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May 23, 2017

Scott Gottlieb, MD
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Building 1, Room 2217
Silver Spring, MD 20993

Dear Commissioner Gottlieb,

Congratulations on your confirmation as U.S. Food and Drug Administration (FDA) Commissioner. As you assume this important role, I want to offer the Infectious Diseases Society of America (IDSAs) as a resource and a partner for advancing policies to improve patient care, protect public health, and promote biomedical research and innovation. As a fellow physician, I and the members of IDSAs appreciate the medical expertise and passion for patients that you will bring to this role.

IDSAs represents over 10,000 infectious diseases (ID) physicians and scientists devoted to patient care, prevention, public health, education, and research in infectious diseases. Our members care for patients with or at risk of serious infections such as HIV, hepatitis C virus (HCV), infections caused by antimicrobial resistant pathogens, and opportunistic infections afflicting transplant patients and other immunocompromised individuals. ID physicians are also on the front lines responding to public health emergencies recently examples include outbreaks of Ebola, Zika, MERS-CoV, and pandemic influenza viruses.

With the goals of improving patient safety and stimulating cutting edge research, IDSAs advocates for developing urgently needed new antimicrobial drugs, diagnostics, and vaccines. IDSAs members serve on a variety of federal advisory committees, including the Presidential Advisory Committee on Combating Antibiotic Resistant Bacteria (PACCARB), FDA's Antimicrobial Drugs Advisory Committee (ADAC), the Advisory Committee on Immunization Practices (ACIP), the National Vaccine Advisory Committee (NVAC), and the National Preparedness and Response Science Board. We look forward to collaborating with you and your staff on all relevant infectious diseases issues. We also wish to share more information about two critical priority areas: antimicrobial resistance and the urgent need to stimulate new antibiotic research and development (R&D), and infectious disease diagnostics issues.

Antimicrobial Resistance and Antibiotic R&D

IDSAs has been sounding the alarm on the public health crisis of antimicrobial resistance for well over a decade, beginning with our [2004 Bad Bugs, No Drugs report](#). Our recommendations served as a key basis for significant new

federal investment to combat antimicrobial resistance beginning in 2016 with Congress's approval of new funding for this priority. As you know, pathogens are increasingly resistant to available antimicrobial drugs, making some previously easily treatable infections life-threatening and requiring much longer hospital stays.

Simultaneously, [antibiotic research and development](#)¹ (R&D) has dwindled, due to regulatory and economic challenges. From a regulatory perspective, it can be difficult to enroll a sufficient number of patients with targeted infections for antibiotic clinical trials. Moreover, feasible regulatory pathways for developing the most urgently needed new antibiotics to treat the most highly resistant infections have been elusive. Bad economic realities for antibiotics compound the problem. Particularly those for the growing unmet needs, antibiotics are difficult and costly to develop, used for a short duration, inexpensive compared to most other types of drugs, and appropriately held in reserve to protect their utility from the development of resistance.

We were encouraged to see this issue raised during your Senate confirmation hearing, and empathize with your experience of having lost patients to infections caused by multidrug resistant organisms. IDSA launched the [Faces of Antimicrobial Resistance](#)² campaign to demonstrate the real-life impact of multidrug resistant infections on patients, and we are eager to work with you to combat this serious threat to patients.

The 21st Century Cures Act included a provision that enjoyed broad bipartisan support in Congress to establish a new limited population antibacterial/antifungal development (LPAD) approval pathway for new antibiotics and antifungals that treat a serious or life-threatening infection and address an unmet medical need. Under LPAD, new antibiotics and antifungals may be studied in smaller, more rapid clinical trials. If FDA approval is gained, it is only for the limited population of patients who are most in need. This approach is essential because some of the most dangerous and highly resistant pathogens are currently occurring in a relatively small number of patients. According to statute, LPAD drugs must be clearly labeled as "limited population," their promotional materials must be pre-reviewed by the FDA, and their use must be monitored. These safeguards help ensure these drugs are used appropriately. In addition, antimicrobial stewardship programs led by expert ID physicians will be essential for ensuring the optimal use of these and all antimicrobial drugs. We look forward to supporting and advising on FDA's implementation of this important new policy that should speed the development of new antibiotics and antifungals.

We are pleased that over the past year the FDA has already taken steps to create a more feasible approach for developing antibiotics that address unmet needs, including narrow spectrum antibiotics and even antibiotics that treat a single pathogen. Narrow spectrum agents would be extremely useful to treat infections with unmet needs without causing undue collateral damage, such as fostering resistance or causing *Clostridium difficile* infections,

¹http://www.idsociety.org/uploadedFiles/IDSA/Policy_and_Advocacy/Current_Topics_and_Issues/Advancing_Product_Research_and_Development/Bad_Bugs_No_Drugs/Press_Releases/IDSA%20Antibiotic%20Incentives%20Infographic%202016%20Final.pdf

²<http://www.idsociety.org/uploadedFiles/IDSA/FOAR/FOAR%20Report%201-up%20final.pdf>

associated with broad spectrum antibiotics. Last July, the FDA held a productive [public workshop](#)³ on this topic, in which participants acknowledged the challenges associated with clinical development of these antibiotics, but emphasized the urgent need to find a path forward. This April, the FDA Antimicrobial Drug Advisory Committee held a [meeting](#)⁴ on this topic, at which IDSA was honored to [present](#).⁵

IDSA recently published a [white paper](#)⁶ on this issue. Key recommendations focused on novel and pragmatic approaches to feasible trial designs for narrow spectrum antibiotics that meet unmet needs by combining four ideas: small clinical datasets (made more possible by 21st Century Cures), pharmacokinetic/pharmacodynamic data, well validated animal models, and well validated external controls. While we recognize that there may be criticism from some stakeholders surrounding this type of an approach, we must emphasize the following in response: 1) ID clinicians are already having to make prescribing decisions based upon incomplete data due to the increasing number of difficult-to-treat infections and our rapidly depleting antibiotic arsenal; 2) safeguards such as antibiotic stewardship programs and those included in 21st Century Cures will provide extremely valuable tools to help clinicians optimally use antibiotics, including those developed through non-traditional pathways; and 3) the status quo for antibiotic development is not an option. Given the increasing numbers of patients who are running out of therapeutic options for their life-threatening infections, the risk of inaction far outweighs the risks associated with more nimble antibiotic development approaches.

While an improved regulatory climate for antibiotic R&D is essential, it alone is insufficient to spur the development of the life-saving new therapeutics our patients desperately need. While providing economic incentives (such as tax credits, market entry rewards, etc.) is not under FDA's purview, we hope that you will utilize your new role to help highlight the need for new antibiotics and create a sense of urgency among Congress and your colleagues in the administration to advance policies that will stimulate antibiotic R&D. Likewise, we hope you will be a champion for broader solutions to address antimicrobial resistance in both human and animal health.

[Diagnostics](#)⁷

IDSA has long stressed the importance of innovation producing new diagnostic tests for the care of patients suffering from infectious diseases. Such improved diagnostics can allow physicians to rapidly identify the pathogen infecting a patient and prescribe the most appropriate treatment, increasing the likelihood of a positive patient outcome. Notably, high quality ID diagnostics have a unique ability to protect the broader public health by alerting

³ <https://www.fda.gov/drugs/newsevents/ucm497650.htm>

⁴ <https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/ucm551361.htm>

⁵ <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM553385.pdf>

⁶ <https://academic.oup.com/jid/article/3798533/White-Paper-Developing-Antimicrobial-Drugs-for?searchresult=1>

⁷ http://www.idsociety.org/uploadedFiles/IDSA/Policy_and_Advocacy/Current_Topics_and_Issues/Diagnostics/Better%20Tests%20Better%20Care.pdf

health officials of potential ID outbreaks and guiding the appropriate clinical use of antimicrobial drugs to help limit the development of resistance.

We hope that FDA will work to ensure appropriate regulatory pathways for advancing critical ID diagnostics such as laboratory developed tests (LDTs), ID next generation sequencing (ID NGS)-based tests, diagnostics for viruses afflicting patients with transplants, and other areas of unmet need. IDSA would like to offer its members' expertise to help appropriately classify tests' risk. We were greatly encouraged by the [FDA's November 2016 panel meeting](#)⁸ regarding classification of diagnostic tests for transplant-associated viruses. We urge you to advance efforts to classify such tests as Class II. As we outlined in our [comments](#)⁹, these tests have years of robust data supporting their use that demonstrate their positive impact on patient outcomes. The potential risk of use is mitigated as they are but one tool interpreted in a broader clinical context. Importantly, a Class II classification is likely to spur needed innovation in this area.

IDSA also strongly [supports](#)¹⁰ FDA's continuing efforts to promote timely and coordinated development of antimicrobial drugs and antimicrobial susceptibility tests (ASTs) that are vital for providing high quality patient care through guiding appropriate antibiotic use. Significant delays between the approval of a new antimicrobial drug and the availability of susceptibility testing for that drug currently greatly hamper clinicians' ability to use new drugs. FDA's [September 2016 workshop](#)¹¹ on AST development highlighted many of the challenges in this area. We look forward to continued engagement with FDA to address this issue. Both the FDA's draft guidance on the coordinated development of ASTs and the 21st Century Cures Act provision aimed at speeding updates of antimicrobial susceptibility breakpoints are important steps forward. We encourage you to consider additional opportunities to speed the development and the approval of ASTs for progress that should also include developing clinical trial networks and providing increased economic incentives for test developers.

In response to [questions](#)¹² about LDTs submitted by Senator Patty Murray during your confirmation process, IDSA was pleased to see you acknowledge the need to balance Clinical Laboratory Improvement Amendments (CLIA) and FDA regulatory requirements encouraging innovation while making sure patients and providers can be confident in the clinical validity of test results. We agree with your [assertion](#)¹³ that different types of

⁸<https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/MicrobiologyDevicesPanel/ucm515517.htm>

⁹http://www.idsociety.org/uploadedFiles/IDSA/Policy_and_Advocacy/Current_Topics_and_Issues/Diagnostics/Letters/IDSA%20Comments%20on%20FDA%20Notice%20of%20Meeting%20RE%20Microbiology%20Devices%20Panel%20102616.pdf

¹⁰http://www.idsociety.org/uploadedFiles/IDSA/Policy_and_Advocacy/Current_Topics_and_Issues/Advancing_Product_Research_and_Development/Antimicrobials/Letters/IDSA%20Comments%20to%20FDA%20RE%20AST%20Devices%20111716.pdf

¹¹<https://www.fda.gov/drugs/newsevents/ucm512519.htm>

¹²<http://www.cq.com/flatfiles/editorialFiles/healthBeat/reference/docs/4042403.pdf>

¹³<https://www.forbes.com/sites/scottgottlieb/2016/04/28/theranos-woes-offer-lesson-in-how-labs-should-be-regulated/#51e1cf5048d9>

regulation are required for new laboratory tools (such as ID LDTs developed by academic and not-for-profit laboratories) than for laboratory services, which are designed for commercial use by for-profit developers. We also understand that increased regulation of LDTs may be appropriate to ensure safety and effectiveness in select cases, but for the vast majority of ID LDTs there is no data to support the assertion that these cause harm. Access to rapid diagnostic tests for rare diseases, public health emergencies, antimicrobial resistance, and other unmet needs will improve patient care and advance our defenses against ID threats. IDSA looks forward to continuing to work with FDA and Congress to help determine an appropriate risk-based pathway for the regulation of ID LDTs that does not suffer from an over-reliance on the premarket review process.

IDSA recognizes the significant demands on your time and attention. Preventing and treating infectious diseases are central to high quality patient care and to improving our nation's health. We greatly appreciate your medical expertise and look forward to opportunities to work with you.

Sincerely,

A handwritten signature in cursive script that reads "Bill Powderly". The signature is written in dark ink and is positioned above the typed name and title.

William G. Powderly, MD, FIDSA
President, IDSA