IDSA Headquarters
1300 Wilson Boulevard
Suite 300
Arlington, VA 22209
TEL: (703) 299-0200
FAX: (703) 299-0204
EMAIL ADDRESS:
info@idsociety.org
WEBSITE:
www.idsociety.org

IDSA
Infectious Diseases Society of America

January 7, 2019

Martin J. Blaser, MD, FIDSA
Chair
Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria
Office of the Assistant Secretary for Health
U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 715-G
Washington, DC 20201

Dear Dr. Blaser:

Thank you for the opportunity to provide recommendations to the Presidential Advisory Council on Combating Antibiotic Resistant Bacteria regarding priorities to include in the next phase of the CARB National Action Plan. As you know, addressing antibiotic resistance is a top priority of the Infectious Diseases Society of America. We are pleased to partner with the PACCARB and the federal government on this important effort. While the current National Action Plan marshals federal resources in a more coordinated fashion and continues to demonstrate progress on a number of fronts, we remain deeply concerned that antibiotic resistance continues to tax our healthcare system, costing patients their lives and jeopardizing the very foundation of modern medicine.

New data indicate that as many as 162,044 people die in the US annually due to multidrug-resistant infections. The estimates, nearly seven times higher than 2013 estimates from the U.S. Centers for Disease Control and Prevention, are based on 2010 mortality data and indicate that infections resistant to treatments were the third leading cause of death that year.

Increased investments and meaningful policy changes are needed to drive necessary progress with regard to stewardship, prevention, surveillance, research and innovation in the US and globally. In addition to replying to the PACCARB request for information, IDSA is writing to provide you with more in-depth feedback on the National Action Plan, gaps in progress and recommendations for future directions. We hope you find this feedback useful and encourage you to call upon us any time we may be of help.

Goal 1: Slow the emergence of resistant bacteria and prevent the spread of resistant infections.

Recommended Priority: Increase federal investment in workforce and resources needed to implement antimicrobial stewardship and infection

prevention in all health care settings. IDSA is greatly encouraged by the progress made in implementing stewardship programs as 76% of hospitals in the US now have stewardship programs that align with the Core Elements developed by the Centers for Disease Control and Prevention. A Medicare requirement for stewardship would be an important step toward ensuring universal adoption. Many of the hospitals that have not yet implemented robust stewardship programs may lack the resources and expertise to do so. CDC is helping state and local health departments foster partnerships between ID physicians with expertise in stewardship and infection prevention and smaller community hospitals, long-term care facilities, and outpatient settings to help build stewardship and infection prevention capacity. Additional investment is needed to sustain these efforts and reach additional health care facilities. Federal investment is needed to ensure that stewardship leaders have protected time and resources to provide necessary support and education to additional facilities. New funding mechanisms could be created through the Centers for Medicare and Medicaid Services, the Agency for Healthcare Research and Quality or the CDC to support the training of a stewardship workforce, similar to the K awards provided by the National Institutes of Health to foster the biomedical research workforce. In addition, the federal government should encourage greater use of telemedicine to extend the reach of stewardship and infection prevention experts. According to a 2015 report from CDC, "If best infection control practices and antibiotic stewardship were nationally adopted, more than 600,000 infections and 37,000 deaths could be prevented over 5 years."

Recommended Priority: Increase federal funding to support research on stewardship implementation. As progress continues in the implementation of stewardship, it is essential that we study stewardship to evaluate specific approaches and interventions rigorously. Research should drive innovative methods to enhance stewardship and improve patient outcomes. Additional funding through NIH and CDC is needed to support research on stewardship and to share data to inform implementation.

Goal 2: Strengthen national One Health surveillance efforts to combat resistance.

Recommended Priority: Develop, implement and fund strategies to significantly boost the number of healthcare facilities reporting antibiotic use and resistance data to the CDC National Healthcare Safety Network. As of April 1, 2018, 776 out of the over 5,500 U.S. hospitals have voluntarily reported antibiotic use data, and 317 hospitals have reported antibiotic resistance data to the CDC NHSN Antibiotic Use and Resistance (AUR) module. While this represents progress, we are significantly short of the current goal for 95% of hospitals to report these data by 2020. Increased federal resources must be provided to help more healthcare facilities report these data in a standardized fashion. The Centers for Medicare and Medicaid Services and the Office of the National Coordinator for Health Information Technology should explore the use of existing policy levers to encourage or require reporting. Comprehensive data on antibiotic use and resistance are essential to inform and evaluate stewardship activities.

Recommended Priority: Expand funding and maintain flexibility for public health surveillance capabilities. Current funding has allowed CDC to support seven regional laboratories with specialized capabilities to rapidly detect and identify emerging antibiotic-resistant threats. Data have led to response activities where state and local health departments worked with facilities to stop the spread of resistance, further enhance surveillance of resistant

strains, monitor emerging resistance, and validate molecular detection methods. In addition, the CDC Emerging Infections Program (EIP), which monitors antibiotic resistance across a population of about 44 million people, and measures risk by population and community, expanded in 2018 to include more sites conducting surveillance for invasive *Staphylococcus aureus* infections, candidemia, carbapenem-resistant *Enterobacteriaceae* (CRE), carbapenem-resistant *Pseudomonas*, extended-spectrum beta-lactamase producing gram-negative bacteria, and sepsis. However, even this expanded surveillance is insufficient to detect and track continually emerging and evolving threats. Additional resources are needed to support surveillance, and flexibility must be maintained as threats emerge and change over time.

Recommended Priority: **Strengthen data collection and stewardship in agricultural settings.** FDA's recently released data on antibiotics sold for use in food-producing animals during 2017 - the first year that the FDA policy to eliminate growth promotion and establish veterinary oversight went into effect - demonstrates an encouraging 33 percent reduction in sales volume compared to the previous year. However, these data are not sufficiently detailed to fully evaluate antibiotic use and resistance patterns in production settings or to assess stewardship practices. To improve the surveillance, FDA should 1) finalize its proposed biomass adjustment methodology and apply its adjustment to antibiotic sales data to provide appropriate context regarding the size and the composition of the animal population at risk of requiring treatment; 2) continue the annual reporting of data regarding the quantities of antibiotics sold for use in food-producing animals, including the provision of species-specific estimates; 3) continue and expand the collaboration with USDA, CDC and other governmental, academic, and private-sector parties to collect and evaluate on-farm data on antibiotic use, resistance and stewardship practices; 4) further define and implement the FDA goal, outlined in the agency's recent 5-year roadmap, to establish an on-farm antibiotic consumption surveillance and monitoring system; 5) harmonize antibiotic use and resistance data collection across the human, animal and environmental sector; 6) expand collaboration and support for diagnostic laboratories associated with state departments of agriculture or public health, veterinary schools, academia and the private sector.

Other elements of the Agency five-year roadmap would also support the FDA long-term efforts to reduce unnecessary antibiotic use and promote stewardship activities in production agriculture, including the Agency plans to bring all remaining antibiotic drugs under veterinary oversight, and to require drug sponsors to update antibiotic labels to reflect appropriate duration limits and indications that meet the FDA definition of judicious use. It is vital to involve growers and veterinarians in the FDA and USDA efforts to promote antibiotic stewardship. The federal government should develop and deliver effective and high-quality training and technical assistance on stewardship and antibiotic use and alternatives to agricultural stakeholders.

Goal 3: Advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria.

Recommended Priority: Reverse cuts to diagnostics reimbursement that threaten innovation and patient access to testing. CMS has reduced reimbursement for most diagnostic tests by 10 percent in 2018, and an additional 10 percent in 2019, with another 10 percent cut anticipated in 2020. Inadequate reimbursement can limit patient access to testing, which can drive increased empiric antibiotic use often in direct conflict with the goals of stewardship. Also,

inadequate reimbursement can discourage innovation of urgently needed new tests. Diagnostic developers already struggle to recoup the investment made in creating new tests and bringing them to market, and cuts to reimbursement will only exacerbate this challenge.

Recommended Priority: Provide federal resources for diagnostics outcomes studies and other tools to support provider education and appropriate clinical integration of diagnostic tests. Additional support is needed to ensure optimal utilization of diagnostic tests across health care settings. New investments, such as through NIH, CDC or Agency for Healthcare Research and Quality, to support outcomes studies would be very helpful to demonstrate to clinicians the impact specific diagnostic tests could have on patient outcomes and how to best incorporate them into stewardship activities. Further investment in provider education could help expand the appropriate use of diagnostic tests.

Recommended Priority: Increase federal funding in diagnostics research, including through NIH and the Biomedical Advanced Research and Development Authority. Current funding through BARDA and NIAID is supporting several important diagnostics studies and research projects to foster the development of innovative tests for multidrug-resistant pathogens. The AMR Diagnostic Challenge, supported by NIH and BARDA, has yielded five impressive finalists. The NIAID supported Antibacterial Resistance Leadership Group is pioneering several diagnostic studies and collaborating with companies to implement a master diagnostics protocol through which multiple tests could be validated simultaneously. Additional resources are needed to support this type of research, particularly as new resistance threats emerge.

Goal 4: Accelerate basic and applied research and development for new antibiotics and other therapeutics, including vaccines.

Recommended Priority: Develop, implement and fund a "pull" incentive to allow companies to achieve a predictable, reasonable return on investment for new antibiotics that address unmet medical needs. Incentive should align with stewardship and appropriate access goals. While some new antibiotics have been approved over the last few years—demonstrating the important positive impact of deepening federal investment through BARDA, NIH and the GAIN Act—the small pharmaceutical companies largely responsible for recent antibiotic innovation are in grave danger. Over the last 18 months, stock prices for all late-stage antibiotics companies have fallen significantly. Two companies—Achaogen and Melinta—announced massive layoffs in the second half of 2018 due to significant financial difficulties despite their recent FDA approvals. With virtually no opportunity for these companies to be acquired by large pharmaceutical companies (as these companies see no financial gain to such an investment), small companies are faced with very high infrastructure costs to bring new products to market. Securing investment to fund commercial infrastructure is extremely difficult given minimal opportunities for return on investment. If these companies fail, not only will they be unable to continue antibiotic R&D, but such failures could send even worse signals to investors and other companies, further weakening the antibiotic pipeline. We must act quickly to prevent this potentially catastrophic downturn.

Multiple policy opportunities exist to provide incentives that would allow antibiotic developers to earn a reasonable return on their investment. For example, novel reimbursement mechanisms

outside of the traditional Medicare DRG, market entry awards that are de-linked from the sales and use of the antibiotic, and refundable tax credits provided at the time of approval to repay R&D costs should all be pursued. It is likely that a combination of several incentives will be necessary to foster the robust and renewable antibiotic pipeline necessary to address current and future public health needs.

Recommended Priority: Increase funding for "push" incentives. Investments from BARDA and the National Institute of Allergy and Infectious Diseases through CARB-X and other mechanisms continue to be an essential form of support for antibiotic R&D without which even the modest progress we have seen in antibiotic development in recent years would have been impossible. Continuing to strengthen and increase these investments will be essential to broader efforts to secure the antibiotic pipeline.

Recommended Priority: Support a robust AMR research workforce. To strengthen basic and applied research on AMR and new therapeutics, we must build and support a strong scientific workforce. NIAID is a critical source of funding to support training for early career researchers, and NIAID and Congress have prioritized this effort in recent years. However, significant challenges remain. While IDSA greatly appreciates that NIAID has raised the payline for K awards—a key funding source for young investigators—from a proposed 14 to 18 for 2019, IDSA remains deeply concerned that this payline is significantly lower than the paylines for many other NIH institutes. This could make it much more challenging for an emerging scientist to pursue AMR or infectious diseases research as compared to other areas of biomedical research. Stronger investments in the pipeline of AMR physicians and scientists are just as important as investments in the antibiotic pipeline.

Goal 5: Improve international collaboration and capacities for antibiotic resistance prevention, surveillance, control and antibiotic research and development.

Recommended Priority: Strengthen and expand global AMR surveillance and ensure global alignment of systems and approaches. AMR is a global issue. Resistance threats in any country pose a danger to all of us given the interconnected nature of our world. Therefore, it is essential that we detect and track resistance threats throughout the world. The Global Health Security Agenda is providing important support for basic infectious diseases surveillance systems in targeted countries, and US investment in the GHSA must be continued. CDC AMR projects build upon this work to create AR specific surveillance capacities. Further, CDC AMR resources can extend to countries beyond GHSA to focus on geographic areas in which resistance is particularly worrisome. CDC is also helping countries build the capacity necessary to report data to the WHO Global AMR Surveillance System (GLASS), which helps to ensure uniform, comparable data.

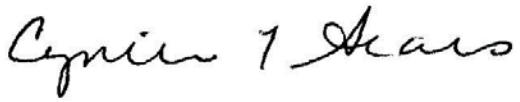
Recommended Priority: Streamline bureaucratic processes to foster multinational AMR clinical trials. To understand the global AMR burden, challenges in different settings, and the impact of interventions, it is important to study AMR globally. Further, international research allows scientists to study pathogens and mechanisms of resistance that may not be prevalent in the US yet, helping us to prepare. The CDC, NIH and DoD all have research sites around the globe. However, there are significant bureaucratic challenges for scientists aiming to conduct

multinational research with government agencies. These challenges pose significant delays to trial enrollment and can discourage many from even attempting multinational studies. Wherever feasible, efforts should be made to streamline processes for multinational AMR research.

Recommended Priority: Strengthen and expand global antimicrobial stewardship and infection prevention and control efforts. In many parts of the world, basic infection prevention and control infrastructure is severely lacking, which contributes to the preventable spread of resistant infections. With additional resources, CDC could extend its expertise to additional countries to scale up prevention efforts. Preventing infections at their source is the most effective way to prevent them from reaching the US. Similarly, we lack basic information about AMR and approaches to stewardship. Additional CDC funding to support global AMR awareness and to build capacities and expertise for stewardship in more countries will be essential to turn the tide against resistance. Such global efforts are an essential complement to domestic efforts to address AMR, as any pathogen or resistance threat anywhere in the world is merely a plane ride away from the US.

Once again, IDSA thanks you for your leadership on this important issue and looks forward to continuing to collaborate with you. Thank you for this opportunity to provide feedback, and please do not hesitate to contact us if we can be of any help in advancing solutions to antimicrobial resistance.

Sincerely,



Cynthia Sears, MD, FIDSA
President, IDSA