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# IDSAs

Infectious Diseases Society of America

February 9, 2015

Representative Fred Upton  
Chairman  
Energy and Commerce Committee  
2183 Rayburn House Office Building  
Washington, DC 20515

Representative Diana DeGette  
Ranking Member  
Subcommittee on Oversight and Investigation  
Energy and Commerce Committee  
2368 Rayburn House Office Building  
Washington, DC 20515

Dear Chairman Upton and Representative DeGette:

On behalf of the Infectious Diseases Society of America (IDSAs), I write to thank you for the hard work to date by you and your staff in compiling a comprehensive draft to advance the 21<sup>st</sup> Century Cures Initiative. IDSAs appreciates the opportunity to comment on the January 26, 2015 discussion draft and is particularly pleased that this draft represents a strong commitment to advancing the development of urgently needed new antibiotics. Our patients continue to suffer from multi-drug resistant infections that we cannot effectively treat with our current arsenal of antibiotics, and provisions in this draft bill can have a significant impact for such patients. Further, antibiotic research and development (R&D) faces very unique scientific, economic and regulatory challenges that necessitate specific, targeted federal policies. In addition, we appreciate the draft bill's focus on diagnostics and vaccines, and are pleased to offer additional ideas to strengthen the bill in these areas.

More broadly, we greatly appreciate the Committee's commitment to fostering overall research. These are critical priorities worthy of additional investment. We are eager to support policies that will maintain America's status as a leader in biomedical innovation, and to do so, we believe it is critical that our leading federal agencies, such as the National Institutes of Health (NIH), maintain their authority to drive research based upon the best available science and evolving scientific opportunities.

Below please find specific comments on individual sections of the discussion draft. We hope the Committee will find these helpful as you continue working on this important effort.

## **Title I, Subtitle D—Antibiotic Drug Development**

### *Sec. 1061 Approval of certain drugs for use in a limited population of patients*

IDSAs enthusiastically supports the creation of a new limited population drug approval pathway for antibacterial and antifungal drugs to treat serious or life-threatening infections where there exists an unmet medical need. We thank the Committee for including this important provision in the Cures discussion draft, and urge you to continue to advance this important component as you work toward bipartisan introduction of the legislation. In September, the President's Council of Advisors on Science and

Technology (PCAST) issued a Report to the President on Combating Antibiotic Resistance that also recommended this approach. Last Congress, [multiple stakeholders](#) joined together to express support for this concept as addressed in the bipartisan Antibiotic Development to Advance Patient Treatment (ADAPT) Act. This provision would speed patient access to important antibacterial and antifungal drugs to treat serious or life-threatening infections where there exists an unmet medical need by allowing such drugs to be approved based upon smaller, more rapid clinical trials. As you may know, it is often not feasible for these antibiotics to be developed using traditional, large clinical trials due to the limited numbers of patients in whom the targeted infections currently occur. While IDSA strongly supports advancing this provision and appreciates the committee's work on this provision, we urge the Committee to consider improving this language by addressing the following issues.

Given that this provision would establish a new Food and Drug Administration (FDA) approval pathway, we recognize that there has been interest in clarifying the process that companies wishing to pursue a new drug approval under ADAPT would utilize with FDA, and we appreciate the Committee's efforts to clarify what such a process may look like in this provision. We agree with the goal of fostering productive communications between FDA and drug sponsors and appreciate the committee's and ADAPT Act sponsors' work to clarify this process. However, like you, we want the provision to be feasible to ensure its successful implementation.

- Page 37, lines 4-11 and lines 16-22, and page 38, lines 15-22: We are unclear whether this language could require the FDA to agree upon (1) postapproval commitments, (2) the efficacy or safety data necessary to support expansion of the approval or licensure of the drug beyond use in the limited population, and (3) the clinical development program before a new drug application is even submitted. We agree with the need to hold meetings and discuss such issues as early as possible, but recommend that specific references to making agreements during such early meetings be removed from the discussion draft as we are concerned that asking FDA to make such agreements so early in the process, before reviewing relevant data in the application, could result in this important new pathway not being fully utilized.

In addition, on page 36, lines 12-16, the draft bill specifies timeframes within which FDA must hold particular meetings with drug sponsors. IDSA appreciates efforts to speed this process and ultimately shorten the time it takes for urgently needed new antibiotics to reach patients. However, we also recognize that FDA should have flexibility to respond to unpredictable emergencies, such as the current Ebola outbreak. We encourage the Committee to continue working with FDA to ensure this language provides that necessary flexibility, while still maintaining the inherent goals of this legislation.

It is important that drugs approved under this pathway be used judiciously, particularly given that they will be approved for limited populations, not the broader population of patients with non-serious infections that can be treated effectively with existing drugs. Appropriate use is critical to deliver optimal patient care and limit the development of drug resistance. IDSA strongly supports provisions in the draft legislation to help guide appropriate use, including pre-review of marketing materials and monitoring the use of drugs approved under this pathway, as well as patterns of resistance. We also support the language on page 39, lines 8-16, which would

require the labeling of drugs approved under this pathway to prominently include the following statement: “This drug is indicated for use in a limited and specific population of patients.” However, IDSA would like to see the Committee strengthen this language by requiring the labeling of these drugs to also include a prominent visual element to make it simple for the health care community to quickly recognize that these drugs are approved for a limited population and must be used prudently.

*Sec. 1062 Susceptibility test interpretive criteria for microbial organisms*

IDSA strongly supports this provision to ensure that susceptibility test interpretive criteria (commonly referred to as “breakpoints”) for antimicrobial drugs are regularly updated in a timely fashion, and that updated breakpoints are made publicly available via FDA’s website. A breakpoint provides information that helps to predict whether a patient infected with a specific pathogen will have a good clinical response to standard doses of a drug (i.e., whether an antimicrobial drug is expected to successfully treat an infection). Prescribers need accurate and up-to-date breakpoints to guide the selection and dosage of antimicrobial drugs to maximize patients’ chances for positive clinical outcomes. Breakpoints are used in antimicrobial susceptibility testing (AST) devices, results of which serve as the basis for drug selection by clinicians. Inaccurate (including out-of-date) breakpoints can result in health care providers unknowingly selecting ineffective treatments or incorrect dosing, putting patient safety and lives at risk.

Updated and accurate breakpoint information is crucial not only for individual patient care, but also for the broader public health. Updated and accurate breakpoint information is crucial not only for individual patient care, but also for the broader public health. Inaccurate breakpoints lead to the removal of potentially effective drugs from the clinician’s already limited therapeutic options, and possibly the use of drugs with greater toxicity or that are overly broad-spectrum that could further contribute to the development of antimicrobial resistance. Even more troubling, inaccurate breakpoints risk use of a potentially ineffective drug that fails to resolve the infection and may also drive the development of resistance.

Moreover, health care facilities often rely on accurate AST devices to identify patients with dangerous, multi-drug resistant infections for whom certain infection control protocols must be activated to prevent the further spread of the resistant organism. Without updated breakpoints, an AST device may misclassify the susceptibility of infecting pathogens to antibiotic agents, putting patients at risk of misguided and ineffective care, and putting other patients, family members, and others at risk of exposure.

*Sec. 1053 Election to convey a portion of extended exclusivity period applicable to qualified infectious disease products*

IDSA has long advocated for a variety of economic incentives to spur antibiotic development. Significant unique economic barriers persist that are hampering the development of urgently needed new antibiotics. 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 research and development (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.

This provision to allow a company developing a new antibiotic to transfer some of that antibiotic's extended exclusivity to a different product would provide an important economic incentive for antibiotic development and we urge the committee to continue to advance this provision as you work toward introduction. As you may know, IDSA recommended a similar approach in our *Bad Bugs, No Drugs* report in 2004. However, our proposal at that time recommended utilizing patent extension rather than exclusivity. IDSA appreciates that the discussion draft requires that companies electing this transferable exclusivity option be required to donate a portion of their profits to the National Institutes of Health (NIH) for research on antimicrobial resistance. IDSA made a similar recommendation in its 2004 report and believes that this policy will help bolster NIH research in this critical area, which is particularly important given the recent climate of fiscal austerity that has impacted all federal research funding.

*Sec. 1064 Encouraging the development and use of new antimicrobial drugs*

IDSA supports the inclusion in the discussion draft of this provision to provide increased reimbursement to new antimicrobial drugs that treat a serious or life-threatening infection with high rates of morbidity or mortality and that address an unmet medical need. This narrowly focused incentive is an important complement to the other provisions in this subtitle and will appropriately target limited federal resources toward the development of the drugs that patients most urgently need. Given that these drugs can be even more challenging to develop than the broader set of antibiotics to treat serious or life-threatening infections, it is important to provide additional incentives to ensure that these urgently needed products reach patients. IDSA also appreciates that this provision would allow a company to seek a designation for a product as eligible for this incentive during the drug's development, rather than requiring a company to wait until its new drug has been approved by the Food and Drug Administration (FDA) in order to apply for increased reimbursement. This approach will give companies the predictability they need in order to target their development programs to the areas of greatest patient need and serve as a strong incentive for them to invest in antibiotic research.

In addition to spurring the development of new antimicrobial drugs, it is equally critical that we also take steps to help ensure their appropriate use in order to protect patients and safeguard these precious drugs from rapid development of resistance caused by misuse. We appreciate that this provision would require prescribing hospitals to participate in the Antimicrobial Use and Resistance (AUR) module of the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) or a similar reporting program to track the use of these important drugs. IDSA continues to work with CDC, health care institutions, and other key stakeholders to improve data collection on antibiotic use and resistance, and we hope that this legislation can help advance this important effort. We are also working with CDC and related stakeholders to help expand the type of data collected to ultimately include use indication, site of infection, organism, basic patient demographics, treatment duration, and outcomes (efficacy and side effects). These data are crucial for evaluating the effectiveness strategies to address

resistance, targeting antimicrobial drug and diagnostic development priorities, and defining clear benchmarks for progress.

### **Subtitle E—Priority Review for Breakthrough Devices**

IDSA is pleased to support this subtitle which would establish priority review for PMA, de novo, and 510(k) breakthrough devices. This provision will speed approval of devices, including diagnostic tests, for which no alternatives exist, as well as tests that offer significant advantages for patients over existing approved or cleared tests. In 2014, the FDA issued [draft guidance](#), which IDSA supported, that would similarly expedite access to PMA devices that address an unmet medical need. By extending priority review to lower risk tests that still meet the breakthrough criteria, this provision could speed patient access to a much wider variety of diagnostic tests that could provide much more rapid and reliable results in patients suffering from infectious diseases. Such tests have tremendous potential to improve patient outcomes and shorten hospital stays by facilitating administration of appropriate treatment much earlier in the course of a disease. These diagnostics may also be extremely useful in identifying patients eligible for antimicrobial drug clinical trials.

### **Subtitle F—Accelerated Approval for Breakthrough Devices**

IDSA supports this subtitle that would provide accelerated approval for PMA, de novo and 510(k) breakthrough devices that have an impact on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway is already utilized successfully for drug development and approval, and IDSA supports similar efforts to speed patient access to urgently needed diagnostic tests. For a patient with a serious or life-threatening infection that cannot be identified in a sufficiently rapid manner to substantively impact care and outcomes, FDA must appropriately weigh the risk of approving a new diagnostic test based upon a smaller premarket data set against the risk of not having urgently needed new diagnostics. Importantly, this provision provides for the conduct of post-market studies to verify clinical benefit. Post-market data can allow FDA to continue to clarify uncertainties regarding the benefits and risks of the device without inappropriately slowing or blocking patient access to an urgently needed test. We believe this provision is appropriately aligned with [draft guidance issued by the FDA](#) in 2014 regarding the balance of premarket and post-market data collection for PMA devices.

This provision will be particularly helpful in developing viral load tests for infections such as cytomegalovirus (CMV) that impacts transplantation patients. These tests can clearly identify and reliably establish viral load in patients, and can also be used to establish the duration of treatment with optimal efficacy, cost-effectiveness, and patient outcome. However, clinical trials for these tests are extremely difficult because clinical endpoints are rarely reached due to preemptive treatment of high risk patients. This provision would allow trials to use a surrogate endpoint like quantification of viral load as related to a comparator test, greatly simplifying the trials process. By allowing accelerated approval of these tests, post-market data can be collected

to better validate the medical benefits of using these tests as guides for treatment response while not unnecessarily delaying patient access to these important tools.

### **Subtitle G—Expanded Access**

IDSA appreciates the Committee’s attention to the important issue of providing patient access to experimental therapies outside of a clinical trial. The Expanded Access program can be life-saving for patients with a variety of infectious diseases, including for example emerging infections, Ebola virus disease, and infections caused by multi-drug resistant organisms. IDSA appreciates the inclusion of Qualified Infectious Disease Products (antibiotic or antifungal drugs to treat a serious or life-threatening infection) in this provision. In the field of infectious diseases, we see patients with a variety of infections that are extremely difficult or impossible to treat with existing antimicrobial drugs. In such instances, an experimental therapeutic may be the best option for some patients and this provision seeks to improve the information, metrics and speed by which patients in great need can utilize this option. We do not seek any changes to this provision, but we would like to share with the Committee the unique challenges that infectious diseases present in this area.

First, speed is essential. For serious infections, a delay of even a few hours in effective treatment may significantly impact patient outcomes and even mean the difference between life and death. For some patients who present earlier in the course of a serious infection, access to an experimental treatment within 48 hours may provide a meaningful impact on patient outcome. However, expanded access programs that take several days or weeks to provide an experimental drug to a patient would typically not be useful for most bacterial or fungal infections. We appreciate that the provision seeks more information on the time it takes patients to access such treatments and seeks to improve the overall process to reduce unnecessary delays.

Second, antibiotic and antifungal development is already extremely challenging, and the drug pipeline remains very fragile. The few companies who are trying to develop new antibiotics and antifungals already face significant challenges enrolling patients in clinical trials. Some of the most deadly infections are currently occurring in a relatively small number of patients, which severely limits the number of people eligible for a clinical trial. The lack of rapid diagnostics creates significant difficulty in identifying patients eligible for a clinical trial. For patients who are severely ill, we must often initiate antimicrobial drug therapy before there is time to enroll that patient in a clinical trial. Given these factors, IDSA appreciates that this provision does not alter existing FDA regulation that stipulates that a patient can only get access to an investigational drug through expanded access if the Secretary of Health and Human Services “determines that provision of the investigational drug or investigational device will not interfere with the initiation, conduct, or completion of clinical investigations to support marketing approval.”

### **Title II, Subtitle A—21<sup>st</sup> Century Cures Consortium Act**

IDSA is very encouraged by the inclusion of this provision to establish the 21<sup>st</sup> Century Cures Consortium in the draft Cures bill and believes it is a necessary step to advance antimicrobial drug and diagnostic research and development in the U.S. IDSA has long urged Congress and

the Administration to establish a complementary effort to the European Union’s Innovative Medicines Initiative (IMI), specifically its New Drugs for Bad Bugs (ND4BB) and Rapid Point-of-care test Platforms for Infectious Diseases (RAPP-ID) projects. Such public private partnerships are essential to furthering the R&D process for new antibiotics and diagnostics because they convene the required diverse stakeholders to tackle the complex scientific and economic challenges that currently impede the development of these products. For example, ND4BB brings together government leaders, academia, industry and other experts for an unprecedented sharing of information and multi-disciplinary collaboration. The focus of the overall program is to develop better networks of researchers, create fluid and innovative clinical trial designs and provide incentives for companies to meet the challenges of antibiotic resistance quickly and efficiently. RAPP-ID convenes similar diverse groups of experts to develop fast and reliable point-of-care tests for the detection of various pathogens. RAPP-ID is gathering input from clinicians to focus its activities on areas of greatest need that can most significantly impact patient care. This effort is focused on diagnostics for blood infections, lower respiratory tract infections (including community-acquired pneumonia and ventilator-associated pneumonia) and tuberculosis.

Multiple IDSA leaders have been engaged with the IMI’s activities, and we are pleased to offer their expertise as the Committee continues to refine this provision. We would also like to offer specific recommendations to strengthen the current discussion draft.

- Page 183, lines 10-14: The discussion draft would allow the consortium to provide grants to individual non-profits or small businesses. IMI instead provides grants to partnerships that include academic groups, informatics groups, and large and small companies. IDSA recommends that the Committee modify the discussion draft to explicitly provide grants to such partnerships for two key reasons: First, this approach fosters better collaboration across stakeholders by explicitly requiring that they work together in order to receive funding. Other existing public private partnership models in the U.S., such as the Biomedical Advanced Research and Development Authority (BARDA) and the Reagan-Udall Foundation already provide grants to individual entities. Providing grants instead to partnerships would make this new entity unique and allow it to fill a current void in the U.S. Second, providing grants to partnerships that include a variety of stakeholders would allow for participation by large companies. IDSA believes such participation is necessary to stimulate development of urgently needed new antibiotics and diagnostics. In the IMI, large companies do not directly receive government funds, but through the partnerships described above, they actively participate in projects and contribute significantly through “in-kind” resources. For example, large companies donate their researchers’ time and provide access to research facilities or resources. Further, in the IMI’s ND4BB project, new antibiotics from large pharmaceutical companies are often among those studied. The ND4BB project is allowing these new antibiotics from large companies to be studied when they otherwise would not.
- Page 132, lines 1-5: In describing the purpose of the Consortium, the bill lists “innovative cures, treatments, and preventive measures,” as the areas the Consortium should address. IDSA strongly recommends adding “diagnostics” to that list. Similarly, to ensure that

diagnostics are included in this important effort, we recommend the following changes: Sec. 281B Duties, page 132, lines 19-22, add “diagnostics”; Sec. 281D, Grants, Contracts, and Other Assistance, page 137, line 18, add “diagnostics.” While it was unclear whether or not the Committee intended for diagnostics to be included in this provision, we strongly urge that the Committee make the above changes to explicitly ensure their inclusion. We urgently need new infectious diseases diagnostic tests that provide rapid results, are easy to use, and accurately identify the pathogen causing an infection and the best drug to use. New and improved diagnostics can significantly improve patient care by giving physicians the information they need to more rapidly provide appropriate treatment. For example, currently, 20-30% of patients with sepsis receive inadequate initial treatment because the cause of the infection can take several days to diagnose. Better diagnostics can also improve public health by identifying patients for whom isolation or other infection control measures are needed, improving the tracking of outbreaks and emerging infectious disease threats. Improved diagnostics can also guide the appropriate use of antimicrobial drugs, and therefore are critical to the campaign to address antimicrobial resistance. Unfortunately significant barriers persist that hamper the development of these new tests, including high research and development costs, difficulty accessing clinical samples and clinical and laboratory expertise, and scientific challenges. Public private partnerships, such as those that could be supported through the new Consortium, are ideal for overcoming these hurdles.

- Page 139, lines 6-13: The draft bill would terminate the Consortium in 2021. IDSA suggests that rather than statutorily terminate the Consortium, the Committee instead include language calling for a reassessment. In the field of infectious diseases, new pathogens are always emerging and mutating, necessitating the need for new drugs, diagnostics and vaccines. In addition, we suggest that the reassessment occur in 2026, rather than 2021 as proposed in the draft bill, as we think that a 10-year timeframe would more appropriately allow the Consortium sufficient time to advance projects and demonstrate an impact.
- Page 139, lines 16-21. We note that the funding amount is left blank in the draft bill. As a point of reference, the IMI has a 3.3 billion Euro budget for 2014-2024, with approximately half of the funding coming from government sources and the remainder from the European Federation of Pharmaceutical Industries and Associations (EFPIA) companies. IDSA recommends that a similar level of funding is needed for the proposed new Consortium to have a similarly significant impact. We recognize that securing new federal funding remains very challenging in the current environment. However, we urge the Committee to consider that the new antimicrobial drugs and diagnostics this Consortium could help develop have the potential to significantly lower health care costs by reducing the administration of ineffective or unnecessary treatment and shortening hospital stays by enabling more rapid administration of effective treatments. Currently it is estimated that antibiotic resistant infections are responsible for an additional 8 million hospital days in the U.S. every year and cost our health care system \$21-\$34 billion annually.

## **Title II, Part 2—Improving Clinical Outcomes for Patients and Program Integrity through CMS Data**

### *Sec. 2085 Expanding availability of Medicare data*

IDSA welcomes legislative action that would facilitate access to Medicare data for purposes of quality and patient care improvement activities. Whereas there are some limitations to the use of these data, given the lack of granularity due to the limited information captured on the Medicare claim, access to these data will be of great value to medical societies such as IDSA. In the past, IDSA has purchased Medicare data in order to establish the [positive impact of an infectious diseases physician's involvement on inpatient stays](#). This type of research is important in order to confirm the value of ID specialty care as the health care system moves to alternative payment models (bundled payments) in a value-based, integrated delivery system. It is unclear to us what activity might be allowable under this provision regarding the promotion of published literature, based on research resulting from access to Medicare data. IDSA asks the Committee for more clarity on the intent of subparagraph (C) of this provision, pertaining to prohibitions of the use of such data for marketing purposes. Specifically, IDSA hopes that a non-profit organization's promotion of published research would be permissible.

## **Title II, Part 3, Subtitle L—NIH Federal Data Sharing**

IDSA supports this provision, which requires any entity receiving NIH funding to release its findings to the public and share with the public data generated through such research. Improving access to such scientific data in this manner makes sense and may help strengthen and accelerate additional research.

## **Title II, Part 3, Subtitle M—Accessing, Sharing, and Using Health Data for Research Purposes**

IDSA supports this provision, which creates an exception to the Common Rule in cases where clinical data registries, as well as other individuals or entities, are collecting identifiable patient information, but are not engaged in direct human subjects intervention or interaction. IDSA has previously supported improving access to patient information as long as privacy remains appropriately protected.

Improving access to clinical data registries would accelerate critical infectious diseases health care operations research, such as studies regarding the clinical integration of rapid diagnostic tests into patient care settings. New rapid infectious disease diagnostics require improved coordination between laboratories, attending physicians, infectious diseases specialists, antimicrobial stewards, and public health professionals. For example, if a test can yield results in 30 minutes, but the treating physician does not receive the results for several hours, the rapid test's ability to impact patient care is not realized. Further, rapid results must also be communicated swiftly to public health and infection control professionals to allow them to trigger protocols designed to limit the spread of infection. Access to clinical data registries can allow researchers to examine the processes for communicating diagnostic test results between these parties, and how to optimize such processes to realize the patient care and public health benefits of a rapid diagnostic test.

### **Title III, Subtitle A—Clinical Research Modernization**

*Sec. 3001 Protection of Human Subjects in Research; Applicability of Rules*

*Sec. 3002 Use of Institutional Review Boards for Review of Investigational Device Exemptions*

IDSA has long supported efforts to streamline the regulatory process while maintaining research participant protections. We are pleased to support both of these sections, which we believe are appropriately aligned with a recently released [draft NIH policy](#) on the use of a single institutional review board (IRB) for multi-site research. Currently, duplicative review of multicenter studies by local IRBs delays study initiation, requires substantial resources from local investigators and IRBs and does not improve protocol or human subject protections.

### **Title IV, Subtitle A—National Institutes of Health**

*Sec. 4003. NIH Travel*

Although the Committee has not yet released draft language for this section, IDSA would simply like to take this opportunity to highlight the importance of federal scientists' participation in scientific conferences, which often require some travel. These meetings allow for analytical discussion and interaction between experts and other physicians and scientists that are crucial to scientific advancements. Further, scientific conferences provide leading federal scientists with the opportunity to educate and mentor junior researchers and physicians—a critical priority as we seek to develop the next generation of innovators. Unfortunately, policies such as sequestration have caused federal attendance at scientific conferences to decline significantly in recent years. We look forward to the Committee's proposals to address this important issue.

### **Title IV, Subtitle C—Vaccine Access, Certainty, and Innovation**

IDSA is pleased that the draft bill includes an extensive subtitle on vaccines. Vaccines are our best tools for preventing infectious diseases, and IDSA supports policies that promote access and stimulate innovation and licensure of new and better vaccines where there is an unmet need. IDSA is pleased to support several of the provisions in this subtitle, further described below. However, we must also raise concerns about a few of the provisions as drafted and offer recommendations that we believe would more effectively advance the goals of this subtitle.

#### **Part 1—Development, Licensure, and Recommendations**

*Sec. 4041. Prompt Review of Vaccines by the Advisory Committee on Immunization Practices*

IDSA appreciates the goal of this section to ensure that the Advisory Committee on Immunization Practices (ACIP) promptly reviews vaccines and makes recommendations with respect to the route of administration, dosage and frequency of administration for specific populations. Quick review subject to a set timeframe may be beneficial for public health planning purposes, including quickly educating parents and patients and distributing vaccines to providers; however, IDSA has strong concerns with this provision as currently drafted.

Several IDSA members currently or have previously served on the ACIP, and we are pleased to offer their expertise as the Committee works to refine this draft legislation. IDSA has a deep appreciation of ACIP's important work as well as the challenges faced by ACIP members to analyze scientific data and make deliberate, well-informed recommendations. For each vaccine recommendation under consideration, ACIP members must review considerable microbiological, clinical, and epidemiological data, typically stretching the committee's workload to capacity.

It is also important to note that unlike FDA, the ACIP does not have a model for expedited approval requiring manufacturers to provide additional funding to support additional staff time to perform an expedited review process. As such, this provision would place strict constraints on ACIP members without providing any additional support to help them meet new requirements. IDSA is deeply concerned that as written, this provision could jeopardize the integrity of ACIP's recommendations by failing to provide sufficient time for a thorough review of relevant data.

#### *Sec. 4042. Review of Transparency and Consistency of ACIP Recommendation Process*

IDSA strongly supports measures to ensure that the U.S. government's vaccine recommendation process is transparent and communicated clearly to the public. However, we are unaware of any problems in this area, and as such do not see the need for this provision. As a Federal Advisory Committee, ACIP is governed by federal standards of transparency and public engagement. All regular ACIP meetings are accessible to the public. All working group decisions and accompanying rationale are shared publicly at regular ACIP meetings.

This provision would also require review of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to the review and analysis of scientific and economic data. There is already extensive literature pertaining to GRADE. Both GRADE and the cost-effectiveness analyses used by ACIP have been presented at CDC in great detail, and have been posted on the internet or otherwise published.

As written, we are concerned that this provision could divert already strained CDC resources from other activities that would have a more significant impact on public health.

#### *Sec. 4043. Guidance on Vaccine Development*

IDSA strongly supports this provision to require FDA to issue final guidance to facilitate the use of accelerated and expedited pathways for the development and licensure of urgently needed vaccines, specifically those to prevent emerging, re-emerging or rare infectious diseases and vaccines for infectious diseases for which current vaccines are not addressing the full scope of public health needs. This provision would be helpful for rapidly emerging diseases that currently affect relatively few Americans, such as coccidiomycosis (valley fever) and Chikungunya fever. It would also be helpful for vaccines that need to be improved, such as those for pertussis and influenza.

Clear FDA guidance for vaccine manufacturers is important to ensure clear communication about licensure pathways available for vaccine products, as well as the clinical trial data and

other regulatory requirements with which companies will need to comply. With a better understanding of the licensure pathways and respective regulatory requirements, vaccine manufacturers and their investors will be better able to make informed decisions about vaccine R&D and target their resources to areas of greatest need. FDA guidance will also help to ensure that Biologics License Applications (BLA) meet FDA expectations earlier in the process, thus saving FDA staff time and manufacturer time and expediting public access to vaccines. As with other guidance for industry documents, public comment should be considered before finalizing any draft.

*Sec. 4044. Meetings Between CDC and Vaccine Developers*

Open communication between public health authorities and vaccine manufacturers is a worthy goal, and we understand that CDC priorities and epidemiological changes over time can significantly impact the potential market for a new vaccine product. However, IDSA has significant concerns with this provision. We believe that requiring CDC to meet with any vaccine manufacturer within 90 days of a request is unreasonable given very limited CDC staff resources. Unlike the FDA, which has access to user fees and designated full time employees to hold meetings with medical product sponsors, the CDC has no such dedicated financial or staff support for these activities. IDSA has consistently advocated for increased CDC funding. We are concerned that requiring CDC to accommodate these activities, without providing the agency with additional resources, may divert CDC resources from other critical priorities.

IDSA strongly supports ensuring that federal policies promote, and do not inhibit, the development of urgently needed new vaccines. As such, we would be interested in working with the Committee to better understand exactly what epidemiological data is currently unavailable to vaccine developers and the public through existing means so that we may better recommend more appropriate policies to ensure its availability. We would also look forward to working with the Committee to explore other more practical ways to facilitate more open communication between CDC and vaccine developers, such as through a regular open forum.

*Sec. 4045. Modifications to the Priority Review Voucher Program for Tropical Diseases*

IDSA supports this provision. IDSA strongly supported legislation enacted in December 2014 to add Ebola virus to the Priority Review Voucher (PRV) program. That legislation made additional important improvements to the program, and we believe this provision builds upon those efforts by providing more clarity about the process and methodology with which the FDA will determine what diseases will qualify for the program. This language may facilitate the addition of other appropriately qualifying diseases to the PRV program, such as Chagas disease. Chagas disease is a tropical disease caused by the parasite *Trypanosoma cruzi*, which is commonly transmitted to humans by insect vectors. Trypanosomes may also be spread through blood transfusion and organ transplantation, ingestion of food contaminated with parasites, and from a mother to her fetus. It is estimated that as many as 8 million people in Mexico, Central America, and South America have Chagas disease. Chagas disease is a very painful, debilitating disease. As the disease progresses, serious chronic symptoms can appear, such as heart disease and malformation of the intestines. If untreated, the chronic disease is often fatal. Nearly all of the victims of Chagas disease are poor people living in developing countries. There is almost no

private sector research for Chagas disease. IDSA also recognizes that additional improvements to this program may be appropriate to ensure it meets continually evolving needs, and we look forward to working with the Committee and other stakeholders to periodically assess how this program functions and how it may be strengthened.

*Sec. 4048. Expanding NIH Research on Vaccines*

IDSA strongly supports expanding vaccine R&D programs at NIH, especially in areas where there is an unmet need or where better vaccines are needed, such as pertussis and influenza. Influenza vaccines are currently our best interventions for prevention of seasonal influenza, even when vaccines are less than perfectly matched to the circulating virus strains. The relatively low level of protection offered by this season's vaccine underscores the need for greater research in this area.

Pertussis outbreaks in various U.S. regions in recent years highlight the need for an improved vaccine for this disease. IDSA supports a national research agenda that includes investigation of the pathogenesis of pertussis and modes of protection against *Bordetella pertussis* infection, informed by molecular microbiology, immunology, and epidemiology. We support a comprehensive approach to systemize, coordinate, and strengthen vaccine R&D across all relevant agencies and between the federal government and the private sector.

**Title IV, Subtitle C, Part 2—Medicare, Medicaid and Other Provisions**

*Sec. 4061. Requiring Prompt Updates to Medicare Program upon Issuance of ACIP Recommendations*

IDSA supports this provision. We believe that ACIP recommendations, once formally adopted by the CDC, should be implemented as soon as possible to ensure access to the vaccine for the indicated population. For the Medicare population, access to a vaccine depends largely upon whether the Medicare program covers it. These coverage decisions should be made as expediently as possible following the ACIP recommendation. We believe the 60-day timeframe specified in this provision provides the Centers for Medicare and Medicaid Services (CMS) with a reasonable amount of time to update the Medicare Benefit Policy Manual to reflect new vaccine recommendations. In addition, IDSA is eager to work with the Committee and other relevant stakeholders to facilitate greater CMS involvement with ACIP and CDC's vaccine recommendation process to ensure that Medicare officials can adequately anticipate and respond to important new recommendations that impact the Medicare population.

*Sec. 4062. Encouraging Health Plans to Establish Programs to Increase Adult Immunization*

IDSA has long highlighted the troublingly low rates of adult immunizations, and the resulting burden of vaccine-preventable illnesses. Increasing adult immunization rates is a critical public health priority. We are grateful that the Committee included a provision that explicitly acknowledges the need for greater efforts across the public and private sectors to improve adult immunization rates. Public and private insurance plans have an important role to play in ensuring access to recommended vaccines for adults. Allowing plans to include programs to

increase adult immunization as a quality improvement activity for purposes of calculating the Medical Loss Ratio is a strong incentive. However, programs to increase adult immunization by themselves will not necessarily result in an actual increase in immunization rates. We urge the Committee to explicitly require plans to show an actual immunization increase among their beneficiary population in order to qualify for the MLR benefit.

Given the Committee's strong interest in improving adult immunization rates, we also offer an additional suggestion that we believe will provide an even greater impact. The current discrepancy between Medicare Part B and Part D coverage of important vaccines is a significant barrier to seniors' access to vaccines. Under current law, Medicare Part D plans are responsible for covering vaccines not covered under Medicare Part B, including those protecting seniors from herpes zoster, pertussis, tetanus, and diphtheria. Unfortunately, not all seniors have Part D plans, and even those who do are often subject to prohibitively expensive copays for these vaccines. In addition, the existing fractured coverage imposes significant administrative challenges for patients, physicians, and pharmacists. For example, patients who need the herpes zoster vaccine to prevent shingles must obtain the vaccine from a pharmacist but then have it administered by a health care provider. This policy leads to fewer seniors receiving this vaccine. We strongly recommend that the Committee include in this bill a provision requiring coverage for all ACIP recommended vaccines through both Medicare Part B and D to ensure that no senior falls through the cracks.

#### **Title IV, Subtitle E—FDA Hiring, Travel, and Training**

Although the Committee has not yet released draft language for this section, IDSA would simply like to take this opportunity to highlight the importance of federal scientists' participation in scientific conferences, which often require some travel. As we explained above regarding a similar section on NIH travel, we note that scientific meetings allow for analytical discussion and interaction between experts and other physicians and scientists that are crucial to scientific advancements. We look forward to the Committee's proposals to address this important issue.

#### **Title IV, Subtitle I—Telemedicine**

##### *Sec. 4181 Advancing telehealth opportunities in Medicare*

IDSA greatly appreciates the Committee's recognition of the value that telemedicine can offer with more widespread use of this technology. ID specialists continue to leverage telemedicine to extend timely care to patients who have severe and complex infections. As many infectious diseases physicians practice in or near academic centers, telemedicine has the potential to provide specialty infectious diseases care to patients outside these areas where unmet need exists, including rural areas and correctional facilities. [Telemedicine can be used to link patients directly to infectious diseases specialists or to facilitate consultations between primary care providers and specialists.](#) Moreover, telemedicine expansion holds promise for improvements in management of chronic infectious diseases like hepatitis C (HCV) and HIV/AIDS, clinical decision support systems, and disaster preparedness and response. This provision would facilitate the extension of ID specialty care to applications that are not dependent on geographical or health care provider type limitations and that, we believe, will actually result in

improved outcomes with lower costs. We support the plan calling for collaboration through the use of State medical board compacts to create common licensure requirements for telehealth services and to define the terms that may allow such services across state lines.

### **Subtitle L—Global Surgery Services Rule**

IDSA does not support this Subtitle that would prohibit the Secretary from implementing any provision of the Medicare CY2015 Physician Fee Schedule Final Rule with respect to transitioning and revaluing the 10-day and 90-day global surgery services with 0-day global periods. IDSA understands the rationale that CMS has presented in both the proposed and final rules and deems the work involved in carrying this out to be worthwhile to pursue at this point. Already, this change called for in the final rule has led to productive conversations among medical specialty societies as to how to consider a revaluation of the global bundles and candid, general discussions around new methods to explore towards more accurate valuation of physician services. Therefore, we urge the Committee to remove this provision and instead continue to monitor CMS activities in this area to assess their impact.

### **Subtitle S—Continuing Medical Education Sunshine Exemption**

*Sec. 4381. Exempting from manufacturer transparency reporting certain transfers used for educational purposes*

IDSA is pleased to support this provision, which would ensure that peer-reviewed journals, journal reprints, journal supplements, and medical textbooks are included in existing Sunshine Act reporting exclusion for continuing medical education (CME) activities. The importance of up-to-date, peer reviewed scientific medical information as the foundation for good medical care is well documented. Independent, peer reviewed medical textbooks and journal article supplements and reprints represent the gold standard in evidence-based medical knowledge and provide a direct benefit to patients because better informed clinicians render better care to their patients. In August, 2014, IDSA joined a significant number of national and state medical societies to urge CMS to exempt these materials from Sunshine Act reporting requirements, and we are grateful for the Committee's attention to this important issue.

### **Additional Recommendations**

In addition to the very comprehensive discussion draft that the Committee has compiled, IDSA has a few additional recommendations that we believe are central to the overall goal of this legislation to spur innovation that will benefit patients. The following recommendations specifically focus on fostering the development of new infectious diseases diagnostics. In addition to the summaries below, we are also attaching draft legislative language for the first two proposals, which we hope the Committee will find helpful.

**Biorepositories: Direct the National Institute for Allergy and Infectious Diseases (NIAID) to examine opportunities to support the development of virtual biorepositories for viruses, fungi and other pathogens, utilizing samples already being collected under existing NIAID-funded research, similar to the existing bacteria virtual biorespository. Provide incentives and support for institutions to save de-identified specimens and to participate in virtual**

**biorepository catalogues when possible.** A key challenge in clinical trials for new diagnostics is access to clinical samples, particularly those containing rare pathogens. Many clinical laboratories no longer freeze specimens containing novel or unusual organisms for further use. Even when such critical samples are available, the cost of accessing them has, in many cases, become prohibitive. The Antibacterial Resistance Leadership Group (ARLG), a strategic research team funded by NIAID, established a [Virtual Biorepository \(VB\) Catalogue](#), a web-based system that provides researchers with unique access to clinically well-characterized bacteria for the development of diagnostic tests and other research. The bacteria are already being collected through other ARLG research projects and are housed at multiple locations. This approach requires significantly less resources than traditional physically centralized biorepositories. Researchers are able to search the virtual biorepository catalogue to locate the samples they need. This approach could be very useful in other areas of infectious diseases diagnostics development (e.g. virus, fungi, etc.).

**Conflict of Interest: Clarify, through report language, that institutions receiving federal funding should implement conflict of interest (COI) policies that appropriately enable transparent industry/institutional research collaborations. Direct the Food and Drug Administration (FDA) to clarify and revise its COI policy to enable more effective recruitment of subject matter experts while retaining objective regulatory review.** Often expert input or independent validation of a potential test is needed during development. Institutional COI policies are often much more strict than the National Institutes of Health (NIH) [COI regulatory framework](#), which was intended to provide guidance to institutions on how to manage COI. Unfortunately, institutional COI policies often bar those best suited for these activities, sometimes even if the expert is willing to work for free on his or her own time. Even when an institution does not explicitly ban such activities, policies are sometimes misinterpreted, resulting in a stifling of collaboration between academic researchers and industry. This forces developers to forgo expert input or use laboratories lacking expertise for independent testing. This loss of expert input and the resources diverted to train and supervise testing at labs lacking expertise can add considerable time and cost to diagnostic development.

**Strong educational programs to inform physicians about the utility of new diagnostics: Direct the Agency for Healthcare Research and Quality (AHRQ), specifically through its Center for Evidence and Practice Improvement (CEPI), to conduct or support research to demonstrate the impact of new ID diagnostics on patient care and outcomes, and to disseminate the results of that research to physicians to encourage them to appropriately utilize new diagnostics.** Many physicians and other health care providers may be hesitant to use new diagnostic tests, in part because they are often uncertain of how best to integrate them in their practice and how to interpret results. Physicians often look to education, such as clinical guidelines developed by their professional societies, such as IDSA, and government bodies, such as the AHRQ, to suggest the best methods to diagnose and treat an infection. Little guidance currently exists on the use of diagnostic tests for a particular type of infection, or what bundles of tests should be used if a patient has a particular set of symptoms. The ability to construct useful guidelines is hampered by the lack of clearly designed outcomes studies demonstrating patient benefit when tests are used as part of clinical decision making. IDSA is open to this type of research being conducted or supported elsewhere in the federal government. However, CEPI is well-suited to address this need, as the Center is tasked with conducting and supporting research

on health care delivery and improvement and advancing decision and communication sciences to facilitate informed treatment and health care decision making by patients and their health care providers.

Once again, IDSA is grateful to the Committee for the hard work evident in this comprehensive discussion draft. We hope our comments will be helpful as you seek to refine and advance this important effort. We look forward to continue working with you toward policies that will benefit patients and public health. Again, we are excited to see the focus this discussion draft places on antibiotic development and believe these policies will truly make a difference in the patient care and public health.

Sincerely,

A handwritten signature in purple ink that reads "Stephen B. Calderwood". The signature is written in a cursive, slightly slanted style.

Stephen B. Calderwood, MD, FIDSA  
IDSA President