for understanding and addressing AMR emergence and impact.

Improved diagnostics will be critical in both preventing the continued overuse of antimicrobials as well as the need to be able to maximize the treatment of patients infected with antimicrobial resistant infections. We need investment in research in novel diagnostic approaches. In addition, with ongoing personnel shortages in clinical microbiology laboratories we need to recognize and incentivize people to pursue medical microbiology as a career. This will allow for the increased adoption of current improved laboratory practices to optimize prescribing and for testing and therefore use of newly developed antimicrobials as well as adoption of newer technologies which streamline prescribing.

Written Testimony of

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Chairman Griffith, Vice Chair Lesko, Ranking Member Castor and distinguished members of the subcommittee, thank you for holding a hearing on antimicrobial resistance (AMR) and inviting me to testify here today and share my expertise and perspective.

I am Dr. Amy Mathers, MD, clinical director of antimicrobial stewardship, associate director of clinical microbiology and associate professor in the school of medicine at the University of Virginia (UVA). I am here today representing the American Society for Microbiology (ASM), one of the largest life science societies with more than 30,000 members in the U.S. and around the globe focused on advancing the microbial sciences. I serve in multiple volunteer leadership roles through ASM, including as an elected leader of the Council on Microbial Sciences for the Antimicrobial Agents and Resistance community. Addressing antimicrobial resistance (AMR) through science, clinical practice, global health programs and policy is a top priority for ASM. I am also a fellow of the Infectious Diseases Society of America.

As an infectious disease physician who sees hospitalized patients with serious infections, I am motivated by the negative impact that antimicrobial resistance has had on many patients I have cared for. This hearing is very timely as I have been seeing first-hand several types of antimicrobial resistant bacteria and fungi that are emerging and re-emerging in the wake of the public health emergency. In fact, even within the last week one of our transplant patients succumbed to an untreatable infection. I bring a "bench to bedside" perspective when it comes to AMR. I conduct research at the bench, in the hospital and in the community. I also work at the interface of public health and medical research. My expertise is in detecting and tracking antibiotic-resistant bacteria and my research works to advance the understanding of where antibiotic-resistant pathogens originate and how they spread in even the most sterile places like hospitals. My colleagues and I do this by conducting research on the following areas: development of novel interventions for the hospital built environment to prevent transmission; development of technologies to better detect antimicrobial resistance and emergence; the utilization of diagnostic tools which help in the treatment and how to curtail antimicrobial overuse. Finally, we work at a basic level to understand how antimicrobial resistance evolves especially at the interface between patients and the environment. We have worked to develop genomic tools to understand transmission and emergence of AMR resistant pathogens with one of the only clinical labs in the country that utilizes next generation sequencing to track AMR pathogens. More recently in collaboration with UVA's Biocomplexity Institute (Drs. Madhave Marathe and Christian Reidy) we are working to use large data sets to build models to understand emergence of antimicrobial resistance. In my clinical practice through antimicrobial stewardship, I work with other physicians and hospital leadership to minimize the impact that antimicrobial overuse can have on selecting for resistant bacteria. In this role, I work with pharmacists and laboratorians to pair cutting edge diagnostics in the clinical lab to maximize appropriate use of antimicrobial in patients. We are here today because antimicrobial resistance (AMR) is one of the most daunting public health challenges facing the United States and the world.

Recent estimates demonstrated AMR associated deaths of almost 5 million and over 1 million directly attributable to AMR. The complexity and the urgency of the problem means it must be tackled with a multi-faceted approach and with multiple stakeholders—from health care and clinical laboratory settings to agricultural and environmental microbial research perspectives, in the United States and around the world. It requires an understanding of the connection between the health of people, animals, and the environment – what we refer to as a "One Health" model. ASM supports policy solutions that, in the spirit of One Health, comprehensively address AMR from multiple angles and, when possible, with integrated strategies. With past support from Congress, we have made progress against AMR, but more work can and should be done to address this crisis.

My testimony today will focus on several components of the One Health aspects of AMR that I have been engaged as a scientist and clinician, and also on which ASM focuses its advocacy work. Specifically, I will discuss the importance of basic and translational research and development, including on diagnostics; the important role diagnostics play and need for antimicrobial stewardship; the role of public health surveillance and use of genomic sequencing technology to track, prevent and predict resistance; and the need to address medical microbiology workforce shortages.

Basic and Translational Research is Foundational to Addressing AMR

To address AMR's pressing challenge, our nation must continue to invest in basic and translational research on microbes through the National Institutes of Health and other federal science agencies including how they interact and persist in the environment, how they develop resistance, and how we can prevent, detect, and treat antimicrobial resistant infections. It is critical that this research focuses across the spectrum of microbial pathogens including bacteria and fungi. For example, tracking specific genes that drive AMR and which can be exchanged by unique bacterial species and not just confined to a single pathogen adds a great deal of complexity to the issue. We need to understand resistance as it emerges across pathogens and between non-pathogenic and pathogenic bacteria. Research in the area of resistance gene exchange between bacteria will be crucial for understanding the drivers of emerging antibiotic resistance. Research and development of novel diagnostic tools and approaches is an extremely important investment to prevent resistance emergence and utilization of new therapeutics. While optimizing current diagnostics is extremely critical, developing the next generation of diagnostics that can provide rapid point of care analysis on resistance remains elusive. In addition, diagnostic testing which more conclusively demonstrated who had an infection warranting antimicrobials and those who do not would also limit unnecessary antimicrobials.

Antifungal resistance in particular is a serious emerging threat that requires more research to understand and address effectively. Resistant fungal infections have emerged more recently and pose a serious threat to plant, animal and human health in the U.S. and around the world. Perhaps the most prominent example is the rapid spread of *Candida auris (C. auris)* in U.S. healthcare facilities, which is now considered an urgent threat according to the CDC. We have large knowledge gaps surrounding emergent resistant fungi and we have fewer therapies to combat fungal infections and those we have are often highly toxic. It is especially important that we devote resources to this particular facet of AMR. Without sustained funding for research at all levels, we will not be able to make progress against AMR.

The Role of Diagnostics in AMR

Diagnostics play a central role in preventing, detecting and combatting AMR and in practicing antimicrobial stewardship in healthcare settings. The lack of rapid and affordable diagnostic tools to detect microbial pathogens is a major, often overlooked contributor to AMR. The state of diagnostics is directly connected to the long-term effectiveness of antibiotics already in the marketplace. Poor diagnostics can lead to incorrect prescribing of antibiotics and their overuse. Congress has an opportunity to expand investments in the Biomedical Advanced Research and Development Authority (BARDA) to focus on innovative diagnostics in the upcoming Pandemics and All-Hazards Preparedness Act reauthorization later this year. The newly established Advanced Research Projects Agency for Health (ARPA-H) also offers a new model for the development of novel diagnostics and therapeutics to address AMR.

An effective antibiotic marketplace requires effective use of diagnostics in addition to investments in research and development on novel diagnostics. The appropriate use of laboratory testing to guide patient management, including treatment, is important to optimize clinical outcomes and limit the spread of antimicrobial resistance. During the pandemic it became very clear how essential clinical testing was to preventing COVID-19 transmission by detection of infected persons who could then go into isolation to prevent transmission. Some of the same principles also apply to AMR as knowing who is carrying or infected with highly resistant bacterial and fungal infection can aid in isolating and preventing transmission. Supporting clinical laboratories in though workforce development to adopt diagnostics for improved AMR detection as well as supporting research to develop novel and improved diagnostics are both critical in combatting toe spread as well as managing patients impacted by AMR.

Prescribing appropriate and timely therapy is critical to the proper management of infectious diseases. For example, when a patient is in the hospital for an infection, the first line of therapy is usually a broad-spectrum antibiotic while we wait for the results of the test to come back. Because current diagnostics take time to inform the practitioner of the type of infection, the consequence is that while we wait, we could be inadvertently using the wrong antibiotic or the wrong dose of antibiotic. This delay results in worse patient outcomes with antimicrobial resistant infections but also contributes to resistance emergence, increases hospital stays and as a result, increases health care costs. Rapid diagnostics can promote the prevention of unnecessary antimicrobials as well as by allowing the targeting of antimicrobials earlier. In addition, for patients with antimicrobial resistant infections novel diagnostics can be used to detect resistance sooner and employ novel antimicrobials which are reserved largely for the treatment of patients with AMR infections.

Another aspect of diagnostics is critical to the practice and treatment of antimicrobial resistant infections is through up-to-date susceptibility testing. Research and development in the area of pharmacology, clinical infectious diseases and microbiology all work together to make sure that susceptibility testing and reporting of resistance is accurate and using the most current research to inform clinicians how to treat infections. This is done though a consensus process and sometimes results in changes suggested in antimicrobial susceptibility testing and interpretation. It is critical that clinical laboratories are supported in making changes to use the most current and clinically informed susceptibility testing and reporting standards to detect, report and give information to clinicians for how to treat antimicrobial resistant bacteria. We know that there has been a lag between the updating of testing recommendations and updates made by the Food and Drug Administration. This in turn often slows the adoption of new and updated breakpoints by clinical microbiology laboratories, leading to an underestimation of emerging resistance as well as the potential for worse outcomes for patients with serious infections. The 21st Century Cures bill championed by this Committee made strides to improve this process, but there is still work to be done.

The Role of Public Health Monitoring and Genomic Sequencing in Addressing AMR

Historically antimicrobial resistance is detected in clinical laboratories, but this has not necessarily been publicly reported or coordinated with state or regional epidemiology. Monitoring emergence of resistant organisms plays a unique and important role in combating antimicrobial resistance. As we will not have endless antimicrobials to count on in the future, prevention of antimicrobial resistance transmission will be critical. Using detection of resistance and reporting to understand where and how resistance is emerging can prevent the spread of resistant infections generally, allowing for fewer cases of drug resistant infections and elongating the effectiveness of current therapies. Deploying systems in the health care setting such as improved reporting and data sharing between clinical facilities, clinical laboratories and public health where antibiotic resistant infections are endemic and emerging is paramount to developing and targeting interventions. The current challenge lies in setting up systems and coordinating their data to drive a larger understanding of the problem and allowing targeted solutions to be deployed.

Leveraging next generation sequencing technologies both in research and in public health is an important way to detect and track resistance in both healthcare and environmental settings. We thank Congress for making important investments in this space and authorizing expanded partnerships and programs, but we need robust and sustained funding for programs funded through the Centers for Disease Control and Prevention's (CDC) National Center for Emerging and Zoonotic Infectious Diseases, which are critical to addressing AMR and complement the research and development taking place in academic centers and in the private sector. The CDC Advanced Molecular Detection (AMD) program supports technologies that help public health laboratories detect existing and emerging antibiotic-resistant organisms, including some of the biggest threats we face such as *Clostridioides difficile* (*C. diff*), "nightmare bacteria" carbapenem-resistant Enterobacteriaceae (CRE), the fungus *Candida auris, Mycobacterium tuberculosis*, and *Neisseria gonorrhoeae*. By adding AMD technologies to antibiotic resistance surveillance, scientists can look more deeply at these pathogens to understand their emergence and prevent transmission. Ultimately this type of data can also assist healthcare providers select the most effective medications to treat infections.

Thanks to recent, supplemental investments made by Congress in the AMD program, the CDC has established innovative public health-academic partnerships to advance the technology and capitalize on the potential synergistic strengths of public health and research entities. Last September, the Centers of Disease Control announced 5-year awards to five public health departments to establish the Pathogen Genomics Centers of Excellence (PGCoE) network. The PGCoE network is meant to foster and improve innovation and technical capacity in pathogen genomics, molecular epidemiology, and bioinformatics to better prevent, control, and respond to microbial threats of public health importance. Using many of the lessons from the COVID-19 pandemic, the network also represents an unprecedented opportunity to expand and deepen collaboration between U.S. public health agencies and academic institutions to form a national resource to better prevent, control, and respond to microbial threats of public health importance.

Each center of excellence consists of a health department and one or more academic institutions. I am proud to be an academic partner from one of these centers with a large portion of the research devoted to the emergence of AMR. Our partnership is between the Virginia Division of Consolidated Laboratory Services, the Virginia Department of Health, Virginia Commonwealth University, and my institution, the University of Virginia. UVA's role as part of the Center focuses on how "superbugs" which often do not respond to existing antibiotics, can emerge and be tracked by public health using next generation sequencing. We propose to develop genomic tools for improved use of data to understand AMR emergence including tools to better track AMR gene sharing between bacteria. In addition, we will perform the further refinement of wastewater surveillance to detect antibiotic resistance, as well as other infectious diseases. We hope to develop more accurate models and analyses of both future infectious disease outbreaks as well as the effects of antibiotic resistance through the data and information we collect.

This program has enormous potential, but it will not be sustainable without a strong commitment from Congress moving forward.

Another novel approach has been in wastewater surveillance. This method has already been shown during the COVID-19 pandemic to be an extremely useful metric for measuring the disease and guiding response to outbreaks and was significantly expanded during the public health pandemic. That said, the applications for AMR are still a new surveillance technique, and there is a lot of research needed to hone this into a fully operational and routine tool in our arsenal. Given viruses only live in humans or host animals, the signal we are receiving from wastewater likely reflects active shedding from hosts. Some bacteria however can live in persist in the environmental waste stream and may end up being too far divorced from what is going on in humans to replicate the same use as viral surveillance. However, wastewater AMR surveillance research is ongoing and our ability to understand emerging pathogens including the possibility that the environment is an ideal location for AMR gene exchange will be critical. No doubt, wastewater surveillance is on the cutting edge or frontier of surveillance and time will tell the extent of its effectiveness in identifying AMR pathogen emergence and impacts on human health.

We very much appreciate that Congress is funding this work and Centers as part of the supplemental funding provided in 2021, and I hope Congress will continue to fund this and other such initiatives as they have enormous value and future potential.

The Role of Medical Microbiologists in Fighting AMR

ASM appreciates the Committee’s attention to the needs of the healthcare workforce and the threat that shortages have on patient care and the broader medical ecosystem. Clinical laboratories, including microbiology laboratories, have experienced personnel shortages for many years now, and the COVID-19 pandemic shone a spotlight on the critical need to bolster this workforce. Without medical microbiologists to validate, develop and conduct antimicrobial susceptibility testing and infectious disease diagnostics, we cannot make progress against AMR. Shortages not only compromise diagnostic and antimicrobial stewardship efforts, but also prevent laboratories from updating susceptibility testing methods, bringing new testing platforms online and also lead to unacceptable delays due to the need to “outsource” the tests.

The pandemic only exacerbated an existing shortage in medical laboratory scientists and infectious disease laboratory professionals. In 2016, several years prior to the pandemic, the Bureau of Labor Statistics predicted we needed 12,000 new clinical laboratory professionals annually to meet rising demand. At that time the vacancy rate for medical laboratory scientists working in clinical microbiology laboratories was 6.25% and the vacancies for supervisory positions was nearly 4%. By 2018-19, the vacancy rates had grown to 10.56% and nearly 7%, respectively. These facts, coupled with the anticipated retirement of 20% of staff in microbiology departments over the coming years, set the stage for what has now become a full-blown crisis.

We must address these shortages and plan for the future. While the challenges facing the profession are myriad, the federal government can provide incentives and support. These include the establishment of loan forgiveness programs that include medical microbiologists and other medical laboratory scientists, both in and outside of public health settings and the establishment of federal training grants for medical microbiologists and other medical laboratory scientists and professionals. Diagnostic tests in infectious disease also are reimbursed at lower rates than other types of tests; sometimes not fully covering the cost of the test. This has the downstream effect of devaluing the work of the laboratory and subsequently the profession, depressing salaries and in some cases, leading to substandard care.

AMR is a Global Threat

Lastly, we must think globally when considering strategies to address AMR. AMR is not only a public health threat but a national security threat, and rising resistance anywhere is a threat everywhere. As a global scientific society, ASM urges Congress to consider how federal support here in the U.S. can also extend to addressing research, surveillance, stewardship efforts in countries around the world. Aligning US domestic AMR policy with the global policy infrastructure is critical to tackling the problem, and U.S. policy must reflect the global challenges while also reflecting specific domestic concerns. One area where the US experience can be instructive is laboratory capacity. Globally, laboratory availability and capacity can be limited, particularly in lower-middle income countries. And the labs that do exist often do not have access to the necessary infrastructure to perform the basic surveillance and testing required to assess AMR. Congress must continue to support the U.S. Antimicrobial Resistance (AR) Laboratory Network funded through CDC and which is now authorized to focus on global laboratory capacity to provide technical assistance to countries around the world to address AMR.

In closing, on behalf of ASM and myself I want to thank the Chairman, Ranking Member and the Subcommittee for inviting me to testify at this important hearing on a topic that affects each and every one of us. ASM and its members look forward to working with you and your colleagues to advance policies that will enable us to address the daunting challenge of AMR head on for the benefit of all humankind.