Testimony of the Infectious Diseases Society of America on U.S. Biodefense, Preparedness, and Implications of Antimicrobial Resistance for National Security
Prepared for the U.S. House of Representatives Committee on Oversight and Reform Subcommittee on National Security
Submitted by Helen Boucher, MD, FACP, FIDSA, IDSA President on June 26, 2019, 14:00

On behalf of the Infectious Diseases Society of America (IDSA), my fellow ID physicians and most importantly, our patients, I thank the Subcommittee for holding today's hearing and inviting me to testify. I am an infectious diseases physician, Professor of Medicine in the Division of Geographic Medicine and Infectious Diseases at Tufts Medical Center in Boston, Massachusetts, and the Director of the Tufts Center for Integrated Management of Antimicrobial Resistance (CIMAR). I also serve as the Director of the Heart Transplant and Ventricular Assist Device Infectious Diseases Program and the Infectious Diseases Fellowship Program at Tufts Medical Center and as the Treasurer of IDSA. I established the antimicrobial stewardship program at Tufts in 2002. In addition, I serve as a voting member of the Presidential Advisory Council for Combatting Antibiotic-resistant Bacteria (PACCARB). My comments today are my own and delivered on behalf of IDSA and do not reflect the views of the United States government.

In 2013, both the United States Center for Disease Control and World Health Organization declared antimicrobial resistance (AMR) a public health crisis. Combating antimicrobial resistance (AMR) and strengthening the antibiotic pipeline are top priorities for IDSA. We welcome the opportunity to work with the Subcommittee and other key stakeholders to advance solutions. IDSA members routinely see patients with infections that are extremely difficult or in some cases impossible to treat due to resistance and our dwindling arsenal of safe and effective antibiotics.

I am first and foremost a clinician, so I would like to start by telling you about two patients we recently treated. The first is a young lady with a history of injection drug use who has had two prior heart valve infections related to opioid use. Over the course of 2 years she had 2 separate heart valve infections, the 2nd of which was due to methicillin-resistant *S. aureus* (MRSA) and involved her tricuspid valve that was surgically repaired for the first infection. Her treatment was complicated by kidney failure due to vancomycin (an antibiotic) and required prolonged hospitalization. Her course was further complicated with a chest wound infection, also due to MRSA. We saw her again when she was 22 weeks pregnant and the MRSA infection of her sternum extended into her chest. She had to have several surgeries and to receive another long course of antibiotic therapy while pregnant. She had several more hospitalizations, including time spent in the ICU, but ultimately delivered a healthy full-term baby. Her problems have continued, however, and she may require another valve replacement. Sadly, hers is not an isolated case. We and most other health care facilities in the US have large numbers of patients with drug-resistant infections related to opioid use.

The second patient is a middle-aged lady I took care of in the hospital recently. She had undergone chemotherapy for leukemia and was in remission (she had no cancer in her body). We were called when she developed pneumonia with bloodstream infection due to a gram-negative bacteria resistant to every available drug tested. When I sat to deliver this news, my patient said,

"how can this be…surely you'll find something to treat this." We successfully did fancy testing in the lab, collaborated with a world expert on these infections, obtained permission and help from the FDA and help from a company to give her an investigational drug called cefiderocol plus a combination of other antibiotics, but she died ten days later. So this lady in the prime of her life who had beat cancer died from an antibiotic-resistant infection. It's important to point out that even with our best efforts, and help from many all over the country, it took 4 days to get the emergency use antibiotic to our patient. This is actually better than most of these types of requests go and emphasizes how vital it is for us to have effective drugs in our hospital pharmacies ready to use when our patients need them.

These are only two of the many other stories of patients who died or suffered devastating complications caused by antibiotic-resistant infections--stories that motivate me and so many of my infectious diseases colleagues to fight for solutions to this crisis.

Antimicrobial Resistance and Key Drivers

While bacteria develop resistance in nature, the use of antimicrobial drugs, including antibiotics, places selective pressure on microbes, including bacteria. This leads to bacteria and other microbes developing resistance to available antimicrobial drugs. Bacteria are also able to pass their resistance genes easily to one another, facilitating rapid spread of antibiotic resistance. Ultimately, some bacteria become utterly resistant to all known antibiotics. We fear that what is now uncommon will be common, effectively bringing us back to a pre-antibiotic era.

According to data published in 2018, as many as 162,000 people in the US lose their lives every year due to multidrug-resistant infections, which would make resistant infections the third leading cause of death in the US.[1] According to 2013 data from the Centers for Disease Control and Prevention (CDC), at least 2 million people in the US suffer from an antibiotic-resistant infection each year, a very conservative estimate.[2] The AMR Review published in the UK estimated in 2014 that at least 700,000 people globally lose their lives every year due to resistant infections. This study estimated that if we do nothing, by 2050, 10 million people will die due to AMR annually worldwide, surpassing cancer deaths.[3] The opioid epidemic is one factor driving increases in resistant infections. CDC estimates that in the US, individuals who inject drugs are 16 times more likely to develop a methicillin-resistant *S. aureus* (MRSA) infection.[4] CDC also estimates that antibiotic-resistant infections result in $20 billion in excess health care costs annually, due in large part to longer hospital stays for patients whose infections are not easily treated.[5] As the subcommittee considers the costs of proposals to address antibiotic resistance and strengthen the antibiotic pipeline, I strongly urge you to consider the far higher cost of inaction.

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[1] Burnham JP, et al. (2019). Re-estimating annual deaths due to multidrug-resistant organism infections. Infection Control & Hospital Epidemiology 2019, 40, 112–113. doi: 10.1017/ice.2018.304

[2] Antibiotic Resistance Threats in the United States, 2013. US Centers for Disease Control and Prevention.

[3] Review on Antimicrobial Resistance. Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations. 2014.

[4] Jackson KA, Bohm MK, Brooks JT, et al. Invasive Methicillin-Resistant Staphylococcus aureus Infections Among Persons Who Inject Drugs — Six Sites, 2005–2016. MMWR Morb Mortal Wkly Rep 2018;67:625–628. DOI: http://dx.doi.org/10.15585/mmwr.mm6722a2external.

[5] Antibiotic Resistance Threats in the United States, 2013. US Centers for Disease Control and Prevention

CDC data indicate that roughly 30 percent of antibiotics used in hospitals are unnecessary or prescribed incorrectly. Total inappropriate use in outpatient settings approaches 50 percent of antibiotic prescriptions.[6] We must reduce the improper use of antibiotics to reduce resistance. But it is important to remember that ANY antibiotic use, even appropriate use, will lead to the emergence of resistance. We can and we must slow resistance, but we cannot stop it.

Further, we continue to identify new resistance threats as they continue to emerge. As physicians, we need new drugs to treat our patients as resistant organisms are inevitable. We need a robust antibiotic pipeline that is capable of meeting today's threats and those that will emerge, threatening our children and future generations.

Antibiotic use in animals and agricultural settings also contribute to AMR. Environmental factors, such as the release of antibiotics and other chemicals and wastes into water and soil, play significant roles. IDSA embraces a One Health approach to address AMR with solutions that span human health, animal health, agriculture and the environment. This testimony will focus primarily on human health, which is IDSA's area of greatest expertise.

Americans are concerned about antibiotic resistance. IDSA partnered with Research!America to commission a nationwide public opinion poll conducted in October 2018 by Zogby Analytics, with support from Pfizer. Sixty-five percent of those polled believe antibiotic resistance is a public health problem, and 76 percent agreed that the federal government should increase funding for research and public health initiatives to address antibiotic resistance. That support was strong across political affiliations, with 81 percent of Democrats, 76 percent of Republicans and 70 percent of Independents in agreement. A majority of 73 percent agree that the federal government should provide incentives to encourage increased private sector investments in the development of new antibiotics.

There is significant recognition of the antibiotic resistance crisis and the need for action. This issue was the focus of the Aspen Health Strategy Group this June, co-chaired by two former Secretaries of Health and Human Services, Kathleen Sebelius (2009-2014) and Tommy Thompson (2001-2005). Expert bodies, including the World Health Organization and the President's Council of Advisors on Science and Technology, have also called for action to combat antibiotic resistance and foster the research and development of urgently needed new antibiotics. These challenges are a key focus of IDWeek—IDSA's annual scientific meeting—at which we convene experts aimed at advancing scientific approaches to resistance, antibiotic development and antibiotic stewardship. Antibiotic Stewardship refers to programs of coordinated interventions designed to improve and measure the appropriate use of antibiotic agents by promoting the selection of optimal antibiotic regimens including the optimal dosing, duration of therapy, route of administration (e.g. intravenous or oral); the purpose of which is to improve patient outcomes and decrease antimicrobial resistance.

Antibiotic pipeline challenges

[6] Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. JAMA: The Journal of the American Medical Association 2016; 315(17): 1864-73.

As the threat of resistance continues to spread and claim lives, our toolbox of antibiotics to treat these infections is shrinking. While the numbers of antibiotics annually approved for marketing in the US has increased in recent years following a decline in the previous decade, the most recently approved drugs represent modifications to existing classes, rather than more innovative approaches. Unmet needs persist, with far too few treatment options available for multidrug-resistant infections.

Nearly all large pharmaceutical companies have left the antibiotic development field. The small companies that are responsible for most of the antibiotic innovation are struggling to stay in business, as the new antibiotics they have developed and launched provide very little opportunity for return on investment. In April 2019, one small antibiotics company—Achaogen—filed for bankruptcy, despite having launched an important new antibiotic plazomicin in 2018. In June 2019, another small antibiotics company—Tetraphase—announced massive layoffs, including eliminating its research function. The few remaining small antibiotics companies face similar fates. Indeed, these companies are struggling financially to manufacture these medicines. These new antibiotics were developed in part with federal taxpayer dollars meant to stimulate research and development of innovative antimicrobials. Yet, after these federal expenses, the drugs developed and FDA-approved may not be available to patients who need them. Further, these companies are unable to conduct necessary post-market studies to support the use of their drugs in precisely the infections for which new therapies are direly needed. And these companies cannot fund continued investment into the development of additional new antibiotics.

There are currently 42 antibiotics in development, 15 in Phase 1 clinical trials, 11 in Phase 2, 13 in Phase 3, and three have had new drug applications submitted. Of these, 16 have the potential to treat gram-negative infections—which ID physicians consider to be among the worst, most highly resistant, and most difficult to treat threats.[7] It is important to remember that the drug development process is long (approximately 10 years), expensive (up to 2.7 Billion USD) and risky. Most of these drugs in clinical development do not ultimately achieve Food and Drug Administration (FDA) approval (estimates are that 1 out of every 5-10 drugs that reach human testing will make it to FDA approval).

The very nature of infectious diseases and antibiotic resistance necessitates a robust and renewable antibiotic pipeline capable of meeting current and future patient, public health and national security needs. New threats will continue to emerge, and existing threats will continue to evolve. Patients with multidrug-resistant infections often have other health problems which may limit the types of antibiotics that will be safe and effective for them. For example, many patients develop kidney problems when they are ill. This further limits antibiotic options as many antibiotics can't be given to patients with kidney problems.

Impact of resistance and lack of new antibiotics on national security

AMR poses a significant threat to our national security. Resistant pathogens complicate our soldiers' combat wounds, increasing the risk of limb loss and death, and compromise our military's combat readiness and effectiveness. Between 2004 and 2009, over 3,300 American

[7] Tracking the Global Pipeline of Antibiotics in Development. The Pew Charitable Trusts. March, 2019.

soldiers in Iraq and Afghanistan became severely ill from a single resistant Gram-negative pathogen—*Acinetobacter*, which has become even more resistant to treatment over time.[8]

Alarmingly, resistant pathogens are also a prime candidate for weaponization by our nation's enemies, both state and non-state actors. The former Soviet Union engineered multidrug-resistant strains of both plague and anthrax.[9] Studies have concluded that the aerosolized release of a weaponized, resistant pathogen in just a single incident of bioterrorism in the Washington, DC area would result in a death toll of over 3 million.[10] The death toll from a coordinated bioterrorist attack using a weaponized resistant pathogen would be many magnitudes higher. Any mass casualty event is likely to result in severe wounds and burns, which can quickly become infected and further complicated by resistance.
AMR also puts our health security at risk, both within the US and globally. An outbreak of a serious resistant infection with limited or no treatment options could overwhelm health systems, harm economies, and even destabilize communities or entire countries.

Impact of resistance and lack of new antibiotics on patient care and public health
While AMR is a serious national security concern, it is also a life-threatening crisis that impacts patients every day and threatens to undo decades of medical progress. Many life-saving procedures—cancer chemotherapy, organ and bone marrow transplants, other complex surgeries--are made possible by safe and effective antibiotics. These procedures significantly increase patients' risk of infections by weakening their immune systems or opening their bodies up to bacteria. We can only manage that risk with antibiotics, but resistance is spreading. Our antibiotic pipeline is dwindling, severely limiting our ability to support this crucial medical care.

Joint replacements are one of the most common surgeries in the US. Any cut of the skin or placement of an artificial item inside a patient increases that patient's risk of infection. We have strong processes in place to limit that infection risk, but we cannot prevent every infection. We already see patients whose new hips or knees become infected with untreatable infections and who then face amputation or worse. We do not want to lose the ability to perform joint replacement surgeries—which enhance the lives of millions of individuals, providing increased mobility and freedom from pain—because we cannot manage the associated infections.

Infections that are not typically life-threatening are also becoming far more difficult to treat as a result of resistance, dramatically increasing health care costs and burdening patients. Consider urinary tract infections, a very common illness among women, that were once reliably treated with oral antibiotics. As resistance to all available oral antibiotics has increased, and intravenous antibiotics become the only remaining treatment option, many more patients now face a hospital stay to treat a urinary tract infection.

Current federal efforts to address resistance

[8] Fighting Superbugs: DoD's Response to Multidrug Resistant Infections in Military Treatment Facilities. Hearing before the Subcommittee on Oversight and Investigations of the Committee on Armed Services. US House of Representatives, September 29, 2010
[9] Microbial Threats to Health: Emergence, Detection, and Response. Smolinski, M.S., Hamburg, M.A., and Lederberg, J. 2003.
[10] Rosen J et al. Cybercare: A System for Confronting Bioterrorism. National Academy of Engineering. Engineering and Homeland Security, December 3, 2008.

Legislation
IDSA greatly appreciates previous and ongoing efforts by Congress and the federal government to combat antibiotic resistance and strengthen the antibiotic pipeline. The Generating Antibiotic Incentives Now (GAIN) Act, enacted in 2012 as part of the Food and Drug Administration Safety and Innovation Act (FDASIA), provided an important first step to support antibiotic R&D by granting an additional five years of exclusivity to new antibiotics and antifungals that treat serious or life-threatening infections. The 21st Century Cures Act, enacted in 2016, established the Limited Population Antibacterial Drug (LPAD) pathway, which makes clinical trials more feasible for the most urgently needed new antibiotics to address unmet medical needs. Under LPAD, urgently needed antibiotics can be studied in smaller, more rapid clinical trials, which is essential because some of the most highly resistant pathogens infect relatively small numbers of critically ill patients who are challenging to enroll in clinical trials. It is important to note that so far, no company has successfully utilized the new LPAD mechanism. IDSA has made recommendations to the FDA for more novel clinical trial designs that we believe could support the stronger implementation of LPAD. We look forward to continuing to work with the agency on these approaches.

National Action Plan for Combating Antibiotic Resistant Bacteria
The National Action Plan for Combating Antibiotic Resistant Bacteria (CARB) set forth several critical goals and objectives to drive progress in the areas of infection prevention, antibiotic stewardship, surveillance, therapeutic and diagnostic innovation, and enhanced global coordination. In Fiscal Year 2016, Congress allocated an increase of $380 million across multiple federal agencies to support implementation of the CARB National Action Plan and has sustained that funding in subsequent years, providing some modest but important increases for key programs at CDC, the Biomedical Advanced Research and Development Authority (BARDA) and the National Institute for Allergy and Infectious Diseases (NIAID). These efforts have driven important progress, though significant work remains to be done.

With regard to antibiotic R&D funding, the BARDA broad-spectrum antimicrobials program remains an essential support for the advanced research and development of antibiotics that have a biothreat indication. BARDA and NIAID joined with multiple private partners across the globe to launch CARB-X, which supports early development of new antibiotics, vaccines, rapid diagnostics and other products to prevent, diagnose and treat life-threatening bacterial infections. CARB-X is expected to support more than 60 promising products by the end of this year, many of which represent highly innovative approaches to antibiotic-resistant infections.

IDSA greatly appreciates growing investment for AMR research at NIAID. One important example of supported research is the Antibacterial Resistance Leadership Group (ARLG), which was launched in 2013 to prioritize, design and execute clinical research that will reduce the public health threat of antibacterial resistance. ARLG research focuses on several key areas, including early clinical evaluation of new antibacterials, strategy trials to optimize the use of current antibacterials, treatment-based prevention measures, diagnostics testing, and effective infection control and stewardship programs and activities.

Since June 2013, the ARLG has initiated over 40 studies that include over 18,000 patients. The ARLG also activated over 130 clinical trial sites and established collaborations in 19 countries. The ARLG developed a virtual biorepository catalog, a web-based system that provides researchers with access to well-characterized bacteria for the development of diagnostic tests, novel antimicrobial compounds and for studies evaluating mechanisms of resistance. The ARLG has shipped over 1400 strains to 28 approved requestors.

Additional funding would allow the ARLG to expand its efforts for more high priority pathogens as well as additional study sites in more states and countries. If funded, plans include embarking on ambitious but essential interventional trials to define best treatments for highly antibiotic-resistant bacterial infection enabling optimal use of newly approved antibiotics. The knowledge gained from ARLG research will be essential in guiding further government and private sector efforts to address AMR and development of new antimicrobial drugs, diagnostics and preventive measures. In addition, a clinical trials network built off of the ARLG infrastructure would be an important resource to support registration trials for new antibiotics. Such a network would require additional federal funding and should be done collaboratively with international and non-governmental partners.

We have been encouraged to see an increase in the number of hospitals that have implemented antibiotic stewardship programs that align with CDC Core Elements of Hospital Antibiotic Stewardship Programs. As of 2017, 76 percent of hospitals had implemented such programs, an increase from 65 percent in 2016 and 48 percent in 2015. IDSA continues to promote universal adoption of stewardship so that all patients and communities can benefit from the improved patient outcomes, reduced rates of resistance and lower health care costs associated with stewardship. We strongly support a requirement that hospitals establish stewardship programs as a condition of participation in Medicare, and we are pleased that both the PACCARB and the CDC Board of Scientific Counselors have also expressed support for this important policy. We are encouraged that the administration recently extended this proposed rule for one year, rather than allowing this proposal to expire. Examples of the impacts of stewardship programs include[11]:

- Tufts Medical Center (started 2002): documented improved patient outcomes with decreased length of stay and improved rates of initial appropriate antimicrobial therapy for ventilator-associated pneumonia[12] and decreased antibiotic use in patients with COPD who underwent rapid diagnostic testing.[13]
- Vanderbilt University Hospital in Tennessee found that the proportion of healthcare-acquired infections caused by multidrug-resistant gram negative pathogens decreased from 37.4 percent in 2001 to 8.5 percent in 2008.
- A university-affiliated community hospital in Queens, NY realized an 80.1% reduction in hospital-wide cephalosporin use, which led to a 44.0% reduction in the incidence of ceftazidime-resistant *Klebsiella* infection and colonization throughout the medical center,

[11] IDSA and SHEA present evidence and justification for antibiotic stewardship programs to be a Condition of Participation in Medicare.
[12] Lancaster JW et al Impact of an institution-specific hospital-acquired pneumonia protocol on the appropriateness of antibiotic therapy and patient outcomes. Pharmacotherapy. 2008 Jul;28(7):852-62. doi: 10.1592/phco.28.7.852.
[13] Tickoo et al, in press, BMC Pulmonary Medicine

a 70.9% reduction within all intensive care units, and an 87.5% reduction within the surgical intensive care unit.

- Saint Joseph Mercy Community Hospital in Ann Arbor, MI, studied one aspect of its stewardship program—prospective audits of antimicrobial orders—and found that this intervention yielded an approximately 50 percent reduction in the risk of contracting *Clostridioides difficile*, a life-threatening diarrheal infection associated with antibiotic use.
- Cost savings associated with the implementation of stewardship programs include:
    - Tufts Medical Center – $400,000/year currently, yielding approximately $6MM savings over the last 17 years.
    - Community hospital (120 beds) in Monroe, LA saved $177,000 over one year.
    - Long term acute care hospital (60 beds) in Dallas, TX saved $159,580 over 15 months.
    - Community teaching hospital (159 beds) in Dorchester, MA saved $200,000-$250,000 in one year.
    - Large tertiary teaching hospital in Baltimore (800 beds) in Baltimore, MD saved nearly $3 million in 3 years.
    - Academic medical center (880 beds) in Winston-Salem, NC saved $920,070 to $2,064,441 per year over 11 years.

These examples reflect the experiences of hospitals with robust antimicrobial stewardship programs across the country.

Since 2016, the CDC continues to advance our nation's public health responses to resistance. CDC has expanded its epidemiology and laboratory capacity, working with states, communities and healthcare facilities to more rapidly detect emerging resistance threats and outbreaks and to prevent and contain the spread of resistant infections. In April, 2018, CDC published a Vital Signs report focused on controlling unusual resistant bacteria, which are resistant to all or most antibiotics tested and carry special resistance genes. With the new funding allocated by Congress, CDC was able to identify an aggressive containment strategy which CDC estimated could prevent 1,600 cases of CRE (a highly resistant pathogen known as the "nightmare bacteria") in a single state over three years. Additional resources for the CDC Antibiotic Resistance Solutions Initiative will support implementation of this and other strategies to prevent the development of resistance and the spread of resistant infections in additional health care settings and communities.

The CDC National Healthcare Safety Network (NHSN) offers a module through which healthcare facilities may report data on antibiotic use and resistance. As of January 1, 2018, over 616 facilities from 48 states are reporting antimicrobial use data and over 231 facilities from 27 states submitted at least some antimicrobial resistance data. This represents a 40 percent increase for hospitals reporting use data and a 27 percent increase for resistance data over the previous six months. While the upward trend is encouraging, there are still significant gaps in reporting, which hinder our understanding of antibiotic prescribing and resistance trends and how to best improve them. CDC also collaborates with state and local health departments, academic partners, and health care facilities in the US and abroad to identify and implement best practices in infection prevention and antibiotic stewardship. Additional resources are needed to allow CDC

to support additional healthcare facilities, such as smaller hospitals, long-term care facilities and outpatient settings.

National Biodefense Strategy
IDSA supports the AMR goals and objectives included in the National Biodefense Strategy issued by the White House in 2018:

- Strengthen awareness of drug-resistant pathogens and their associated diseases and improve stewardship of medically important drugs.
- Strengthen understanding of the drivers of drug resistance and improve the development and adoption of effective mitigation measures.
- Promote the use of preventive and therapeutic options other than antimicrobial drugs.
- Accelerate basic and applied research and development of new antimicrobials, novel preventatives and therapeutics, vaccines, and diagnostic tests.

These topics represent key issues that need to be addressed to combat AMR effectively. We now need more specific policies and resources to drive progress toward these goals. Efforts to implement this strategy should also be coordinated with ongoing efforts under the CARB National Action Plan to ensure the most meaningful outcomes and the most effective use of federal resources.

Global Health Security Strategy
Like any other infectious disease threat, antimicrobial resistance does not respect international borders. As we become an increasingly interconnected world with frequent international travel, resistant pathogens that emerge in other parts of the world quickly spread to the US. In 2015, a new resistance gene (MCR-1) was discovered in China. This gene attaches to *E. coli* and other common bacteria that cause urinary tract, blood, gut and other infections and makes these common bacteria resistant to colistin—an antibiotic that is toxic and causes kidney damage but is used as a last resort to treat multidrug-resistant infections. Within a few months, patients in the US were infected with bacteria that had the MCR-1 gene. A similar threat (NDM-1) was discovered in India over a decade ago and has been infecting US patients since 2009.

Given the global nature of the threat of AMR, IDSA supports the AMR provisions in the Global Health Security Strategy, released by the White House in 2019:

- Improve the capacity of laboratories to identify priority WHO AMR pathogens and perform susceptibility testing on them;
- Prevent AMR transmission in health care facilities and the community through infection prevention and control measures;
- Train human and animal health care workers on basic infection prevention and control policy guidelines and practices;
- Implement evidenced-based internationally endorsed guidelines on appropriate antimicrobial use within humans and animals; and
- Implement drug quality surveillance.

Additional Solutions Needed

Despite important progress made in combating antibiotic resistance and investing in the research and development of new antibiotics, additional solutions are urgently needed to meet current and future patient needs, promote public health and protect our national security. Some of the solutions may fall under the scope of other congressional committees, and IDSA encourages members of this subcommittee to work with your colleagues on other committees to advance the necessary policies and investments.

Reimbursement Reform

When new antibiotics are brought to the market, they are rarely used. This is due in part to appropriate stewardship policies ensuring that such antibiotics are only used when they are truly needed, and IDSA strongly supports stewardship programs. However, the Medicare reimbursement system can also make it challenging for patients to access new antibiotics even when they are clinically appropriate. The Medicare bundled payment (known as the Diagnosis Related Group or DRG) is too low to cover the costs of new antibiotics, making it difficult in many instances for new antibiotics to be added to hospital formularies or prescribed even when they are medically the best choice for the patient. IDSA supports carving new antibiotics out of the DRG and allowing them to be reimbursed separately. This will help ensure that patients who need these drugs can access them, and will help stabilize the precarious antibiotic marketplace for developers.

IDSA believes it is essential that reimbursement reform or any other policies aimed at incentivizing new antibiotic R&D must be paired with robust stewardship policies to guide appropriate antibiotic use and preserve the effectiveness of new antibiotics, thereby preserving our nation's investment in the discovery and development of those new antibiotics. In order to receive higher reimbursement for antibiotics, hospitals must be required to implement stewardship programs that align with CDC recommendations and report antibiotic use and, in parallel, report resistance data to the National Healthcare Safety Network.

IDSA is delighted that Senators Johnny Isakson and Bob Casey have introduced the DISARM Act that would enact these reimbursement reforms and stewardship proposals. We understand that Representatives Danny Davis and Kenny Marchant plan to introduce DISARM in the House. We are grateful to these bipartisan champions, and hope members of the subcommittee will consider supporting this important bill. While we understand that this bill falls under another committee's jurisdiction, its provisions will directly protect Americans from the national security threat of AMR.

Pull Incentive

While reimbursement reform would be an important way to stabilize the antibiotics market, it alone is highly unlikely to deliver the antibiotic pipeline we need from the perspective of patient care or national security. Even with reimbursement reform, use of new antibiotics is likely to remain too low as compared to products in other therapeutic areas to allow developers to earn a reasonable and predictable return on investment necessary for companies and venture capitalists to remain in or re-enter the antibiotics field. A new model, one not linked to sales volume, is necessary. IDSA is proud to be working closely with other stakeholders to develop a consensus proposal on a novel pull incentive, such as a market entry reward, for targeted, urgently needed new antibiotics that address our greatest unmet needs. Pull incentives are resources provided to a

developer after the FDA approval of a new product, whereas push incentives are provided during the research and development process to help defray costs. IDSA believes that a pull incentive must be sustainably funded, sufficient in size to meaningfully impact the antibiotic pipeline, and paired with stewardship requirements for the developer. IDSA looks forward to following up with the subcommittee with more specific ideas for a pull incentive later this year.

Push Funding

While reimbursement reform and a novel pull incentive will be critical, they cannot take the place of push funding, primarily through BARDA and NIAID that has been essential in bringing new candidates to the pipeline and maintaining industry participation in antibiotic R&D. Push funding must be paired with reimbursement reform and market entry pull incentives to ensure that newly approved antibiotics are accessible for patients who need them and that the companies who develop them can remain in business to maintain supply of the new antibiotic as well as develop additional antibiotics.

Stewardship

In addition to requiring all hospitals to implement stewardship programs and to report antibiotic use and resistance data to CDC, there are other steps the federal government should take to strengthen antibiotic stewardship. Additional funding should be provided to the CDC to study and advance the science of stewardship to ensure optimal, up-to-date approaches. CDC should also receive additional funding to expand its work to additional healthcare facilities, particularly outpatient settings, where a great deal of work remains to be done to improve antibiotic prescribing.

Once again, we offer our deepest thanks to the Subcommittee for holding this hearing and for inviting us to participate. We look forward to continued collaboration to address the public health crisis and the national security threat of antimicrobial resistance.