

**Committee on Energy and Commerce
Subcommittee on Health
United States House of Representatives
Hearing on
“FDA User Fees 2012: Hearing on Issues Related to Accelerated Approval,
Medical Gas, Antibiotic Development, and Downstream Pharmaceutical
Supply Chain”
Written Testimony of
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Chairman Pitts, Ranking Member Pallone, and Members of the Subcommittee, thank you for the opportunity to testify on the urgent need to spur greater innovation and accelerate the development of new therapeutics to combat the threat of antimicrobial resistant bacterial infections.

Introduction

I am Dr. Barry Eisenstein, Senior Vice President of Scientific Affairs at Cubist Pharmaceuticals. Cubist is a biopharmaceutical company focused on the research, development and commercialization of pharmaceutical products – especially antibiotics -- that address critical needs in the acute care environment. Headquartered in Lexington, Massachusetts, we currently market CUBICIN® (daptomycin for injection), the first intravenous (IV) antibiotic from a class of anti-infectives called lipopeptides. CUBICIN received FDA approval in 2003 for the treatment of complicated skin and skin structure infections caused by certain susceptible strains of Gram-positive microorganisms, including methicillin-resistant *Staphylococcus aureus* (MRSA). CUBICIN is also approved in the U.S. for the treatment of *S. aureus* bloodstream infections (bacteremia), and is the only IV antibiotic approved for this indication based on the results of a prospective, randomized, controlled registration trial. In the wake of a highly successful launch

of CUBICIN, the company has a growing pipeline that includes two antibiotics for difficult to treat infections planned for Phase 3 clinical trials in 2012 – one for *Clostridium difficile* and one for serious Gram-negative infections, including those caused by multi-drug resistant *Pseudomonas aeruginosa*.

As Senior Vice President of Scientific Affairs, I am responsible for leading the efforts at Cubist to understand the medical needs best answered by CUBICIN, and other antibiotics we are developing, interacting with leading scientists and health care providers in the United States and elsewhere, and advising our scientific staff regarding infectious diseases, particularly those due to resistant bacteria. I am trained in internal medicine, infectious diseases, and microbiology. I have been a hospital epidemiologist, chief of an Infectious Diseases division, chair of an academic department of microbiology and immunology, the leader of infectious diseases discovery and clinical development at a major pharmaceutical company, and am presently, in addition to my job at Cubist, Clinical Professor of Medicine at Harvard Medical School, where I teach. I hold or have held leadership positions with the Infectious Diseases Society of America, the National Foundation for Infectious Diseases, and the American Society for Microbiology, and am currently an editor of the journal, Antimicrobial Agents and Chemotherapy. I am also a member of the Foundation for the National Institutes of Health, Biomarkers Consortium. I have been studying antibiotic resistance and treating patients with infectious diseases for over three decades, have edited major textbooks, and published over 100 scholarly articles in the field.

I. Congress Has Crafted Consensus Legislation to Help Combat Antimicrobial Resistance.

On behalf of patients, infectious disease specialists, nurses, scientists, and public health experts who work in clinical settings, academia and industry nationwide, I wish to commend this Subcommittee, led by Chairman Pitts and Mr. Pallone, Chairman Upton and Mr. Waxman, for working so actively and patiently to better prepare the United States against the serious public health threat of antimicrobial resistant organisms. Also, I commend Congressmen Gingrey and

Green for introducing the GAIN Act along with the many members of this committee who are co-sponsors, especially our home state congressman, Representative Markey.

For more than six years, since before the last reauthorization of the Prescription Drug User Fee Act (PDUFA) in 2007, you have systematically convened hearings, heard expert testimony, participated in multilateral meetings, and pursued intensive dialogues with patient groups, public health and specialty societies, and innovative industry, in order to develop and introduce focused, well-reasoned legislation that could greatly accelerate the discovery of new antimicrobials. This legislation has the support of many major national organizations engaged in the struggle to combat antimicrobial resistance.

Just a few years ago, it was not at all certain that Congress and the infectious disease community would respond to this crisis as quickly and capably as it has. Two years ago, I testified before this Subcommittee that “We [were] approaching a ‘crisis point’ with antimicrobial resistance and the lack of new therapies against Gram positive bacteria such as ‘staph’ and Gram negative bacteria such as *Acinetobacter*.” Four years ago, I testified to your Senate colleagues on the Health, Education, Labor and Pensions (HELP) Committee that “we must implement effective measures to combat antimicrobial resistance.”

Today, I am happy to return to this Subcommittee, as it considers enacting critically important legislation to combat antimicrobial resistance, and report that your concern over this public health crisis, and your desire to take timely, targeted action to increase innovation, now constitute a national consensus that is broadly shared by the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the Food and Drug Administration (FDA); the Infectious Disease Society of America (IDSA) ; independent authorities such as The Pew Charitable Trusts and Extending the Cure; governors of life science-leading States like Massachusetts; 35 military and veterans associations; St. Jude’s

Children's Research Hospital; and the innovative biopharmaceutical companies like Cubist.

Together over the past several years, we have confirmed that the risks to public health at home and abroad are great and the gaps in our medical preparedness and our therapeutic options are not only substantial, but also growing with every passing month. Together, we have identified the market failure that has hollowed out antimicrobial innovation, and we have tailored policies that could serve as concrete solutions and make a critical difference in the lives of millions of Americans annually.

Mr. Chairman, the result of this sustained collaboration is H.R.2182, the Generating Antibiotic Incentives Now, or GAIN, Act of 2011. This consensus, bipartisan public health measure – introduced by Dr. Gingrey and his colleagues I mentioned, and cosponsored by many of the present members of this Subcommittee – would extend Hatch-Waxman exclusivity only for select “qualified infectious disease products” that would significantly improve our therapeutic and clinical abilities to combat infections caused by resistant pathogens. The GAIN Act would, in addition, assure that novel antibiotics receive priority review or fast track status under the Food and Drug Administration's (FDA) existing authority. The bill also provides for additional exclusivity for “qualified infectious disease products” developed in conjunction with a companion diagnostic test. Finally, the Act calls for the FDA to revise its guidelines for clinical trials of antibiotic drugs to reflect the latest developments in science and clinical knowledge.

These clear and impactful policies would directly promote the research and commercialization of new drugs and diagnostics against resistant pathogens. Taken together, the provisions in the GAIN Act offer our best hope to stimulate American innovation and strengthen the hand of clinicians and scientists in the fight against antimicrobial resistance both here and abroad.

II. Antimicrobial Resistance is a National Public Health Threat

As the Subcommittee is aware, during the last several decades, the prevalence of antimicrobial resistant organisms in U.S. hospitals and medical centers has increased. According to 2002 data from the Centers for Disease Control and Prevention (CDC), more than 1.7 million people acquire bacterial infections in U.S. hospitals each year, and 99,000 die as a result. CDC estimates that up to 70 percent of those bacterial infections are resistant to at least one drug, at a cost of approximately \$5 billion annually.

The IDSA estimates that the treatment of resistant pathogens costs more than \$20 billion annually to our health care system and result in Americans spending more than 8 million additional days in the hospital. A study published in the *Journal of the American Medical Association* extrapolated data from nine U.S. communities to estimate that there were 94,360 invasive MRSA infections alone in the U.S. in 2005 which resulted in 18,650 deaths—to say nothing of the prevalence of other drug resistant pathogens.

Intensive care patients in American hospitals and our troops in the Middle East conflicts alike are suffering untreatable *Acinetobacter* infections at alarming rates. Two years ago, the House Armed Services Oversight Subcommittee received testimony from the U.S. Air Force on the “challenging epidemic” of “multi-drug resistant . . . infections [that] has resulted in a shortage of safe and effective antibiotics.” Then - Chairman Vic Snyder of the House Armed Services Committee, Oversight and Investigations Subcommittee, stated “. . . [T]he problem could get worse in the next several years, because there are few new antibiotic treatments expected from the drug research pipeline.”¹ You are also well aware of the disturbing rates of MRSA and the emergence of vancomycin-resistant enterococci (VRE) increasingly leave infectious disease doctors with few, if any, effective therapies for certain strains of bacterial infection. Just as antimicrobial

¹ Press Release, Fighting Superbugs: Oversight and Investigations Subcommittee Holds Hearing on Military’s Efforts to Prevent Outbreaks of Multidrug-Resistant Infections in Military Hospitals; United States House of Representatives Armed Services Committee Democrats. September 30, 2010

resistance is rising, we are faced with a disturbing and dangerous lack of new antibiotic drugs, particularly against Gram negative bacteria.

III. Multiple Solutions Are Being Applied to Antimicrobial Resistance But At This Time, None Can Generate New Antibiotics

Mr. Chairman, there is no question that limiting the spread of serious infections, as well as improving practitioners' use of antibiotics, are critically important to combating resistant pathogens. Infection prevention and control programs, the use of clinical practice guidelines, and basic steps like proper hygiene in health care settings, can all have a substantial impact on limiting the emergence of resistance and the number of patients infected. Improving the quality, timeliness, and usefulness of infectious disease surveillance is also of great importance, as is the need to sustain our Federal investment in biomedical research through the National Institutes of Health (NIH).

Over the past decade, Congress and the infectious disease community have cooperated to develop, enact, implement, and assess many new policies and Federal initiatives to combat resistant pathogens. For example:

- The federal Interagency Task Force on Antimicrobial Resistance in focused federal R&D funding was authorized in 1999 after a hearing on the dangers of antimicrobial resistance.
- In 2002, Congress further broadened this funding authority in the aftermath of the deliberate biological attacks against the Capitol and in New York, New Jersey and Florida.
- In the 2007 PDUFA reauthorization, at our encouragement, this Subcommittee authored provisions directing FDA to update its regulatory guidance and revise critical clinical breakpoints for antibiotics, as well as to determine whether the Orphan Drug Act could be made available to promote development of new antimicrobial drugs.
- In 2009, the Affordable Care Act included provisions to improve the quality of inpatient care against hospital-acquired infections, created a

short-term incentive called the Qualifying Therapeutic Discovery Project Tax Credit, and provided CDC and States with additional infection control funding.

In short, these policies are important and necessary, but they will not and simply cannot, fill our medicine cabinets. They cannot close the dangerous gaps in our therapeutic options: our efforts to improve the education of clinicians, better manage the prescribing of antibiotics, reduce health-care acquired infections, and conduct more basic research can only accomplish so much. Just as our medicine cabinets are becoming empty, so too our policy toolbox has been emptied.

IV. GAIN Act Would Target Market Failures, Accelerate Antimicrobial Innovation

As a result, Mr. Chairman, The Pew Charitable Trusts warns us that “[t]he antibiotic pipeline is dwindling, and a global crisis looms.” That is why the GAIN Act is so urgently needed. The Act builds on previous Federal and congressional enactments, by specifically targeting the market failures and policy gaps that have led us to this crisis point.

The antibiotic pipeline is running dry because antibiotics, uniquely, are “wasting assets.” Bacteria evolve so quickly that the development of resistance is inevitable. Thus, each new antibiotic only has a finite lifespan. Appropriate stewardship is an important component of antibiotic use, as its primary goal is to optimize clinical outcomes while minimizing the unintended consequences of antimicrobial use (e.g. toxicity, selection of pathogenetic organisms, emergence of resistance). But it paradoxically reduces the commercial returns necessary to induce the investment, research and clinical trials that lead to new, approved antibiotics. In addition, antibiotics are used for acute conditions and for a short period. Consequently, much of the biopharmaceutical industry does not invest in antimicrobial development and has instead turned its efforts to products and more chronic diseases with the potential for greater commercial returns on investment.

The GAIN Act is targeted at precisely this problem. By extending the new drug exclusivities created by the 1984 Hatch-Waxman Amendments, it would dramatically improve the prospects for attracting new investments for the development and approval of new antibiotics so needed by our patients. The Act would send a powerful signal to scientists and investors exploring new molecules and forming new companies, as well as to large, established biopharmaceutical companies, that Congress recognizes the unique commercial challenges in this area, and is opening the door to new innovation, new investigations, and greater investor interest.

As this Subcommittee knows, the GAIN Act deliberately builds on current law and the foundation of the Hatch-Waxman Amendments to support innovation. The enhanced exclusivity for antibiotics, as well as the straightforward designation of “qualified infectious disease products”, is based upon what Dr. Janet Woodcock of the FDA recently described as the “wildly successful”² Orphan Drug Act, which has led to more than 2,150 orphan drug designations and 358 new, approved therapies for rare diseases and disorders. . .”

We believe implementation of the GAIN Act is certain to succeed because the Act envisions early consultations between companies and the FDA based on the orphan drug model, and a designation that is based on clear criteria that target the most serious infections. Finally, the review of FDA’s guidances, and the assurance of priority review or fast track status on the basis of FDA’s current authorities, promise to further expedite the development and approval of new antibiotics.

Conclusion

Mr. Chairman, this Subcommittee has a unique opportunity to take timely action against a serious public health threat. The market failure that has

² Janet Woodcock, June 9, 2010 Hearing in Energy and Commerce; Transcript p. 65. Available at: <http://democrats.energycommerce.house.gov/documents/20100609/transcript.06.09.2010.he.pdf>

drained our pipeline of important new antibiotics remains. As Congress acts to reauthorize the Prescription Drug User Fee Act in a timely and bipartisan manner before the end of this fiscal year, so too should it enact the GAIN Act. I urge the Members of this Subcommittee to move the GAIN Act through Committee and enact it into law during this 112th Congress.

Thank you for the opportunity to testify today. I look forward to your questions.