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July 10, 2018

Scott Gottlieb, MD

Commissioner

U.S. Food and Drug Administration

10903 New Hampshire Avenue

Building 1, Room 2217

Silver Spring, MD 20993

Seema Verma, MPH

Administrator

Centers for Medicare & Medicaid Services

7500 Security Boulevard

Baltimore, MD 21244

Dear Commissioner Gottlieb and Administrator Verma:

The Infectious Diseases Society of America (IDSAs) was pleased to see Commissioner Gottlieb's June 12 announcement regarding the urgent need to provide incentives for the research, development and judicious use of antibiotics to address the growing public health threat of antimicrobial resistance. IDSAs represents over 11,000 infectious diseases physicians and scientists, and our members are seeing increasing numbers with extremely difficult or impossible to treat infections. While we greatly appreciate ongoing work across the federal government to address this crisis, we agree wholeheartedly with Commissioner Gottlieb that additional efforts are needed to stimulate the development of antimicrobials to treat these resistant infections safely.

We were heartened to hear that Food and Drug Administration (FDA) and Centers for Medicare and Medicaid Services (CMS) are exploring new models for antibiotic reimbursement, including an approach similar to software licensing. IDSAs is pleased to offer our ideas regarding antibiotic R&D incentives and stewardship as well as feedback on the specific idea raised by Commissioner Gottlieb. As you further consider these issues, IDSAs would be happy to offer input and work to build support among key stakeholders for policies to strengthen the antibiotic pipeline and advance antimicrobial stewardship.

Need for Antibiotic R&D Incentives and Stewardship

As you know, the Centers for Disease Control and Prevention (CDC) have estimated that at least 2 million individuals in the US are sickened by antibiotic-resistant bacteria every year, and at least 23,000 die. The crisis of antimicrobial resistance threatens to undo decades of medical progress. The antibiotic pipeline is nowhere near sufficient to meet current needs or to anticipate future patient demands. Antibiotics are difficult and costly to develop, while providing very little opportunity for return on investment given their typically limited treatment courses and as they must be held in reserve for when they are truly needed. As a result, most large pharmaceutical companies have exited antibiotic R&D. Numerous bodies of experts, including the Presidential Advisory Council on

Combating Antibiotic Resistant Bacteria and the President’s Council of Advisors on Science and Technology, have recommended necessary, new incentives for antibiotic R&D.

Stewardship is equally necessary to combat resistance effectively. Studies indicate that 30 to 50 percent of antibiotics prescribed in hospitals are unnecessary or inappropriate. There is no doubt that overuse and misuse of antibiotics are driving the development of antibiotic resistance. Antibiotic stewardship programs have been found to reduce inappropriate antibiotic use, but many hospitals do not yet have stewardship programs. CDC has reported that in 2016, 69.5 percent of general acute care hospitals had implemented stewardship programs aligned with the CDC core elements for stewardship. This is an increase from 53.1 percent in 2015 and 44 percent in 2014. While this progress is encouraging, we remain deeply concerned about those facilities that have not yet implemented robust stewardship programs and assert that additional policies are urgently needed to advance the adoption of stewardship.

Overarching Principles of Antibiotic Incentives

As you consider new policies to spur antibiotic R&D, we urge you to keep the following principles in mind. An incentive should be sufficiently robust, understandable and predictable to truly motivate industry and private investors. An incentive should be targeted to the areas of greatest unmet medical need. We appreciate that federal resources are limited. We believe they should be geared toward developing new antibiotics for infections with few or no existing treatment options. Incentives also should be well aligned with efforts to promote stewardship, which is essential to protect antimicrobial clinical utility and the federal government’s investments in antibiotic R&D. There are many policy options that we urge you to consider, including market entry rewards that the federal government pays directly to antibiotic developers and transferable exclusivity, which allows an antibiotic developer to transfer a portion of the antibiotic’s exclusivity to another drug.

Potential Antibiotic Licensing Model

IDSA is pleased to offer suggestions and raise some questions about a potential new licensing model for antibiotics.

Financing and Process

IDSA would appreciate greater clarity regarding financing for the licensing model and how the process would operate. Key questions include:

- How large would the payments to the drug developer be?
- What entity would finance these payments? Would hospitals be expected to pay the licensing fees or would a federal agency provide support?
- How would insurers or patients be charged for antibiotics in this model?
- Through what process would payments be administered?

Research and modeling conducted by DRIVE-AB—a project of the European Union’s Innovative Medicines Initiative involving multiple countries, academic institutions, and

industry— developed the following estimates to demonstrate the likely impact of post-approval payments for new antibiotics that target an unmet medical need.

Post-Approval Payments	Total New Antibiotics for Unmet Needs Over 30 Years	First in Class New Antibiotics* for Unmet Needs Over 30 Years
\$0	23	4
\$400 million	27	6
\$600 million	46	11
\$1 billion	74	19

*First-in-class, new antimicrobials are especially sought as they are the most likely to have durable efficacy against multidrug resistant organisms

While it is not necessary for all of this investment to come from a single source or even from a single country, we hope these data points will be useful as you further develop your ideas. You may also wish to consider that payments may be made over a multi-year period, rather than in a single lump sum, which could provide an opportunity for the US government to hold developers accountable to the regulatory maintenance of the antibiotic as well as to commitments regarding stewardship.

Access

While stewardship is essential, it is equally vital to ensure that patients who truly need antibiotics have access to them. IDSA appreciates the concept of driving appropriate use by allowing hospitals within a new licensing agreement only a small supply of new antibiotics. Care must be taken to ensure that hospitals are provided with a sufficient quantity for appropriate use, considering the numbers of complex patients and serious infections that individual hospitals typically treat. Further, we must recognize that it is impossible to predict future outbreaks, and plans must be established to ensure that hospitals can access new antibiotics quickly when needed, regardless of whether the hospital is in the licensing agreement.

An alternative approach to drive appropriate use, provide revenue to antibiotic developers, and maintain sufficient flexibility with regard to antibiotic supply may be to charge a licensing fee for antibiotic use. Such a fee could be administered per prescription, per gram, or per day. To raise sufficient revenue to finance an incentive and to encourage appropriate use in all settings, such a fee could also be applied to antibiotic use in outpatient settings and antibiotic use in animals and agricultural settings. This approach was also recommended by the President’s Council of Advisors on Science and Technology.

Antimicrobial Stewardship Programs

IDSA believes firmly that the suggested licensing model will work best if all hospitals have antimicrobial stewardship programs that can guide the appropriate use of antibiotics. Without such an infrastructure, hospitals may struggle to manage the new antibiotics under new payment models appropriately. Stewardship programs have been found to reduce healthcare costs, reduce inappropriate antibiotic use and improve patient outcomes. Infectious disease physicians, by

virtue of their training and expertise in managing infectious diseases and antibiotic use, are uniquely well suited to lead stewardship programs that have been proven to improve patient outcomes. As you advance new payment models for antibiotics, we urge you to simultaneously advance new requirements for all hospitals to adopt ID physician-led antimicrobial stewardship programs that align with the CDC core elements as a condition of participation in the Medicare program.

Monitoring Antibiotic Use and Resistance

Monitoring antibiotic use and resistance are essential to evaluate the impact of efforts to limit antibiotic use as well as to understand how different antibiotic incentives and payment models may impact use and resistance. The CDC National Healthcare Safety Network offers an antibiotic use and resistance module through which healthcare facilities may report these data. As of January 1, 2018, over 616 facilities from 48 states are reporting antimicrobial use data and over 231 facilities from 27 states submitted at least some antimicrobial resistance data. This represents a 40 percent increase for hospitals reporting use data and a 27 percent increase for resistance data in the past six months. While the upward trend is encouraging, there are still significant gaps in reporting which hinder our understanding of antibiotic prescribing and resistance trends and how to best improve them. We strongly encourage you to require any hospital participating in a new antibiotic payment model to report data to NHSN on antibiotic use and resistance so that we can effectively track the impacts of a new antibiotic payment model.

Once again, IDSA thanks you for your attention to the serious issue of antimicrobial resistance and the urgent need to strengthen the antibiotic pipeline and promote stewardship. IDSA stands ready to assist you in this important work.

Sincerely,

A handwritten signature in black ink, appearing to read "Paul Auwaerter". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Paul G. Auwaerter, MD, MBA, FIDSA
President, IDSA