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For Profit or For Health? It is Time to Reckon With the Current Pharmaceutical Landscape Through a Systematic Analysis of Monoclonal Antibodies

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For Profit or For Health? It is Time to Reckon With the Current Pharmaceutical Landscape Through a Systematic Analysis of Monoclonal Antibodies

Alexander Snyder*

I. INTRODUCTION

When the Food and Drug Agency (“FDA”) was created in 1938, no person at the time could have envisioned how important its role would become.¹ Nor could any person have envisioned the types of medical breakthroughs the agency would be required to facilitate, and in certain instances, regulate. At the time of the FDA’s inception, acetylsalicylic acid, more commonly known as aspirin, was prescribed and used for almost every common ailment, with certain members of public choosing to take it every day for its “wonder” drug properties.² Today, aspirin is only prescribed as a blood thinning agent after a cardiac event or stroke.³ In truth, aspirin would probably not have passed through the current regulatory and clinical processes to receive FDA approval; it has instead been “grandfathered” into current medical treatment.⁴

Since its inception, not only has the FDA seen significant medical advancements, it has also seen fourteen administrations and numerous iterations of Congress. In that time, it has evolved to accommodate new and innovative therapies along with ever increasing costs associated with research and development. But it is time for the agency to evolve once again, to learn from its past mistakes, and rekindle its relationship with its true purpose—the health and welfare of the public. It is time for the agency and its controlling government to reckon with its place in the pharmaceutical landscape.

The goal of this Note is to look at the background and history of the FDA regulatory landscape and its effects on drug prices as a result. Part II of this Note will

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¹ Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399.

² Jeff Nilsson, *Aspirin: The First Wonder Drug*, THE SATURDAY EVENING POST (Mar. 6, 2019), <https://www.saturdayeveningpost.com/2019/03/aspirin-the-first-wonder-drug/>.

³ *Id.*

⁴ *Id.*

conduct an in-depth analysis of the FDA and related legislation concerning small molecule drugs and biologics. Part III will introduce monoclonal antibodies, a type of biologic, that is commonly associated with soaring drug prices today. Part IV will then focus on legislation and regulatory recommendations that could allow the FDA to shift its focus from favoring innovation to supporting competition and accessibility.

II. FDA REGULATORY BACKGROUND

A. *Inception*

The FDA began with the enactment of the Food, Drug & Cosmetic Act (“FDCA”).⁵ Like most legislation in this nation’s history, it was enacted in response to a crisis. “Dr. Massengill’s Elixir Sulfanilamide,” a drug marketed as a new anti-infective treatment, led to the deaths of 107 citizens.⁶ Congress viewed this event as a preventable tragedy that required immediate legal change.⁷ The real crux of the issue was that the elixir violated federal law because it was misbranded; the drug posed no actual danger to the public.⁸ However this misconception led to the FDA’s birth, which primarily focused on protecting the population from dangerous drugs.⁹ The FDCA complimented the creation of the FDA by defining what a drug was and ensuring that all drugs that met that definition would be subject to regulation.¹⁰ Under the FDCA, a drug is an article recognized by the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia, or National Formulary that is intended for the use in the diagnosis, cure, mitigation, treatment, or prevention of disease; or intended to affect the structure or any function of the body.¹¹ This definition of a drug is precise and inclusive, leaving room for articles that are used as drugs to fall outside FDA regulations.¹² For example, certain articles, such as dietary supplements, that are still in the healthcare space fall outside of this definition

⁵ Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399.

⁶ Paul M. Wax, *Elixirs, Diluents, and the Passage of the 1938 Federal, Drug and Cosmetic Act*, 122 ANNALS INTERNAL MED. 456, 456–61 (1995).

⁷ *Id.*

⁸ DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA 93 (Ira Katznelson et al. eds., 2010) (citing James Harvey Young, *The ‘Elixir Sulfanilamide’ Disaster*, 14 EMORY UNIV. Q. 230, 230–37 (1958)).

⁹ *Id.*

¹⁰ 21 U.S.C. § 321(g)(1).

¹¹ *Id.*

¹² *Id.*

and are not subject to the FDA regulatory process.¹³ Throughout its existence, the FDA has steadily evolved to match modern medical advancements along with the public desire for safe and efficacious drugs. As drugs become more and more complex, the asymmetrical relationship between producers and consumers has continued to grow. The role of the FDA has evolved to help consumers in bridging that gap, in alignment with the original reasoning for its creation.

B. Evolution

After the enactment of the FDCA, the FDA started its slow climb to its current “gatekeeper” role. Initially, before a “new drug” could be brought to market it had to be submitted to the FDA for pre-market approval via a notification system.¹⁴ In addition, the agency had authority over and ultimate control of the drug approval process.¹⁵ Even though the original FDCA legislation had no efficacious provision, it still gave the FDA and its officials significant control and flexibility in the types of regulations it could pass in regard to pre-market approval.¹⁶ Then, in the U.S. Supreme Court decision *United States v. Dotterweich*, the Court held that the passage of the FDCA in 1938 indicated that the legislature intended to hold the public’s health in high regard, and therefore, criminal liability should extend to those actors in control of the pharmaceutical companies seeking drug approval.¹⁷ This decision essentially gave the FDA teeth, since a violation of one of its regulations would lead to criminal liability of the pharmaceutical executives responsible.¹⁸ Due to a combination of flexible and powerful regulatory authority, the FDA began to slowly introduce efficacy components to its review process.¹⁹ Over time, FDA administrators and pharmaceutical companies began to work almost side-by-side to ensure that new pharmacologic developments would be up to standard of review.²⁰

¹³ *Id.*

¹⁴ See generally CARPENTER, *supra* note 8, at 73–117 (describing the initial legislation surrounding the FDCA and the powers granted to the FDA).

¹⁵ *Id.*

¹⁶ *Id.*

¹⁷ *United States v. Dotterweich*, 320 U.S. 277, 281 (1943).

¹⁸ *Id.*

¹⁹ See generally CARPENTER, *supra* note 8, at 118–227 (describing the growing nature of the FDA regulatory scheme following its inception in 1938 and eventually amendments in 1962 and how there were hints and evidence that the FDA would eventually be given significant power and influence over the drug industry).

²⁰ *Id.*

This allowed the FDA to dictate how research and development was done over the next 20 years.²¹

This increase in regulatory power gave remarkable control over an industry for any agency, resulting in calls for deregulation. Drug regulation became almost a constant tug and pull between the FDA administrators and pharmaceutical company executives. This power struggle came to fruition in 1962 when the Kefauver-Harris amendment to the FDCA was passed.²² This amendment was a result of a mixture of events, most notably the thalidomide disaster of the early 1960's.²³ Thalidomide was a drug intended to treat morning sickness in pregnant women.²⁴ FDA officials and physicians denied marketing of this drug in America due its negative outcomes observed in clinical studies.²⁵ They simply did not believe it was safe enough to be given to the public. Their suspicions turned out to be correct when thalidomide was directly linked to severe adverse outcomes for European children.²⁶ Mothers who had been using the drug were giving birth to children without arms and legs.²⁷ Horrified, the American public turned to the FDA; the agency's denial and resistance to thalidomide served as the perfect catalyst for enhanced support of more government regulation over the drug manufacturing industry.²⁸ The Kefauver-Harris amendment took the original pre-market approval system and built upon it, requiring the manufacturers to wait until the FDA had deliberated over and approved the drug for safety and effectiveness.²⁹ In the past, the drug merely received a stamp of approval from the FDA, but the amendment gave the FDA strict control of what drugs were entered into the market.³⁰ Additionally, the amendment made it a statutory requirement for the drug to not only be safe, but efficacious as well.³¹ Ultimately, the amendment provided the FDA direct authority to examine a drug for

²¹ *Id.*

²² Richard A. Merrill, *Symposium on Regulating Medical Innovation: The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1764 (1996); see generally CARPENTER, *supra* note 8, at 228–97.

²³ Merrill, *supra* note 22, at 1764.

²⁴ See CARPENTER, *supra* note 8, at 228–97.

²⁵ *Id.*

²⁶ *Id.*

²⁷ *Id.*

²⁸ *Id.*

²⁹ *Id.*

³⁰ *Id.*

³¹ *Id.*

its therapeutic effect.³² Lastly, the amendment enlarged the FDA’s authority over the type of clinical trials conducted by manufacturers since the FDCA specified that the effectiveness of a drug must be shown by “substantial evidence,” defined by statute as “evidence consisting of adequate and well-controlled investigations, including clinical investigations, by expert[s] qualified to evaluate the effectiveness of the drug involved. . . .”³³ This gave the FDA broader discretion and control of criteria for clinical efficacy.³⁴ Just as they had with the inception of the FDA, pharmaceutical manufacturers began to model their processes to match these new regulatory barriers.³⁵ These new barriers were designed to prevent drugs with no therapeutic benefit from being marketed.³⁶ By the time the Kefauver-Harris amendment was enacted, there were numerous drugs that were on the market that were neither efficacious nor forgone the FDA pre-market notification process, aptly deemed “not drugs.”³⁷ These older drugs already on the market were simply grandfathered into the scheme.

In 1984, the Drug Price Competition and Patent Term Restoration Act was passed as an amendment to the FDCA.³⁸ It would become better known as the Hatch-Waxman Act.³⁹ The purpose of the act was to address a similar problem that patients of the current day know all too well—drug pricing.⁴⁰ Congress believed that the best way to incentivize research and development, particularly of novel drugs, while keeping drug prices down was to enact different processes for brand and generic manufacturers.⁴¹ Brand manufacturers are the actors that specialize and seek out novel treatments and medicine in the hope that they can monopolize the market for a time. On the other hand, generic manufacturers specialize and produce drugs requiring little to no research and development, which allows them to sell their generic drugs at discounted prices.⁴² The problem Congress sought to address by

³² *Id.*

³³ 21 U.S.C. § 355(d).

³⁴ CARPENTER, *supra* note 8, at 118–227.

³⁵ *Id.*

³⁶ *Id.*

³⁷ *Id.*

³⁸ Dmitry Karshedt, *The More Things Change: Improvement Patents, Drug Modifications, and the FDA*, 104 IOWA L. REV. 1129, 1146 (2019).

³⁹ *Id.*

⁴⁰ *Id.*

⁴¹ *Id.*

⁴² *Id.*

passing the Hatch-Waxman Act is two-fold. First, brand manufacturers were concerned about making money back on their investments in novel medicines and treatments.⁴³ The Act addressed this problem by expanding the patent exclusivity to five years after approval of a New Drug Application (NDA) for market and distribution.⁴⁴ Originally, the drug manufacturers would file for a patent when the original small molecule was synthesized or discovered.⁴⁵ The current patent term lasts for 20 years. This term remains unchanged regardless of whether the NDA of the final product is approved 14 years later or 20 years later.⁴⁶ The patent exclusivity term was added to incentivize drug manufacturers to develop new and effective medical treatments without concern for the traditional 20 year patent limit.⁴⁷ During 20 year patent term, the FDA cannot even consider generic manufacturers' applications.⁴⁸ However, after this term has expired, FDA consideration of generic manufacturers' applications resumes. Such manufacturers are not required to prove that the drug is efficacious or safe. Rather, they simply require that the drug is bioequivalent or biosimilar by filing an Abbreviated New Drug Application (ANDA).⁴⁹ Once an ANDA is approved and the generic drug enters the market, drug prices typically fall for both the branded drug and the additional generic counterparts. While the brand manufacturer has patent exclusivity it can enjoy high profit margins.⁵⁰

Second, the Orphan Drug Act was passed in 1983 to address another pressing issue in the drug manufacturing industry.⁵¹ Diseases such as Huntington's disease, Myoclonus, ALS, Tourette Syndrome, and Muscular Dystrophy dramatically affect the quality of life of the patients diagnosed, but do not affect a large proportion of the overall population.⁵² Therefore, little incentive exists for drug manufacturers to

⁴³ *Id.* at 1147.

⁴⁴ *Id.* at 1148.

⁴⁵ *Id.* at 1214.

⁴⁶ Uruguay Rounds Agreements Act, Pub L. No. 103-465, 108 Stat. 4809 (1994).

⁴⁷ Karshstedt, *supra* note 38, at 1147–48.

⁴⁸ *Id.*

⁴⁹ *Id.* at 1149.

⁵⁰ *Id.* at 1149–50.

⁵¹ U.S. DEP'T HEALTH & HUM. SERV. OFF. INSPECTOR GEN., OIE-09-00-00380, THE ORPHAN DRUG ACT: IMPLEMENTATION AND IMPACT 4 (2001), <https://oig.hhs.gov/oci/reports/oci-09-00-00380.pdf>.

⁵² *Id.* at 5.

develop adequate drugs for treatment.⁵³ Drug manufacturers will abstain from investing greatly into these treatments and medicines because they will incur financial loss due to the small subset of the population affected by these diseases.⁵⁴ The Orphan Drug Act sought to rectify this issue by offering financial incentives to drug manufacturers to create treatments for these types of rare diseases.⁵⁵ The law provides four specific incentives: (1) 7-year market exclusivity to sponsors of approved orphan products, (2) a tax credit of 50% of the cost of conducting human clinical trials, (3) federal research grants for clinical testing of new therapies to treat and/or diagnose rare diseases, and (4) an exemption from the usual drug application or “user” fees charged by the FDA.⁵⁶

C. Current State

With the enactment of the Hatch-Waxman Act and the Orphan Drug Act, Congress relied heavily on the promise and guarantee of patent exclusivity to incentivize innovation and research in an inelastic pharmaceutical drug market. However, when patent exclusivity is the only guarantee of profitability, pharmaceutical companies will go to great lengths to maximize that period.

Over the course of the Orphan Drug Act’s thirty-seven year history, its use has been expanded extensively, causing increased concerns that it is being abused at a detriment to patients.⁵⁷ Although the Act is still being used to incentivize research and development of pharmaceutical treatments for rare diseases, there is reason to believe that drug manufacturing companies are using the Act to circumvent and “game” the system by targeting “mainstream” disease states.⁵⁸ Disease state is an all-encompassing term that refers to any disorder, disease, condition, symptom, or indication.⁵⁹ Essentially, pharmaceutical companies are promoting drugs that are indicated for a type of rare disease, but in reality they are being pushed and marketed for much more common disease states.⁶⁰ This way, pharmaceutical companies acquire all the incentives guaranteed by the Orphan Drug Act and benefit from the

⁵³ *Id.* at 4.

⁵⁴ *Id.*

⁵⁵ *Id.*

⁵⁶ *Id.*

⁵⁷ Michael G. Daniel et al., *The Orphan Drug Act: Restoring the Mission to Rare Diseases*, 39 AM. J. CLINICAL ONCOLOGY 210, 210–13 (2016).

⁵⁸ *Id.*

⁵⁹ *Disease State definition*, LAW INSIDER, <https://www.lawinsider.com/dictionary/disease-state> (last visited Sept. 2, 2021).

⁶⁰ Daniel et al., *supra* note 57, at 210–13.

ability to market the drug to a larger patient population for a much more common disease state.⁶¹ It is easy to see the attractiveness of such an option.

By 2020, orphan drugs, meaning those granted approval by the FDA under the Orphan Drug Act, are believed to make up roughly 20% of the prescription drug market when they made up only 6.3% of the market in 2000.⁶² These orphan drugs regularly come with a premium price tag, and are often 25 times more expensive than drugs that receive an FDA approval via traditional means.⁶³ The cost of orphan drugs have increased over time as well with the average annual price of an orphan drug increasing from \$7,136 in 1997 to \$186,758 in 2017.⁶⁴

Admittedly, the increased price of orphan drugs is multifactorial. For example, most orphan drugs today are biologics that required significant funds relating to research and development. However, a key contribution to this increase in overall drug prices is this exploitation of incentives in the Orphan Drug Act.

The abuse of patent exclusivity does not end with the Orphan Drug Act. There are numerous other examples of patent exclusivity being expanded beyond the traditional five-year exclusivity period granted by the Hatch-Waxman Act. “Product Hopping” is a term used for when manufacturers take an existing drug and file a new patent application for new formulations, different manufacturing processes, or even new indications.⁶⁵ This method allows manufacturers to expand their patent exclusivity for the same active drug ingredient.⁶⁶ Manufacturers also file for “secondary” or “double” patents as a way to extend their exclusivity period.⁶⁷ Secondary patents or “follow-on” patents are similarly related to the initial patent, but they claim to be a new active drug ingredient.⁶⁸ They build off of the existing drug in the form of a new iteration of the active ingredient itself, such as the prodrug,

⁶¹ *Id.*

⁶² *Id.*

⁶³ *Drug Prices for Rare Diseases Skyrocket While Big Pharma Makes Record Profits*, AHIP (Sept. 10, 2019), <https://www.ahip.org/drug-prices-for-rare-diseases-skyrocket-while-big-pharma-makes-record-profits/#:~:text=The%20average%20annual%20orphan%20drug,selling%20drugs%20had%20orphan%20indications.>

⁶⁴ *Id.*

⁶⁵ Christopher M. Holman, *Congress Should Decline Ill-Advised Legislative Proposals Aimed at Evergreening of Pharmaceutical Patent Protection*, 51 UNIV. PAC. L. REV. 493, 496–97 (2020).

⁶⁶ *Id.*

⁶⁷ *Id.* at 499–502.

⁶⁸ *Id.*

salts, isomers or certain drug metabolites.⁶⁹ There is also reason to believe that these types of secondary patents are more frequently sought out when the initial active drug ingredient is more successful.⁷⁰ Double patents are simply the same drug being re-patented. This is strictly precluded by statutory language but there is reason to believe that the “obviousness” standard applied by the USPTO is not a secure bar to prevent this from happening entirely.⁷¹ It makes complete sense from an economic perspective that manufacturers would seek out any way to extend this patent exclusivity. However, as highlighted with the Orphan Drug Act, when patent exclusivity is extended premium drug prices usually follow.

In 2010, the Biologics Price Competition and Innovation Act (“BPCIA”) was passed as a part of healthcare reform.⁷² While the FDCA and Hatch-Waxman Act concern small molecule drugs, more typical medicines such as acetaminophen, lisinopril, or cetirizine, concerns biologics.⁷³ Analogous and parallel to the aforementioned amendments to the FDCA, the BPCIA was enacted to promote innovation by ensuring market exclusivity.⁷⁴ The BPCIA ensures that an innovative biologic will be afforded twelve years of FDA exclusivity.⁷⁵ There is some debate as to whether the exclusivity relates to data or market exclusivity, since the statute was ambiguous.⁷⁶ Regardless, the FDA has interpreted the statute to be referring to market exclusivity.⁷⁷ Again, much akin to the Hatch-Waxman Act, the BPCIA provides an abbreviated pathway for the generic version of biologics, or biosimilars.⁷⁸ The goal is to increase accessibility for manufacturers to produce biosimilars, allowing for a more competitive biologic market driving prices down.⁷⁹

The very nature of biologics and their developmental history is to blame for the two analogous pieces of legislation with seemingly the same exact goal. When the

⁶⁹ *Id.*

⁷⁰ Amy Kapczynski, Chan Park & Bhaven Sampat, *Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of ‘Secondary’ Pharmaceutical Patents*, 7 PLoS ONE 1, 1 (2012).

⁷¹ 21 U.S.C. § 355(d), *supra* note 33.

⁷² Ude Lu, Note, *Biologics Price Competition and Innovation Act: Striking a Delicate Balance Between Innovation and Accessibility*, 15 MINN. J.L. SCI. & TECH. 613, 613 (2014).

⁷³ *Id.* at 615.

⁷⁴ *Id.* at 613.

⁷⁵ 42 U.S.C. § 262(7)(A).

⁷⁶ Lu, *supra* note 72, at 613.

⁷⁷ *Id.* at 636 (citing Notice of Public Hearing, 75 Fed. Reg. 61,498 (Oct. 5 2010)).

⁷⁸ 42 U.S.C. § 262(k).

⁷⁹ Lu, *supra* note 72, at 633–34.

FOR PROFIT OR FOR HEALTH?

Hatch-Waxman Act was being passed, biologic development was in its beginning stages and those writing the statutory language could never have predicted the scientific breakthroughs that biologics would allow.⁸⁰ Whereas small molecule drugs are synthesized, biologics are isolated from a variety of natural sources either human, animal, or microorganism.⁸¹ Biologics production require cutting-edge biotechnology methods at the forefront of biomedical research, but if successful, they may be used to treat a variety of medical conditions that were previously untreatable.⁸² Although biologics is a broad and encompassing term, monoclonal antibodies have garnered increased attention over the past two decades, and rightfully so.

III. MONOCLONAL ANTIBODIES

In recent years there has been a push for personalized medicine and the forefront of that push is monoclonal antibodies.⁸³ The advancements in this type of drug development allows for numerous unique and innovative ways to treat a litany of different disease states.⁸⁴ A complex science, the first monoclonal antibody was generated in 1975 and was first approved in 1986.⁸⁵ In short, a monoclonal antibody is a monovalent antibody that binds to the same epitope and are produced from a single B-lymphocyte clone.⁸⁶ They work by cloning certain white blood cells and almost hijack the body's natural immune system to elicit responses for a variety of disease states including multiple types of cancer, autoimmune diseases and even combat certain types of hyperlipidemia.⁸⁷ The first monoclonal antibodies were generated in mice and other animals but the efficacy and safety has increased steadily over the years as the science of developing humanized or human monoclonal antibodies came to the forefront.⁸⁸

⁸⁰ *Id.* at 615–16.

⁸¹ *What are "Biologics" Questions and Answers*, U.S. FOOD & DRUG ADMIN. (Feb. 6, 2018), <https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/what-are-biologics-questions-and-answers>.

⁸² *Id.*

⁸³ Justin K.H. Liu, *The History of Monoclonal Antibody Development—Progress, Remaining Challenges and Future Innovations*, 3 *ANNALS MED. SURGICAL* 113, 113–16 (2014).

⁸⁴ *Id.*

⁸⁵ *Id.*

⁸⁶ *Id.*

⁸⁷ *Id.*

⁸⁸ *Id.*

Although they have become the face of novel medical advancements, monoclonal antibodies are exceedingly hard to get into the hands of the patients that need them, especially at an affordable price. More specifically, research and development of monoclonal antibodies is extensive and immense which undoubtedly plays a role in the skyrocketing prices.

For example, evolocumab (Repatha) is a human monoclonal antibody that binds to proprotein convertase subtilisin kexin type 9 (PCSK9) preventing it from binding to LDL-receptors that eliminate LDL from blood.⁸⁹ Therefore, it allows for more LDL-receptors to be available to clear out LDL in the blood, which is a lipid that is closely linked to high cholesterol in patients.⁹⁰ For treatment of high cholesterol, it has been shown to decrease LDL levels by as much as 60% and triglycerides by 36% whereas statins, the traditional first-line treatment, decreases LDL levels by 20-55% and triglycerides by 10-30%.⁹¹ Although there are legitimate adverse effect concerns regarding Repatha, such as injection site reactions and back pain, other cholesterol medications are associated with as many or more adverse effects.⁹² Healthcare providers are very resistant to administering this new drug instead of the traditional first-line treatment, statins, in large part because of the cost; the drug's adverse effects do not play a role in healthcare providers' aversion to prescribing this drug.⁹³ Atorvastatin is one of the most common statins prescribed for high cholesterol and is usually first-line treatment.⁹⁴ It costs roughly \$10-20 a month for this medication.⁹⁵ In contrast, Repatha costs \$14,000 a year.⁹⁶

As previously stated, the increase in drug price could be due to the nature of the drug itself and the complex research involved in its development. However, Repatha received orphan drug status. Even though it is indicated as adjunct therapy for high cholesterol, a very common disease state affecting millions of patients, it has received orphan drug status for the adjunct treatment of homozygous familial hypercholesterolemia (HoFH).⁹⁷ HoFH is a genetic disease that is characterized by

⁸⁹ KAREN SHAPIRO ET AL., RXPREP: DYSLIPIDEMIA—CLINICAL GUIDELINES 372–83 (2019).

⁹⁰ *Id.*

⁹¹ *Id.*

⁹² *Id.*

⁹³ *Id.*

⁹⁴ *Id.*

⁹⁵ *Atorvastatin (Lipitor)*, GOODRX, <https://www.goodrx.com/lipitor> (last visited Feb. 12, 2021).

⁹⁶ SHAPIRO ET AL., *supra* note 89.

⁹⁷ *Marketing Authorization With Orphan Designation—USA: Repatha*, ORPHANET, <https://www.orpha.net/consor/cgi->

extremely elevated levels of LDL and a higher risk of atherosclerotic cardiovascular disease.⁹⁸ There are numerous other examples that share a similar fact pattern such as infliximab (Remicade) which originally received orphan drug status as a treatment for Crohn's disease but has since been indicated for more common diseases including rheumatoid arthritis, psoriatic arthritis and ulcerative colitis.⁹⁹

The real risk is when cost of treatments begins to affect the practice of healthcare. Healthcare professionals are acutely aware of the tradeoff between the effectiveness of novel treatments, such as Repatha, and the financial burden of obtaining such treatment. In some instances, it is better practice to prescribe the cheaper and slightly less effective option for patients. When only the wealthy have access to medications not due to government inaction, but instead, government action gone awry, the real issue becomes what is the government's role as a self-appointed regulator of an entire industry.

IV. FDA RECOMMENDATION

The concerns regarding the attack on guaranteed exclusivities are legitimate. In large part, these incentives have allowed for both great progress in medicine and for extraordinary funds to be committed to innovative breakthroughs in medicine. But as previously stated, the FDA has a unique position in relation to the pharmaceutical market that is not typically seen in other markets. They act as the sole gatekeeper to prescription drugs, preventing drugs without pre-market approval from sale.¹⁰⁰ The FDA even monitors and controls drugs once they enter the market via phase IV of the clinical trial process, conducting post-market analysis on the safety and effectiveness of the drug long-term.¹⁰¹ This highlights the FDA pushing the boundaries of statutory authority in the name of public health and they should not stop there.

bin/Drugs_Search.php?lng=EN&data_id=112837&search=Drugs_Search_Simple&data_type=Status&yp=Med (last visited Jan. 24, 2021) [hereinafter *Repatha*].

⁹⁸ Frederick J. Raal et al., *Reduction in Mortality in Subjects With Homozygous Familial Hypercholesterolemia Associated with Advances in Lipid-Lowering Therapy*, 124 CIRCULATION 2202, 2202-07 (2011).

⁹⁹ Laura Joszt, *Orphan Drugs Are Driving Skyrocketing Drug Costs, AHIP Finds*, AJMC (Sept. 12, 2019), <https://www.ajmc.com/view/orphan-drugs-are-driving-skyrocketing-drug-costs-ahip-finds>.

¹⁰⁰ Daniel Carpenter, *Gatekeeping and the FDA's Role in Human Subjects Protection*, AMA J. OF ETHICS (Nov. 2004), <https://journalofethics.ama-assn.org/article/gatekeeping-and-fdas-role-human-subjects-protection/2004-11>.

¹⁰¹ *What are the Different Types of Clinical Research?*, U.S. FOOD & DRUG ADMIN. (Jan. 4, 2018), <https://www.fda.gov/patients/clinical-trials-what-patients-need-know/what-are-different-types-clinical-research>.

The modern drug manufacturing system is convoluted with various statutory and regulatory processes that were initially intended to both improve accessibility and innovation, seeming simultaneously. As with any free enterprise, the market players found ways to circumvent the system to their benefit. Whether it is the abuse of the Orphan Drug Act, product hopping, or double and secondary patents, there are numerous examples of manufacturers taking advantage of the current regulatory scheme.¹⁰² In fact, a review of the patent and market exclusivity extensions among top-selling prescription drugs found a median exclusivity duration of 12.5 (8.5-14.8) years.¹⁰³ The argument defending these long exclusivity periods is centered on the belief that it will spur innovation by providing proper economic incentives for the research and development required for drugs, especially biologics like monoclonal antibodies.¹⁰⁴ While this may be true, drug prices have been soaring as a result. In 2010, the top seven biologics represented 43% of Medicare Part B's total budget.¹⁰⁵ Some analyses have found that by introducing biosimilars to the market competition will cause price discounts of anywhere from 10-50%, while the Congressional Budget Office estimated it could reduce drug spending by \$25 billion over ten years.¹⁰⁶ The average price discount of biosimilars in the European Union is 25-35% while the average savings of biosimilars in the United States resides somewhere between 10-37%.¹⁰⁷ Even though there is a reduction of price in biosimilars, only 29 have been approved by the FDA since the enactment of the BPCIA in 2010.¹⁰⁸ For context, the FDA approved twenty-three biologics just in the year 2019 alone.¹⁰⁹

¹⁰² Holman, *supra* note 65.

¹⁰³ Aaron S. Kesselheim, Michael S. Sinha & Jerry Avorn, *Determinants of Market Exclusivity for Prescription Drugs in the United States*, 177 JAMA INTERNAL MED. 1658, 1658-64; 2017 (citing Bo Wang, Jun Liu & Aaron S. Kesselheim, *Variations in Time of Market Exclusivity Among Top-Selling Prescription Drugs in the United States*, 175 JAMA INTERNAL MED. 635, 635-37 (2015)).

¹⁰⁴ *Id.*

¹⁰⁵ *Id.*

¹⁰⁶ *Id.*

¹⁰⁷ Deana Ferreri, *Potential Cost Savings From Improving Biosimilar Availability in Slovakia*, AJMC (Oct. 1, 2020), <https://www.centerforbiosimilars.com/view/potential-cost-savings-from-improving-biosimilar-availability-in-slovakia>; Lauren Chase, *A Guide to Biosimilars Prices: How Much They Cost and How You Can Save*, GOODRX (Apr. 14, 2020, 11:32 AM), <https://www.goodrx.com/blog/biosimilars-prices-how-much-they-cost-how-to-save/>.

¹⁰⁸ *Biosimilar Product Information*, U.S. FOOD & DRUG ADMIN. (Dec. 17, 2020), <https://www.fda.gov/drugs/biosimilars/biosimilar-product-information>.

¹⁰⁹ *2019 Biological License Applications Approvals*, U.S. FOOD & DRUG ADMIN. (Jan. 1, 2020), <https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/2019-biological-license-application-approvals>.

FOR PROFIT OR FOR HEALTH ?

This Note suggests two broad recommendations for the FDA to take in order to better control monoclonal antibody prices through an overall limitation of FDA regulatory exclusivity. First, broad regulatory market exclusivity of five to nine years with +/- sliding scale adjusting for research and development costs. The Obama administration proposed reducing the twelve year period of exclusivity to seven years on many occasions.¹¹⁰ The PRICED Act was introduced previously and proposed to amend the BPCIA exclusivity period from twelve to seven years.¹¹¹ The bill was proposed in the House of Representative in 2016 but died in Congress.¹¹² The bill has since been reintroduced to amend the exclusivity period from 12 years to 5 years, analogous to the biologic exclusivity period in other developed countries like Australia, but has yet to make any headway in Congress.¹¹³ This recommendation applies a slight extension to the proposed rule, with +/- 2 year sliding scale in either direction based upon costs associated with research and development. The more costs associated with the production of the biosimilar, the greater the length of exclusivity that the FDA will grant and vice versa. The purpose is to provide a mechanism that promotes economic incentives while reducing for the longevity of market exclusivity.

Second, there should be stricter enforcement of the Orphan Drug Act. The statute needs reform to better represent the purpose for which it was created. It has been abused since its inception making up 20% of the prescription drug market in 2020.¹¹⁴ In 2020, legislation was introduced to address a loophole in the Orphan Drug Act relating to manufacturers inability to cover costs of drug development when the previous iteration of the drug actually proved to be profitable.¹¹⁵ However, there has not been legislation to address “gaming” the system to grant seven-year market exclusivity for drugs that can treat profitable “mainstream” disease states in addition to orphan disease states. The monoclonal antibody evolocumab (Repatha) is a prime example of this practice.¹¹⁶ There should be legislative action to address this issue and loophole in its entirety. The proposed legislation should be enacted to steer the

¹¹⁰ Lu, *supra* note 72, at 641.

¹¹¹ *Legislation Tracker: PRICED Act Proposes to Shorten Biologic Exclusivity Period from 12 to 7 years*, BIG MOLECULE WATCH (June 24, 2016), <https://www.bigmoleculewatch.com/2016/06/24/legislation-tracker-priced-act-proposes-to-shorten-biologic-exclusivity-period-from-12-to-7-years/>.

¹¹² *Id.*

¹¹³ Priced Act, H.R. 3379, 116th Cong. (2019).

¹¹⁴ Daniel et al., *supra* note 57.

¹¹⁵ Aaron L. Josephson, *Closing the Orphan Drug Act Loophole*, THE NATIONAL LAW REV. (Feb. 18, 2020), <https://www.natlawreview.com/article/closing-orphan-drug-act-loophole>.

¹¹⁶ *Repatha*, *supra* note 97.

act back to its original purpose of incentivizing drug development for rare and unprofitable disease states.¹¹⁷ If the drug, such as a monoclonal antibody, treats a rare disease but also happens to treat a more common disease state, there is no need to provide additional incentive through the Orphan Drug Act since the traditional economic incentives associated with a common disease state are present. However, there should be clear effort and emphasis to ensure that the amendments made to the Act do not result in a drug, like a new monoclonal antibody used in the treatment a rare disease, not being produced.

V. CONCLUSION

Soaring drug prices are one of the greatest challenges the American healthcare system is facing today. Among the most expensive of these prescription drugs is a type of biologic called monoclonal antibodies.¹¹⁸ Although the research and development of these cutting-edge biomedical entities is extensive, there are ways the FDA can operate as a gatekeeper to ensure increased market competition with the goal of driving prices down. Through legislation, the FDA can limit the stranglehold the exclusivity periods have on drug prices, allowing generics or biosimilars to enter the market sooner driving prices down or at least providing cheaper alternatives to patients. This Note suggests tipping the scales from favoring innovation to instead favoring competition and accessibility through implementing a sliding scale market exclusivity for biosimilars. The stricter and fairer enforcement of the Orphan Drug Act, more in line with the original intent of the legislation when it was passed in 1983, will also aid to help tip the scales from innovation to competition and accessibility.¹¹⁹ Legislation and regulation regarding patient care should always be driven by improving health outcomes of the patients by making drug prices cheaper and more accessible. Somewhere along the way, legislation and regulation focused more on ensuring that pharmaceutical companies can make a sizable profit. It is time to decide whether the goal of the pharmaceutical industry is to be for profit or for health.

¹¹⁷ U.S. DEP'T HEALTH & HUM. SERV. OFF. INSPECTOR GEN., *supra* note 51.

¹¹⁸ Inmaculada Hernandez et al., *Pricing of Monoclonal Antibody Therapies: Higher if Used for Cancer?*, 24 AM. J. MANAGED CARE 109, 109–12 (2018).

¹¹⁹ U.S. DEP'T HEALTH & HUM. SERV. OFF. INSPECTOR GEN., *supra* note 51.