



Testimony
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BARDA Efforts to Counter Antimicrobial Resistance

Statement of

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Good morning Chairman Pallone, Ranking Member Shimkus and other distinguished Members of the Subcommittee. I am Dr. Robin Robinson, Director of the Biomedical Advanced Research and Development Authority (BARDA), an office within the Assistant Secretary for Preparedness and Response of the Department of Health and Human Services. Antimicrobial resistance is of major concern to this Congress, the Federal government, and the Nation. I appreciate the opportunity to talk with you today about BARDA's role in countering this growing problem.

Overview of Antimicrobial Resistance for Biodefense

Antimicrobials, a class of drugs that includes antibiotics, agents that kill or inhibit bacteria, and antivirals, which kill or inhibit viruses, are primary weapons in the fight against infectious disease. The discovery and development of antibiotics in the mid-twentieth century is among the greatest advances in the history of medicine and public health. Further, the advent of antiviral drugs provides new options for controlling previously untreatable viral infections. Antimicrobials are today, and will remain for the foreseeable future, an indispensable tool of medical practice and a cornerstone of public health, providing safe, simple, and effective treatments for serious communicable diseases.

Our ability to rely upon the availability of effective antimicrobial drugs is severely threatened. Ironically, this threat arises in large part from the use of the drugs themselves. Antimicrobial resistance occurs in microorganisms as a

manifestation of their ability to adapt to the environment. Under pressure by antimicrobials, bacteria have inevitably responded by evolving mechanisms for reducing their susceptibility to the drugs, resulting in the phenomenon known as antibiotic resistance.

As a result of this phenomenon, resistance to entire common antimicrobial classes, including β -lactams, quinolones, tetracyclines, glycopeptides and macrolides, is emerging rapidly and is already prevalent in health care and community settings. As widespread use of antibiotics has become common, the extent of the problem of antimicrobial resistance has grown.

Although antimicrobial resistance occurs naturally in microorganisms as a mechanism of adaptation to the environment, an additional concern is that the capability for resistance to current antimicrobials could be intentionally introduced by genetic manipulation into otherwise susceptible bacteria, including bioterror agents, producing a biological super-weapon that would render our stockpiles of antibiotics for treatment useless during a bacterial threat agent attack. Further, naturally occurring drug resistant isolates of several biodefense pathogens, including plague and meliodiosis, have been detected by environmental or clinical surveillance, suggesting that the obtainment of these strains by nefarious parties is technically feasible. Thus, the increasing prevalence of antimicrobial-resistant bacteria is a matter of concern for both public health and national security biodefense.

Although the phenomenon of resistance has been evolving since the first introduction of antibiotics, its impact has been mitigated because new antibiotics

have continually been developed and introduced to replace those that have lost effectiveness due to resistance, with a robust antimicrobial development pipeline maintained by the combined enterprise of academic, government and commercial interests. However, in the last 25 years, the number of new antimicrobials has steadily and dramatically decreased, reflecting in part an erosion of interest by the private sector in developing novel antimicrobial drugs.

The decrease in pharmaceutical company commitment to new antimicrobial development reflects an unfavorable assessment of the economics of the market for these products. The process of taking an antibiotic drug from discovery through development and testing to approval by the Food and Drug Administration (FDA) requires considerable time and financial resources. To justify this investment, drug companies look for a commensurate level of return in sales. However, the market dynamics of antibiotics are influenced by factors that make this outcome far from certain. The limited duration of most antibiotic regimens, leading to a cure, does not result in the continued sales that can be expected with drugs for chronic conditions. In addition, a new, effective antibiotic is likely to be initially reserved for severe infections that do not respond to other antibiotics, further limiting sales. Squeezed between the increasing cost of developing new drugs and uncertain prospects for a profitable market return, the commercial pharmaceutical industry has turned its attention to other drugs that command higher prices and are aimed at treating chronic conditions and diseases.

The consequences of the interrupted antibiotic pipeline are being felt by medical practitioners and observed in public health monitoring, with tragic outcomes for a growing number of individual patients. And the situation is likely to worsen before it improves. The lengthy drug development process means that new classes of drugs to supplement or replace current ones are still years away at best.

Faced with this looming crisis, a concerted effort is needed to provide short-term relief and long-term solutions to the problem of antibiotic resistance. The public health and biodefense interests of this effort call for the Federal government to take the lead in providing the necessary support and incentives to restore the commercial antibiotic pipeline and ensure the continuous availability of effective drugs to treat all bacteria that cause human disease.

BARDA's Efforts to Counter Antimicrobial Resistance

BARDA was established by the Pandemic and All-Hazards Preparedness Act of 2006 (PAHPA) to ensure that the United States has a sufficient supply of vaccines and drugs to respond to public health emergencies caused by pandemic influenza, emerging infectious diseases, and chemical, biological, radiological, and nuclear (CBRN) threats. BARDA addresses a critical niche in the public health and medical infrastructure to fill in the gap for enabling those types of medical countermeasures that the commercial markets have rejected based on current market forces. BARDA has designed and implemented programs that create partnerships between government and industry based on

support and incentives that induce the commercial enterprises to address public health and biodefense priorities.

Filling Market Gaps: BARDA as a Bridge over the “Valley of Death”

BARDA has taken a multi-faceted approach to its programs for stimulating drug and vaccine development. Pursuant to the Project BioShield Act of 2004, BARDA initially created markets for CBRN threats by committing to procure certain drugs and vaccines that would create a stockpile of treatments to be used in case of a bio-terror attack. From the experiences implementing Project BioShield, PAHPA was enacted in 2006 and authorized the award of up to half the contract amount for drugs and vaccines that reached critical “milestones” to be made before the projects have been completed. These contracts allow the government to effectively support advanced product development and ensure that companies have sufficient resources and incentives to take these products to licensure, thus bridging the “valley of death” between the funding of applied research and completed projects. Further, the development of antibiotics for the treatment of biological threat agent exposure concurrently increases the robustness of the developmental pipeline, as these candidate antibiotics also seek FDA approval for clinically relevant infectious diseases. BARDA has also provided support for the building of U.S.-based infrastructure for the development and manufacturing of vaccines, strengthening our overall capability for preparing for and responding to public health and bio-terror threats.

BARDA is currently applying these approaches and authorities to programs focused on pandemic influenza and high priority biodefense threats. BARDA is authorized to implement programs whose goal is the development of new antibiotics, as well as other tools for reducing infectious diseases, as part of an overall approach to the problem of antibiotic resistance. BARDA can conduct this work as a two-phase, coordinated strategy on countering antimicrobial resistance, comprised of 1) funding the acceleration of new antimicrobial product pipeline, and 2) supporting advanced development of vaccines for high-priority microbial pathogens.

Antimicrobial Strategy

For reasons discussed earlier, commercial market incentives are no longer driving a robust antibiotic development pipeline, necessitating government initiative to ensure that the system operates in the public interest. Our sister agencies within HHS are doing their part to stimulate activity at the discovery end of the pipeline, and to facilitate progress at the approval end. BARDA's role is to ensure progress through the critical development and manufacturing phases of the enterprise. Development of dual-purpose antibiotics useful for both bio-threats and public health pathogens is a key in the BARDA strategy.

BARDA's initial programs in antibiotic development have approached the development of new antibiotics from the perspective of filling gaps in our ability to respond to bacterial threat agents. Some of these threat agents do not currently have an FDA-approved treatment and some have the potential for becoming

resistant to current treatments through natural or intentional means. BARDA has supported the development of new formulation of existing antibiotics, including an inhalational (gentamicin) product for plague and tularemia. In the President's FY 2011 budget, BARDA requested funds to support advanced development of new classes of broad-spectrum antimicrobials that address critical gaps in antimicrobials against bio-threats and public health pathogens. In addition, on May 17, 2010 BARDA published a sources sought notification/ request for information regarding animal model development. The development of animal models is a key element in the successful development of medical countermeasures for CBRN threats, particularly since efficacy of products against most of these threats could never be verified using clinical studies. Of particular concern is the lack of animal models to demonstrate antibiotic efficacy for bacterial threats such as plague and tularemia. Lastly, BARDA supports efforts to develop appropriate animal models to support licensure of products, including antimicrobials, to address CBRN threats.

Further, BARDA has the authority to expand the scope of existing and new Broad Agency Announcement to include requests for submissions for advanced research and development for emerging infectious disease, including the development of novel therapies to treat multi-drug resistant microorganisms.

BARDA has the authority to develop new antibiotics for public health. BARDA can focus on antibiotic resistance as an emerging threat of imminent risk to the United States. Specific initiatives could also be designed to support commercial enterprises in the advanced development of new antibiotics that are

effective against bacteria that have become extensively resistant to current antibiotics and are an urgent concern for medical practitioners.

Vaccine Strategy

One of the ways BARDA can address the problem of antibiotic resistance is through the development of antibiotics; another way would be through the development of vaccines. Specifically, antibiotic resistance can be reduced by preventing disease, and thus decreasing the need for and usage of antibiotics. For this purpose, the availability and use of vaccines can play a key role. For bacterial pathogens that quickly develop resistance to each new antimicrobial, vaccines provide more reliable and long-term protection. Vaccines also have the potential, with widespread distribution, to drastically decrease treatment costs. The development and use of vaccines for bacterial diseases that cause high demand for antibiotics or have demonstrated a particular tendency to develop resistance can be a powerful complement in the strategy for preserving antibiotic effectiveness.

BARDA is authorized to play a role in supporting advanced research and development of vaccines against high-priority bacterial diseases. Since vaccines are specific for a single bacterial pathogen, as opposed to antibiotics, which may be effective against multiple pathogens in a class of organisms, these initiatives will be carefully targeted to bacteria that have already shown high levels of resistance to existing antimicrobials, such as *Staphylococcus aureus* (MRSA). In combination with BARDA's broad spectrum antibiotic development initiatives,

these vaccine programs will help maximize our ability to address the problem of antibiotic resistance and ensure the long-term security of this valuable medical resource well into the future.

Conclusion

In conclusion, BARDA's mission and capabilities make it well-suited to contribute to a national strategy to combat antimicrobial resistance. We view this effort as a key part of our current and future program direction, and are fully committed to addressing this important problem.

Again, I would like to thank the Subcommittee for the opportunity to testify, and look forward to your questions.