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## Repairing the Antibiotic Pipeline: Can the GAIN Act Do It?

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## REPAIRING THE ANTIBIOTIC PIPELINE: CAN THE GAIN ACT DO IT?

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### ABSTRACT

*Antibiotic resistance, according to the World Health Organization, is one of the greatest threats to public health. To combat the problem, new antibiotics need to be developed. However, antibiotic research and development is fraught with scientific and economic problems. Recognizing these problems and the public health threat posed by antibiotic resistance, Congress passed the GAIN Act, which President Obama signed into law in June 2012. The GAIN Act (Act) incentivizes pharmaceutical companies to invest in antibiotic research and development. This Article will outline the incentives in the Act and suggest why the Act may not solve the growing antibiotic resistance problem. There are, however, areas of promise in the Act that may mitigate its shortcomings and pave the way to the possibility of the Act's success.*

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## INTRODUCTION

Antibiotic resistance is a worldwide epidemic. It is an acute domestic problem, as well. In 2006, methicillin-resistant *Staphylococcus aureus* (MRSA) killed more Americans (19,000) than emphysema, HIV/AIDS, Parkinson's disease, and homicide combined.<sup>2</sup> Furthermore, "[a]lmost 2 million Americans per year

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<sup>2</sup> Infectious Diseases Society of America (IDSA), *Statement of the*

develop hospital-acquired infections (HAIs), resulting in 99,000 deaths, the vast majority of which are due to antibiotic-resistant pathogens.”<sup>3</sup>

Antibiotic resistance and the lack of activity along the antibiotic development pipeline are problems worthy of Congress’ attention. Existing antibiotics are losing their effectiveness due to antibiotic resistance and yet, antibiotic development efforts are slow to respond to this crisis. Antibiotic development is stunted because the pharmaceutical companies spearheading research and development are primarily concerned with maximizing profits and feel the scientific and economics challenges are not worth the investment. Antibiotics are typically not profitable for pharmaceutical companies because they are prescribed sparingly to stem antibiotic resistance.<sup>4</sup> Moreover, consumers only purchase small quantities of antibiotics as they are typically used for 7–14 days, whereas some profitable pharmaceuticals are taken for the duration of the consumer’s life.<sup>5</sup>

Congress diverted its attention to the problem and recently passed the GAIN (Generating Antibiotic Incentives Now) Act. The GAIN Act incentivizes pharmaceutical companies to develop antibiotics. However, the GAIN Act’s many incentives for antibiotic research and development are unlikely to repair the antibiotic pipeline and stem the problem of increasing antibiotic resistance.

Part I of this Article will discuss why Congress felt the need to implement the GAIN Act. Part II will discuss the Act’s incentives for antibiotic development. Part III will discuss the Act’s potential problems and explain why it may not repair the antibiotic pipeline.

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*Infectious Diseases Society of America Promoting Anti-Infective Development and Antimicrobial Stewardship through the U.S. Food and Drug Administration Prescription Drug User Fee Act (PDUFA) Reauthorization Before the House Committee on Energy and Commerce’s Subcommittee on Health, IDSOCIETY.ORG, [http://www.idsociety.org/uploadedfiles/idsa/policy\\_and\\_advocacy/current\\_topics\\_and\\_issues/advancing\\_product\\_research\\_and\\_development/bad\\_bugs\\_no\\_drugs/statements/idsa%20pdufa%20gain%20testimony%20030812%20final.pdf](http://www.idsociety.org/uploadedfiles/idsa/policy_and_advocacy/current_topics_and_issues/advancing_product_research_and_development/bad_bugs_no_drugs/statements/idsa%20pdufa%20gain%20testimony%20030812%20final.pdf) (last visited June 10, 2013).*

<sup>3</sup> *Id.*

<sup>4</sup> IDSA, *supra* note 2.

<sup>5</sup> *Id.*

Part IV, however, will address potential areas of promise in the Act and will suggest how these provisions may mitigate the Act's problems.

### I. THE NEED FOR THE GAIN ACT

Antibiotic resistance occurs when bacteria become resistant to antibiotics after being exposed to them.<sup>6</sup> This resistance is often due to a spontaneous gene mutation during bacterial cell replication that allows a cell to continue to divide and replicate, unlike its counterparts that were killed off by the antibiotic.<sup>7</sup> Increased antibiotic use correlates to a rise in antibiotic resistance because antibiotic use exacerbates natural selection of antibiotic-resistant bacteria.<sup>8</sup> Antibiotic resistance due to overuse is an increasing problem in the United States due to (1) the inappropriate use of antibiotics, when physicians prescribe antibiotics without first determining whether a patient has a bacterial infection that can only be cured with antibiotics; (2) the increased presence of antibiotics in our food supply, which potentially introduces more antibiotic-resistant bacteria into the human population; and (3) the extensive use of antibiotics in hospitals.<sup>9</sup> Because hospitals frequently prescribe antibiotics for patients, hospitals are prime breeding grounds for antibiotic-resistant bacteria.

The social and economic impact of antibiotic resistance is enormous and cannot be ignored. "Each year, antibiotic-resistant infections are responsible for tens of thousands of deaths, hundreds of thousands of hospitalizations and up to \$26 billion in extra costs to the U.S. health care system."<sup>10</sup> For example, antibiotic resistant

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<sup>6</sup> *FDA's Strategy on Antimicrobial Resistance—Questions and Answers*, U.S. FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm216939.htm> (last visited Nov. 25, 2012).

<sup>7</sup> *General Background: About Antibiotic Resistance*, ALLIANCE FOR THE PRUDENT USE OF ANTIBIOTICS, [http://www.tufts.edu/med/apua/about\\_issue/about\\_antibioticres.shtml](http://www.tufts.edu/med/apua/about_issue/about_antibioticres.shtml) (last visited July 1, 2013).

<sup>8</sup> *Id.*

<sup>9</sup> *Id.*

<sup>10</sup> Pew Health Group, *Bill Summary: The Generating Antibiotic Incentives Now Act of 2011*, <http://www.pewtrusts.org/uploadedFiles/wwwpewtrustsorg/>

infections (ARIs) increase patient care costs and wage losses because ARIs typically lead to hospital stays that are up to two weeks longer than they would be if the patients had not contracted ARIs.<sup>11</sup> Alliance for the Prudent Use of Antibiotics, a nongovernmental organization, suggests that a mere 20% reduction in antibiotic resistant infections would save up to 5.2 billion U.S. healthcare dollars a year.<sup>12</sup> Despite the extent of the problem, few pharmaceutical companies are willing to devote the time and resources to antibiotic development.

There are several reasons why pharmaceutical companies are reluctant to pursue new antibiotics. One reason is that antibiotic development poses unique scientific challenges. For example, over a 10-year period, it took 72 candidate antibiotics to yield one FDA-approved product, whereas other pharmaceuticals required only 15 candidates to yield an FDA-approved product.<sup>13</sup> Drug development is facing increasing economic challenges—it currently costs \$400–\$800 million per approved agent.<sup>14</sup> Further, there are fewer perceived economic incentives for pharmaceutical companies to develop antibiotics than other drugs. Antibiotics do not generate as much revenue as other pharmaceuticals because they (1) are only used for short time periods, typically 7–14 days; (2) are priced low to keep the public health free of communicable diseases; and (3) are sparingly prescribed to curb the problem of antibiotic resistance.<sup>15</sup> Further still, because there are some generic antibiotics that are still effective against many bacterial infections, physicians often relegate newly developed antibiotics to a second

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Fact\_Sheets/Antibiotics\_and\_Innovation/Antibiotics\_GAIN\_FactSheet.pdf (last visited July 1, 2013).

<sup>11</sup> *The Cost of Antibiotic Resistance to U.S. Families and the Health Care System for Consumers, Patients, Policy-Makers*, ALLIANCE FOR THE PRUDENT USE OF ANTIBIOTICS, [http://www.tufts.edu/med/apua/consumers/personal\\_home\\_5\\_1451036133.pdf](http://www.tufts.edu/med/apua/consumers/personal_home_5_1451036133.pdf) (last visited July 1, 2013).

<sup>12</sup> *Id.*

<sup>13</sup> IDSA, *supra* note 2.

<sup>14</sup> B. Spellberg et al., *The Epidemic of Antibiotic-Resistant Infections: A Call to Action for the Medical Community from the Infectious Diseases Society of America*, 46 CLINICAL INFECTIOUS DISEASES, 155–64 (2008).

<sup>15</sup> *Id.*

or later line of defense against these pathogens.<sup>16</sup>

Due to these disincentives, the antibiotic pipeline is running dry. “In the 1980s, the . . . FDA approved 29 new systemic antibiotics. That number dropped to . . . nine in the 2000s.”<sup>17</sup> This comes as no surprise considering that, “compared to the revenues generated from sales of ‘blockbuster’ high blood pressure or cholesterol medications that patients take for many years or even a lifetime, the returns from antibiotics are low.”<sup>18</sup> It is for this reason that legislative attention has become necessary to combat the tide of antibiotic resistance.

## II. THE GAIN ACT’S INCENTIVES

The GAIN Act provides pharmaceutical companies many incentives to develop new antibiotics to combat the growing problem of antibiotic resistance. While there are many provisions in the Act, this Article focuses only on those that will serve as the most powerful incentives for antibiotic development and that are most likely to be effective in combatting antibiotic resistance.

### A. *The Act Adds Exclusivity Periods to Qualified Antibiotics*

Exclusivity is a special protection under FDA rules, independent of patent protection. Exclusivity provides the holder of new approved drugs protection from competition in the marketplace by limiting FDA approval of similar drugs during the exclusivity period.

Because getting an antibiotic drug market-ready is especially time-consuming and costly, patent protection does not provide sufficient incentive to pharmaceutical companies. Pharmaceutical

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<sup>16</sup> Chantal Morel & Elias Mossialos, *Stoking the Antibiotic Pipeline*, 340 BRIT. MED. J. 1115, 1115 (2010).

<sup>17</sup> Allan Coukell & Sharon Ladin, *Testimony before the House Committee on Energy and Commerce, Subcommittee on Health*, <http://www.pewtrusts.org/uploadedFiles/wwwpewtrustsorg/Speeches/Testimony%20of%20Allan%20Coukell%20and%20Sharon%20Ladin%20re%20GAIN.pdf> (last visited Oct. 10, 2012).

<sup>18</sup> Pew Health Group, *supra* note 10.

companies typically obtain patents at the beginning of the drug discovery process. However, “taking a novel compound through pre-clinical testing into clinical studies and all the way to approval takes a significant period of time—and . . . patents have a limited lifespan.”<sup>19</sup> By the time a candidate antibiotic is approved by the FDA and put on the market, the 20-year term of a patent is likely to be nearing its end.<sup>20</sup> Pharmaceutical companies thus need additional FDA exclusivity to protect their inventions on the market after both the lengthy clinical testing and the FDA approval processes.

One of the Act’s key provisions adds five years of exclusivity to qualified new antibiotics at the time of their entry into the market.<sup>21</sup> This five year exclusivity is in addition to the applicable Hatch-Waxman five-year new chemical entity (NCE) exclusivity, Hatch-Waxman three-year new clinical studies exclusivity, seven-year orphan drug exclusivity, or six-month pediatric exclusivity.<sup>22</sup>

The Act similarly adds an additional six months of exclusivity for approved antibiotics that have been paired with a companion diagnostic test.<sup>23</sup> Companion diagnostic tests are tests that identify both individuals who will most likely benefit from the antibiotic and individuals who will most likely have a serious adverse reaction to the antibiotic.<sup>24</sup> Drugs paired with companion tests are eligible for extended exclusivity because they further the goals of the GAIN Act. Specifically, if physicians use companion diagnostic tests to determine the likelihood of success in the patient before prescribing a certain antibiotic, such antibiotic will be used less and will reduce the speed of antibiotic resistance.

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<sup>19</sup> Robert G. Hibbert et al., FOOD, BEVERAGE, AND DRUG LAW CLIENT STRATEGIES 109 (Eddie Fournier, 2008).

<sup>20</sup> *Id.*

<sup>21</sup> *Id.*

<sup>22</sup> *Id.*

<sup>23</sup> *Id.* Bill Summary: *The Generating Antibiotic Incentives Now Act of 2011* (H.R. 2182), *supra* note 10.

<sup>24</sup> *Id.*; Celia Henry Arnaud, *Diagnostics-Drugs Pairings Advance Personalized Medicine*, CHEMICAL AND ENGINEERING NEWS, (July 23, 2012), <http://cen.acs.org/articles/90/i30/Diagnostics-Drugs-Pairings-Advance-Personalized.html>.



*B. The Act Provides for Priority Review and Fast-Track Approval of Qualified Antibiotics*

Under the GAIN Act, antibiotic applications will be eligible for both priority review and fast-track approval through the FDA new drug application process.<sup>25</sup> The FDA's priority review and fast track processes are complex, but new drugs that are able to get priority and fast track "labels" will get to market significantly faster.<sup>26</sup> The faster the antibiotics get to market, the sooner the pharmaceutical companies can reap the benefits of costly research and development. Because pharmaceutical companies can in turn invest time and money into new antibiotic research and development after their previously developed antibiotic is on the market and bringing in revenue, it is likely that a faster antibiotic FDA approval process will ultimately bring more antibiotics into the market more quickly. In 2003, antibiotics under priority review and fast-track approval had a median approval time of six months, whereas the median review and approval time was 13.8 months.<sup>27</sup> Together with added exclusivity periods, faster approval time makes the protection term effectively longer and allows products to enter the market sooner.

*C. The Act Creates a Study on Incentives for Qualified Infectious Disease Biological Products*

Another provision in the Act "direct[s] the Government Accountability Office (GAO) to conduct a study to determine the need for incentives to encourage research, development, and marketing for qualified infectious disease biological products."<sup>28</sup>

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<sup>25</sup> Pew Health Group, *supra* note 10.

<sup>26</sup> *Fast Track, Breakthrough Therapy, Accelerated Approval and Priority Review: Expediting Availability of New Drugs for Patients with Serious Conditions*, U.S. FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccessToImportantNewTherapies/ucm128291.htm> (last visited July 1, 2013).

<sup>27</sup> *Id.*

<sup>28</sup> H.R. REP. NO. 112-495 (2012), available at [http://thomas.loc.gov/cgi-bin/cpquery/?&sid=cp1121EYgl&r\\_n=hr495.112&dbname=cp112&&sel=TOC\\_102426&](http://thomas.loc.gov/cgi-bin/cpquery/?&sid=cp1121EYgl&r_n=hr495.112&dbname=cp112&&sel=TOC_102426&).

Biological products (biologics) include vaccines, blood and blood components, allergenics, somatic cells, gene therapy agents, tissues, and recombinant therapeutic proteins.<sup>29</sup> Congress' focus on these qualified biologics could prove instrumental in addressing the problem of antibiotic resistance and infectious disease control. Indeed, the near disappearance of mortality from diseases such as typhoid fever, cholera, typhus, smallpox, polio, and the Bubonic plague can be attributed to biologics and the development of immunizations.<sup>30</sup>

The Act does not yet delineate specific incentives for qualified infectious disease biologics, but rather commits the GAO to devoting the time and focus necessary to find compelling research and development incentives. The requirements of this provision are vague in light of the specific problems posed by biologics research and development. While "[d]rugs generally have well-defined chemical structures, and a finished drug can usually be analyzed to determine all its various components" it can be nearly impossible to characterize a biologic.<sup>31</sup> As such, biologics "manufacturers must ensure product consistency, quality, and purity by ensuring that the manufacturing process remains substantially the same over time."<sup>32</sup> Drug manufacturers do not face this same quality assurance problem.

### III. THE GAIN ACT'S PROBLEMS

The GAIN Act, despite its many antibiotic development incentives, is not likely to keep antibiotic resistance at bay. The Act is problematic because (1) there are no provisions encouraging appropriate use and marketing of new antibiotics to prevent antibiotic resistance to these new antibiotics, (2) the additional five

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<sup>29</sup> Vaccines, Blood, and Biologics: Consumers (Biologics), U.S. FOOD AND DRUG ADMINISTRATION <http://www.fda.gov/BiologicsBloodVaccines/ResourcesforYou/Consumers/default.htm> (last visited July 1, 2013).

<sup>30</sup> Peter Barton Hutt et al., *Food and Drug Law Cases and Materials* 876 (Robert C. Clark et al. eds., 3d ed. 2007).

<sup>31</sup> *How do Drugs and Biologics Differ?*, BIOTECHNOLOGY INDUSTRY ORGANIZATION (Nov. 10, 2010), <http://www.bio.org/articles/how-do-drugs-and-biologics-differ> (last visited Aug. 9, 2013).

<sup>32</sup> *Id.*

years of exclusivity at the end of new antibiotic's patent terms will increase healthcare costs and thus, limit the beneficiaries of the new antibiotics to only those who can afford them, (3) the financial incentives will likely still not be enough to encourage pharmaceutical companies to invest the necessary time and money into cumbersome and low-yielding antibiotic research and development, and (4) the FDA drug approval process is still too complicated and unpredictable for pharmaceutical companies to expend drug development costs at the risk of facing eventual non-approval by the FDA.

*A. The Act is Void of Meaningful Antibiotic  
Conservation Incentives*

The Act, while incentivizing antibiotic development, does not incentivize appropriate antibiotic use.<sup>33</sup> The use of new antibiotics without appropriate conservation techniques will allow infectious diseases to be exposed to, adapt to, and ultimately resist these new antibiotics. The Act's proposed remedy—new antibiotic development—could therefore exacerbate the very problem it was enacted to address.

Incentives are one of the only tools possible under current law to ensure appropriate antibiotic conservation. This is because the FDA currently lacks authority to restrict a physician's prescription of antibiotics. Alternatively, antibiotics could be classified in a scheme similar to the DEA's scheduled drug classifications. The restrictions placed on antibiotic prescriptions could mirror antibiotic stewardship recommendations. In such a situation there would be real authority to restrict antibiotic prescriptions. However, since the scheduling classifications for controlled substances are based on the potential for dependency, it may be impractical to create an analogous program for antibiotics.

Hospitals and other healthcare providers will likely need more incentives to implement antibiotic conservation measures. Indeed, hospitals can reduce antibiotic use by undertaking infection control

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<sup>33</sup> Ed Silverman, *The Op-Ed: No Gain From Antibiotic Incentives*, PHARMALOT (June 21, 2012, 7:50 AM), <http://www.pharmalot.com/2012/06/the-op-ed-no-gain-from-antibiotic-incentives> (last visited Aug. 9, 2013).

measures, such as screening patients for infectious pathogens and isolating infected patients. These procedures, however, take hospital manpower, time and resources, and are not reimbursed by insurance. Insurance reimbursement indeed is a powerful tool that is currently "not well deployed to promote continued antibiotic effectiveness."<sup>34</sup> Insurance reimbursement "hinders conservation [of antibiotics] and allows hospitals and physicians to receive additional payments for out-of-control infections and unnecessary prescriptions."<sup>35</sup> To meaningfully reduce health care providers' antibiotic use, the magnitude of financial incentives must at least match that of the reimbursements they currently receive for antibiotic prescriptions.

The Centers for Medicare and Medicaid services have enacted such a financial incentive. Under pay-for-performance programs, Medicare does not reimburse hospitals for treatment required due to hospital-acquired infections. As such, the hospital is financially responsible for the services it provides to these infected patients.<sup>36</sup> At the state level, California led the way in creating meaningful incentives for healthcare providers to appropriately prescribe antibiotics. In January 2008, California Senate Bill 739 became effective, requiring general acute care hospitals "to monitor and evaluate the utilization of antibiotics and charge a quality improvement committee with the responsibility for oversight of the judicious use of these medications."<sup>37</sup>

The Infectious Diseases Society of America (IDSA) proposed many changes during the congressional hearings on the GAIN Act,

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<sup>34</sup> Kevin Outterson, *The Legal Ecology of Resistance: The Role of Antibiotic Resistance in Pharmaceutical Innovation*, 31 CARDOZO L. REV. 613, 616 (2010).

<sup>35</sup> *Id.*

<sup>36</sup> Department of Health and Human Services, Centers for Medicare & Medicaid Services, *Hospital-Acquired Conditions (HAC) in Acute Inpatient Prospective Payment System (IPPS) Hospitals*, <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalAcqCond/Downloads/HACFactsheet.pdf> (last visited June 12, 2013).

<sup>37</sup> *The California Antimicrobial Stewardship Program Initiative*, CALIFORNIA DEPARTMENT OF PUBLIC HEALTH, <http://www.cdph.ca.gov/programs/hai/Pages/AntimicrobialStewardshipProgramInitiative.aspx> (last visited June 10, 2013).

but Congress failed to incorporate the proposals into the enacted bill. Among the proposed changes was a stewardship proposal whereby the GAIN incentives would be limited only to those pharmaceutical companies that were careful with how new antibiotics were used.<sup>38</sup> Noting the inherent problem with providing market protections for new antibiotics, commentators Robert Weissman and Anthony So of the *Huffington Post* noted that “[r]esistance to an antibiotic increases as the drug is used more frequently, so the use of new antibiotics must be reserved for resistant infections ... monopoly protections [however] conflict with the need for preservation by encouraging companies to sell as much of the new drug as possible.”<sup>39</sup>

### *B. The Act Will Likely Increase Healthcare Costs*

The GAIN Act will also likely increase healthcare costs. Since the Act will add five years of exclusivity on top of the 20-year patent terms for qualified antibiotics, the introduction of generic antibiotics will be delayed five years, costing the United States health care system several billion dollars in prescription drug expenses.<sup>40</sup> However, many Americans are already unable to purchase needed antibiotics due to prohibitive expense. These individuals will have to wait out the GAIN Act–approved antibiotics’ patent and FDA exclusivity phases before an affordable generic equivalent to come on the market.

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<sup>38</sup> Kevin Outterson, *All Pain, No GAIN: Need for Prudent Antimicrobial Use Provisions to Complement the GAIN Act*, *Alliance for the Prudent Use of Antibiotics*, ALLIANCE FOR THE PRUDENT USE OF ANTIBIOTICS, <http://www.tufts.edu/med/apua/news/news-newsletter-vol-30-no-1-4.shtml> (last visited June 14, 2013).

<sup>39</sup> Robert Weissman and Anthony So, *Generating Antibiotic Incentives Now: GAIN—Or Just Greed* (June 6, 2012, 5:36 PM), HUFFINGTON POST, [http://www.huffingtonpost.com/robert-weissman/antibiotic-resistance-\\_b\\_1572284.html](http://www.huffingtonpost.com/robert-weissman/antibiotic-resistance-_b_1572284.html) (last visited Aug. 9, 2013).

<sup>40</sup> Silverman, *supra* note 33.

*C. The Act's Incentives Are Likely Not Enough to Incentivize  
Pharmaceutical Companies to Undertake Costly and Risky  
Research and Development*

Moreover, the Act's many incentives will likely not be enough to encourage pharmaceutical companies to invest in antibiotic research and development. Because antibiotic research and development is notoriously risky and unpredictable, some pharmaceutical companies may be incentivized to act only when they are sure they will be able to recoup all of their expenses in the marketplace. While the five-year exclusivity period will help pharmaceutical companies recoup *more* of their research and development expenses, it likely will not result in the recovery of *all* of these expenses. The Act, then, will likely not compel these companies to undertake antibiotic research and development.

The Act also does not include a potentially powerful incentive—tax credits. The IDSA, in its report before Congress, proposed that tax credits would incentivize pharmaceutical companies to undertake antibiotic research and development.<sup>41</sup> Tax credits relieve a company of some percentage of the tax burden on its revenues and therefore are attractive to large firms that already have products on the market.<sup>42</sup> Tax credits can similarly be attractive to smaller companies, as tax credits can be transferred or even redeemed as a cash refund for a company with a low tax bill.<sup>43</sup>

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<sup>41</sup> Brad Spellberg et al., *The Epidemic of Antibiotic-Resistant Infections: A Call to Action for the Medical Community from the Infectious Diseases Society of America*, 46 *Clinical Infectious Diseases* 155, 160 (2008).

<sup>42</sup> Priya Sharma & Adrian Towse, *New Drugs to Tackle Antimicrobial Resistance: Analysis of E.U. Policy Options*, United Kingdom Office of Health Economics (2011).

<sup>43</sup> ELIAS MOSSIALOS ET AL., *POLICIES AND INCENTIVES FOR PROMOTING INNOVATION IN ANTIBIOTIC RESEARCH* (European Observatory on Health Systems & Policies 2010).

*D. The Complicated and Oft-Maligned FDA Drug Approval Process Remains Largely Unchanged*

The FDA drug approval process is known among pharmaceutical companies to be unpredictable and complicated, especially when compared to other countries' processes. While welcoming the GAIN Act's provisions, drug developers and the IDSA think "more needs to be done to improve the regulatory landscape and the economics of antibiotic drug development."<sup>44</sup> In a letter to HHS Secretary responding to Congress' passing of the Act, the IDSA president stated that "regulatory disincentives resulting from the lack of clear and feasible antibacterial clinical guidance for industry has become a towering impediment to antibiotic development."<sup>45</sup> Biopharmaceutical executives have similarly suggested that the United States look to Europe as a successful example of how to implement "a more robust strategy for funding antibiotic R&D to address public health priorities."<sup>46</sup>

In its testimony before Congress, the IDSA recommended that the GAIN Act include a new FDA approval mechanism—Special Population Limited Medical Use (SPLMU) Drugs. Under the SPLMU mechanism, a "drug's safety and effectiveness would be studied in substantially smaller, more rapid, and less expensive clinical trials than traditionally required."<sup>47</sup> As such, a drug would be approved for use only in a small subset "of patients for whom the benefits of the drug have been shown to outweigh the risks."<sup>48</sup> The smaller clinical trials under the SPLMU mechanism would make it easier for companies to get FDA approval for new antibiotics given that the FDA currently requires two large clinical trials that cost between \$50-100 million and take many years to complete.<sup>49</sup> Further, the SPLMU designation is not dispositive

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<sup>44</sup> Steve Usdin, *GAIN Act, FDA stance only first steps to refilling antibiotic pipeline in U.S.*, BIOCENTURY (Nov. 19, 2012), <http://www.biocentury.com/biotech-pharma-news/coverstory/2012-11-19/gain-act-fda-stance-only-first-steps-to-refilling-antibiotic-pipeline-in-us-a1>.

<sup>45</sup> *Id.*

<sup>46</sup> *Id.*

<sup>47</sup> IDSA, *supra* note 2.

<sup>48</sup> *Id.*

<sup>49</sup> *Id.*

because the drug sponsor can later go “through a traditional study route for an indication for the anti-infective the limited use designation could be removed.”<sup>50</sup> As SPLMU drugs would be used only in those patients with a highly resistant pathogen, antibiotic resistance to these novel drugs would be slowed.<sup>51</sup>

#### IV. AREAS OF PROMISE IN THE GAIN ACT

##### *A. The Act's Antibacterial Drug Development Task Force May Address Some of the IDSA's Proposals Not Expressly Adopted in the Act*

The Act's creation of the “Antibacterial Drug Development Task Force” may address some of the problems under the current provisions. The task force is comprised of “scientists and clinicians from throughout CDER [the Center for Drug Evaluation and Research]” who “will work with other experts from academia, regulated industry, professional societies, patient advocacy groups, and government agencies.” The task force's many goals include (1) exploring “novel scientific approaches to facilitate [antibiotic] development;”<sup>52</sup> (2) “identify[ing] issues related to unmet medical needs for antibacterial drugs, reasons for the lack of a robust pipeline for antibacterial drug development, and new approaches for weighing the risks, benefits, and uncertainties of potential new drugs;”<sup>53</sup> and (3) “participat[ing] in think tanks . . . to address various issues that could enable [antibiotic] development, including study design, statistical analytical methods, and approval pathways.”<sup>54</sup> However, it is currently unclear how much power the task force will have to suggest further legislative action or to advise the FDA.

The task force should pick up some of the IDSA proposals that

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<sup>50</sup> *Id.*

<sup>51</sup> *Id.*

<sup>52</sup> *Antibacterial Drug Development Task Force*, U.S. FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm317207.htm> (last visited Oct. 7, 2012).

<sup>53</sup> *Id.*

<sup>54</sup> *Id.*



were not incorporated into the actual text of the Act to address some of the problems addressed in this Article. One proposal made to congressional staff could address the potential problem of new antibiotic development and use leading to bacterial antibiotic resistance of those new antibiotics. This proposal called “for the CDC to spend \$10 million per year in surveillance, to track the resistance profiles of the new drugs approved under GAIN.”<sup>55</sup> Such a surveillance program could ensure that infectious diseases do not rapidly become resistant to new antibiotics due to overuse or poor inherent antibiotic properties. While the task force will likely not contribute to the economic incentives of the Act, it could ensure appropriate antibiotic use. The more appropriate the antibiotic use, the less dire the situation in the antibiotic pipeline will become because antibiotic resistance to the newly developed antibiotics will be minimized.

*B. The Act's Recognition of Biologics as Another Solution to the Antibiotic Resistance Problem is Promising*

The Act's recognition that biologics, such as vaccines, may also combat infectious diseases demonstrates that Congress took a comprehensive approach in shaping the Act. Had the Act solely focused on chemical pharmaceutical development, the pipeline would be missing one of its greatest potential solutions—the development of biologics to complement the use of chemical antibiotics to which infectious diseases can easily build resistance.

Despite these areas of promise, however, the Act does not go far enough to make up for its shortcomings in other areas. Congress should consider amendments if they desire to *fully* address the twin problems of antibiotic resistance and the dry antibiotic development pipeline.

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<sup>55</sup> Kevin Outterson, *supra* note 36.

## CONCLUSION

“Although we think of [antibiotics] narrowly in connection with treating acute infections, their use underpins much of modern care—from routine surgical procedures to organ transplants and cancer treatment.”<sup>56</sup> If the GAIN Act is unable to solve the twin problems of antibiotic resistance and a dried-up antibiotic development pipeline, the modern healthcare we take for granted may cease to exist in the near future. While the GAIN Act contains numerous provisions that incentivize pharmaceutical companies to develop antibiotics, the incentives will likely not be enough to encourage companies to invest in antibiotic development over more profitable drugs. In focusing primarily on antibiotic *development*, the Act fails to adequately address the *responsible use* of antibiotics. Regardless of whether the Act incentivizes antibiotic development, it will be for naught if no stewardship protocols are implemented to stem antibiotic resistance to newly developed antibiotics.

As antibiotic development and approval is a notoriously lengthy process, it will be years before the Act’s policies really take effect. With this in mind, the Health and Human Services Department recently agreed to pay GlaxoSmithKline \$40 million to develop antibiotics. The agreement further provided an option whereby the federal government will give GlaxoSmithKline as much as \$200 million over the next five years.<sup>57</sup>

Assuming, *arguendo*, that the incentives are effective, new antibiotic development alone will not solve the problem of antibiotic resistance. There ought to be a continued focus on the appropriate use of these antibiotics along with the exploration of alternative infectious disease combatants—namely biological derivatives—to ensure we do not experience the catastrophic effects that could result from complete antibiotic resistance.

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<sup>56</sup> *Pew Health Group*, *supra* note 10.

<sup>57</sup> Barry Meier, *Pressure Grows to Create Drugs for ‘Superbugs’*, CNBC (June 3, 2013, 1:45 AM), <http://www.cnbc.com/id/100783270>.

## PRACTICE POINTERS

- Hospitals and other healthcare providers should consider antibiotic stewardship protocols to ensure that infectious diseases do not quickly become resistant to the newly developed antibiotics incentivized by the Act.
- Should further legislative action be taken to amend the Act, Congress should examine other countries' antibiotic research and development programs that have been lauded by pharmaceutical and biologics companies as superior to the United States.
- Congress should consider restricting physicians' antibiotic prescribing authority by implementing a DEA-regulated scheme analogous to scheduled drug classifications and corresponding restrictions on prescriptions.
- The fact that antibiotic resistance itself could be a powerful incentive for pharmaceutical companies to enter the market should not be overlooked. Antibiotic resistance may actually stimulate rather than retard innovation, as resistance makes existing antibiotics obsolete, paving the way for new drug entry.