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IDSA
Infectious Diseases Society of America

June 16, 2016

The Honorable Sylvia Burwell
Secretary
US Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Secretary Burwell:

The Infectious Diseases Society of America greatly appreciates your leadership in our nation's efforts to combat antibiotic resistance through a multipronged strategy including incentivizing the development of new antibiotics and rapid diagnostics. We are pleased that you asked the Presidential Advisory Council on Combating Antibiotic Resistant Bacteria (PACCARB) for advice on antibiotic and diagnostic incentives and hope you will consider our recommendations on this important issue as well.

IDSA has been sounding the alarm about the public health crisis of antibiotic resistance and the urgent need for new antibiotics and diagnostics for over a decade, including with our 2004 Bad Bugs, No Drugs report and our 2011 Combating Antimicrobial Resistance: Policy Recommendations to Save Lives report. Our physician members are on the front lines of this crisis, seeing more and more patients who cannot be safely and effectively treated with existing antibiotics. The first US case of a colistin-resistant strain of E. coli detected in a Pennsylvania woman last month underscores the fact that we are on the very real, very frightening precipice of a post-antibiotic area. The lack of new safe and effective antibiotics jeopardizes our ability to successfully perform many life-saving medical interventions, including organ and bone marrow transplants, cancer chemotherapy, many surgeries, and the care of preterm infants. IDSA strongly supports the Administration's efforts to prevent the development of resistance through antibiotic stewardship, and IDSA members are leading stewardship programs at health care facilities throughout the country. But we must recognize that even with our best efforts, we can only slow the development of resistance. We cannot stop it entirely, and we therefore need a robust pipeline of new antibiotics.

The market has failed to sufficiently stimulate the research and development (R&D) of antibiotics for a variety of reasons. Antibiotics are difficult and costly to develop. Unlike other types of drugs, the use of antibiotics decreases their effectiveness over time due to the development of resistance by the bacteria that infect patients. Antibiotics are typically priced low compared to other new drugs, used for a short duration, and held in reserve to protect their utility, making them far less economically viable investments for companies than other types of drugs. In 1990, there were nearly 20 pharmaceutical companies with large antibiotic R&D programs. Today, there are only 2 or 3 large companies with strong and active programs and a few small companies with more limited programs.

IDSA's 2015 Better Tests, Better Care: Next Generation Diagnostics report calls attention to the equally urgent need for new diagnostic tests that provide rapid results, are easy to use, and accurately identify the pathogen causing an infection and its antimicrobial susceptibility, in order to guide initial antibiotic therapy. By guiding appropriate antibiotic use, diagnostics are crucial to effective stewardship. Better diagnostics are also important for identifying patients for whom isolation or other infection control measures are needed when first seen, improving the tracking of outbreaks and emerging infectious disease threats. In addition, rapid diagnostics can help identify patients who are eligible for antibiotic clinical trials. But greater investment and improved regulatory policies are needed to ensure that scientific advancements translate into the development and use of new diagnostics.

Economic Incentives for Antibiotics

Despite stronger support through existing mechanisms such as the Generating Antibiotic Incentives Now (GAIN) Act and increased funding through the Biomedical Advanced Research and Development Authority (BARDA) and National Institutes of Allergy and Infectious Diseases (NIAID), antibiotics remain an economically unattractive and infeasible investment for many companies. More incentives are needed to help level the playing field and allow antibiotics to compete against more profitable, easier-to-develop drugs for companies' resources.

As part of the National Action Plan for Combating Antibiotic Resistant Bacteria (CARB), the Administration pledged to release a report and provide recommendations on antibiotic incentives. Multiple stakeholders continue to call for the release of the report and recommendations to help guide needed progress in this area.

IDSA is extremely encouraged by recent announcements by BARDA and NIAID regarding the establishment of a biopharmaceutical accelerator to support antibiotic R&D. IDSA has long called for such a public-private partnership to help encourage companies to pursue antibiotic R&D and bring urgently needed new antibiotics to market.

IDSA is also very pleased that Congress maintains strong bipartisan support for antibiotic incentives. The Reinvigorating Antibiotic and Diagnostic Innovation (READI) Act, H.R. 3539, was introduced by Representatives Boustany (R-LA) and Thompson (D-CA) and has been endorsed by over 40 organizations and companies. This bill, modeled after the successful Orphan Drug law, would provide a 50% tax credit for new antibiotics that would treat a serious or life-threatening infection and address an unmet medical need. An analysis of this bill by Ernst and Young indicated this would add an additional 5-6 new antibiotics to the pipeline every year.

Regulatory Incentives for Antibiotics

While economic incentives are critical, we must also address regulatory barriers to antibiotic R&D to ensure there is a feasible path to Food and Drug Administration (FDA) approval for the most urgently needed new antibiotics. Some of the most deadly, highly resistant pathogens are currently infecting relatively small numbers of critically ill patients—making it extremely challenging and sometimes impossible to enroll a sufficient number of patients in a traditional large trial. The Promise for Antibiotics and Therapeutics for Health (PATH) Act, by Senators

Orrin Hatch (R-UT) and Michael Bennet (D-CO) would allow new antibiotics that treat a serious or life-threatening infection and address an unmet medical need to be studied in smaller, more rapid clinical trials and approved only for the limited population of patients in whom the studies are done and who need them most.

Not only would this approach facilitate the R&D of urgently needed new antibiotics, it would also help guide the appropriate use of these new antibiotics. The drugs' narrow indication and clear "limited population" labeling would signal to the healthcare community the importance of using these drugs judiciously. Further, PATH would direct monitoring of antibiotic use and FDA pre-review of any promotional materials for limited population antibiotics.

In April the Senate Health, Education, Labor and Pensions Committee passed the PATH Act with strong bipartisan support, and IDSA is urging the full Senate to vote upon the bill right away. Similar legislation was included in the 21st Century Cures Act, which passed the House of Representatives last year.

Incentives for Diagnostics

New policies are also needed to stimulate diagnostic R&D. Diagnostics continue to face high R&D costs. For example, many laboratories available to conduct diagnostics research lack the particular expertise needed to evaluate specific new tests, requiring companies to provide costly training and supervision. Locating or developing a sufficient number of laboratories with the appropriate expertise to process the large number of samples needed for a clinical trial is becoming too costly for many companies to pursue. Further, participating laboratories may need to run multiple tests in order to validate a new diagnostic. This strategy is very expensive, dramatically increasing the cost of clinical trials. The cost of one effective validation method, nucleic acid sequence analysis, can add over $100,000 to the cost of a clinical trial. That may be prohibitive, particularly for smaller companies. In addition, accessing test materials for rare pathogens also can be very difficult. Even when such crucial samples are available, the cost of accessing them has become prohibitive, in many cases.

In addition to targeting antibiotic R&D, the READI Act would also provide a 50% tax credit for phase two and three clinical trials for new diagnostic tests that provide results in four hours or less. In fact, the READI Act is the first antibiotic incentives bill that includes an explicit provision to stimulate diagnostic R&D as well.

In addition to high R&D costs, diagnostics often do not provide significant return on investment. If new tests are more expensive than older counterparts, they often do not receive reimbursement levels that cover the cost of the test until a new procedural code has been assigned. Even when new codes are assigned, they still often do not adequately reimburse the full cost of testing. IDSA greatly appreciates that the Protecting Access to Medicare Act (PAMA) of 2014 directing the Centers for Medicare and Medicaid Services (CMS) to make improvements to diagnostic reimbursement, including forming an expert advisory panel to guide CMS activities in this area and collecting data from laboratories on payment rates for existing tests to help inform new reimbursement rates. Unfortunately, the expert panel does not include sufficient representation from the infectious diseases field. However, IDSA has continued to engage with CMS on this

important issue to provide ID input. Last year, CMS published a proposed rule requiring laboratories that receive 50% of their Medicare revenues and over $50,000 annually for services billed under the Clinical Lab Fee Schedule (CLFS) or Physician Fee Schedule (PFS) to report reimbursement rates and volumes on which the new weighted median reimbursement level for a test will be calculated. These thresholds exclude nearly all hospital based laboratories, which may have higher costs than commercial laboratories due to differences in volume of tests. Exclusion of hospital based laboratories may result in inappropriately low new reimbursement rates for tests, making it difficult for physicians to access these tests and even creating disincentives for companies to develop new tests. IDSA believes that reporting requirements may be overly burdensome for hospital laboratories. To help ensure that CMS collects data for the purposes of determining reimbursement rates that reflects the broad scope of the market, and the value of local, rapid laboratory services that are critical to impact ID patient care early in illness, IDSA has recommended that CMS seek data from private insurers on the rates paid to hospital laboratories and physician offices for diagnostic tests. If that is not possible, IDSA recommends CMS consider a mechanism that allows hospital laboratories and physician offices to submit their information voluntarily.

ID Physician-Scientists

While IDSA strongly supports the Administration's focus on incentivizing antibiotic and diagnostic R&D, we must also underscore the need for a robust pipeline of infectious diseases (ID) physician-scientists—the very people who will be needed to undertake the research necessary to bring forward new antibiotics and diagnostics. Like many medical and scientific societies, patient organizations and other advocates, IDSA is greatly concerned that fewer and fewer young people are pursuing research careers. Significant student loan debt and concerns about the ability to secure research funding are key drivers of this problem. We continue to support robust federal funding for research through the National Institutes of Health (NIH), Patient Centered Outcomes Research Institute (PCORI), Agency for Healthcare Research and Quality (AHRQ), Department of Defense (DoD), and other agencies.

IDSA was also encouraged by the NIH Physician-Scientist Workforce Working Group Report, which was released in 2014 and made a number of recommendations that we support, including novel pilot approaches to increase the award rate for new investigators, a new grant mechanism to facilitate the transition from training to independence, and expansion of loan repayment programs. We encourage you to remain mindful of the need for ID physician scientists to lead R&D efforts for new antibiotics and diagnostics, and hope you will work with the NIH to advance these recommendations.

Unfortunately, the future of ID physician-scientists faces additional challenges because fewer and fewer young physicians are pursuing ID specialization. Data from the National Residency Match Program (NRMP) indicate a disturbing decline in the number of individuals applying for ID fellowship training, with 342 applicants in the 2010-2011 academic year and only 221 in 2016-2017. For 2016-2017, only 65% (or 218 out of 335) of available ID fellowship positions filled. In many other specialty areas, all, or nearly all, available fellowship positions are typically filled.

In 2014, IDSA surveyed nearly 600 internal medicine residents about their career choices, and very few planned to go into ID. A far higher number reported that they were interested in ID but chose another field instead. Among that group, salary was the most often cited reason for not choosing ID. Average salaries for ID physicians are significantly lower than those for most other specialties and only slightly higher than the average salary of general Internal Medicine physicians, even though ID training and certification requires an additional 2-3 years. Young physicians' significant debt burden ($200,000 average for the class of 2014) is understandably driving many individuals toward more lucrative specialties, often with faster paths to practice.

Over 90% of the care provided by ID physicians is accounted for by evaluation and management (E&M) services. These face-to-face, cognitive encounters are undervalued by the current payment systems compared to procedural practices, which accounts for the significant compensation disparity between ID physicians and specialists who provide more procedure-based care. IDSA is urging the Centers for Medicare and Medicaid Services (CMS) to undertake research to identify better inputs to value E&M codes in the cognitive specialties such as ID

Once again, IDSA greatly appreciates your tremendous commitment to combating antibiotic resistance and stimulating the development of urgently needed new antibiotics and diagnostics. Your leadership can drive the policy changes needed to protect public health and save lives. IDSA is grateful for the opportunity to work with you on these important efforts. Should you have any questions, please feel free to contact Amanda Jezek, IDSA's Vice President for Public Policy and Government Relations, at ajezek@idsociety.org.

Sincerely,

Johan S. Bakken, MD, PhD, FIDSA
IDSA President

Cc: Presidential Advisory Council on Combating Antibiotic Resistant Bacteria (PACCARB)