

**The Infectious Diseases Society of America's (IDSA) Statement on
Defending Against Public Health Threats**

**Before the Senate Appropriations Subcommittee on Labor, Health and Human Services,
Educations and Relations Agencies**

September 29, 2010

The Infectious Diseases Society of America (IDSA) appreciates this opportunity to speak before the Senate Labor, Health and Human Services (HHS), and Education Appropriations Subcommittee as you examine our nation's readiness and ability to deal with public health threats, particularly through the development of countermeasures to address biodefense, pandemic influenza and emerging infectious diseases. My name is Andrew Pavia, MD, FIDSA, FAAP. I am an infectious diseases specialist and the George and Esther Gross Presidential Professor and Chief of the Division of Pediatric Infectious Diseases at the University of Utah. I am the chair of IDSA's Pandemic Influenza Task Force. I am also a member of the National Biodefense Science Board, which was created under the authority of the Pandemic and All-Hazards Preparedness Act, to provide expert advice and guidance to the HHS Secretary and the HHS Assistant Secretary for Preparedness and Response (ASPR) to prepare for, and respond to, public health emergencies resulting from chemical, biological, nuclear, and radiological events, whether naturally occurring, accidental, or deliberate.

IDSA represents more than 9,000 infectious diseases physicians and scientists devoted to patient care, prevention, public health, research and education. Our members care for patients of all ages with serious infections, including meningitis, pneumonia, tuberculosis (TB) and HIV/AIDS, emerging infections like the 2009 H1N1 influenza virus, food-borne diseases caused by *Salmonella*, *Campylobacter*, and *Escherichia coli* (*E. coli*), and diverse infections caused by antimicrobial-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus*, *E. coli*, *Salmonella*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and the newly emerging New Delhi metallo-beta-lactamase (NDM-1). NDM-1 is an enzyme that makes bacteria resistant to a broad range of antibacterial drugs. It was first identified in December 2009 in a patient hospitalized in New Delhi with an infection caused by *Klebsiella pneumoniae*. It has since rapidly spread to other areas of the world, and three cases recently have been reported in the United States. IDSA's testimony will primarily focus on new medical countermeasures essential to address pandemic influenza and antimicrobial-resistant infections.

HHS' End-to-End Countermeasure Review

IDSA commends HHS Secretary Kathleen Sebelius and the Administration for undertaking the comprehensive end-to-end review of our medical countermeasures enterprise. As the final report (*The Public Health Emergency Medical Countermeasure Enterprise Review: Transforming the Enterprise to Meet Long Range National Needs*), prepared by the ASPR, Nicole Lurie, MD, MSPH and her staff, makes clear, there are many components and organizations which are critical to the development, deployment and use of medical countermeasures, including urgently

needed investments in the U.S. public health system. The goal of an efficient and effective medical countermeasure enterprise is to be able to rapidly produce effective responses, not only to known threats or biologic attacks, but to previously unrecognized threats and emerging infectious diseases.

We are pleased that the Administration is taking a comprehensive approach to developing a medical countermeasure strategy. Many of the recommendations in HHS' end-to-end review mirror policy improvements IDSA has suggested over the past several years, including in our 2004 report "Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates, a Public Health Crisis Brews", which called attention to the dry antibacterial pipeline and the need for the U.S. government to financially support and incentivize the development of novel antibacterial drugs. The Administration's report also reflects several recommendations found in IDSA's 2007 report, "Pandemic and Seasonal Influenza Principles for U.S. Action." In this report, IDSA recommended that HHS and ASPR move quickly to:

1. Strengthen pandemic vaccine efforts by establishing a Multinational Pandemic Influenza Vaccine Master Program
2. Strengthen anti-infective pharmaceutical research and development and stockpiling efforts
3. Improve quality and availability of diagnostic tools for influenza
4. Accelerate development of countermeasures to prevent, treat, and diagnose pandemic influenza through additional legislative action and continue to streamline regulatory approval processes
5. Update plans for countermeasure distribution and prioritization of use
6. Expand vaccine uptake, stabilize vaccine manufacture, and test and evaluate vaccine distribution plans during annual influenza seasons
7. Protect the health care workforce during a pandemic
8. Build national, regional, and local health care systems capable of responding to mass casualty events
9. Develop and test community mitigation measures
10. Improve and coordinate influenza surveillance
11. Continue to strengthen leadership, international collaboration, and communication, and
12. Allocate significant and sustainable funding for long-term planning and action.

The implementation of these policy improvements is essential to reduce the threat Americans and the world community faces from the public health threats of greatest concern. Copies of IDSA's Bad Bugs, No Drugs report and the Pandemic and Seasonal Influenza Principles for U.S. Action document are available through IDSA's website at: <http://www.idsociety.org/10x20.htm> and <http://www.idsociety.org/influenza.htm>. Additionally, IDSA is hosting a meeting on January 27-28, 2011, "Seasonal and Pandemic Influenza 2011", where the influenza principles will be reviewed and further updated to include lessons learned from the novel H1N1 influenza pandemic, with a focus on specific actions and timelines.

Pandemic Influenza and Antimicrobial Resistance

Infectious diseases and public health experts believe that another influenza pandemic is inevitable. The key questions that remain are when it will occur, which influenza virus will cause the pandemic, how severe it will be, and whether the world will be ready. Experts also are extremely concerned about the growing threat of antimicrobial-resistant infections. The need for novel products (drugs, diagnostics and vaccines) to address these threats is urgent.

There are three types of influenza viruses, classified as A, B, or C, based on their protein composition. Public health experts are most concerned with type A influenza virus. Pandemic influenza typically is a virulent new strain of human influenza that causes a global outbreak of serious illness. Four influenza pandemics have occurred during the past 100 years: the 1918-19 “Spanish flu,” the 1957-58 “Asian flu,” the 1968-69 pandemic or “Hong Kong flu” and the H1N1 pandemic from 2009-2010. The 2009 H1N1 influenza pandemic proved to be the mildest of these in overall deaths, killing an estimated 9,000 to 18,000 Americans according to CDC estimates. The virus did not develop resistance to oseltamivir (Tamiflu), the only widely available antiviral to treat influenza. Focusing solely on the number of deaths, however, masks the overall impact of the H1N1 pandemic. More than 1200 children younger than 18 died of H1N1 influenza and between 200,000 and 400,000 Americans were hospitalized.

The 2009 H1N1 influenza pandemic was perhaps a best case scenario. If a pandemic similar in virulence to the 1918 influenza strain were to occur, up to 2 million Americans could die and the number of hospitalizations and need for Intensive Care Unit beds would overwhelm our health care system and cripple our infrastructure.

On the issue of antimicrobial-resistant infections, the U.S. Centers for Disease Control and Prevention (CDC) has described antimicrobial resistance as “one of the world’s most pressing health problems”, while the World Health Organization (WHO) calls it “one of the three greatest threats to human health.” Infectious diseases physicians agree. NDM-1, for example, poses a new threat of great concern and illustrates how antimicrobial-resistant infections will continue to emerge wherever antimicrobial drugs are used. NDM-1 also illustrates how a drug-resistant organism created in one area of the world can quickly threaten all regions. The costs due to antimicrobial resistance, both in the numbers of lives lost or devastated and in economic terms, are exceedingly high. Drug-resistant bacteria, such as MRSA resistant *E. coli*, *Acinetobacter baumannii* and *Clostridium difficile* (*c. diff.*) currently affect many hospitalized patients and a growing number of people in the community, including healthy athletes, parents, working people, and children. CDC reports that nearly 2 million health care-associated infections (HAIs) and 90,000 HAI-related deaths occur annually in the U.S. Most of these infections and deaths involve antimicrobial-resistant bacteria. The direct and indirect economic costs associated with antimicrobial-resistant infections are also enormous in terms of dollars spent, length of hospital stay, and loss of productivity. A recent study indicated that annually in the U.S. antimicrobial-resistant infections are responsible for more than \$20 billion in excess health care costs, more than \$35 billion in societal costs, and more than 8 million additional hospital days. Antimicrobial resistance is a critical issue in viral diseases as well. In 2008, the dominant circulating seasonal influenza strain had become resistant to oseltamivir (Tamiflu) leaving limited options for treatment. For now, this strain has largely disappeared, but if it re-emerges we have few drugs in the pipeline to deal with the threat.

There also is an alarming connection between influenza and antimicrobial-resistant bacterial infections. In addition to the morbidity and mortality caused by the influenza virus itself, many people with influenza will develop life-threatening secondary bacterial infections, many of which are resistant to antibacterial drugs. In recent years, MRSA has been the most lethal cause of post-influenza bacterial infections.

Reengineering the Pandemic Influenza Vaccine Production Enterprise

As we stated in our 2007 Pandemic and Seasonal Influenza Principles for U.S. Action, IDSA believes the widespread use of a pandemic vaccine should be the central strategy for protection of human health during a pandemic event. IDSA supports a coordinated effort led by the federal government working with public and private partners and the international community to outline a comprehensive approach that will coordinate, and strengthen vaccine research and development, increase production capacity, accelerate licensure, guarantee equitable global distribution, and monitor vaccine performance and safety.

In August 2010, the President's Council of Advisors on Science and Technology (PCAST) issued a report focused on reengineering the pandemic influenza vaccine production enterprise. In its report, the PCAST emphasized that existing technology for influenza vaccine will never deliver enough vaccine in time to respond to a pandemic. However, they said that targeted investments in key areas could shorten by weeks the time needed to produce enough doses. They found that the development of new types of influenza vaccines is of critical importance, and no single new technology has a high likelihood of success. To ensure success of one, we must pursue several potential vaccine strategies simultaneously. The PCAST recommendations provide a blueprint to significantly increase our nation's ability to produce vaccine in a timely manner. The recommendations would speed up not only flu vaccines, but also a number of other medical countermeasures against infectious diseases that could emerge naturally or as the result of a bioterrorism attack.

Although the PCAST did not determine anticipated costs for the projects required to make the improvements necessary to reengineer the influenza vaccine production enterprise and has not attempted to allocate the share of financial responsibility to be borne by the governmental agencies or the companies, they did state that it is fair to assume an initial \$1 billion in Federal funds—and at least similar sums over the subsequent few years—would be required to make the changes that will allow the Nation to mount a vigorous effort that can protect its population as well as possible in the event of another pandemic, an event that could have catastrophic consequences.

On-going strong investment in pandemic vaccine technologies is justified on a cost-benefit basis, in part because large numbers of lives could be saved through relatively inexpensive improvements in current methodologies and in part because federal investments in influenza pandemic response would speed development of technical platforms and production facilities that would support medical countermeasures against a variety of other dangerous pathogens.

Antimicrobial and Diagnostics Discovery and Development

The development of both antiviral and antibacterial drugs as well as point-of-care diagnostics must be treated as priorities in the U.S. medical countermeasure development strategy. In IDSA's view, there is an urgent need to address the factors that have resulted in a dearth of new antimicrobials and other countermeasures in development. These include:

- Lack of financial incentives of sufficient strength to make companies choose to engage;
- Regulatory uncertainty caused by the lack of consistent approval pathways and limited regulatory scientific resources at the Food and Drug Administration (FDA);
- Insufficient federally supported research and development efforts; and
- Lack of a coordinated management structure

In addition, as pointed out in the end-to-end medical countermeasure review, lack of coordination between federal agencies and complex contracting regulations add additional barriers.

To create a sustainable, national and global medical countermeasures R&D enterprise, it is necessary to determine the right combination of financial incentives ("push" and "pull" mechanisms) to entice industry to invest and to help companies, big and small, with innovative technology to succeed. Examples of the push incentives are grants, contracts, and tax credits. Examples of the pull incentives are milestone payments, guaranteed markets, liability protection, patent extensions or data exclusivity, and prizes. These incentives are intended to change the "return on investment" or net present value calculation of countermeasures to make them more competitive with other medical products. The strategic investment firm envisioned by the medical countermeasure review report also supports the development of high priority products by sharing the risk of development with companies. The HHS report highlights the need for the strategic investment firm to first focus on novel antimicrobials to address drug-resistant infections. IDSA wholeheartedly supports this effort. We caution, however, that the proposed initial funding level for the strategic investment firm is \$200 million, which is wholly insufficient to increase the likelihood of bringing successful antimicrobial drugs and other medical countermeasures to the marketplace. We also strongly believe that additional "push" and "pull" incentives are needed, particularly to address the withering antibacterial pipeline, and urge Congress to act quickly to pass strong legislation in this area. Risk sharing and incentives that stimulate the development of new rapid diagnostics also should be adopted.

FDA must quickly assure a clear regulatory pathway for the review and approval of new countermeasures. For many years, industry representatives have identified regulatory uncertainty as one of the primary obstacles to new antibacterial development, in particular. IDSA acknowledges the strong commitment expressed by current FDA leaders and staff to address the multi-faceted problem of regulatory uncertainty. Despite good faith meetings, workshops, and advisory committee meetings, the situation today for antibacterial review and approval appears no better than it was at this time last year. In some respects, the level of uncertainty has increased. In its medical countermeasure review report, HHS identified a critical need to upgrade FDA science and regulatory capacity. HHS hopes to make a significant investment to provide FDA scientists with the resources they need to develop faster ways to analyze promising new discoveries and give innovators a clear regulatory pathway to bring their

products to market. This year, IDSA, FDA, the National Institute of Allergy and Infectious Diseases (NIAID), and pharmaceutical companies have begun to participate in an important effort being led by the Foundation of the National Institutes of Health (FNIH) to study new endpoints that will more easily demonstrate antibacterial effectiveness. The FNIH effort is promising, but to develop this knowledge and quickly implement changes in the regulatory process requires people and money. This spring, IDSA testified in support of additional funding to allow FDA to hire additional staff to develop much needed clinical trial guidance documents and to fund Critical Path initiatives specific to antimicrobial drug development. We also requested \$13.25 million to support a focus on new antibiotics within FDA's new regulatory science initiative with the National Institutes of Health (NIH).

We recognize the strains on the federal budget due to the economic crisis and the budget deficit, but significantly increased federal research dollars are urgently needed to advance scientific knowledge about pandemic influenza and antimicrobial resistance, as well as to support countermeasure discovery and development. IDSA has for the past several years supported consistently strong funding for these activities throughout HHS. We appreciate that this Subcommittee has provided substantial funding for pandemic influenza response, as it did last year in the Supplemental Appropriations bill. However, IDSA strongly believes that some pandemic preparedness efforts require funding over multiple years. For example, companies considering investing in countermeasures development need assurance that the financial commitment will be secure in future years or they will not engage.

We strongly support significantly boosting funding for HHS' Biomedical Advanced Research and Development Authority (BARDA). This year, IDSA testified in support of at least \$1.7 billion of multi-year appropriations for BARDA in FY 2011 to fund the development of new therapeutics, diagnostics, vaccines, and other technologies, including antimicrobials. Such funding would significantly enhance BARDA's support of countermeasures through the advanced stages of development, as well as BARDA's flexibility to partner effectively with industry. IDSA also wishes to see BARDA take a much stronger role in advancing the development of new antimicrobials and related diagnostics to detect, identify and treat pathogens that presently are affecting a significant number of Americans in hospitals annually. With modern molecular biology techniques, the resistance genes found in these highly resistant "superbugs" can be readily introduced into bioweapons such as anthrax or tularemia. Specific to NIAID research funding for antibacterial resistance and antibacterial discovery research, this year IDSA testified in support of a substantial funding increase in these areas for FY 2011 to a total of \$500 million. Current NIAID funding levels in these areas are extremely limited in IDSA's view and do not match the threats we face from antibacterial-resistant infections.

Moreover, to further strengthen the countermeasures pipeline, we must invest in appropriate infrastructure for clinical trials. Such clinical trials infrastructure should be flexible and agile, with the ability to rapidly respond to new or re-emerging infections as they arise. Further, it must balance both pediatric and adult unmet infectious diseases needs. We are gratified to see NIAID taking steps to achieve part of this goal, as NIAID is broadening its AIDS Clinical Trials Group (ACTG) to expand its tuberculosis and, likely, its hepatitis C clinical research portfolios. Earlier this year, IDSA urged NIAID to build clinical trials infrastructure in areas beyond HIV/AIDS including to address serious bacterial, viral (particularly influenza), and fungal

infections. The creation of an NIAID-funded in-patient clinical trials network in these areas will help to create an environment supportive of high-quality research, incorporating experienced investigators and study sites, robust statistical support, specialized laboratories (e.g., pharmacokinetics, immunology) and organizational structures to support clinical trials. Such additional clinical trials infrastructure could contribute substantially to the critical need for advancements in the diagnosis and treatment of drug-resistant bacterial infections, pandemic and seasonal influenza and other serious infections. Furthermore, the clinical trial infrastructure we have proposed fits squarely within and is supportive of HHS' medical countermeasure review effort. IDSA believes such additional infrastructure is urgently needed.

The global H1N1 pandemic is a striking reminder of the importance of making sustained investments in research as well as public health infrastructure. Investments made over the past several years in surveillance, vaccine capacity and preparedness clearly limited the impact of the H1N1 pandemic. However, in other areas the pandemic showed our continued vulnerabilities. These include early international detection, and rapid production and distribution of vaccines, and antivirals that are appropriate for critically ill patients. The threat of another pandemic remains. The nation's public health system must maintain robust disease surveillance, epidemiologic investigation, education and outreach, and communications capacity.

Strengthening Leadership, Coordination and Management Structure

In 2007, IDSA called for strengthened leadership and collaboration in influenza preparedness. We called for HHS and the federal government to clarify lines of authority and key responsibilities, involve technical experts and stakeholders, issue and update national standards for planning, and continue to lead international collaborative efforts related to pandemic preparedness. HHS responded and many improvements were considered and implemented. The PCAST report recommends that the Administration further strengthen its management structure by vesting authority with the ASPR at HHS to coordinate and task component agencies at HHS with supporting and implementing the influenza vaccine recommendations. In addition, it recommends that HHS create a small advisory committee comprised of representatives from the biotechnology, pharmaceutical and investment communities, to guide the Department's engagement with industry. This coincides with the recommendation in HHS's end-to-end medical countermeasure review that changes are needed in how the enterprise is managed to greatly strengthen its decision-making. The review suggests that HHS identify a leader who would work with program leaders and managers across the span of medical countermeasure development activities as well as with commercial partners and other key stakeholders. The congruence of these three recommendations emphasizes the critical role of integrated and coordinated planning between all levels of government in pandemic preparedness and medical countermeasure development.

Having the necessary infrastructure in place to both monitor and respond to current and emerging antimicrobial-resistant infections also will play a crucial role in ensuring that we are protecting the health and safety of our citizens. Congress began to address this need several years ago when it passed legislation that became Section 319E, "Combating Antimicrobial Resistance" of the Public Health Service Act. This law directed the Secretary to establish an Antimicrobial Resistance Task Force to coordinate Federal programs relating to antimicrobial resistance. This Task Force developed the Public Health Service Action Plan to Combat Antimicrobial

Resistance, published in 2001, which has not been sufficiently funded. Comprehensive legislation introduced in the Senate during the last Congress and in the House of Representatives in each of the last two Congresses, the "Strategies to Address Antimicrobial Resistance (STAAR) Act" (H.R. 2400 in the 111th Congress), will advance the key elements in the federal Action Plan and authorize adequate funding for these strategies. The STAAR Act strengthens existing efforts by establishing within HHS an Antimicrobial Resistance Office (ARO). The Director of this new office also will serve as the director of the existing interagency task force to facilitate the coordination of activities. The legislation also would establish a Public Health Antimicrobial Advisory Board (PHAAB) comprised of infectious diseases and public health experts who will provide much-needed advice to the ARO Director and interagency task force. Finally, the bill, when enacted and sufficiently funded, will strengthen existing surveillance, data collection, and research activities as a means to reduce the inappropriate use of antimicrobials, develop and test new interventions to limit the spread of resistant organisms, and create new tools to detect, prevent and treat drug-resistant "bad bugs."

Conclusion

It is easy to dismiss hyperbolic news reports because of sensationalism and inaccuracies, but the danger posed to the United States by biological threats, including pandemic influenza, biologic weapons and emerging infections, including antimicrobial-resistant infections, is very real and very great. Continued thoughtful investment in science, filling the pipeline, evaluating and licensing countermeasures and efficient management of the enterprise will provide Americans with the protection they expect and deserve. IDSA stands ready to assist this Subcommittee and the federal government in any way that we can, and we are grateful for this opportunity to express our views.

Thank you.