



## All pain, no GAIN: need for prudent antimicrobial use provisions to complement the GAIN Act

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*The development of new antibiotics without having mechanisms to insure their appropriate use is much like supplying your alcoholic patients with a finer brandy.* (Dennis Maki, IDSA meeting, 1998 [1, 2])

Only one health care bill is likely to pass Congress in this election year: the Prescription Drug User Fee Act V (PDUFA V). Every five years, the FDA and the drug and device industries renegotiate the user fees and regulatory priorities for the FDA. PDUFA V is the fifth generation in this process. This bill is very likely to pass Congress this summer because many jobs at the FDA are no longer funded from general federal appropriations, but come from these user fees. If the bill doesn't pass, many people at the FDA will be furloughed or fired.

Since it is a "must pass" bill with bipartisan support, PDUFA V has attracted additional provisions, hoping to hitch a ride and thus become law. The Generating Antibiotic Incentives Now (GAIN) Act is one prominent example. The GAIN Act is prominently featured in both the House and Senate versions of PDUFA V.

The stated objectives of the GAIN Act include increased surveillance of resistant bacteria, more responsible use of existing antibiotics, and increased incentives to develop new antibiotics. However, the current draft of

the GAIN Act does not provide any binding requirements to implement antimicrobial stewardship, appropriate use, and conservation. It focuses exclusively on bringing new antibiotics to market quickly, without any changes whatsoever to patterns of use in either human or animal populations. More brandy for the alcoholics.

It didn't start out this way. The Infectious Diseases Society of America (IDSA) testified before Congress on March 8, 2012, and asked for both "strong incentives to spur new anti-infective research and development (R&D) and promote antimicrobial stewardship." [3] While the IDSA's primary focus has long been on promoting new antimicrobial drugs, this testimony notably included many proposals (advocated by public health organizations such as APUA) for preserving and extending the useful life of existing treatments as well. They suggested creating a new regulatory pathway for "special purpose limited medical use drugs" which would be strictly limited to appropriate antimicrobial use. IDSA called for payors to take a more active role in appropriate use and value-based reimbursement for diagnostics. IDSA called for implementation of effective antimicrobial stewardship programs as a condition of participation in Medicare and Medicaid. IDSA also specifically recom-

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mended a robust surveillance system to “promote measurement of antibiotic usage across all health care settings and support adoption and implementation of comprehensive antimicrobial stewardship programs across all health care settings to promote the appropriate use of antibiotics.” Finally, they suggested that drug companies develop a plan for educating health care providers on the appropriate use of new antibiotics and “to reinforce precautions to reduce the risk of resistance.”

As of late April 2012, none of these provisions are included in the latest House or Senate versions. What has survived is an entirely one-sided emphasis on bringing new antibiotics to market quickly, even if the safety data is less complete and without regard to appropriate use. The GAIN Act will add 5 or more years of data exclusivity on to the end of patent terms for “qualified infectious disease products,” extending the effective patent period by about 40%, from 12 to 17 years. In economic terms, these extensions in effective patent life will eventually cost the US health care system several billion dollars in prescription drug expenses due to the delayed introduction of generic antibiotics. But, in a perfect Washington game, these expenses will not count against the GAIN Act when the Congressional Budget Office scores the bill. As the IDSA testimony points out: “IDSA’s exclusivity proposals will likely not score a cost to the federal government for the next decade or two, given the average amount of patent life typically remaining on new antibiotics at the time they are approved. Major companies, including GlaxoSmithKline (GSK) and Pfizer, agree with IDSA’s assessment.”

In addition to the IDSA testimony, in early April 2012, several stewardship proposals were made to congressional staff during bipartisan discussions on the GAIN Act. One proposal was to limit the new GAIN incentives to companies that met appropriate use or stewardship targets set by the FDA. In other words, the federal government would agree to spend billions to bring new antibiotics to market, but only if the companies were careful with how they were used. Another proposal

called for the Centers for Disease Control and Prevention (CDC) to spend \$10 million per year in surveillance, to track the resistance profiles of the new drugs approved under GAIN. Neither proposal made the cut. The only amendment that might be considered friendly to appropriate use is proposed section 906 of the Senate bill, which calls for a study by the National Academies on alternative business models for antimicrobial R&D, including prize funds. [4-5]

At this point, public health would be better served if GAIN did not pass as part of PDUFA V. Any new incentives for rushing antibiotics to market must be matched by similar commitments to stewardship and appropriate use. [6-7] Value-based reimbursement of both antibiotics and companion diagnostics should include strong support for appropriate use. [8-9] Otherwise, we might succeed at meeting the IDSA’s goal of 10 new drugs by 2020, but fail in the ultimate goal of having effective antimicrobials at the moment of need due to accelerating resistance. [10]

The correct policy isn’t simply conservation or new production; we need both, in a balanced approach. As currently drafted, GAIN is not balanced, but this could be corrected this summer in the Conference Committee before Congress passes PDUFA V.

*Professor Outterson is an appointed member of the Antimicrobial Resistance Working Group of the OID/ Board of Scientific Counselors, CDC and a faculty associate at the Harvard Center for Communicable Disease Dynamics.*

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## OUTTERSON

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## Fewer drugs, more superbugs: strategies to reverse the problem

**Jennie Choe, M.S.**

Staff Reporter, Alliance for the Prudent Use of Antibiotics

Resistance to antibiotics among the world's most dangerous pathogens is a serious public health threat, but hardly a new phenomenon. Alexander Fleming himself warned as early as 1945 that penicillin and similar antibiotics would eventually make themselves obsolete, through natural selection and the very nature of bacteria. [1] Today, ever-increasing types of resistant bacteria and fewer new antibiotics being developed against them portend a post-antibiotic era on the horizon rather than a regression to the pre-antibiotic era. [2] A post-antibiotic era would again be plagued by common, potentially fatal medical conditions, but have far less hope of finding effective treatments.

### Societal consequences of drug resistance

What would medical treatment look like in a post-antibiotic era? Many types of surgery would become impossible, including organ transplants. So would cancer chemotherapy and care for both premature infants and the critically ill. Two million patients in the U.S. develop drug-resistant healthcare-associated infections every year, of which 99,000 will die. [3] Direct expenses alone cost the healthcare system anywhere from \$21 billion to \$34 billion. Additional medical expenses, restrictions on in-

ternational travel, and decreased tourism, trade, and commerce could incur far greater economic losses to society.

Infectious disease and drug resistance is never just one country's problem. Drug-resistant pathogens like XDR-TB, hypervirulent *C. difficile*, and multidrug-resistant *S. pneumoniae* and *N. gonorrhoeae* incur huge costs not only to human life but also to the global economy and international security. Resistant infections in the U.S. required more than 8 million additional days spent in the hospital compared to non-resistant infections. The same loss of labor (and with higher mortality rates, the loss of working-age citizens) in developing countries such as those in the sub-Saharan region can cost up to 20% GDP. [4] The resulting difficulty in developing resources and creating products for export, and the decreased demand for imports from their trading partners, makes the crisis bleed over from developing countries into industrial ones. Developed countries end up shouldering much of that burden through both federal funding and private aid from philanthropic organizations, to prevent other countries' losses from becoming their own. Moreover, the Bipartisan WMD Terrorism Research Center warns that a terrorist attack using a drug-resistant pathogen could cause a "potentially uncontrollable" num-