

**President's Council of Advisors on Science and Technology
Public Meeting on Antibiotic Resistance
April 4, 2014
Infectious Diseases Society of America Comments**

The Infectious Diseases Society of America welcomes this opportunity to offer comments on antibiotic resistance to the President's Council of Advisors on Science and Technology (PCAST). IDSA represents over 10,000 infectious diseases physicians and scientists. Antibiotic resistance and the lack of new antibiotics in development are serious threats to our nation's public health, patient safety, and national security. While we are encouraged to see the federal government paying closer attention to this public health crisis, we are overdue for comprehensive, concrete actions. The longer we wait to address antibiotic resistance, the larger and more costly the problem will become.

In 2011, IDSA published [Combating Antimicrobial Resistance: Policy Recommendations to Save Lives](#). While some progress has been made, significant work remains. The US needs high level leadership and a comprehensive action plan, including well-defined goals and timelines for activities, to address antibiotic resistance and the stagnant antibiotic pipeline. Efforts to address resistance must involve all relevant government and non-government stakeholders. Below, please find a summary of our recommendations with updated detail that we hope will be of use to PCAST.

1. Adoption of Economic Incentives and Support for Other Collaborative Mechanisms to Address the Market Failure of Antibiotics

Background

The current marketplace fails to incentivize antibiotic research and development (R&D). In 1990, there were almost 20 pharmaceutical companies with large antibiotic R&D programs. Today, there are only two or three large companies and a handful of small companies remaining. [A 2013 IDSA report](#) identified only seven new drugs in development for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (GNB). There is no guarantee that any of these drugs will actually reach the finish line and receive Food and Drug Administration (FDA) approval, particularly given the significant scientific and regulatory challenges facing antibiotic R&D.

There are multiple economic reasons why drug companies have retreated from antibiotic R&D. Antibiotics are typically priced low, taken for a short duration, and held in reserve to limit the development of resistance. Economic incentives are desperately needed to counteract these factors and level the playing field for antibiotics so that companies may find it economically feasible to reenter this space.

Solutions

The European Union is far ahead of the United States in encouraging innovation in this area. The EU has launched an impressive public private partnership (PPP), New Drugs for Bad Bugs (ND4BB), under its Innovative Medicines Initiative (IMI). PPPs are needed to convene the diverse stakeholders required to tackle the challenges facing antibiotic R&D. 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 in order to meet the challenges of antibiotic resistance quickly and efficiently. IDSA urges US government leaders to establish a complementary effort to ensure that we do not continue falling behind.

Economic modeling has indicated that a variety of push and pull incentives are necessary to stimulate antibiotic R&D. The U.S. took an important first step in 2012 by enacting the Generating Antibiotic Incentives Now (GAIN) Act, which provides an additional 5 years of exclusivity for new antibiotics that treat a serious or life-threatening infection. However, much more work is needed. IDSA recommends a new tax credit to support antibiotic R&D. Analysis by Ernst & Young found that IDSA's antibiotic tax credit proposal would yield an additional 5-7 new drugs in the pipeline every year. Lastly, the Biomedical Research and Development Authority (BARDA) and the National Institute of Allergy and Infectious Diseases (NIAID) continue to be important sources of funding for research in this area. However, stagnant funding for these agencies over the last several years severely curtails their ability to make progress.

2. New Regulatory Approaches to Facilitate Antimicrobial Development and Approval

Background

In addition to economic barriers to antibiotic R&D, regulatory hurdles continue to hamper progress. IDSA has long noted that infeasible clinical trial designs must be revised. We are pleased that the FDA has begun making progress and look forward to continuing to work with the agency. In addition, IDSA recommends statutory changes to further improve the regulatory environment for antibiotic R&D.

Solutions

Specifically, IDSA urges establishment of a Limited Population Antibacterial Drug (LPAD) pathway, very similar to the Special Medical Use (SMU) pathway that PCAST recommended. It is often not feasible to study new antibiotics to treat some of the most serious or life-threatening infections in traditional, large scale clinical trials, due to the limited number of patients in which these infections currently occur. The LPAD pathway would allow new antibiotics to treat serious or life-threatening infections for which there is an unmet medical need to be studied in smaller, more rapid clinical trials. LPAD drugs would be approved for use in the limited population for whom they were proven to be safe and effective under current FDA standards. LPAD drugs must be appropriately labeled and monitored to ensure their appropriate use. [The Antibiotic Development to Advance Patient Treatment \(ADAPT\) Act](#), would establish the LPAD pathway and enact safeguards for appropriate use of LPAD drugs. IDSA is working to advance this legislation and strengthen it by requiring a logo on the labeling of LPAD drugs.

3. Greater Coordination of Relevant Federal Agencies' Efforts

Background

The problem of antibiotic resistance is complex and multi-factorial and it requires a well-coordinated, multi-pronged approach involving all relevant government and non-government

stakeholders working in a well-integrated fashion. While many federal agencies and private entities are currently engaged in activities on this issue, the efforts are sometimes fragmented and lack centralized leadership.

The Interagency Task Force on Antimicrobial Resistance was established 15 years ago to help coordinate the federal response to resistance. The ITFAR agency representatives have worked to advance efforts to address resistance. The ITFAR's most recent action plan highlights many of the areas where stronger activity is needed, but the ITFAR needs more resources and better accountability to ensure that progress is made.

Solutions

The ITFAR needs strong, high-level, centralized leadership and dedicated funding. Specifically, IDSA calls upon the Secretary of Health and Human Services (HHS) to designate an office and director within the Assistant Secretary for Health (ASH) or the Assistant Secretary for Preparedness and Response (ASPR) to oversee coordination of ITFAR activities. We continue to call for the inclusion of benchmarks in the Action Plan to establish timelines for completing projects and measuring progress. Finally, public private partnerships are necessary to the success of public health initiatives of this scale. IDSA continues to advocate for the creation of a formal advisory board of non-government experts to meet with the ITFAR on a regular basis and intends to host a meeting of government and non-government stakeholders at IDWeek in October 2014.

IDSA supports the [Strategies to Address Antimicrobial Resistance \(STAAR\) Act](#), which would enact many of the recommendations discussed in this section. But the Administration could also take many of these steps without action from Congress.

4. Enhancement of Antimicrobial Resistance Surveillance Systems

Background

Surveillance and data collection of antibiotic resistance and antibiotic usage are sporadic and contains many gaps. Antibiotic usage drives resistance and these data are sorely lacking. Real time, publicly available information is critical for determining the prevalence of resistant infections, monitoring the impact of measures such as antibiotic stewardship and infection prevention, determining antibiotic and diagnostic development priorities, and defining metrics and allowing benchmarking.

Solutions

The Centers for Disease Control and Prevention (CDC) new [Detect and Protect Against Antibiotic Resistance Initiative](#) (as proposed in the President's Budget Request for Fiscal Year 2015 at \$30 million) would improve surveillance. One piece of the initiative would create a detection network of five regional labs to speed up identification of the most concerning threats and increase susceptibility testing for high priority bacteria.

The President's Budget also requested a \$14 million increase for the National Healthcare Safety Network (NHSN). This additional funding would support increased uptake of the antibiotic resistance and antibiotic use modules — two tools that allow for centralized reporting of

antibiotic resistance data and antibiotic use data. Currently, 12,000 facilities report some type of data through NHSN, but more funding is needed to expand reporting.

While these funding increases are a step forward, the US should aim for the robust level of surveillance and data collection achieved in the EU. The European Surveillance of Antimicrobial Consumption (ESAC) system collects antibiotic use data from 34 countries, while the European Antimicrobial Resistance Surveillance System (EARSS) collects resistance data.

Lastly, it is critical that antibiotic resistance and use data, and gaps in those data, be made public on a regular basis. IDSA greatly appreciated the [2013 CDC report](#) on this issue and recommends that these data be reported every two years.

5. Strengthening Activities to Prevent and Control Antimicrobial Resistance

Background

Over the last several decades there has been a dramatic increase in antibiotic use in hospitals. Antibiotics are often prescribed needlessly and continued when no longer necessary. Such overuse and misuse is driving the development of antibiotic resistance. Antibiotic stewardship is a critical tool to protect antibiotics from misuse and overuse. Antibiotic stewardship can better patient care, improve outcomes, and lower the healthcare costs associated with antibiotic overuse as well as costs associated with infections and antibiotic resistance. In addition, multiple studies have indicated that stewardship programs provide significant cost savings.

Solutions

IDSA recommends that all healthcare facilities be required to implement an antibiotic stewardship program as a Medicare condition of participation. The STAAR Act (mentioned in section 3 above), would direct CDC to provide grants for the development, implementation and evaluation of stewardship programs. The STAAR Act would also direct CDC to pilot and test antibiotic appropriate use quality measures.

IDSA also recommends funding more research on novel strategies, best practices and evaluation of methods to prevent, control and eradicate antibiotic resistant organisms. CDC's prevention EpiCenters (a partnership with academic investigators) conduct valuable work in this area regarding healthcare associated infections, but flat funding over the last several years is preventing these collaborations from expanding their critical work. The STAAR Act would direct the EpiCenters to support evaluation of interventions to prevent or limit resistance.

CDC's proposed new antibiotic resistance initiative (mentioned under Section 4 above) would also establish prevention collaboratives. These are envisioned to be groups of healthcare facilities in communities across the country that work together to implement best practices for antibiotic prescribing and preventing infections.

6. Significant Investments in Antimicrobial-Focused Research

Background

Stagnant funding for NIAID continues to compromise the Institute's ability to fund needed research on resistance and serves as a disincentive for individuals interested in pursuing infectious diseases research, including research on resistance. IDSA was heartened to see NIAID establish a new Clinical Research Network on Antibacterial Resistance. The scientific areas this effort is expected to cover include: conducting early-stage clinical evaluation of new antibacterial drugs, performing clinical trials to optimize currently licensed antibacterial drugs to reduce the risk of resistance, testing diagnostics, and examining best practices in infection control programs to prevent the development and spread of resistant infections. Unfortunately, the \$62 million over 6 years that NIAID plans to allocate to this initiative is inadequate.

Solutions

IDSA recommends that the new Clinical Research Network on Antibacterial Resistance be codified in statute (under the STAAR Act) and allocated \$100 million annually to carry out its objectives. Overall, IDSA recommends NIAID be provided sufficient funding to allocate \$500 million annually to antibiotic resistance research. To ensure that an infusion of new funds is used in the most effective manner, and that key research areas are not missed, IDSA continues to recommend the development of an antibiotic resistance strategic research plan. Such a plan should result in a robust, well-directed, and targeted antibiotic resistance program, define high priority research needs, and address scientific challenges.

7. Greater Investment in Rapid Diagnostics R&D and Integration into Clinical Practice

Background

New diagnostic tools are also crucial for combating resistance. Diagnostic tests help guide appropriate use of antibiotics and decrease antibiotic misuse and overuse by lessening the need for clinicians to treat patients empirically and permitting use of narrow spectrum agents to minimize collateral damage to normally present host microorganisms. However, there are significant challenges to the development, regulatory approval and clinical integration of new diagnostic tests.

Solutions

IDSA's recently released report, [Better Tests, Better Care: Improved Diagnostics for Infectious Diseases](#) makes policy recommendations to help spur the development of new and more rapid diagnostic tests and encourage their use in patient care and public health, including:

- Provide robust funding for diagnostics research through NIAID, BARDA and tax credits.
- Reduce regulatory barriers to diagnostics R&D, specifically working with the FDA Center for Devices and Radiological Health (CDRH) to facilitate development of point of care tests.
- Ensure appropriate levels of reimbursement for diagnostics.
- Provide funding for the Agency for Healthcare Research and Quality (AHRQ) and the Health Resources and Services Administration (HRSA) to assist healthcare institutions and professional societies with educational programs about the utility of diagnostic tests.

8. Eliminating Non-Judicious Antibiotic Use in Animals, Plants, and Marine Environments

Background

The relationship between antibiotic-resistant infections in humans and antibiotic use in agriculture is complex, but well-documented. A large and compelling body of scientific evidence demonstrates that antibiotic use in agriculture contributes to the emergence of resistant bacteria and their spread to humans. IDSA is working to eliminate inappropriate uses of antibiotics in food-producing animals and other aspects of agriculture and aquaculture. This includes expanding surveillance of antibiotic use and resistance on the farm; ending the use of antibiotics for growth promotion, feed efficiency, and routine disease prevention purposes in food animals; and requiring prescriptions and veterinary oversight of all antibiotics given to animals.

Solutions

The EU has far outpaced the US in curbing the inappropriate use of antibiotics in food-producing animals. IDSA strongly supports a federal ban on antibiotic use in food-producing animals for growth promotion purposes. Recent FDA Guidance for Industry (GFI) # 213 would phase out such use and require changes to drug labeling, but on a voluntary basis. IDSA remains concerned that such voluntary measures may not be enough to change bad practices. As such, IDSA supports legislative measures to strengthen FDA's regulatory authority, such as the Preservation of Antibiotics for Medical Treatment Act (PAMPTA) of 2013 (H.R. 1150 in the 113th Congress) and the Preventing Antibiotic Resistance (PAR) Act (S. 1256 in the 113th Congress).

IDSA also supports a strong federal requirement that antibiotic prescriptions for animals be overseen by a veterinarian knowledgeable of the place and intended use of these drugs. FDA's recent Veterinary Feed Directive (VFD) proposed rule provides an important framework governing a veterinarian's oversight role in the use of certain drugs in animal feed, but strong veterinarian-client-patient relationship (VCPR) standards must be enforced to ensure proper oversight. In addition, five-year recordkeeping should be required and FDA should publish periodic reports so the public can monitor whether the regulation is achieving the underlying policy goals.

Finally, IDSA supports regulatory measures to expand FDA surveillance of antibiotic use in agriculture, and legislation where new authority is necessary. The Delivering Antimicrobial Transparency in Animals (DATA) Act (H.R. 820 in the 113th Congress) would provide the FDA and the public with better information on the use of antimicrobial drugs in food animals. Such data will enable public health officials and scientists to better understand and interpret trends and variations in antimicrobial resistance, to improve the understanding of the relationship between animal uses of these drugs and antimicrobial resistance in animals and humans, and to identify interventions to prevent and control resistance.

Again, IDSA thanks PCAST for this opportunity to provide comments and for its work on the issue of antibiotic resistance. IDSA looks forward to working with PCAST, our partners in the federal government, and other key stakeholders to move forward with comprehensive, aggressive strategies to address antibiotic resistance.