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ODA and GAIN: The Key to Promoting Innovation

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Abstract

Medicine has greatly advanced in recent decades, but has it reached its peak? With increasing costs for getting the Federal Drug Administration's ("FDA") approval and for performing clinical trials, pharmaceutical companies and drug companies are hesitant to research and develop drugs that do not have a significant market despite protections offered through patents. For example, companies are more reluctant to research and develop drugs for rare diseases and drugs for antibiotic-resistant strains of microorganisms as there is not enough demand for such drugs, even if the drug is able to obtain a patent. Pharmaceutical drug developers rely strongly on the patent system and regulatory incentives in developing drugs. The patent system, for example, allows the drug developer to control the market for a certain period of time so that it can recover its drug development costs and get rewarded for its innovative efforts. Because drugs for rare diseases and antibiotic resistant strains of pathogens have such a small market and affect a limited number of people, pharmaceutical developers often lack incentives to research and develop such drugs. However, regulations such as the Orphan Drug Act ("ODA") and Generating Antibiotic Incentives Now ("GAIN") Act attempt to provide incentives to pharmaceutical developers for rare diseases, also called orphan diseases, and antibiotic resistant ailments. However, are these incentives enough? Is the current patent system still working for all pharmaceuticals? This paper seeks to address these questions and other issues concerning the pharmaceutical industry and its relationship to the patent system, specifically related to the Orphan Drug Act and Generating Antibiotic Incentives Now.

Keywords: Antibiotic, Antibiotic-Resistance, ODA, GAIN, FDA, Pharmaceutical Industry

I. Introduction

In the past few decades, advances in modern medicine have been significant. The rise of new antibiotics and new medicines have cured diseases once thought to be incurable. For example, in 2014, Gilead manufactured Sovaldi, a drug to treat Hepatitis C

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in a safe manner.[1] Sovaldi is an example of a "miracle drug": it boasts an 84% – 96% cure rate of Hepatitis C.[2] In 2014 alone, Sovaldi earned $7.9 billion dollars.[3] Pharmaceutical companies take the profits from successful blockbuster drugs to finance research and development for new innovate drugs. Advancements in the pharmaceutical industry are largely due to the patent system and the protections afforded to pharmaceuticals. Companies are able to utilize patent protections to maximize profits from blockbuster drugs through exclusivity periods provided by patents. This allows companies to make enough profits to recover for the costs in developing the drug. In fact, "pharmaceutical innovation is thought to be the patent system's greatest success story."[4] Were it not for the patent system, it is very likely that the pharma industry would not be as successful as it is today.

Yet despite such marvelous advances, the "United States is suffering one of the largest drug shortages in history."[5] Specifically, drugs and cures for rare diseases and advanced strains of antibiotic resistant microorganisms are in short supply, particularly antibiotics.[6] There are many reasons why the number of new drugs entering the market is declining.[7] Research and development costs for pharmaceutical companies are rising, drugs are often repurposed to avoid the demanding FDA approval requirements for new drugs,[8] and many diseases do not affect enough of the population to entice pharmaceutical companies to research and develop new drugs.[9]

While there have been many blockbuster and novel drugs developed in recent years,[10]

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[1] Alyssa Clark, *Projected Top 3 earning drugs in 2014*, HEALTHCARE GLOBAL, Feb. 7, 2014, http://www.healthcareglobal.com/hospitals/692/Projected-Top-3-earning-drugs-in-2014.

[2] Lacie Glover, *The Top-Selling Drugs in America*, NERDWALLET, June 26, 2015, https://www.nerdwallet.com/blog/health/top-selling-drugs-in-america/.

[3] *Id.*

[4] Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503, 504 (2009).

[5] Amanda Fachler, *The Need for Reform in Pharmaceutical Protection: The Inapplicability of the Patent System to the Pharmaceutical Industry and the Recommendation of A Shift Towards Regulatory Exclusivities*, 24 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 1059, 1061 (2014).

[6] *See infra* Part II.C.

[7] Fachler, *supra* note 5, at 1061.

[8] *Id.* at 1069 ("After receiving patent approval but before entering the market, a pharmaceutical product must receive FDA approval, which assures that the new product is both safe and effective enough to be made commercially available." Repurposed drugs do not need to obtain another approval if it has already been approved by the FDA).

[9] *Id.* at 1061.

[10] For example, Abilify, Humira, Nexium, and Crestor all earned more than $5.8 billion dollars each

there is nevertheless a shortage of new drugs entering the market. This paper first briefly discusses the pharmaceutical industry, orphan drugs and diseases, and antibiotic resistance in Part II. Part III discusses patent law, the FDA, the ODA, and the GAIN Act. Finally, Part IV discusses potential reform with respect to the GAIN Act to mirror the ODA, followed by a brief conclusion.

II. The Pharmaceutical Industry and Obstacles

A. Success of the Pharmaceutical Industry

Pharmaceuticals constitute a "multi-billion dollar industry" in the U.S., and have been responsible in part for the increase in life expectancy in the U.S. in recent years.[11] Along with Sovaldi making $7.9 billion dollars in 2014, Abilify ($7.8 billion), Humira ($7.2 billion), Nexium ($5.9 billion), and Crestor ($5.8 billion) ranked among the top 5 earning drugs in the U.S.[12] These profits are largely due to the patent system. Companies are able to utilize patent protections to maximize profits from blockbuster drugs through exclusivity periods provided by patents, thereby avoiding any competition. The success of these patented drugs allows pharmaceutical companies to invest in and research less profitable drugs, thereby promoting the pharmaceutical industry. Thus, the patent system promotes innovation for pharmaceuticals through this cycle.[13] However, despite the success of the pharma industry in conjunction with the patent system, there is still a need for new and innovative drugs, specifically for orphan diseases and antibiotic resistant strains of pathogens.

B. What are Orphan Drugs and Diseases?

An orphan disease is a "rare disease or condition" based on a patient population in which the subject disease or condition affects less than 200,000 people in the United

in 2014. *See* Glover, *supra* note 2.

[11] Fachler, *supra* note 5, at 1063.

[12] Glover, *supra* note 2.

[13] Roin, *supra* note 4, at 504.

States.[14] An orphan drug is therefore any drug designated to treat an orphan disease or condition. Examples of orphan diseases and conditions include Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), and Tourette syndrome.[15] The issue with orphan diseases is that only a limited number of people are affected by such diseases and ailments. Consequently, there is not a large demand for pharmaceuticals related to these diseases. Given the high costs involved in bringing a new drug product to the market, pharmaceutical companies are hesitant to work on orphan drug products because there is only a small demand for the drug. This small demand means that companies will not be able to sell enough of the drug to cover the costs involved in bringing the drug to market. Congress recognized this disjunction between the need for orphan drug products and the incentives to make a profit, and thus enacted the Orphan Drug Act to bridge this gap.[16]

C. The Problem of Antibiotic Resistance

Each year, "at least 2 million people become infected with bacteria that are resistant to antibiotics and at least 23,000 people die each year as a direct result of these infections."[17] Antibiotic resistance occurs when an antibiotic can no longer "effectively control or kill bacterial growth."[18] In other words, the bacteria or other microorganism[19] becomes resistant to the antibiotic drug, which was previously effective. In the same way that our bodies use vaccines (comprised of dead disease-causing microorganism) to create antibodies and develop resistance to certain pathogens, bacteria and other microorganisms can develop a resistance to a drug that would otherwise kill that organism. At a molecular and genetic

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[14] *See* 21 U.S.C. § 360bb.

[15] *Orphan Drug Act Relevant Excerpts*, FDA, Nov. 3, 2015, http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/ucm364750.htm.

[16] *Id.*; *See also* Enrique Seoane-Vasquez et al., *Incentives for orphan drug research and development in the United States*, ORPHANET JOURNAL OF RARE DISEASES, Dec. 16, 2008, http://ojrd.biomedcentral.com/articles/10.1186/1750-1172-3-33.

[17] *Antibiotic/Antimicrobial Resistance*, CDC, Apr. 19, 2016, http://www.cdc.gov/drugresistance/index.html.

[18] *What is Antibiotic Resistance and Why is it a problem?*, APUA (2014), http://www.tufts.edu/med/apua/about_issue/antibiotic_res.shtml.

[19] *Promoting Anti-Infective Development and Antimicrobial Stewardship Through the U.S. Food and Drug Administration Prescription Drug User Fee Act (PDUF) Reauthorization*, IDSA, Mar. 8, 2012, http://www.tufts.edu/med/apua/index_363_626155726.pdf at 3 (The "problem of antimicrobial resistance is not specific to bacteria — medically important fungi (e.g., Candida spp.), viruses (e.g., HIV, influenza), and parasites (e.g., malaria) also develop antimicrobial resistance").

level, this resistance forms as a result of "a spontaneous gene mutation during bacterial cell replication" that allows the cells with the mutation to continue to divide and replicate even in the presence of an antibiotic killing the remaining cells.[20] Antibiotic resistance mutations can occur even without the presence of antibiotics.[21] Furthermore, in the same way that many insects form a resistance to pesticides, bacteria form resistance to antibiotics through the process of natural selection.[22] Increased antibiotic use "correlates to a rise in antibiotic resistance because antibiotic use exacerbates natural selection of antibiotic-resistant bacteria"[23]

There are many factors and ways through which antibiotic resistance is increasing through increased antibiotic use. First, antibiotics are often prescribed inappropriately when "physicians prescribe antibiotics without first determining whether a patient has a bacterial infection that can only be cured with antibiotics."[24] This is a problem both domestically and worldwide, and many physicians feel that this is the leading problem with respect to antibiotic resistance.[25] Second, a common practice of self-medication of antibiotics for minor sicknesses contributes to the increasing problem of antibiotic resistance both domestically and worldwide.[26] This problem is more common in developing countries with limited access to medical care and effective treatments.[27] In such countries, doctors generally only have access to cheaper and older antibiotics. Accordingly, many pathogens may already be resistant to such medications and the problem of antibiotic resistance is exacerbated through natural selection, yet the same medications are being prescribed and are used through self-medication.

Third, an increased presence of antibiotics in our food supply, specifically in the U.S., may be in fact adding to the antibiotic resistance problem.[28] Many animals

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[20] Caitlin Forsyth, *Repairing the Antibiotic Pipeline: Can the Gain Act Do It?*, 9 WASH. J.L. TECH. & ARTS 1, 4 (2013).

[21] Anthony S. Frauci & Hillary D. Marston, *The Perpetual Challenge of Antimicrobial Resistance*, 311 JAMA 1853, 1853 (2014).

[22] *Id.* at 4.

[23] *Id.*

[24] *Id.* at 4.

[25] In an informal interview with Dr. Harcharan Singh Narang, he explained that antibiotic overuse is the leading cause for antibiotic resistance.

[26] *What is Antibiotic Resistance*, *supra* note 21.

[27] *Id.*

[28] Forsyth, *supra* note 23, at 4.

are fed antibiotics to prevent diseases from spreading and many pesticides are also coated with antibiotics. Such use of antibiotics in food increases the general population's overall exposure to antibiotics, thereby limiting those antibiotics' effectiveness. Finally, antibiotics are extensively used in hospitals, making hospitals prime breeding grounds for antibiotic-resistant bacteria.[29] For example, doctors often prescribe broad spectrum antibiotics when they are not sure about the specific nature of the bacterial infection. This can lead to an increase in antibiotic resistance because the broad spectrum antibiotic would not be as effective at killing the bacteria compared to a more specific and stronger antibiotic.

Antibiotic resistance is both a domestic and worldwide epidemic.[30] In fact, if proper antibiotics are not created and properly prescribed to deal with new and advanced resistant strains of pathogens, "superbugs" or pathogens that are completely antibiotic-resistant may soon develop.[31] Antibiotic resistance is "one of the world's most pressing public health problems."[32] Drug-resistant infections cost the U.S. health care system "an estimated $20 billion annually, with an additional estimated $35 billion in lost productivity."[33] An increase in antibiotic resistance leads to ineffective treatments, treatment complications, and increased healthcare costs.[34] For example, in the U.S. alone, *Clostridium Difficile* causes life-threatening diarrhea and nearly 15,000 deaths with an estimated excess in medical costs in about $1 billion per year.[35] Even though current "antibiotics are losing their effectiveness due to antibiotic resistance," antibiotic development efforts are slow and stagnant.[36] This is primarily because pharmaceutical companies "are primarily concerned with maximizing profits and feel the scientific and economics challenges are not worth the investment."[37] Simply put, newer antibiotics

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29 *Id.*

30 Forsyth, *supra* note 23, at 2 (In the U.S. in "2006, methicillin-resistant Staphylococcus aureus (MRSA) killed more Americans (19,000) than emphysema, HIV/AIDS, Parkinson's disease, and homicide combined").

31 Lacie Glover, *Does the US drug approval process need an overhaul?*, FOX NEWS HEALTH, July 1, 2015, http://www.foxnews.com/health/2015/07/01/does-us-drug-approval-process-need-overhaul.html.

32 *Antibiotics and Antibiotic Resistance*, FDA Sep. 18, 2014, http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/AntibioticsandAntibioticResistance/default.htm.

33 Frauci & Marston, *supra* note 24, at 1853.

34 *What is Antibiotic Resistance*, *supra* note 21.

35 *Biggest Threats*, CDC, Aug. 26, 2015, http://www.cdc.gov/drugresistance/biggest_threats.html.

36 Forsyth, *supra* note 23, at 3.

37 *Id.*

would not be profitable for researchers and developers.[38] Unlike medicines for conditions that take many years to deal with, such as high blood pressure or cholesterol medications, antibiotics are typically prescribed only for a few days and newer antibiotics would only be "sparingly prescribed to curb the problem of antibiotic resistance."[39] Pharmaceutical companies would rather invest in drugs that will have higher demands so that they can reap a profit and cover costs, and new antibiotics are worthless to a business. Consequently, antibiotic resistance is becoming an increasing problem while new antibiotics are not being developed.[40] In fact, only "2 new antibiotics were approved by the FDA between 2008 and 2012."[41]

III. Current Legal Setting

A. Patents for Pharmaceuticals

Part of the reason the pharmaceutical industry has made such significant achievements is largely due to the patent system. In fact, "pharmaceutical innovation is thought to be the patent system's greatest success story."[42] Patents provide pharmaceuticals with an essential protection that ensures that the developer "is both compensated for its investments in research and development ("R&D") and made profitable by its competitive advantage in the form of exclusivity."[43] Patent protection allows firms to enjoy a lengthy monopoly over their drugs, "providing them an opportunity to profit" and recover investment costs before having to compete with generic drug competition.[44] Thus, patents play a pivotal and an "essential role in motivating" companies to invest in pharmaceutical research and development.[45] While some may

[38] Many large pharma companies have abandoned R&D on antibiotics. *See* Matthew A. Cooper and David Shlaes, *Fix the Antibiotic Pipeline*, 472 NATURE 32, 32 (2011).

[39] Forsyth, *supra* note 23, at 5-6.

[40] *Id.* at 6 (For example, in "the 1980s, the … FDA approved 29 new systemic antibiotics. That number dropped to … nine in the 2000s").

[41] Frauci & Marston, *supra* note 24, at 1853.

[42] Roin, *supra* note 4, at 504.

[43] Fachler, *supra* note 5, at 1066.

[44] Roin, *supra* note 4, at 508.

[45] *Id.* at 504.

argue that pharmaceutical companies charge exorbitant prices for new drugs during such periods of exclusivity, these high prices are necessary.[46] Without being able to enjoy its monopoly, it is highly unlikely that pharmaceutical companies would recover its costs and investments in developing the drug.[47] Furthermore, this protection is necessary so that the company may make profits after it recovers its costs and invest some of these profits towards new drugs. Thus, many drugs probably would not be developed without this protection.[48]

Patents serve a vital role in stimulating new drug development and innovation, and as a result, the "benefits of drug patents far outweigh their costs."[49] Patents provide the broadest level of protection and patents can cover "pharmaceutical compositions, indications or uses, dosage forms, or manufacturing processes."[50] Patent protection for pharmaceuticals "has significant social value because the security granted to pharmaceutical companies is meant to fuel innovation and thereby provides health benefits for the public."[51] However, patents alone may not be enough to promote innovation for orphan drug products and new antibiotics.

Despite the success of the pharma industry, it faces many problems. Namely, "the United States is suffering one of the largest drug shortages in history."[52] Likewise, "research and development costs for pharmaceutical companies are rising; the number of new drugs entering the market is declining; and pharmaceutical innovation is stifled."[53] However,

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46 *Id.* at 508.

47 *Id.*

48 *Id.* at 512 ("The public may suffer for a time from the higher prices charged for a patented invention, but that harm is necessarily smaller than the injury that would result if no one ever created or developed the invention in the first place, or if it had taken much longer for the invention to reach the public. As a rule of thumb, therefore, patents are socially desirable when, in their absence, the public would not otherwise benefit from the invention or there would be a substantial delay in the public's receipt of that benefit").

49 *Id.* at 508.

50 Seoane-Vazquez et al., *supra* note 16.

51 Fachler, *supra* note 5, at 1066.

52 *Id.* at 1075 ("The nationwide drug shortage in the United States has persisted for several years; hundreds of drugs appear on a federal notice shortage list including cancer drugs, anesthetics for surgery, drugs for emergency medicine, and electrolytes for intravenous feeding … Drug shortages are a unique feature of the pharmaceutical industry because the supply and demand of necessary drugs operates differently than supply and demand in other markets given that prices cannot fix the need for essential medications").

53 *Id.* at 1061 ("The ever-increasing cost — in both time and money — of successfully receiving patent protection and FDA approval of a new drug excessively burdens drug companies and suppresses their incentive for innovation").

the patent system is not to blame for these issues. Without the patent system, the pharmaceutical industry would not be as prosperous as it is today. Costs to bring a drug product to the market are increasing, specifically research and development costs (R&D), while benefits allowed by patents remain unchanged to allow companies to bring orphan drugs and antibiotics to the market. The problem is that companies do not have enough incentives to bring a drug to the market that would only be sold to a small number of people, thereby preventing the company from recovering its costs in bringing the drug to the market in the first place. Thus, it takes acts by Congress, such as the ODA and GAIN, to help pharmaceutical companies to bring new drugs to the market before the drug can reap the benefits of the patent system. Simply put, pharmaceuticals are a business. A company that has no incentive to innovate cannot be forced to do so despite public health concerns. Rare diseases and antibiotic resistant infections affect a small portion of the population and are not very profitable. Thus, in order to help incentivize a company to bring a drug to a small market, Congress must limit costs in obtaining a patent and research and development costs related to bringing a pharmaceutical to the market. By decreasing costs in obtaining a patent, more companies will be willing on to take on drug development for rare ailments. With extremely high R&D costs, a company will never be able to make a profit by selling a drug to a tiny market no matter how long the patent exclusivity period. The biggest hurdle to drug development are R&D costs due largely to the regulations of the FDA.

B. The FDA

After a new drug receives patent approval, it must then receive FDA approval showing that the new drug is safe and effective before it is allowed to reach the public.[54] All drugs must be FDA-approved before they can be lawfully sold and marketed in the United States.[55] The process for FDA approval is either through (1) a new drug application ("NDA"); (2) an abbreviated new drug application ("ANDA" or "section 505(b)(2)" application); or (3) compliance with the appropriate preapproved monograph.[56]

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[54] *Id.* at 1069.

[55] N. Nicole Stakleff, *A Drug Life: The Chemistry of Patent and Regulatory Exclusivity for Pharmaceuticals*, 16 FLA. COASTAL L. REV. 27, 33 (2014).

[56] *Id.* ("In the last category, the FDA has preapproved regulations specifying conditions where certain

For a NDA to meet the FDA's standards, it must include investigatory reports of clinical trials demonstrating safety and efficacy, a list of the drug's chemical ingredients and composition, a report on how and where the drug was manufactured, processed, and packaged, samples of the drug, the proposed drug label, and the patent for the drug if there is one.[57] The FDA approval process entails "animal testing and an outline for proposed human testing in the preclinical period, three phases of human testing and studies in the clinical period, meeting time, application submission, application review, research review, labeling review, and facility review in the New Drug Application review period," a final decision from the FDA, and then an additional phase of "safety monitoring and risk assessment" during the post-marketing period.[58] In sum, the time spent on getting a patent approved and the "time spent conducting clinical trials to satisfy FDA approval can result in a market-entry process that lasts as long as fourteen years."[59]

The FDA approval process and requirements are not cheap. On average, pharmaceutical companies "spend upwards of $800 million on R&D" for each new drug developed.[60] Roughly half of that amount is spent on the "FDA's clinical-trial requirements to establish the safety and efficacy of new drugs."[61] In fact, "only three out of ten FDA-approved drug products recover their R&D costs,"[62] and costs are steadily increasing. This high cost acts as a barrier for pharmaceutical companies from researching drugs that affect a limited number of people. In sum, bringing a new drug to the market after all approvals are received can cost up to $2.6 billion.[63] Without the success of blockbuster drugs,

drugs are generally recognized as safe and effective if they are labeled in accordance with their applicable drug monograph as set forth in the regulations"); *See also* 21 C.F.R. §§ 310.200.

57 Fachler, *supra* note 5, at 1070.

58 *Id.* at 1070-71.

59 Fachler, *supra* note 5, at 1065.

60 Roin, *supra* note 4, at 510; Christopher P. Adams & Van V. Brantner, *Estimating the Cost of New Drug Development: Is It Really $802 Million?*, 25 HEALTH AFF. 420, 420 (2006) (estimating an average R&D cost per drug of $868 million); Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGERIAL & DECISION ECON. 469, 469, 475 (2007) (estimating an R&D cost per drug of $1.24 billion for large molecule biopharmaceuticals); Fachler, *supra* note 5, at 1065 (A study from "Tufts University revealed that the average cost-per-drug for new-drug development is roughly $802 million. Though initially challenged, the Tufts study was later confirmed by further estimates, which revealed even higher calculated averages for companies introducing one drug into the market").

61 Roin, *supra* note 4, at 510-11.

62 *The Orphan Drug Act: An Engine of Innovation? At What Cost?*, 55 FOOD & DRUG L.J. 125, 131 (2000).

63 Nadla Kounang, *Why pharmaceuticals are cheaper abroad*, CNN, Sep. 28, 2015, http://www.cnn.com/2015/09/28/health/us-pays-more-for-drugs/.

pharma companies would not be able to innovate new drugs.

Given the high R&D costs, pharmaceutical companies are more inclined to pursue generic drugs[64] or repurpose reference listed drugs (RLDs), thereby avoiding clinical trial costs and saving hundreds of millions of dollars.[65] This also leads some companies to use existing products on the market to get orphan drug status for orphan diseases by repurposing the drug.[66] This saves the companies millions in costs and further provides for an additional exclusivity period under ODA to market their drug for a new purpose. If a company is able to bypass a large portion of R&D costs, they are able to capitalize on the market and reap large profits.[67] Thus, many pharmaceutical companies act strategically in bringing particular drugs to the market rather than focusing on what public health policy would dictate.[68] As a result, orphan drug products antibiotics are often ignored by large companies.

C. Orphan Drug Act

Acknowledging that adequate drugs for many rare diseases have not been developed and knowing that developing some drugs with potentially small sales would result in a financial loss, Congress enacted the Orphan Drug Act ("ODA") in 1983.[69] There are three main benefits conferred by the ODA: "1) federal funding of grants and contracts for clinical trials of orphan products;[70] 2) tax credit of fifty percent of [research] costs;[71] and 3) grant of an exclusive right to market the orphan drug for seven years

64 Roin, *supra* note 4, at 511.

65 *Id.* ("[G]eneric-drug manufacturers spend on average only about $2 million on the approval process").

66 Companies often repurpose drugs and thus save time and money on clinical trials used to prove that drugs are safe. A repurposed drug is one that is subsequently marketed for an off label use. Companies would rather spend more time determining if an existing drug can have any other affects rather than researching a new drug for a rare disease or rare antibiotic-resistant bacteria.

67 For example, for a generic drug seeking FDA approval through an ANDA, there is no need to conduct animal studies or clinical studies. Rather, there must be a showing of bioequivalence with the previously approved reference-listed drug. The FDA is required to approve or deny the application within 180 days of submission, but it is common for the FDA and applicant to agree to extensions. Thus, generic drugs save on R&D costs.

68 Large companies prioritize drugs with larger potential for profits. *See* Seoane-Vazquez et al., *supra* note 16.

69 *Orphan Drug Act Relevant Excerpts*, *supra* note 15.

70 *See* 21 U.S.C. § 360ee.

71 Of the three incentives, I think this 50% credit is the most beneficial to companies along with the government grants. It can save them nearly hundreds of millions of dollars over time. While the additional

from the date of FDA marketing approval.[72]"[73]

In a study conducted in 2008, findings showed that "the minimum effect patent and market exclusivity life (including orphan drug market exclusivity) was 9.9 ± 3.7 years for orphan [new molecular entities ("NME")] and 10.5 ± 4.1 years for other NMEs."[74] In essence, the "orphan drug market exclusivity provision increased the maximum effective patent and market exclusivity life of orphan NMEs by an average of 0.8 years."[75] On the other hand, the ODA exclusivity period has decreased generic competition when compared to NMEs without the extra exclusivity.[76] While sponsors and developers are enticed by the extra exclusivity, other benefits of the ODA may have a more profound affect.[77] Both tax incentives and grants reduce R&D costs, which is arguably the biggest market barrier for new drug products. The tax incentives work even once the patent exclusivity expires and thus gives companies an incentive to seek orphan drug status.[78] The tax credit allows a company to save on current costs of other drugs, freeing up more overhead to work on other projects. So far, the ODA seems to be working and helping more orphan drug products reach the market since its enactment.[79]

D. GAIN Act

Noting antibiotic resistance as a public health threat, Congress passed the GAIN Act in 2012 in an attempt to spur new development of innovative antibiotic drug products, or qualified infectious disease products (QIDP).[80] QIDP is defined as an

exclusivity is also extremely beneficial, cutting the R&D costs in half could end up saving the developer more than additional exclusivities.

72 *See* 21 U.S.C. § 360cc; see also *The Orphan Drug Act*, *supra* note 62, at 131 ("Market exclusivity under the Act, however, is different from a traditional product or process patent in several ways. Coverage is narrower than a patent; it only applies to orphan drug use for the rare disease for which it was approved").

73 *Id.* at 128 (internal quotations and footnotes omitted).

74 Seoane-Vazquez et al., *supra* note 16.

75 *Id.*

76 *Id.* (With less generic drug competition, the original drug product can make more profits).

77 *Id.*

78 *Id.*

79 Oliver Wellman-Labadie, *The US Orphan Drug Act: Rare disease research simulator or commercial opportunity?*, 95 HEALTH POLICY 216, 217 (2009).

80 *Generating Antibiotic Incentives Now (GAIN) Act Legislative Summary*, THE HILL (2010), http://thehill.com/images/stories/blogs/healthwatch/gainact.pdf.

antibiotic or any drug for "treating, detecting, preventing, or identifying a qualifying pathogen," which include resistant gram positive pathogens, multi-drug resistant gram negative bacteria, multi-drug resistant tuberculosis, or any other infectious pathogen identified for the purposes of the GAIN Act.[81] The main incentives provided by the GAIN Act include an extension to the Hatch-Waxman Act by providing 5 extra years of exclusivity for QIDPS first approved or licensed on or after the GAIN Act, "6 months additional exclusivity for products with companion diagnostics," priority review by the FDA, and fast-track designation eligibility by the FDA allowing for expedited review procedures.[82] However, it is too soon to tell if GAIN has been effective as it was only enacted in 2012. Further reform will only help make GAIN more effective to combat antibiotic-resistance.

IV. Proposed Reform

A. Orphan Drug Act: A Step in the Right Direction

The ODA is a great first step to facilitate innovation. With over 2,000 orphan designations and over 300 approved orphan drugs, the ODA appears to be successful or at least a big step in the right direction.[83] Recently, the FDA awarded 18 new research grants totaling $19 million to boost the development of products for patients with rare diseases, which affect nearly 30 million Americans in total.[84] The research and grants were specifically awarded for 17 different rare diseases, "many of which have little, or no, available treatment options."[85] The FDA has been taking steps in the right direction and should continue to do so. Since 1983, the Orphan Products Grants Program has provided "more than $350 million to fund more than 570 new clinical studies" and has supported the marketing approval of over 50 products.[86]

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81 *Id.*

82 *Id.*

83 Wellman-Labadie, *supra* note 85, at 217.

84 *FDA awards 18 grants to stimulate product development for rare diseases*, FDA, Sep. 21, 2015, http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm463539.htm.

85 *Id.*

86 *Id.*

As it stands today, there is no reason to try to change or alter the ODA to promote innovation. The patent system along with the benefits offered by the ODA have promoted innovation and should continue to do so. Yet despite the success of the ODA, there are still many orphan diseases without any designated drug products. For example, coral snake bites affect about 100 people per year.[87] Coralmyn is an existing potential anti-venom but the manufacturer does not want to invest millions of dollars to test the drug despite the incentives offered by the ODA because the market for the drug is extremely small.[88] Likewise, other rare diseases do not yet have drug products.[89]

The FDA and Congress have not taken the same steps with antibiotic resistance or with GAIN as with the ODA. While ODA allows for a tax credit on R&D and awards grants for research on orphan rare diseases, the same efforts have not been made for antibiotic resistant pathogens. Furthermore, among drug products that do ultimately receive orphan designation, the largest portion of these designations are in the realm of cancer and do not focus on antibiotics.[90] The next step in reform should be to aid researchers and developers to deal with antibiotic resistance. Decreasing R&D costs is extremely important because some drug markets are so small that even an unlimited patent market exclusivity would not allow a company to recover costs. Thus, by incentivizing and reducing costs, more companies would be able to innovate drugs with smaller markets.

B. Adding More Benefits to GAIN

The problem of antibiotic resistance is increasing globally and it will continue to do so. As time passes, antibiotic resistance increases. The next step in the war against antibiotic resistance should be to extend similar benefits from the ODA to GAIN, specifically, the tax credit on R&D and research grants. Extending these benefits to researchers and developers will help not only the innovators, but the general public as well.

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87 Michael Abramowicz, *Orphan Business Models: Toward A New Form of Intellectual Property*, 124 HARV. L. REV. 1362, 1387-88 (2011).

88 *Id.*

89 Examples include Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), and Tourette syndrome. *See Orphan Drug Act Relevant Excerpts*, *supra* note 15.

90 Seoane-Vazquez et al., *supra* note 16.

By providing a tax credit on research and development and providing more grants, innovators will be more inclined to research and develop drugs to combat antibiotic resistance. The biggest hurdle to developing and researching antibiotics is money. R&D costs exceed profit potentials, thereby hindering antibiotic development. By decreasing the R&D cost, more developers and innovators could be willing and able to take on the scientific challenges of creating drugs that are more effective against harmful pathogens.

First and most importantly, the patients would benefit. One of the necessary evils associated with the pharma industry is the high price of brand-name drugs. If the costs in developing the drugs are decreased, then the innovator can slightly adjust its prices so that it can still recoup its costs and profit during its patent exclusivity period. Plus, there will be more drugs on the market to treat antibiotic resistant illnesses.

Second, overall healthcare costs will decrease. Currently, hospitals and patients have to bear excess costs when dealing with an antibiotic resistant pathogen, such as *Clostridium Difficile*.[91] If new drugs to combat antibiotic resistance are developed, then it follows that an effective treatment and drug regimen will save the patient and the hospital time and unnecessary medical costs. Finally, as more and more illnesses caused by GAIN-qualified pathogens are dealt with properly, the problem of antibiotic resistance will decline both domestically and globally.

Proper *treatment* of illnesses will prevent and limit antibiotic resistance. Thus, to promote innovation for antibiotics, Congress needs to provide tax credits and grants to products covered under GAIN. GAIN already provides for an exclusivity period, but as research showed with respect to the ODA, additional exclusivity to patent exclusivity is not that helpful because the market size is so small.[92] Through government grants and tax credits, companies will be able to enter the pharmaceutical market more easily with new antibiotics. The exclusivity and benefits of patents alone are simply not enough to promote innovation for new antibiotics. Therefore, Congress should simply extend the other benefits of the ODA to GAIN in an effort to promote the development of antibiotics. Changes must be made sooner rather than later in order to curb antibiotic resistance.

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[91] *Biggest Threats*, *supra* note 39.

[92] Additional years of exclusivity on a small market would not make a difference to a company trying to recover millions spent in R&D.

V. Conclusion

While Congress has made great strides in its efforts to promote innovation for orphan diseases and conditions, efforts to combat antibiotic resistance are more stagnant. In short, the ODA provides three primary economic incentives: "1) federal funding of grants and contracts for clinical trials of orphan products;[93] 2) tax credit of fifty percent of [research] costs; and 3) grant of an exclusive right to market the orphan drug for seven years from the date of FDA marketing approval.[94]"[95] The benefits awarded by the ODA must extend to GAIN to aid the combat against antibiotic resistance. Not only is antibiotic resistance a domestic problem, it is a worldwide problem. Increased efforts in the U.S. alone will eventually trickle down to other countries to help limit antibiotic resistance and superbugs in the future.

Research and drug development costs are at an all-time high and are steadily increasing. Patents play a vital role in providing developers and innovators time to recover costs associated with developing drugs. Even though this allows companies to charge high prices for patented drugs, the patent system provides developers with an incentive to create. Without patent protection, companies would be hesitant to spend hundreds of millions of dollars on drug research and development. Thus, the goal Congress and the FDA should have is to incentivize innovation so that new antibiotics can be developed. Therefore, in order to best combat the issue of antibiotic resistance, FDA and Congress need to limit R&D costs by providing tax credits and grants for QIDP's for GAIN as with the ODA.

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93 *See* 21 U.S.C. § 360ee.

94 *See* 21 U.S.C. § 360cc.

95 *The Orphan Drug Act: An Engine of Innovation? At What Cost?*, 55 FOOD & DRUG L.J. 125, 128 (2000) (Internal quotations and footnotes omitted).