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IDSA
Infectious Diseases Society of America

August 14, 2012

The Honorable Kathleen Sebelius
Secretary, Department of Health & Human Services
200 Independence Avenue S.W.
Washington, DC 20201

Dear Secretary Sebelius:

On behalf of the Infectious Diseases Society of America (IDSA), which represents nearly 10,000 infectious diseases physicians and scientists, I write regarding Section 805 of the Food and Drug Administration Safety and Innovation Act (FDASIA). As you know, this provision calls upon the Department of Health and Human Services (HHS) to issue a study in no later than five years to reassess qualified infectious disease product incentives. I write to supply additional information to assist the Department in implementing the Section.

IDSA's members care for patients of all ages with serious infections, including an increasing number of patients with serious and life-threatening antimicrobial-resistant infections against which we have frighteningly few, and in some cases no, effective therapeutics available. Addressing the anemic antimicrobial pipeline and combating antimicrobial resistance have been IDSA's top policy priorities for the past decade and have included our launch of the "Bad Bugs, No Drugs" advocacy campaign in 2003; "the 10 x '20 initiative" in 2010, which seeks the development of ten new systemic antibacterial drugs by 2020; and recently a new website, www.AntibioticsNow.org, that highlights the growing number of patients succumbing to serious and life-threatening drug-resistant bacterial infections.

IDSA strongly advocated for the inclusion of Section 805 in FDASIA, because it is critical to ensure that public policy keeps pace with scientific advancements and emerging threats. The study HHS issues as a result of the Section 805 provision should build upon current knowledge of the economic, regulatory and scientific challenges to antibiotic research and development (R&D) in the United States and address which incentives, or combination of incentives, will serve as "game-changers" in this space. Multiple economic models have indicated that a variety of push and pull incentives are needed to effectively stimulate antibiotic R&D. Advancing the development of related diagnostics also is essential both to antibiotics' development as well as appropriate use.

Public Private Collaborations

New risk-sharing approaches are necessary to overcome existing challenges to antibiotic R&D and to yield the antibiotics our patients desperately need. In IDSA's opinion, public private collaborations (PPC) will be part of the ultimate solution.

In FDASIA, Congress recognized the potential benefits PPCs can provide and explicitly called upon HHS to examine PPCs through the study Section 805 requires. We hope HHS's study will include a review of the existing European Union (EU) PPC, the NewDrugs4BadBugs initiative, which is focused on antibiotics for serious resistant pathogens. The effort was launched through the EU's Innovative Medicines Initiative (IMI), and will target priority pathogens: Gram-negative pathogens (e.g., Enterobacteriaceae, *Acinetobacter*, *Pseudomonas*), *Clostridium difficile*, and oral agents for methicillin-resistant *Staphylococcus aureus* (MRSA).

The IMI PPC is built on the premise that the extent of action required to significantly impact the scientific challenges facing antibiotics is too great for any single entity. An unprecedented sharing of information (among companies, academic institutions and government entities) will be a significant and valuable outcome from the EU initiative. A committee will be formed to develop a website that can facilitate the sharing of information, including specifics on failed targets and clinical trial data. The focus of the overall program will be to develop better networks of researchers, create more fluid trial designs and provide incentives for companies to participate. The diversity of skill sets needed to tackle these challenges requires contributions from a number of key stakeholders.

IMI's Call for Proposals[1] was issued in May 2012. IMI will provide €119 million ($149.6 million) in funding, while the private companies involved – GlaxoSmithKline Inc., Sanofi, AstraZeneca PLC, Janssen Pharmaceutica NV, and Basilea Pharmaceutica International, Ltd. – will contribute €114.7 million ($144.1 million) for the first phase of the initiative. Over the next 7 years, the IMI expects this initiative to utilize up to €600 million ($741.84 million) in public and private funding combined.

Government leadership is necessary to launch a PPC. Dr. David Payne, head of GSK's Antibacterial Discovery Performance Unit, noted that it was European Commission leaders' commitment to do something concrete to address the antibacterials R&D problem that got the IMI PPC up and running.[2] With this same goal in mind, IDSA urges **HHS to provide Congress with recommendations for how the U.S. could build a PPC that works in collaboration with or parallel to the EU initiative. IDSA recommends that HHS also work with the Department of Defense (DoD) on this collaboration, given that DoD has a key role and is already working to address serious and life threatening infections being faced by soldiers in combat. Finally, HHS should consider opportunities to establish PPCs for related diagnostics given their importance to the future development and appropriate use of antibiotics.**

Additional Incentives and Timing of Study Release

In reviewing the need for antibiotics and related diagnostics incentives, IDSA encourages HHS to think broadly. For example, **IDSA encourages HHS to support the creation of R&D tax**

[1] http://www.imi.europa.eu/content/6th-call-2012 and http://www.imi.europa.eu/events/2012/05/11/imi-6th-call-webinars

[2] LaMotta, Lisa. "Antibiotic Policy Solutions An Ocean Apart Between U.S., EU," *The Pink Sheet Daily*, May 24, 2012.

incentives such as the 50% credit that has successfully spurred orphan drug R&D. However, we would make such a credit transferable so that start-up companies with no profit might sell credits earned and then reinvest that income into additional R&D. We also would apply the tax credit to related diagnostics. In addition, **further strengthening the Biomedical Advanced Research and Development Authority (BARDA) and National Institute of Allergy and Infectious Disease (NIAID) investments in antibiotic and related diagnostic R&D and announcing that BARDA and NIAID investment in these areas will remain priorities for the foreseeable future will lead to strengthened private investment as well.** IDSA has called upon NIAID to increase its funding for antibiotic and related diagnostic R&D to $500 million annually.

Although Section 805 calls for HHS to release its report in no later than five years, IDSA strongly urges the Department to move much more quickly. **Waiting a full five years to complete the HHS report would fail to recognize the urgency of the antibiotic crisis and would miss the opportunity to provide valuable information to Congress in advance of congressional consideration of the next Prescription Drug User Fee Agreement (PDUFA) reauthorization.** The Eastern Research Group (ERG) is expected to release its HHS-commissioned study on antibiotic incentives within the next six months, and it would be to everyone's benefit if HHS published its study within a reasonable timeframe thereafter in order to build upon the ERG effort.

Regulatory Disincentives

Regulatory disincentives resulting from lack of clear and feasible FDA antibacterial clinical trial guidance for industry has become a towering impediment to antibiotic approvals in this country. Although FDA continues to work to address the problem, the impact on antibiotic development over the past decade has been staggering. IDSA continues to work with FDA and industry stakeholders to address the regulatory issues, but the solution ultimately is in FDA's hands and requires continued leadership on the agency's part. Recently IDSA proposed the establishment of a Limited Population Antibacterial Drug (LPAD) approval mechanism, which has garnered support within the agency, as well as from public health and medical societies, and companies focused on antibacterial R&D[3]. **We genuinely hope that LPAD will be adopted and other remaining regulatory issues will be resolved long before the next PDUFA reauthorization and HHS' report is submitted to Congress. In the meantime, IDSA welcomes the opportunity to provide input to HHS on this topic so that the report required by Section 805 incorporates the reflections of IDSA leaders who have been concerned about and working to address the regulatory issues for more than a decade.**

Antimicrobial Stewardship

In addition to providing incentives to spur antibiotic R&D, Congress also recognized it is critical to protect the federal investment in these precious drugs by ensuring they do not rapidly become obsolete due to the overuse that drives resistance. As you know, Section 805 directs HHS to examine the adoption of programs to measure the use of antibacterial drugs in health care settings

[3] http://www.idsociety.org/2012_LPAD_Proposal_Backing/

along with the implementation and effectiveness of antimicrobial stewardship protocols across all health care settings. Further, HHS is to make recommendations for ways to encourage further development and establishment of stewardship programs.

Antimicrobial stewardship refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy and route of administration. The major objectives of antimicrobial stewardship are to achieve best clinical outcomes related to antimicrobial use while minimizing adverse events and the emergence of antimicrobial resistance. Antimicrobial stewardship also may reduce excessive costs attributable to suboptimal antimicrobial use.

IDSA, in conjunction with the Society for Healthcare Epidemiology of America (SHEA), and the Pediatric Infectious Diseases Society (PIDS) released a joint policy statement on antimicrobial stewardship[4] in which **we recommended that the Centers for Medicare and Medicaid Services (CMS) require participating healthcare institutions to develop and implement physician-led antimicrobial stewardship programs in all healthcare facilities, including hospitals, long-term care facilities, long-term acute care facilities, ambulatory surgical centers, and dialysis centers. We urge HHS to consider and adopt this position as its own.**

Conclusion

IDSA understands that HHS is working to address multiple priorities related to FDASIA's implementation. However, if the U.S. fails to act quickly to address the dying antibiotic pipeline, we risk losing many more patients to devastating antibiotic-resistant infections and further eroding our competitive edge as more companies focus their antibiotic R&D in other countries. Thus, we would appreciate the Department's prompt action in undertaking the study and producing the report FDASIA requires under Section 805.

Continuing to evaluate current approaches, including the recently enacted incentives, as well as additional incentives is critical to ensure that the U.S. is maximizing the impact of its investments in this area and devoting sufficient resources to the areas of greatest need. IDSA stands ready to work with you in these endeavors, and we are happy to provide you with any useful information we can as you develop the study and report on antibiotic incentives and antimicrobial stewardship. Should you have any questions, please contact Robert J. Guidos, JD, IDSA's vice president for public policy and government relations at 703-299-0202 or rguidos@idsociety.org.

Sincerely,

Thomas G. Slama MD

Thomas G. Slama, MD FIDSA
President

[4] *Infection Control and Hospital Epidemiology* , Vol. 33, No. 4, Special Topic Issue: Antimicrobial Stewardship (April 2012), pp. 322-327
http://www.jstor.org/stable/10.1086/665010

cc: Margaret Hamburg, M.D., Commissioner, Food and Drug Administration
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