Infectious Diseases Society of America's (IDSA) Testimony Concerning Fiscal Year 2011 Funding at the Food and Drug Administration

Submitted to the House Appropriations Subcommittee on Agriculture, Rural Development, Food and Drug Administration and Related Agencies

March 19, 2010

The Infectious Diseases Society of America (IDSA) appreciates this opportunity to speak in support of federal efforts to prevent, detect and respond to infectious diseases in the United States and abroad as part of the Fiscal Year (FY) 2011 funding cycle. IDSA supports an **overall increase of $495 million** for the Food and Drug Administration (FDA) for FY2011. Within this overall increase, we support an **additional $20 million for FDA's antimicrobial resistance and antibacterial drug review programs**, which will allow FDA to more aggressively address staffing problems within the agency's division with oversight over antibacterial human drug reviews to enable that division to quicken its pace in developing critical guidance for industry on antibacterial drug clinical trial designs; fund Critical Path initiatives specific to antibacterial drug development; update antibacterial drug and antimicrobial susceptibility testing (AST) device susceptibility breakpoints for inclusion in product labeling; and review the safety of antibacterial drug use in food animals. We also support **an increase of $13.25 million** f**or FDA's new regulatory science initiative** to address scientific issues related to antibacterial drug development and an **increase of $3 million for the National Antimicrobial Resistance Monitoring System (NARMS**).

IDSA represents more than 9,000 infectious diseases physicians and scientists devoted to patient care, prevention, public health, education and research. Our members care for patients of all ages with serious infections, including meningitis, pneumonia, tuberculosis (TB), resistant infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli* (*E. coli*) and *Salmonella*, food poisoning, and HIV/AIDS, emerging infections like the 2009 H1N1 virus and severe acute respiratory syndrome (SARS), and cancer and transplant patients who have life-threatening infections caused by unusual microorganisms.

OVERALL FDA FUNDING RECOMMENDATION

The increases in FDA's appropriations over the past few years have been critical to strengthening the agency. Nonetheless, there remains an extraordinarily large gap between FDA's responsibilities and its resources. Every year, the agency's job becomes more complex scientifically and more difficult to perform. Moreover, new laws affecting FDA recently have been enacted, further straining the FDA's ability to meet the expectations of the Congress and the American people. It is also important to note that FDA's appropriation is quite small, especially when matched against its jurisdiction over one-quarter of consumer spending, 80% of the food supply and all of the drugs, biologics, medical devices, animal drugs, cosmetics and dietary supplements used anywhere in the United States. FDA must also deal with the food and medical products that are sourced from overseas. IDSA is recommending a $495 million increase for FDA in FY2011. This is the amount we believe is needed to enable FDA to make further progress in carrying out its existing responsibilities.

SPECIFIC FUNDING RECOMMENDATIONS

Within this increased funding, IDSA supports a strengthening of efforts which will support FDA's antimicrobial resistance programs and antibacterial drug review efforts. Specifically, we support at least a $36.25 million increase for FDA's activities in these areas in FY2011, including an increase in FDA funding for the new regulatory science initiative and an increase for the National Antimicrobial Resistance Monitoring System (NARMS).

THE ANTIBIOTIC PIPELINE: PROBLEMS AND SOLUTIONS

Since antibiotics were first discovered and used in the 1940s to save American soldiers during World War II, they have saved millions of lives and eased patients' suffering. In fact, antibiotics often have been referred to as "miracle drugs," since patients only need to take them for a few days to completely resolve most infections.

However, antibiotics also are unique among all medicines in two very unfortunate ways. First, over time, these drugs lose their ability to treat the diseases for which they were approved—due to antibiotic resistance. And, second, the phenomenon of antibiotic resistance has required that newly approved antibiotics be used sparingly so that we can prolong their effectiveness against life-threatening infections. These two issues, resistance and the resulting need for protective antibiotic stewardship measures, have created very real clinical challenges in physicians' ability to treat infectious diseases. Unfortunately, they also have resulted in a market failure that has caused most pharmaceutical companies to withdraw from antibacterial research and development (R&D). The sad result—the antibacterial pipeline is drying up, placing Americans and other people around the world at serious risk.

A January 2009 IDSA report published in the journal *Clinical Infectious Diseases (CID)* analyzes antibacterials in development and shows the pipeline is bare, particularly for infections caused by a group of bacteria known as the ESKAPE Pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species), so-called because they effectively escape the effects of approved antibacterial drugs. Of significance, these ESKAPE pathogens cause the majority of U.S. health care-associated infections. A report released by the European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) in September 2009 confirms IDSA's assessment finding only 15 antibacterial drugs in development with the potential to offer a benefit over existing antibacterial drugs. Only five of these antibacterials had progressed to clinical trials to confirm clinical efficacy (Phase III or later).

The lack of new antibacterial drugs in development is deeply troubling to health experts and has the potential to change the practice of medicine as we know it. A number of advanced interventions that we currently take for granted, e.g. surgery, cancer treatment, transplantation and care of premature babies, may be impossible to perform if we get to the point where effective antibacterial drugs are no longer available. Our ability to care for patients with serious and life-threatening infections already has been significantly diminished—morbidity and mortality are on the rise.

In addition to market failure due to antibacterial resistance, pharmaceutical companies often report that uncertainty caused by a lack of clear FDA guidance on appropriate clinical trial designs is a significant impediment to antibacterial R & D efforts. IDSA requests that FDA

funding be sufficiently increased to allow the agency to quickly provide regulatory certainty and to explore other incentives needed to motivate major drug companies to become engaged once again in antibacterial R & D.

FDA has made some progress over the past several years in publishing new clinical trial guidelines. However, clear clinical trial design guidance is still urgently needed, including guidances for community-acquired bacterial pneumonia, hospital-acquired bacterial pneumonia, ventilator-associated bacterial pneumonia, complicated skin and skin structure infections and other serious infections. FDA must have adequate funding to hire additional staff to finalize these guidances quickly. Otherwise, more companies will leave this area of drug development.

Moreover, IDSA strongly urges FDA to commission a study through the Tufts Center (or some other similar entity) seeking a report on strengths and weaknesses in the antibacterial and related diagnostics R&D pipelines with a particular emphasis on products needed to treat, detect, and prevent serious and life-threatening infections caused by ESKAPE pathogens. The study also should provide recommendations as to what combination of incentives, considering each phase of product development, will work to spur greater R&D of such products among the biotechnology, pharmaceutical, and diagnostics industries as well as within academic settings.

SUPPORT FOR REGULATORY SCIENCE

IDSA is encouraged by the recent announcement of the initiative between FDA and the National Institutes of Health designed to accelerate the process from scientific breakthrough to the availability of new, innovative medical therapies for patients. The initiative involves two interrelated scientific disciplines: translational science, the shaping of basic scientific discoveries into treatments; and regulatory science, the development and use of new tools, standards and approaches to more efficiently develop products and to more effectively evaluate product safety, efficacy and quality.

In order to improve the regulatory science, the two agencies will jointly make $6.75 million dollars available over three years for work in this area. The research supported through this initiative will add to the scientific knowledge base by providing new methods, models or technologies to inform the scientific and regulatory community about better approaches to evaluating safety and efficacy in medical product development. IDSA is concerned, however, that this amount of funding will be insufficient to lead to the types of breakthroughs needed to bring new antibacterial drug products to the market in a more timely fashion. We support an increase of $13.25 million in this funding, to a total of $20 million, to support science around antibacterial drug development.

ANTIBACTERIAL BREAKPOINTS

Physicians need accurate information on susceptibility interpretative criteria (“breakpoints”) to use antibacterial drugs wisely. Breakpoints are the science behind standard laboratory policy and are the basis upon which antibacterial drug selection determinations are made. The real-life impact of relying upon inaccurate (including out-of-date) breakpoints are thousands of wrong treatment decisions being made every day in this country. Without accurate breakpoint information, patients’ safety and lives are at risk. That is why updating antibacterial drug product labeling and AST instruments/systems in a timely manner are so critically important. Again, FDA must have the funding necessary to allow for additional staff to be able to update these breakpoints on a timely and consistent basis.

ANTIBACTERIAL USE AND RESISTANCE ON U.S. FARMS

Another area of serious concern is the inappropriate use of antibacterial drugs in food animal production. An additional $5 million should be allocated to allow FDA to complete, update and publish reviews on the safety of antimicrobials of importance to human medicine which currently are approved for non-therapeutic purposes in food-producing animals for their role in the selection and dissemination of antibacterial-resistant food-borne pathogens. Since 2003, FDA's Center for Veterinary Medicine (CVM) has required that the pre-approval safety review for all new antibacterial veterinary drugs include an evaluation of the likelihood that the proposed drug use in animals will lead to resistant infections in humans. Because almost all antibacterial drugs being used for growth promotion and other non-therapeutic purposes in livestock production were approved by the FDA before 2003, most have either not undergone reviews with respect to antibacterial resistance or have undergone reviews that are inconsistent with current standards. In order to ensure that these drugs meet current safety standards, it is important to do post-market safety reviews of those classes of antibacterial drugs important to human medicine that are also being used for routine non-therapeutic purposes in animal agriculture. These would include penicillins, tetracyclines, macrolides, lincosamides, streptogramins, aminoglycosides, and sulfonamides. By providing an additional $5 million, the Subcommittee can ensure that FDA completes and publishes these critical reviews.

Finally, an additional $3 million should be provided to the National Antimicrobial Resistance Monitoring System (NARMS). Jointly operated by FDA, the Department of Agriculture (USDA) and the Centers for Disease Control and Prevention (CDC), NARMS is a national public health surveillance system that tracks changes in the susceptibility of certain enteric bacteria to antimicrobial agents of human and veterinary medical importance. Systematic collection and analyses of data is essential to address the growing problem of antibacterial resistant infections.

NARMS has been level-funded at about $7 million for the last several years; however, at that level it has been unable to keep up with life-threatening pathogens, such as MRSA, E. coli and Salmonella. Additional funding will enable increased surveillance, to include additional bacterial species and numbers and/or types of samples, and to allow researchers to utilize more sensitive methods. The additional funding will also allow NARMS to initiate farm-level surveillance of antibacterial-resistant bacteria.

Today's investment in infectious diseases research, surveillance, prevention, and treatments will pay significant dividends in the future by dramatically reducing health care costs and improving the quality of life of millions of Americans. In addition, U.S. leadership in infectious diseases research and prevention will translate into worldwide health benefits. We urge the Subcommittee to continue to demonstrate leadership and foresight in this area by appropriating the much-needed resources outlined above in recognition of the lives and dollars that ultimately will be saved.