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BIOSIMILARS: A LESSON FROM EUROPE

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ABSTRACT

For years, biologics—drugs derived from humans, animals, or microorganisms—have dominated a significant portion of the pharmaceutical market with the aim to tackle life-threatening diseases, such as cancer, diabetes, or specific immune disorders.[1] This new decade introduces an exciting time for innovators, as some of the most widely known biologics face long-awaited patent expiration.[2] In the coming years, patent expiration on brand name drugs will undoubtedly pave the way for cheaper health care alternatives.[3] Economists expect the biosimilar market to increase worldwide from $5.95 billion in 2018 to $23.63 billion by 2023.[4]

This Note will provide a background on the current state of biosimilars in the United States, comparing it with that of Europe. Focus is given to Europe because that is where the first biosimilar medicine was introduced over a decade ago, and is

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1. Michael Eisenstein, *Bring on the Biosimilars*, 569 NATURE S2, S2 (2019), https://www.nature.com/articles/d41586-019-01401-5 (noting that in 2015, 24 percent of drug spending was on biologics); *With 20th Biosimilar Approval, FDA Celebrates Success*, BIOSIMILAR RES. CTR. (June 20, 2019), https://www.biosimilarsresourcecenter.org/20th-biosimilar-approval/ (noting that, as of 2019, biologics account for one third of all new therapies approved by the FDA and 40 percent of all prescription drug spending); WAYNE WINEGARDEN, CTR. FOR MED. & ECON. INNOVATION, INCENTING COMPETITION TO REDUCE DRUG SPENDING: THE BIOSIMILAR OPPORTUNITY 6, (2019), https://www.pacificresearch.org/wp-content/uploads/2019/07/BiosimilarsCompetition_F.pdf (finding that biologics are complicated drugs that are typically administered to patients in a clinical setting to treat life-altering ailments, such as cancer, psoriatic arthritis, and ulcerative colitis).

2. Michelle Derbyshire & Sophie Shina, *Patent Expiry Dates for Biologicals: 2018 Update*, 8 GENERICS & BIOSIMILARS INITIATIVE J. 24 (2019), http://gabi-journal.net/patent-expiry-dates-for-biologicals-2018-update.html.

3. *See id.*

4. Derbyshire & Shina, *supra* note 2, at 26.

where biosimilar approval has continued to see success.[5] *This Note will also briefly explore potential explanations as to why biosimilars have been so slow to enter into the market, especially in the United States. Finally, this Note will address current congressional proposals and will offer other potential solutions to increase the presence of biosimilars in the U.S. market.*

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I. BACKGROUND

In March of 2010, Congress, through the Biologics Price Competition and Innovation Act, created an abbreviated pathway for biological products to obtain approval.[6] To date, biologics account for 38 percent to

5. Martin Schiestl, Markus Zabransky & Fritz Sörgel, *Ten Years of Biosimilars in Europe: Development and Evolution of the Regulatory Pathways*, 11 DRUG DESIGN, DEVELOPMENT AND THERAPY J. 1509, 1510 (2017).

6. *See* Sapna W. Palla & Monica A. Kolinsky, *The New Biosimilars Frontier*, 17 COM. & BUS. LITIG., no. 2, 2016, at 2.

40 percent of all pharmaceutical spending, even though less than 2 percent of Americans use them.[7]

Biologics are larger, more complex pharmaceutical compounds "made by living organisms, such as bacteria or yeast."[8] Due to their complex mixtures, biologics cannot be easily categorized. Importantly, though, some biologics have become the most effective treatment options, especially for illnesses such as arthritis, psoriasis, and other autoimmune diseases.[9] Meanwhile, biosimilars—which can be thought of as generic medicines, though they are technically not alike—are biologic drugs that exhibit "'no clinically meaningful difference' in safety, purity, and effectiveness" when compared to its reference biologic.[10] Due to a less complicated research and development process, biosimilars have the potential to cut annual health care spending by the billions.[11] However, due to a complicated FDA approval process and the anticompetitive behavior of biologic companies, biosimilars are experiencing difficulty reaching the market, thus restricting many Americans' access to life-saving medicines.[12]

Notably, Europe introduced its first biosimilar, Omnitrope, in 2006, and since then, has approved fifty-nine other biosimilars.[13] On the other hand, the United States has been much slower in entering the biosimilar market.[14] The first FDA-approved biosimilar was not introduced until

7. Mike Z. Zhai, Ameet Sarpatwari & Aaron S. Kesselheim, *Why Are Biosimilars Not Living up to Their Promise in the US?*, 21 AMA J. ETHICS 668, 668–69 (2019); Press Release, Susan Collins, Bipartisan Group of Senators Launch Effort to Stop Patent Gaming & Increase Access to Lower-Cost Drugs, (Mar. 6, 2019, 3:51 PM), https://www.collins.senate.gov/newsroom/bipartisan-group-senators-launch-effort-stop-patent-gaming-increase-access-lower-cost-drugs.

8. Wolfgang A. Rehmann & Diana Heimhalt, *Biosimilars in Europe: The Role of the EMA's Guidelines*, 11 SCITECH LAW., no. 3, Spring 2015, at 8.

9. Ariella Cohen, *What's Going on with Biosimilars?*, 28 HEALTH LAW. 36, 36 (2016).

10. WINEGARDEN, *supra* note 1, at 4.

11. *Id.* at 7–8 (showing that as more biologics continue to come off patent, biosimilars are estimated to reduce health care spending by $54 billion between 2017 and 2026); Zhai et al., *supra* note 7, at 669.

12. *See* Zhai et al., *supra* note 7, at 669.

13. Derbyshire & Shina, *supra* note 2, at 26.

14. Alaric Dearment, *Why is Biosimilar Adoption Slow in the U.S., and Can Something Be Done to Boost Uptake?*, MEDCITY NEWS (Oct. 1, 2019, 8:05 AM), https://medcitynews.com/2019/10/why-biosimilars-adoption-is-slow-in-the-u-s-and-can-something-be-done-to-boost-uptake/ (proposing that the United States's slow adoption of biosimilars to largely be the result of a lack of physician education and the market's immaturity).

2015, and to date, only twenty-eight biosimilars have been approved, with even fewer on the market.[15] Moreover, one-third did not even receive approval until 2019.[16]

TABLE 1: FDA-APPROVED BIOSIMILARS

	Biosimilar	Reference Biologic	Biosimilar Manufacturer	Intended Treatment[17]	FDA Approval Date
1	Zarxio	Neupogen	Sandoz, Inc.	Neutropenia	March 6, 2015
2	Inflectra	Remicade	Celltrion, Inc.	Rheumatoid arthritis ("RA"), psoriatic arthritis ("PA"), Crohn's disease ("CD"), ulcerative colitis ("UC"), plaque psoriasis ("PP"), ankylosing spondylitis ("AS")	April 5, 2016
3	Erelzi	Enbrel	Sandoz, Inc.	RA, juvenile idiopathic arthritis ("JIA"), PA, AS, PP	August 30, 2016
4	Amjevita	Humira	Amgen, Inc.	PP, AS, CD, UC, PA, JIA, RA	September 23, 2016
5	Renflexis	Remicade	Samsung Bioepis Co., Ltd.	PA, RA, CD, UC, PP, AS	April 21, 2017
6	Cyltezo	Humira	Boehringer Ingelheim	RA, JIA, PA, AS, CD, UC, PP	August 25, 2017

15. *Id.*; *How Many Biosimilars Have Been Approved in the United States?*, DRUGS.COM https://www.drugs.com/medical-answers/many-biosimilars-approved-united-states-3463281/ (last updated July 8, 2020); *see infra* Table 1.

16. *See How Many Biosimilars Have Been Approved in the United States?*, *supra* note 15.

17. *FDA Approval History*, DRUGS.COM, https://www.drugs.com/history.html (last visited Jan. 2, 2021).

	Biosimilar	Reference Biologic	Biosimilar Manufacturer	Intended Treatment[17]	FDA Approval Date
			Pharmaceuticals, Inc.		
7	Mvasi	Avastin	Amgen, Inc.	Non-small cell lung cancer, colorectal cancer, glioblastoma multiforme, renal cell carcinoma, cervical cancer	September 14, 2017
8	Ogivri	Herceptin	Mylan GmbH	Breast cancer, gastric cancer	December 1, 2017
9	Ixifi	Remicade	Pfizer, Inc.	RA, PA, AS, CD, UC, PP	December 13, 2017
10	Retacrit	Epogen/Procrit	Hospira, Inc.	Anemia	May 15, 2018
11	Fulphila	Neulasta	Mylan N.V.	Neutropenia	June 4, 2018
12	Nivestym	Neupogen	Pfizer, Inc.	Neutropenia	July 20, 2018
13	Hyrimoz	Humira	Sandoz Inc.	RA, JIA, PP, PA, AS, CD, UC	October 30, 2018
14	Udenyca	Neulasta	Coherus BioSciences, Inc.	Neutropenia	November 2, 2018
15	Truxima	Rituxan	Celltrion, Inc.	Non-Hodgkin's Lymphoma	November 28, 2018
16	Herzuma	Herceptin	Celltrion, Inc.	Breast cancer	December 14, 2018
17	Ontruzant	Herceptin	Samsung Bioepis Co., Ltd.	Breast cancer, gastric cancer	January 18, 2019
18	Trazimera	Herceptin	Pfizer, Inc.	Breast cancer, gastric cancer	March 11, 2019
19	Eticovo	Enbrel	Samsung Bioepis Co., Ltd.	RA, AS, PP, PA, polyarticular JIA	April 25, 2019
20	Kanjinti	Herceptin	Amgen, Inc.	Breast cancer, gastric cancer	June 13, 2019
21	Zirabev	Avastin	Pfizer, Inc.	Colorectal cancer, non-small cell lung cancer, giloblastoma	June 27, 2019

	Biosimilar	Reference Biologic	Biosimilar Manufacturer	Intended Treatment[17]	FDA Approval Date
				multiforme, renal cell carcinoma, cervical cancer	
22	Ruxience	Rituxan	Pfizer, Inc.	Non-Hodgkin's lymphoma, chronic lymphocytic leukemia, granulomatosis with polyangiitis, microscopic polyangiitis	July 23, 2019
23	Hadlima	Humira	Samsung Bioepis Co., Ltd.	RA, JIA, PA, AS, CD, UC, PP	July 23, 2019
24	Ziextenzo	Neulasta	Sandoz, Inc.	Neutropenia	November 4, 2019
25	Abrilada	Humira	Pfizer, Inc.	RA, JIA, PA, AS, CD, UC, PP	November 15, 2019
26	Avsola	Remicade	Amgen, Inc.	CD, UC, RA, AS, PA, PP	December 6, 2019
27	Nyvepria	Neulasta	Pfizer, Inc.	Neutropenia	June 10, 2020
28	Hulio	Humira	Mylan Pharmaceuticals, Inc.	RA, JIA, PA, AS, CD, UC, PP	July 6, 2020

A. Importance of Biosimilars

In the United States alone, more than 34 million Americans reported knowing at least one family member or friend who has passed away in the last five years due to an inability to afford needed medical treatment.[18] Sadly, commonalities such as this will not disappear any time soon, as drug prices are only rising. For example, within the past decade, Eli Lilly tripled the price of Humalog, a life-saving insulin

18. Dan Witters, *Millions in U.S. Lost Someone Who Couldn't Afford Treatment*, GALLUP (Nov. 12, 2019), https://news.gallup.com/poll/268094/millions-lost-someone-couldn-afford-treatment.aspx.

medication that now costs approximately $600.[19] This was matched by an increase in other producers' insulin prices as well.[20] With over 30 million Americans currently diagnosed with diabetes, this price increase drastically affected the American population and caused many to die as a result of insulin rationing.[21] These companies are not alone, however. In 2019 alone, more than 3,400 drugs have seen an increase in their prices.[22]

Biologics are at least "22 times more expensive than small molecule drugs, ranging from $25,000 [to] $200,000 annually per patient."[23] High drug costs are attributed to clinical testing, which is understood to be the most expensive phase in bringing a drug to market.[24] Biologics are complex drugs that are much more difficult to manufacture than generic drugs.[25] Clinical testing of biologics is costly, as biologics are created from living organisms and, thus, must satisfy high standards regarding safety and efficacy.[26] Additionally, biologic companies are required to find patients willing to participate in lengthy clinical trials.[27] However, by

19. Jacob Bell, *Lilly Reveals Humalog Pricing Details amid Larger Scrutiny over Insulin Costs*, BIOPHARMA DIVE (Mar. 25, 2019), https://www.biopharmadive.com/news/lilly-humalog-price-list-net-insulin/551236/.

20. *Id.*

21. Sarah Ruth Bates, *Ending the Cycle of Drug Price Hikes, Death and Outrage*, WBUR (June 25, 2019), https://www.wbur.org/cognoscenti/2019/06/25/high-costs-of-prescription-drugs-sarah-ruth-bates; Rich Barlow, *Insulin Inflation is Killing People. Something Needs to be Done*, WBUR (Nov. 27, 2018), https://www.wbur.org/cognoscenti/2018/11/27/protests-insulin-prices-rich-barlow.

22. Aimee Picchi, *Drug Prices in 2019 are Surging, with Hikes at 5 Times Inflation*, CBS NEWS (July 1, 2019, 11:34 AM), https://www.cbsnews.com/news/drug-prices-in-2019-are-surging-with-hikes-at-5-times-inflation/.

23. Cohen, *supra* note 9, at 37.

24. *See id.*; *see, e.g.*, Jonathan J. Darrow, *Crowdsourcing Clinical Trials*, 98 MINN. L. REV. 805, 823 (2014) (estimating clinical trials to account for 50 percent of the cost to develop a new drug).

25. Avik Roy, *Biologic Medicines: The Biggest Driver of Rising Drug Prices*, FORBES: APOTHECARY (Mar. 8, 2019, 8:20 PM), https://www.forbes.com/sites/theapothecary/2019/03/08/biologic-medicines-the-biggest-driver-of-rising-drug-prices/#651411d18b00.

26. Martin McEnrue, Note, *Barriers to Biosimilar Approval: Creating Clarity Through the Publication of Product-Class Specific Guidances*, 31 MD. J. INT'L L. 311, 313–16 (2016); CONG. RSCH. SERV., R44620, BIOLOGICS AND BIOSIMILARS: BACKGROUND AND KEY ISSUES 1–4 (2019). Biologics suppress the immune system and often carry toxins, thus making them quite dangerous if administered improperly or without monitoring. *See id.* at 3–4.

27. *See, e.g.*, *Motivating Condition-Naïve, Difficult-to-Reach Patients to Participate in Clinical Trials*, CONTINUUM CLINICAL (Aug. 12, 2019) ("Finding patients—and sometimes physicians—who understand the potential benefits, accept the potential risks, and are

avoiding the need to conduct clinical trials, biosimilar patent holders are able to market drugs that are highly similar to pre-approved biologics at approximately 15 to 20 percent lower costs.[28]

B. Approval Process for Biosimilars

1. United States

In 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act, commonly referred to as the Hatch-Waxman Act.[29] One central purpose of the Hatch-Waxman Act was to increase competition in the drug industry in order to provide more affordable treatment options for consumers.[30] To do so, the Act allowed "drug companies to obtain approval of generic versions of small molecule drugs" without having to undergo lengthy and expensive clinical trials.[31] Large-molecule biosimilars were not covered under the Hatch-Waxman Act.[32]

It was not until 2009 that Congress enacted the Biologics Price Competition and Innovation Act ("BPCIA") as part of the Patient Protection and Affordable Care Act.[33] Under the BPCIA, a biosimilar could be subject to an abbreviated approval process provided that it demonstrates equivalency with a licensed biologic.[34] In order to demonstrate similarity to a reference product, or biologic, the biosimilar must "'exhibit[] a range of structural similarities' to the reference product."[35] Pursuant to 42 U.S.C. § 262(i)(2), the biosimilar must show it is "highly similar" to the reference biologic with no "clinically meaningful differences" with respect to its safety, purity, and potency.[36] More specifically, the biosimilar must prove that it "use[s] the same mechanism[(s)] of action for the condition[(s)] of use prescribed,

willing to commit their time and energy to a study schedule can be difficult even under the best circumstances.").

28. *What's the Difference? Biosimilar and Generic Drugs*, CANCER TREATMENT CTRS. OF AM. (Dec. 26, 2018), https://www.cancercenter.com/community/blog/2018/12/whats-the-difference-biosimilar-and-generic-drugs.

29. Erwin A. Blackstone & Joseph P. Fuhr Jr., *Biologics & Biosimilars: The Possibility of Encouraging Innovation and Competition*, 11 SCITECH LAW., no. 3, Spring 2015, at 4, 5.

30. *Id.*

31. *Id.*

32. *Id.*

33. *Id.*

34. *Id.*; 42 U.S.C. § 262(k)(2)(A)(i).

35. Cohen, *supra* note 9, at 36.

36. 42 U.S.C. § 262(i)(2).

recommended, or suggested in the proposed labeling . . . [of the approved] reference product."[37] Furthermore, the biosimilar application must contain information demonstrating that:

> [T]he biological product is biosimilar to a reference product based upon . . .
>
> (aa) analytical studies that demonstrate that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components;
>
> (bb) animal studies (including the assessment of toxicity); and
>
> (cc) a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate safety, purity, and potency in [one] or more appropriate conditions of use for which the reference product is licensed . . . .[38]

Additionally, the biosimilar must be "prescribed, recommended, or suggested" only for condition(s) "previously approved for the reference product," as well as abide by the same routes of administration, dosage forms, and strengths.[39] Finally, "the facility in which the bio[similar] is manufactured, processed, packed, or held [must] meet[] standards designed to assure that the bio[similar] continues to be safe, pure, and potent."[40] Only then through an abbreviated biologics licensing application ("aBLA") can the biosimilar receive approval without repeating all of the work of the biologic manufacturer.[41]

It is important to note that this "highly similar" standard is a lower standard than that of "interchangeability," which is when the biosimilar is shown to produce the same clinical result as the reference biologic in any given patient, and can be substituted with no risk in terms of safety or efficacy.[42] Once interchangeability status is achieved, pharmacists

37. *Id.* § 262(k)(2)(A)(i)(II); Cohen, *supra* note 9, at 37.
38. *Id.* § 262(k)(2)(A)(i)(I).
39. *Id.* § 262(k)(2)(A)(i)(III)–(IV).
40. *Id.* § 262(k)(2)(A)(i)(V).
41. *See* Henrik D. Parker, *Shall We Dance? FDA Biosimilar Approval Process Litigation Options*, 27 INTELL. PROP. LITIG. 2, 2 (2016).
42. 42 U.S.C. § 262(i)(2)–(3).

may exchange a biosimilar for the reference biologic without having to consult the patient's prescribing physician.[43] To date, the FDA has yet to approve any interchangeable biosimilars.[44]

Unlike the Hatch-Waxman Act, the BPCIA focuses its provisions on litigation, often referred to as "the patent dance."[45] This dance begins upon the submission of an aBLA to the FDA. Within twenty days after a biosimilar application has been accepted for review, the applicant must provide the reference product sponsor ("RPS") its application and a description of its manufacturing process.[46] Within sixty days of receipt, the RPS is required to provide the applicant a list of all patents the RPS believes could reasonably be asserted against the applicant and identify those patents it would license.[47] Within sixty days from that time, the applicant may provide its own list of potentially infringing patents that the RPS could use against them, as well as either a statement as to why the patents are invalid, unenforceable, or not infringed, or that the applicant will not market its product until the expiration of the listed patent(s).[48] Finally, the RPS may respond, upon which time both parties must engage in negotiations to determine which patents will be litigated.[49] This so-called patent dance is largely responsible for lengthy litigation and subsequent delays in biosimilar approval.[50]

In 2017, the United States began making steps in the right direction through the case of *Sandoz, Inc. v. Amgen, Inc.*[51] In that case, Sandoz sought FDA approval of its biosimilar, Zarxio, a filgrastim, or bone marrow stimulant, based on the reference product, Neupogen, marketed by Amgen.[52] Amgen brought suit against Sandoz for essentially failing to

43. *Id.* § 262(i)(3).

44. *Biosimilar and Interchangeable Biologics: More Treatment Choices*, U.S. FOOD & DRUG ADMIN. (Mar. 23, 2020), https://www.fda.gov/consumers/consumer-updates/biosimilar-and-interchangeable-biologics-more-treatment-choices.

45. *See* § 262(*l*); Palla & Kollinsky, *supra* note 6, at 2 (noting that the complex and lengthy procedure for patent information exchange and litigation between reference product sponsors and applicants is often termed the "patent dance").

46. 42 U.S.C. § 262(*l*)(2)(A).

47. *Id.* § 262(*l*)(3)(A).

48. *Id.* § 262(*l*)(3)(B).

49. *Id.* § 262(*l*)(4).

50. Palla & Kolinsky, *supra* note 6, at 2. Failure to follow these procedures entitles the reference manufacturer to a declaratory patent infringement action. *See, e.g.*, Sandoz, Inc. v. Amgen, Inc., 137 S. Ct. 1664, 1676 (2017).

51. Sandoz, Inc. v. Amgen, Inc., 137 S. Ct. 1664 (2017).

52. *Sandoz*, 137 S. Ct. at 1672–73.

participate in the patent dance.[53] The Court unanimously ruled that the patent dance is not mandatory, as many biologic companies had argued.[54] Although an applicant "must" provide its application and manufacturing information to the reference biologic manufacturer, failure to do so is accounted for in the statute.[55] Moreover, the Supreme Court unanimously ruled that a biosimilar need not wait six months before bringing an FDA-approved biosimilar to market.[56] While the United States has experienced a significant rise in FDA-approved biosimilars since 2017, when *Sandoz* was decided, it has become increasingly clear that the judiciary system cannot fight the battle of immorally high health care costs alone.[57] Thus, recent Congressional proposals, as well as an examination of a more successful regulatory model, will be explored.

2. Europe

In Europe, statutory provisions for generic medicines govern the approval of biosimilars. Analogous to the United States, after a biosimilar applicant has demonstrated similarity to a previously authorized biologic, the applicant may apply for approval under an abbreviated procedure.[58] However, this mode of approval is only applicable once the reference drug's protection period has expired.[59]

53. *Id.* at 1673.

54. *See id.* at 1676–77.

55. *What Is the Patent Dance?*, WINSTON & STRAWN LLP, https://www.winston.com/en/legal-glossary/patent-dance.html (last visited Oct. 9, 2020). The applicant must also file a Notice of Commercial Marketing to the reference biologic sponsor no later than 180 days before the first commercial marketing of the biosimilar. *Sandoz*, 137 S. Ct. at 1669. However, the applicant may file said Notice at any time before marketing, even including a time before the biosimilar receives FDA approval. *Id.* Importantly, though, failure to provide a Notice of Commercial Marketing is not federally enforceable with an injunction. *Id.*

56. *Sandoz*, 137 S. Ct. at 1677.

57. *See How Many Biosimilars Have Been Approved in the United States?*, *supra* note 15.

58. Rehmann & Heimhalt, *supra* note 8, at 9.

59. *Id.* U.S. biosimilar patent holders must also honor biologic patent holders' exclusivity periods in exchange for their drug studies and samples. *See, e.g.*, *Data Exclusivity for Biologics*, PHRMA (May 1, 2016), https://www.phrma.org/en/Fact-Sheet/Data-Exclusivity-for-Biologics. In the United States, biologics are granted twelve years market exclusivity in order to increase competition while incentivizing innovation, while in Europe, biologics receive ten years of market exclusivity. Rehmann & Heimhalt, *supra* note 8, at 9.

Much like the role of the FDA, the European Medicines Agency ("EMA") is responsible for reviewing biosimilar applications in Europe.[60] However, through the use of specific guidelines that are transparent for a manufacturer's benefit, the EMA has created a larger biosimilar market in Europe than that in the United States.[61] Otherwise, the approval processes in the United States and Europe, exhibited in Figure 1, are analogous.

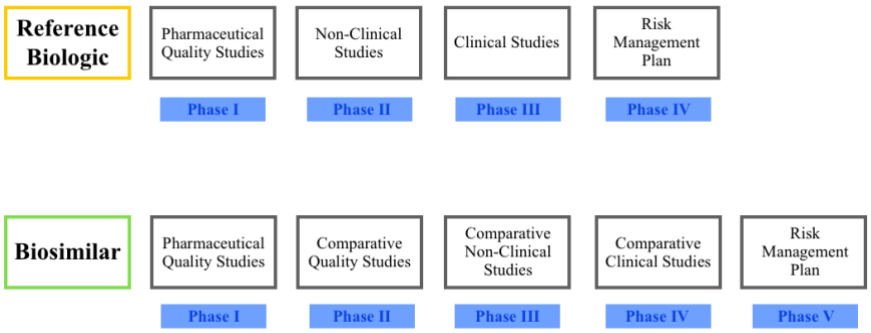

Figure 1: General Approval Process of a Reference Biologic Versus a Biosimilar[62]

In order to receive approval, the biosimilar must again demonstrate "high similarity" to the reference biologic and must not exhibit "clinically meaningful differences" from the reference biologic "in terms of safety, quality, and efficacy."[63] In doing so, biosimilar creators bypass costly and

60. McEnrue, supra note 26, at 312. The EMA's mission is to "foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health in the European Union." *About Us: What We Do*, EUR. MEDS. AGENCY, https://www.ema.europa.eu/en/about-us/what-we-do (last visited Oct. 9, 2020).

61. McEnrue, *supra* note 26, at 311, 324–25, 330. Through the 2004/27/EC Directive, "[t]he EMA has released eight product-specific guidelines for biosimilars," thereby reducing the need for agency intervention. *Id.* at 320, 324–25.

62. EUR. MEDS. AGENCY & EUR. COMM'N, BIOSIMILARS IN THE EU: INFORMATION GUIDE FOR HEALTHCARE PROFESSIONALS 13, https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf (last updated Feb. 10, 2019); *see also supra* Section I.B.1.

63. *Biosimilar Medicines: Overview*, EUR. MEDS. AGENCY, https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview (last visited Oct. 9, 2020).

time-consuming clinical studies. As of May 2019, the EMA has approved fifty-four biosimilars over a timespan of thirteen years.[64]

TABLE 2: EMA-APPROVED BIOSIMILARS

	Biosimilar	Reference Biologic	Biosimilar Manufacturer	Intended Treatment[65]	EMA Approval Date
1	Omnitrope	Somatropin	Sandoz GmbH	Pituitary dwarfism, Prader-Willi syndrome, Turner syndrome	April 12, 2006
2	Abseamed	Epoetin Alfa	Medice Arzneimittel Pütter GmbH & Co. KG	Anemia, cancer, chronic kidney failure	August 28, 2007
3	Binocrit	Epoetin Alfa	Sandoz GmbH	Anemia, chronic kidney failure	August 28, 2007
4	Epoetin Alfa Hexal	Epoetin Alfa	Hexal AG	Anemia, cancer, chronic kidney failure	August 28, 2007
5	Retacrit	Epoetin Zeta	Hospira UK Ltd.	Anemia, autologous blood transfusion, cancer, chronic kidney failure	December 18, 2007
6	Silapo	Epoetin Zeta	Stada Arzneimittel AG	Anemia autologous blood transfusion, cancer, chronic kidney failure	December 18, 2007
7	Ratiograstim	Filgrastim	Ratiopharm GmbH	Cancer, neutropenia, hematopoietic stem cell transplantation	September 15, 2008
8	Tevagrastim	Filgrastim	Teva GmbH	Cancer, neutropenia, hematopoietic stem cell transplantation	September 15, 2008
9	Zarzio	Filgrastim	Sandoz GmbH	Cancer, neutropenia, hematopoietic stem cell transplantation	February 6, 2009

64. Aydin H. Harston, *Biosimilar Approvals Stall During the COVID-19 Pandemic, but the Pipeline Grows*, ROTHWELL FIGG (June 9, 2020), https://www.biosimilarsip.com/2020/06/09/biosimilar-approvals-stall-during-covid-19-pandemic-but-the-pipeline-grows/.

65. For biosimilars #1-55 and #57 in Table 2, *see Biosimilars Approved in Europe*, GABI, http://www.gabionline.net/Biosimilars/General/Biosimilars-approved-in-Europe (Feb. 21, 2020); otherwise, *see Lyumjev FDA Approval History*, DRUGS.COM, https://www.drugs.com/history/lyumjev.html (last visited Jan. 2, 2021) and *Nepexto*, EUROPEAN MEDICINES AGENCY, https://www.ema.europa.eu/en/medicines/human/EPAR/nepexto (last visited Jan. 2, 2021) for biosimilars #56 and #58 in Table 2, respectively.

	Biosimilar	Reference Biologic	Biosimilar Manufacturer	Intended Treatment[65]	EMA Approval Date
10	Filgrastim Hexal	Filgrastim	Hexal AG	Cancer, neutropenia, hematopoietic stem cell transplantation	February 6, 2009
11	Nivestim	Filgrastim	Hospira UK Ltd.	Cancer, neutropenia, hematopoietic stem cell transplantation	June 8, 2010
12	Inflectra	Infliximab	Hospira UK Ltd.	RA, PA, AS, CD, PP, UC	September 10, 2013
13	Remsima	Infliximab	Celltrion Healthcare Co., Ltd.	RA, PA, AS, CD, PP, UC	September 10, 2013
14	Ovaleap	Follitropin Alfa	Teva Pharma B.V.	Anovulation ("IVF")	September 27, 2013
15	Grastofil	Filgrastim	Apotex Europe B.V.	Neutropenia	October 18, 2013
16	Abasaglar	Insulin Glargine	Eli Lilly Regional Operations GmbH	Diabetes	September 9, 2014
17	Accofil	Filgrastim	Accord Healthcare Ltd.	Neutropenia	September 18, 2014
18	Bemfola	Follitropin Alfa	Gedeon Richter Plc.	IVF	March 24, 2014
19	Benepali	Etanercept	Samsung Bioepis Co., Ltd.	RA, PA, AS, PP	January 14, 2016
20	Flixabi	Infliximab	Samsung Bioepis Co., Ltd.	CD, AS, PA, PP, RA, UC	May 26, 2016
21	Inhixa	Enoxaparin Sodium	Techdow Europe AB	Venous thromboembolism	September 15, 2016
22	Thorinane	Enoxaparin Sodium	Pharmathen S.A.	Venous thromboembolism	September 15, 2016
23	Terrosa	Teriparatide	Gedeon Richter Plc.	Osteoporosis	January 4, 2017
24	Movymia	Teriparatide	Stada Arzneimittel AG	Osteoporosis	January 11, 2017
25	Truxima	Rituximab	Celltrion Healthcare Co., Ltd.	Non-Hodgkin's lymphoma, chronic lymphocytic leukemia, granulomatosis with polyangiitis, microscopic polyangiitis, RA	February 17, 2017
26	Amgevita	Adalimumab	Amgen Europe	RA, PA AS, PP, UC, CD	March 22, 2017

	Biosimilar	Reference Biologic	Biosimilar Manufacturer	Intended Treatment[65]	EMA Approval Date
27	Solymbic	Adalimumab	Amgen Europe	RA, PA, AS, PP, UC, CD, hidradenitis suppurativa	March 22, 2017
28	Rixathon	Rituximab	Sandoz GmbH	Non-hodgkin's lymphoma, chronic lymphocytic leukemia, RA, granulomatosis, microscopic polyangiitis	June 19, 2017
29	Riximyo	Rituximab	Sandoz GmbH	Non-Hodgkin's lymphoma, chronic lymphocytic leukemia, RA, microscopic polyangiitis, granulomatosis	June 15, 2017
30	Erelzi	Etanercept	Sandoz GmbH	RA, PA, AS, PP	June 27, 2017
31	Blitzima	Ritruximab	Celltrion Healthcare Co., Ltd.	Non-Hodgkin's lymphoma, chronic lymphocytic leukemia	July 13, 2017
32	Ritemvia	Rituximab	Celltrion Healthcare Co., Ltd.	Non-Hodgkin's lymphoma, granulomatosis, microscopic polyangiitis	July 13, 2017
33	Imraldi	Adalimumab	Samsung Bioepis Co., Ltd.	PP, PA, RA, AS, CD, UC, RA, arthritis, hidradenitis suppurativa, uveitis	August 24, 2017
34	Ontruzant	Trastuzumab	Samsung Bioepis Co., Ltd.	Breast cancer, metastatic gastric cancer	November 15, 2017
35	Mvasi	Bevacizumab	Amgen Europe B.V.	Kidney cancer, lung cancer, ovarian cancer, peritoneal cancer, fallopian tube cancer	January 15, 2018
36	Herzuma	Trastuzumab	Celltrion Healthcare Co., Ltd.	Breast cancer, metastatic gastric cancer	February 9, 2018
37	Semglee	Insulin glargine	Mylan S.A.S.	Diabetes	March 28, 2018

	Biosimilar	Reference Biologic	Biosimilar Manufacturer	Intended Treatment[65]	EMA Approval Date
38	Kanjinti	Trastuzumab	Amgen/Allergan	Breast cancer, metastatic gastric cancer	May 16, 2018
39	Zessly	Infliximab	Sandoz GmbH	RA, CD, UC, AS, PP, PA	May 18, 2018
40	Halimatoz	Adalimumab	Sandoz GmbH	PP, PA, RA, AS, hidradenitis suppurativa, uveitis	July 26, 2018
41	Hefiya	Adalimumab	Sandoz GmbH	PP, PA, RA, AS, juvenile rheumatoid arthritis, hidradenitis suppurativa, uveitis	July 26, 2018
42	Hyrimoz	Adalimumab	Sandoz GmbH	CD, PA, RA, AS, UC, hidradenitis suppurativa, uveitis, papulosquamous skin disease	July 26, 2018
43	Trazimera	Trastuzumab	Pfizer	Stomach neoplasms, breast neoplasms	July 26, 2018
44	Hulio	Adalimumab	Mylan S.A.S.	PP, PA, RA, AS, CD, UC, hidradenitis suppurativa, uveitis	September 17, 2018
45	Pelgraz	Pegfilgrastim	Accord Healthcare Ltd.	Neutropenia	September 20, 2018
46	Udenyca	Pegfilgrastim	Coherus	Neutropenia	September 20, 2018
47	Fulphila	Pegfilgrastim	Mylan S.A.S.	Neutropenia	November 20, 2018
48	Pelmeg	Pegfilgrastim	Cinfa Biotech S.L.	Neutropenia	November 20, 2018
49	Ziextenzo	Pegfilgrastim	Sandoz GmbH	Neutropenia	November 27, 2018
50	Ogivri	Trastuzumab	Mylan S.A.S.	Breast cancer, metastatic gastric cancer	December 12, 2018
51	Zirabev	Bevacizumab	Pfizer	Cancer (kidney, lung, colon, rectum, cervix)	February 14, 2019
52	Idacio Kromeya	Adalimumab	Fresenius Kabi Deutschland GmbH	Arthritis, PP, PA, RA, AS, CD, UC, hidradenitis suppurativa, uveitis	April 2, 2019
53	Grasustek	Pegfilfrastim	Juta Pharma GmbH	Neutropenia	June 20, 2019

	Biosimilar	Reference Biologic	Biosimilar Manufacturer	Intended Treatment[65]	EMA Approval Date
54	Cegfila	Pegfilfrastim	Mundipharma Biologics S.L.	Neutropenia	December 19, 2019
55	Amsparity	Adalimumab	Pfizer	AS, hidradenitis suppurativa, CD, PP, PA, RA, UC, uveitis	February 13, 2020
56	Lyumjev	Insulin Lispro	Eli Lilly Nederland B.V.	Type 1 Diabetes, Type 2 Diabetes	March 24, 2020
57	Ruxience	Rituximab	Pfizer	Chronic lymphocytic leukemia, granulomatosis with polyangiitis, microscopic polyangiitis, Non-Hodgkin lymphoma, RA, pemphigus vulgaris	April 1, 2020
58	Nepexto	Etanercept	Mylan and Lupin	RA, JIA, PP, PA, AS	June 4, 2020

Note: This table does not include biosimilars that received approval but have since been withdrawn.[66]

II. BARRIERS TO ENTRY

Due to a slow regulatory process coupled with stringent, monopolistic biologic companies, the United States has experienced much more difficulty than Europe in getting biosimilars into the hands of consumers. While there are numerous anti-competitive practices exhibited by biologic companies who stand to lose millions upon biosimilar market entry, this Note will examine two commonly seen tactics: sample denials and pay-for-delay settlement agreements.[67]

66. *See Biosimilars Approved in Europe*, GABI, https://www.gabionline.net/Biosimilars/General/Biosimilars-approved-in-Europe (last updated Feb. 21, 2021).

67. Other practices include product-hopping and citizen petitions. Product-hopping occurs when a biologic company reformulates its version of a drug, typically when a biologic's exclusivity period is about to expire. *See* Michael A. Carrier & Steve D. Shadowen, *Product Hopping: A New Framework*, 92 NOTRE DAME L. REV. 167, 168–70 (2016). This almost always negatively affects the similarity of biosimilars to the reference biologic, thus ensuring biologic market monopolization once more. *See id.* On the other hand, citizen petitions, specifically "505(q)" citizen petitions, can delay biosimilar approval by asking the FDA to take specific action against pending abbreviated new drug applications. *See* Michael A. Carrier & Carl Minniti, *Citizen Petitions: Long, Late-Filed, and At-Last Denied*, 66 AM. U. L. REV. 305, 307, 312 (2016) (noting that "[o]nce a generic [or biosimilar] enters the

A. Sample Denials

In order to show that the biosimilar is highly similar to the reference biologic through bioequivalence studies, samples are needed. When a biosimilar manufacturer cannot obtain product samples, it is unable to develop, and ultimately sell, its cheaper version of crucial medicines.[68] Biosimilar companies often are unable to obtain biologic samples due to monopolistic behaviors of biologic manufacturers; such behavior is evidenced through biologic manufacturers' refusal to provide samples to biosimilar companies who are willing to pay high prices for samples at a rate that would be profitable to biologic manufacturers.[69] While this Note disagrees with the belief that the denial of a sale of samples at market price to biosimilar manufacturers makes no sense, it does take the stance that a refusal to sell for values *above* market price stems only from an intent to harm the competition.[70] Understandably, biologic manufacturers are hesitant to offer samples to help their competition succeed at the same price they offer the same medicines to consumers. However, rationalizing this behavior becomes tricky when biologic manufacturers refuse sales that value their medicines at above-market prices. Evidence proves that only on occasion do biologic companies refuse samples in order to protect themselves from liability if biosimilar manufacturers fail to follow adequate safeguards during the use of samples.[71] Most often, however, biologic companies refuse to provide samples with the intent to smother their competition and continue to profit in a monopolized market.[72]

market, the brand product [or biologic] loses 44% to 90% of its market share within the first twelve months.").

68. *See* Monica Chin Kitts, *Biologic Patent Transparency Act Addresses High Biologic Prices*, LEXOLOGY: BIOLOGICS & BIOSIMILARS (May 2, 2019), https://www.lexology.com/library/detail.aspx?g=ac5b4796-8287-45b9-beed-231a72cabfc2.

69. Michael A. Carrier, *Sharing, Samples, and Generics: An Antitrust Framework*, 103 CORNELL L. REV. 1, 38–41 (2017).

70. *But see id.* at 40.

71. *See id.* at 3, 38–41.

72. *See* Michael A. Carrier & Carl J. Minniti III, *Biologics: The New Antitrust Frontier*, 1 UNIV. ILL. L. REV. 1, 46–47 (2018). More specific examples of anti-competitive conduct can be found in the unrelated but seminal Supreme Court cases of *Aspen Skiing v. Aspen Highlands Skiing*, 472 U.S. 585 (1985), and *Otter Tail Power Co. v. United States*, 410 U.S. 366 (1973), wherein company owners were found liable for conduct intended to harm smaller competitors and to maintain their monopolies. *See also* Carrier & Minniti, at 48 & n.408 (discussing the applicability of such antitrust cases to biologic manufacturers' denial

The fear of stifling innovation and competition through the practice of denying samples is so prominent that it garnered bipartisan support in the recently enacted Creating and Restoring Equal Access to Equivalent Samples ("CREATES") Act.[73] Simply put, the Act allows a biosimilar manufacturer to bring suit for injunctive relief against a reference biologic company for its refusal to provide biologic samples for bioequivalence testing.[74] Limited damages may also be awarded as a deterrent to foster competition and the health care market alike.[75] The CREATES Act alone is estimated to lower federal spending on prescription drugs by $3.9 billion.[76]

B. Pay-for-Delay Settlement Agreements

Aside from denying samples, biologic manufacturers have found other ways to prevent biosimilars from reaching the market. One such way is through pay-for-delay settlements, wherein biologic manufacturers pay biosimilar manufacturers large amounts of money to stay off the market.[77] The Supreme Court addressed such settlements a few years ago in the case of *FTC v. Actavis, Inc.*[78] There, Solvay was the patent holder for a new type of drug, AndroGel.[79] Shortly thereafter, Actavis sought to create a generic version of AndroGel to bring to the market.[80] In its application for the generic, Actavis alleged that Solvay's patent was invalid and that Actavis's patent did not infringe on its

of samples). Providing samples of drugs that are already being produced "involves no additional effort." *Id.* at 51.

73. H.R. 1865, 116th Cong. § 610 (2019), https://www.fda.gov/media/136039/download; Kelly Davio, Legislative Hearing Addresses 7 Bills That Target Generic and Biosimilar Competition, CTR. FOR BIOSIMILARS (Mar. 14, 2019), https://www.centerforbiosimilars.com/news/legislative-hearing-addresses-7-bills-that-target-generic-andbiosimilar-competition.

74. *See id.* at § 610(b); *see also* Davio, *supra* note 73.

75. H.R. 1865, 116th Cong. § 610(b)(4).

76. *The Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2019*, U.S. SEN. PATRICK LEAHY OF VT., https://www.leahy.senate.gov/imo/media/doc/020519%20116th%20CREATES%20Fact%20Sheet1.pdf (last visited Nov. 3, 2020).

77. *See* Michael L. Fialkoff, Note, *Pay-for-Delay Settlements in the Wake of* Actavis, 20 MICH. TELECOMMS. & TECH. L. REV. 523, 524 (2014). These "reverse payments" allow biologic companies, or brand-name manufacturers, to reduce competition and continue to charge high prices for crucial medicines. *See id.*

78. 570 U.S. 136 (2013).

79. *Id.* at 144.

80. *Id.*

patent.[81] In response, Solvay brought a claim of patent infringement against Actavis, which was eventually settled after three years of litigation.[82] Under the terms of the settlement agreement, Solvay agreed to pay Actavis tens of millions of dollars over the following nine years.[83] As a result of this settlement, the FTC filed suit, alleging that Actavis had unlawfully abandoned its patent in order to profit from Solvay's monopoly.[84] According to the Supreme Court, such "reverse payment" settlement agreements could violate antitrust laws due to the anticompetitive effects.[85] Ultimately, the Court found that the particular agreement between Solvay and generic companies violated antitrust laws, as the length of time Solvay would be without competition, coupled with the "large and unjustified" amount of money paid to the relevant generic companies, showed an obvious goal of maintaining a monopoly.[86] The Court properly realized that it is actions such as these that harm consumers most.[87]

C. FDA Approval Process

Unlike the FDA, the EMA offers product-specific guidelines for manufacturers seeking biosimilar approval, exhibited in Table 3's

81. *Actavis*, 570 U.S. at 144.
82. *Id.* at 144–45.
83. *Id.* at 145.
84. *Id.*
85. *Id.* at 141, 149. *See also* King Drug Co. of Florence v. Smithkline Beecham Corp., 791 F.3d 388, 393–94 (3d Cir. 2015) (holding that a no-AG settlement, which is a settlement where the brand company agrees not to market its authorized generic during the first-filing generic company's 180 day exclusivity period, has similar anticompetitive effects).
86. *See Actavis*, 570 U.S. at 154–58.
87. *See id.* at 154. Legislative authorities have begun to realize the harmful effects of pay-for-delay settlements, evidenced through the bipartisan proposal of the Preserve Access to Affordable Generics and Biosimilars Act, which essentially prohibits brand-name manufacturers from compensating generic, or in this instance, biosimilar, manufacturers from entering the market. S. 64, 116th Cong. (2019). However, since its most recent proposal which occurred over a year ago, cosponsoring Senators Amy Klobuchar, Chuck Grassley, Patrick Leahy, Joni Ernst, and Kevin Cramer have been unsuccessful in turning this proposed Act into actual law. *See* Press Release, House Comm. on the Judiciary, Nadler & Collins Introduce Preserve Access to Affordable Generics and Biosimilars Act, Legislation to Lower Prescription Drug Prices (Apr. 29, 2019), https://judiciary.house.gov/news/documentsingle.aspx?DocumentID=1142; *see also* Samantha DiGrande, *Klobuchar and Grassley Reintroduce Legislation to Address Pay-for-Delay Practices*, CTR. FOR BIOSIMILARS (Jan. 16, 2019), https://www.centerforbiosimilars.com/view/klobuchar-and-grassley-reintroduce-legislation-to-address-payfordelay-tactics.

example of EMA assistance to biosimilar innovators.[88] The EMA's dedication to transparency has led European biosimilars to experience much greater success in gaining approval than their U.S. counterparts.[89]

TABLE 3: EMA DEFINES SPECIFIC FEATURES OF BIOSIMILAR MEDICINES

"Highly similar to the reference medicine"	"The biosimilar has physical, chemical and biological properties highly similar to the reference medicine's" same properties. Minor differences may be allowed provided they "are not clinically meaningful in terms of safety or efficacy."
"No clinically meaningful differences compared with the reference medicine"	"No differences are expected in clinical performance" with regards to safety and efficacy.
"Variability of biosimilar kept within strict limits"	"Minor variability is only allowed when scientific evidence shows that it does not affect the safety and efficacy of the biosimilar. The range of variability allowed for a biosimilar is the same as that allowed between batches" of its reference drug. "This is achieved with a robust manufacturing process to ensure that all batches of the medicine are of proven quality."
"Same strict standards of quality, safety, and efficacy"	"Biosimilars are approved pursuant to the same strict standards of quality, safety and efficacy that apply to any other medicine."

88. *See* EUROPEAN MEDICINES AGENCY & EUROPEAN COMMISSION, *supra* note 62, at 8 tbl.1, 12 ("[The] EMA has issued scientific guidelines to help developers conform to the strict regulatory requirements for approving biosimilars. The guidelines have evolved to keep pace with rapid advances in biotechnology and analytical sciences, and they take on board increasing experience of clinical use.").

89. Late last year, the EMA offered amendments to the FDA's guidance for biosimilars in an effort to increase clarity for applicants. Zachary Brennan, *EMA Offers Edits on FDA Draft Guidance on Biosimilars*, REGUL. AFFS. PROS. SOC'Y (Aug. 29, 2019), https://www.raps.org/news-and-articles/news-articles/2019/8/ema-offers-edits-on-fda-draft-guidance-on-biosimil. Additionally, unlike the FDA, the EMA is required to disclose information on drug applications withdrawn prior to the conclusion of the evaluation process and publishes assessment reports of withdrawn and refused applications. Giovanni Tafuri et al., *Disclosure of Grounds of European Withdrawn and Refused Applications: A Step Forward on Regulatory Transparency*, NAT'L CTR. BIOTECHNOLOGY INFO. (Aug. 15, 2012), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3612734/ (noting that "transparency about the outcomes of marketing authorization procedures is important for the purpose of a better understanding of the reasons why certain procedures tend to result in either a successful or a failed application").

However, the FDA has seemingly accepted responsibility in slowing the approval of biosimilars and has attempted to mend the harm caused through the FDA's Biosimilars Action Plan ("BAP") aimed to "streamline the [approval] process."[90] The FDA has broken the BAP down into serving four main functions:

> (1) improving the efficiency of the biosimilar and interchangeable product development and approval process; (2) maximizing scientific and regulatory clarity for the biosimilar product development community; (3) developing effective communications to improve understanding of biosimilars among patients, clinicians, and payors; and (4) supporting market competition by reducing gaming of FDA requirements or other attempts to unfairly delay competition.[91]

Unfortunately, BAP's fate remains uncertain.

III. POTENTIAL SOLUTIONS

A. Congress

In the early months of 2019, many bills were introduced in Congress in an effort to address methods to increase prescription drug competition.[92] Three of those bills that would have direct impacts on biosimilars are examined below.

1. The Biologic Patent Transparency Act

The Biologic Patent Transparency Act was proposed in an effort to prevent biologic manufacturers from monopolizing the market, making

90. U.S. FOOD & DRUG ADMIN., BIOSIMILARS ACTION PLAN: BALANCING INNOVATION AND COMPETITION 5 (2018).

91. *Id.* Methods of accomplishing such goals include but are not limited to developing templates for aBLAs to streamline the approval process, developing and adding additional guidance to clarify the regulatory pathway for biosimilars, implementing a Biosimilar Education and Outreach Campaign to spread awareness on biosimilars and their importance to society, and more closely examining and reprimanding a manufacturer's illegal practices intended to delay competition. *Id.* at 5–9.

92. Davio, *supra* note 73.

it nearly impossible for biosimilars to be successful.[93] To do so, the Act "requires the manufacturers of approved [drugs] to disclose and list patents covering their products with the FDA."[94] More specifically, the bill would make the FDA's "Purple Book" publicly available as one searchable list.[95] This would make the Purple Book, a reference on biologics and other large molecule drugs, more closely aligned with the Orange Book that is used in the small molecule context.[96] Aside from the new search mechanism, the Purple Book would also include information on:

- Patents that claim and relate to FDA-approved biological products, for which a claim of patent infringement could reasonably be asserted by the holder, including manufacturing processes;
- Official and proprietary name of each biological product;
- The date of licensure and application number for each product;
- Information related to determinations of biosimilarity and interchangeability;
- Information related to marketing status, dosage form, route of administration, reference product, and any periods of exclusivity related to the product and the date that the exclusivity expires; and

93. *Biologic Patent Transparency Act (S. 659)*, SUSAN COLLINS: U.S. SENATOR FOR ME., https://www.collins.senate.gov/sites/default/files/Biologic%20Patent%20Transparency%20Act%20One%20Pager%20for%20Release.pdf (last visited Nov. 3, 2020).

94. *Id.*

95. *Id.* Currently, the FDA's "Purple Book" for biologic drugs only includes "approved biological products, their date of approval, and any biosimilar or interchangeable biological products licensed by the FDA." Courtenay C. Brinckerhoff, *Will the Biologic Patent Transparency Act Shrink the Biosimilar Patent Dance Floor?*, FOLEY & GARDNER, LLP: PHARMAPATENTS (May 7, 2019), https://www.foley.com/en/insights/publications/2019/05/will-bpta-shrink-patent-dance.

96. Evert Uy Tu & Jeffrey A. Wolfson, *FDA Throws the (Purple) Book at Biosimilars–Purple v. Orange*, HAYNES & BOONE, https://www.haynesboone.com/~/media/files/alert%20pdfs/fdapurplebookvorangebook.ashx (last visited Nov. 3, 2020).

- Approved indications.[97]

Therefore, biosimilar applicants will have more clarity as to what their application must include and what their biosimilar must demonstrate in order to gain FDA approval, which is already required for listings in the Orange Book.[98] Based on Europe's success with a similar transparent model, the passage of the Biologic Patent Transparency Act would likely reduce the need for lengthy communication between the FDA and the applicant, as well as between the applicant and reference product manufacturers, thereby reducing approval time.[99] Importantly, the Biologic Patent Transparency Act would limit the importance and extent of the "patent dance," which does not even exist in Europe.[100] Finally, the bill would modify 35 U.S.C. § 271, the patent infringement statute, by adding with subsection (e)(7) that the owner of a patent that should have been included in the Purple Book but was not may not bring forth a claim for patent infringement.[101]

2. The Forcing Limits on Abusive and Tumultuous ("FLAT") Prices Act

Rising prescription drug prices is one of the main contributors to the high overall health care costs felt across the country. One well-known example is EpiPen—or an Epinephrine Auto-Injector—which has seen an increase in price by approximately 400 percent since its first sale over a decade ago.[102] Years after Mylan's gradual price increases on EpiPen, the company decided to release its own authorized generic at half the cost of

97. Kitts, *supra* note 68.

98. *See id.*

99. *See generally* Sanya Sukduang & Thomas J. Sullivan, *The Patent Dance*, EUR. BIOPHARMACEUTICAL REV. (July 2018), http://www.samedanltd.com/magazine/12/issue/291/article/4846 (highlighting the complexities of the current U.S. regulatory review process, which "consist[s] of several 'rounds' of disclosure and information exchange").

100. *See* Stanton Mehr, *Comparing Biosimilar Approval Progress by the FDA and EMA*, BIOSIMILARS REV. & REP. (Feb. 27, 2019), biosimilarsrr.com/2019/02/27/comparing-biosimilar-approval-progress-by-the-fda-and-ema/; Brinckerhoff, *supra* note 95. The bill would limit patent holders' infringement actions to those patents that were properly listed in the FDA's Purple Book. *Id.*

101. Brinckerhoff, *supra* note 95.

102. Beth Mole, *Years After Mylan's Epic EpiPen Price Hikes, It Finally Gets a Generic Rival*, ARS TECHNICA (Aug. 17, 2018, 10:05 AM), https://arstechnica.com/science/2018/08/fda-approves-generic-version-of-mylans-600-epipens-but-the-price-is-tbd/.

the EpiPen.[103] Unfortunately, by that time, half the cost was still a hefty sum: $300 per two-pack of auto-injectors.[104]

On February 13, 2019, in an effort to combat price hikes and regulate the public interest, the FLAT Prices Act was introduced in Congress.[105] Pursuant to the FLAT Prices Act, pharmaceutical companies, including biologic manufacturers, would be prohibited from partaking in drug "price hikes."[106] The Act defines a price hike as an increase of more than 10 percent over a one-year period, 18 percent over two years, or 25 percent over three years.[107] Moreover, the Act requires drug companies to report price hikes to the Department of Health and Human Services in an effort to combat monopolistic behaviors.[108] Failure to abide by the terms of the Act can result in a reduction of market exclusivity.[109]

3. The Prescription Drug Price Relief Act

Similar to the FLAT Prices Act, the Prescription Drug Price Relief Act of 2019 aims to annually review biologic drugs for excessive pricing.[110] Though not directly targeted at helping the success of biosimilars, the Act still aims to lower billions of dollars spent on medicines for life-altering or life-threating ailments, such as arthritis and cancer.[111] As of last year, approximately one in five Americans could not afford the medicine they needed.[112] Realizing this predominantly U.S.-felt epidemic, lawmakers introduced The Prescription Drug Price

103. *Id.*

104. *Id.*

105. Forcing Limits on Abusive and Tumultuous Prices ("FLAT") Act, H.R. 1188, 116th Cong. (2019).

106. *Id.*; Press Release, Congressman Jared Golden, Golden Introduces New Bill to Stop Drug Companies' Unfair Price Hikes, Address Rising Rx Costs in America (Feb. 13, 2019), https://golden.house.gov/media/press-releases/golden-introduces-new-bill-stop-drug-companies-unfair-price-hikes-address.

107. H.R. 1188 § 2(b).

108. *Id.* § 2(c)(1).

109. *Id.* § 2(c)(2).

110. Prescription Drug Price Relief Act, S. 102, 116th Cong. § 5(b) (2019).

111. Press Release, Congressman Ro Khanna, Sweeping Plan to Lower Drug Prices Introduced in Senate and House (Jan. 10, 2019), https://khanna.house.gov/media/press-releases/release-sweeping-plan-lower-drug-prices-introduced-senate-and-house.

112. For years, Americans have experienced the highest prescription drug prices in the world. *See id.* In fact, in 2017 Americans spent more than double the amount per person on prescription medicines than those in the United Kingdom. *See id.*

Relief Act.[113] If enacted, the Act would require U.S. prescription drug prices to be reduced to the median price paid for the same prescription drugs in Canada, the United Kingdom, France, Germany, and Japan.[114] Refusal on the part of pharmaceutical manufacturers to lower drug costs to the required median price would, in turn, require the federal government to approve cheaper generic versions of those drugs, essentially abrogating any active market exclusivity periods.[115] Clearly, almost all political parties advocating for lower drug prices recognize the importance, symbolically and financially, of the market exclusivity period, and believe that hope for consumers lies in treating such periods as a *privilege* that can be taken away at any time.

B. Patents

Patents are the strongest form of intellectual property that give patent holders the power to exclude competitors from the market for twenty years.[116] The need for such a long exclusivity period is to incentivize research and development, which can cost billions of dollars and take more than ten years.[117] However, through roadblocks, such as sample denials and pay-for-delay settlement agreements, biologic patent holders are able to obtain more than twenty years of exclusivity, greatly harming the public interest and costing the health care market millions of dollars.[118] To receive a U.S. patent, the product must meet five

113. Press Release, Congressman Ro Khanna, *supra* note 111.

114. S. 102 § 2(b)(1).

115. *The Prescription Drug Price Relief Act of 2019*, BERNIE SANDERS https://www.sanders.senate.gov/download/final_-prescription-drug-price-relief-act-of-2019—-summary?id=D3922119-B92C-41F0-997D-2B931E34B2FE&download=1&inline=file. Additionally, the Center for Economic and Policy Research estimates that, if this Act were to become law, the prices of most brand-name drugs would be cut in half. *Id.* (Recognizing that "80 percent of Americans say that drug prices are unreasonable. . . . The Prescription Drug Price Relief Act puts an end to this highway robbery.").

116. 35 U.S.C. § 154(a)(2). Through "patent thickets," manufacturers of biologics are able to block dozens of patents that would otherwise compete with their drugs on the market. Kitts, *supra* note 68. For example, AbbVie's Humira is commonly referred to as a patent thicket, as it is composed of about 136 patents, some of which are not set to expire until 2034. *Id.*

117. *See* 1 PETER S. MENELL, ET AL., INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE: 2019, at 167 (2019).

118. *See What's the Difference?*, *supra* note 28 (stating biosimilars are 15 to 20% cheaper than brand products); Fialkoff, *supra* note 77, at 524–25 (explaining that pay-for-delay settlements cost consumers $3.5 billion in increased prescription drug costs every year);

requirements. The first requirement is that the product is one of patentable subject matter, defined as a "process, machine, manufacture, or composition of matter."[119] Second, the product must have some utility, meaning that there is a practical use for the drug.[120] This is a critical requirement for pharmaceuticals. Third, the patent must be nonobvious and pose a significant technical advance over prior art.[121] Fourth, the product must be novel, meaning it has not been previously published or sold.[122] Finally, there must be sufficient disclosure and enablement so that others may replicate the product upon expiration of the patent.[123]

Patents are crucial in the development of pharmaceuticals, and without patent rights, there would be no incentive to spend millions of dollars for years' worth of research. The protections and exclusivity granted to patent holders provide the incentives to innovate.[124] Once the patent expires, the innovation becomes part of the public domain for other inventors to use.[125] One proposed solution to prevent anti-competitive behavior from biologic companies is to lengthen the patent protection period for pharmaceuticals.[126] Should not drugs, which commonly cost millions to even billions of dollars to research and develop and a decade to formulate, receive longer protections than those for the patent on a kitchen sponge, for example? Perhaps longer exclusivity periods would reduce the urge for biologic companies to participate in illegal anti-competitive practices, helping the public good in the long run.

C. Taking Notes from Europe

As previously noted, Europe has etched the pathway for biosimilar approval. Since the first EMA-approved drug, Omnitrope, began marketing in April 2006, Europe's fast approval process has, to date, saved its country 20 to 30 percent in health care spending on antibody

Carrier, *supra* note 69, at 28 (writing that the practice of sample denials stifles competition).

119. 35 U.S.C. § 101.

120. *Id.*

121. *Id.* §§ 102(a), 103.

122. *Id.* § 102(a)(1).

123. *Id.* § 112(a).

124. BARTON BEEBE, TRADEMARK LAW: AN OPEN-SOURCE CASEBOOK, 30 (6th ed. 2019).

125. *See id.*

126. *See, e.g.*, Natasha Rao, *An Extension to the Life of Pharmaceutical Patents?*, FIELDFISHER (Nov. 28, 2019), https://www.fieldfisher.com/en/insights/an-extension-to-the-life-of-pharmaceutical-patents.

drugs alone.[127] Upon examination of the differences between the United States and Europe's biologic and biosimilar approval processes, pharmaceutical companies' marketing practices, and the benefits offered to incentive innovation in this field, there are at least two clear lessons that the United States could learn from Europe. First, to speed up the already-abbreviated regulatory process and improve approval rates of U.S. biosimilars, the FDA should be encouraged to update its biosimilar application to a format that mimics Europe's with regard to transparency of expectations.[128] Second, as offered in recent proposals to Congress,[129] limits should be placed on biologic drug prices, even during their market exclusivity periods, in an effort to align U.S. prescription drug costs more closely with those of other countries. Thus, Congressional representatives should feel compelled to give the proposals described in this Note some thorough consideration, as the majority of Americans would likely agree that the benefits strongly outweigh the risks.

IV. CONCLUSION

Biosimilars are crucial because they stimulate competition and provide greater access to life-saving medicines. The rise of the biosimilar market lays its origin in Obamacare, or the Patient Protection and Affordable Care Act, which created the BPCIA that offers guidance for biosimilar approval.[130] Under the current administration, biosimilar approval has increased from four approved biosimilars in 2016 to twenty-eight biosimilars approved to date.[131] In the wake of the 2020 U.S. presidential election, it will be interesting to see if the country's biosimilar market will continue to flourish, or if patients and taxpayers will bear the financial burden of biosimilar stagnation.

127. Joanna M. Shepherd, *Biologic Drugs, Biosimilars, and Barriers to Entry*, 25 HEALTH MATRIX 139, 145–46 (2015). Antibody drugs are just one category of biologics. *Introduction to Biologics and Monoclonal Antibodies*, THERAPEUTIC ANTIBODY ENG'G, 2012, at 1.

128. *See supra* text accompanying notes 99–101.

129. *See supra* Section III.A.

130. McEnrue, *supra* note 26, at 311, 315.

131. *See supra* Table 1.