The Patent Trap: The Struggle for Competition and Affordability in the Field of Biologic Drugs

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The biologic drug market in the U.S. suffers from a dearth of competition. Ten years after the passage of the Biologics Price Competition and Innovation Act (BPCIA), competition from biosimilars remains weak, and prices of branded biologics continue to increase at rates that outstrip inflation. This crisis of non-competition has resulted in billions of dollars in lost savings and reduced access to treatment, especially for vulnerable groups. Patent thickets — dense webs of overlapping patents — are one of the main barriers to biosimilar competition. By protecting their products with patent thickets, branded biologic manufacturers are able to deter competition from biosimilars and maintain periods of market exclusivity that far exceed statutory limits. This Note analyzes regulatory gaps in the BPCIA that allow patent thickets to thrive, and recommends both legislative and administrative solutions. Part II assesses the market landscape for biologic drugs in the U.S. and concludes that, of all barriers to biosimilar competition, patent thickets are the most significant. Part III evaluates the BPCIA framework in light of patent thickets and identifies aspects of the statute that allow patent thickets to block biosimilar market entry. Part IV analyzes recent legislative proposals to address the problem of patent thickets, and recommends administrative changes to strike a better balance between innovation and competition in the field of biologics.

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I. INTRODUCTION

The high and rising cost of prescription drugs in the U.S. continues to alarm patients, providers, and payers alike.[1] Biologic drugs in particular have been identified as a main driver of rising drug expenditures.[2] The impact of biologics on national drug spending is staggering: in 2019, net spending on biologics totaled $211 billion, representing 43% of all drug spending in the U.S. and growing at a compound annual growth rate of 14.6% since 2015.[3]

The Food and Drug Administration (FDA) separates pharmaceutical drugs into two categories: small-molecule drugs and biologic drugs. While small-molecule drugs are chemically synthesized, biologic drugs are large, complex molecules typically produced in living cells and then purified.[4] The organic origins of biologic drugs make manufacturing and characterizing these molecules difficult.[5] For this reason, the FDA regulates biologics separately from small-molecule drugs: small-molecules are regulated under the Hatch-Waxman Act,[6] while biologics are regulated under the Biologics Price Competition and Innovation Act (BPCIA).[7]

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1. *See generally* Aaron S. Kesselheim et al., *The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform*, 316 JAMA 858 (2016); Sy Mukherjee, *It's the New Year, and Pharma Companies Are Already Hiking Prices for Popular Drugs*, FORTUNE (Jan. 4, 2021), https://fortune.com/2021/01/04/drug-price-increases-abbvie-humira/ [https://perma.cc/C7ZE-UUGW].

2. Andrew W. Mulcahy et al., *Biosimilar Cost Savings in the United States*, RAND HEALTH Q. (2018), https://www.rand.org/pubs/periodicals/health-quarterly/issues/v7/n4/03.html [https://perma.cc/H8QN-P8C6] ("[B]iologics alone accounted for . . . 70 percent of drug spending growth between 2010 and 2015.").

3. MURRAY AITKEN ET AL., IQVIA INST. FOR HUM. DATA SCI., BIOSIMILARS IN THE UNITED STATES: 2020–2024 2 (Oct. 2020), https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/iqvia-institute-biosimilars-in-the-united-states.pdf?_=1620244510344 [https://perma.cc/8AKW-CKPA] (finding that biologics represented 43% of invoice-level medicine spending in the U.S. in 2019, and had grown at a 14.6% compound annual growth rate over the past five years).

4. *See generally* U.S. FOOD & DRUG ADMIN., BIOLOGICAL PRODUCT DEFINITIONS (2017), https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf [https://perma.cc/AD89-D9LZ] [hereinafter "BIOLOGICAL PRODUCT DEFINITIONS"].

5. *Id.*

6. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585.

7. Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, §§ 7001–03, 124 Stat. 119 (2010). The BPCIA was enacted as Title VII, Subtitle A of the Affordable Care Act. *See* Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119, 804–21 (2010) (codified as amended in scattered sections of the U.S. Code); Michael S. Epstein et al., *Biosimilars: The Need, the Challenge, the Future: The FDA Perspective*, 109 AM. J. GASTROENTEROLOGY 1856, 1857 (2014). Prior to 2010, biologics were regulated under the Public Health Service Act (PHSA), Pub. L. No. 78-410, ch. 373, 58 Stat.

Biologic drugs take many forms, including monoclonal antibodies, vaccines, gene therapy, recombinant proteins, blood and blood products (such as clotting factors), and cell therapy.[8] Biologics hold great therapeutic potential for diseases such as cancer, diabetes, arthritis, and other autoimmune conditions — and are often the only treatment available.[9] However, the therapeutic potential of these drugs comes at a steep price: biologics cost an average of $10,000 to $30,000 per patient, per year, and the most expensive can cost upwards of $500,000 per year.[10]

The high prices of biologics largely result from a dearth of competition. In 2010, Congress enacted the BPCIA to facilitate competition from biosimilars — the biologic equivalent of generics[11] — and deflate the high prices of biologic drugs.[12] A study by the RAND Corporation in 2014 estimated that the market entry of biosimilars would yield cost savings of $44.2 billion in national drug spending between 2014 and 2024.[13] However, these cost savings failed to materialize.[14] Branded biologics continue to dominate the market long past their statutory exclusivity periods, and their prices have increased at rates that outpace inflation.[15]

682, 702 (July 1, 1944). The PHSA had no real approval pathway for biosimilars (biosimilars instead had to be approved as new drugs).

8. *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 [https://perma.cc/9WCB-WYPQ].

9. Michael A. Carrier & Carl J. Minniti III, *Biologics: The New Antitrust Frontier*, 2018 U. ILL. L. REV. 1, 3.

10. Brian K. Chen et al., *Why Biologics and Biosimilars Remain So Expensive: Despite Two Wins for Biosimilars, the Supreme Court's Recent Rulings Do Not Solve Fundamental Barriers to Competition*, 78 DRUGS 1777, 1777 (2018).

11. Generics are small-molecule drugs that are chemically identical to branded small-molecule drugs (e.g., fluoxetine is the generic version of Prozac). Biosimilars are biologic molecules that are highly similar, but not necessarily identical to branded biologic drugs. *See What are "Biologics" Questions and Answers*, *supra* note 8. In the context of biosimilar production, branded drugs are referred to as "reference products" or "originator products."

12. *See Biologics and Biosimilars: Balancing Incentives for Innovation: Hearing Before the Subcomm. on Cts. & Competition Pol'y of the H. Comm. on the Judiciary*, 111th Cong. 1–2 (2009) (statement of Rep. Henry C. "Hank" Johnson) [hereinafter "*Biologics and Biosimilars Hearing*"] (the BPCIA aimed to spur competition from biosimilars while preserving incentives for biologic innovation). The BPCIA established an abbreviated licensure pathway for biosimilars and statutory exclusivity periods for branded biologics. These provisions are discussed in greater detail in Part III.

13. ANDREW W. MULCAHY ET AL., THE COST SAVINGS POTENTIAL OF BIOSIMILAR DRUGS IN THE UNITED STATES 1 (2014), https://www.rand.org/content/dam/rand/pubs/perspectives/PE100/PE127/RAND_PE127.pdf [https://perma.cc/GH33-TMJ4].

14. Y. Tony Yang et al., *Biosimilars — Curb Your Enthusiasm*, 3 JAMA ONCOLOGY 1467, 1467 (2017).

15. I-MAK, OVERPATENTED, OVERPRICED: HOW EXCESSIVE PHARMACEUTICAL PATENTING IS EXTENDING MONOPOLIES AND DRIVING UP DRUG PRICES 11 (2018),

Competition from biosimilars remains significantly weaker in the U.S. than in other countries.[16] The result is billions of dollars in lost savings, persistently inflated prices, and reduced access to treatment — especially for vulnerable groups.[17]

The weak state of biosimilar competition in the U.S. is due in large part to the strategic patenting used by branded biologic manufacturers to insulate their products from competition. Under general patent law, a patent grants the inventor "the right to exclude others from making, using, offering for sale, or selling" the claimed invention for a twenty-year term.[18] Branded biologic manufacturers have effectively extended this term of exclusivity by protecting their products with "patent thickets," or dense webs of overlapping patents, many of which are filed years after the product first enters the market.[19] Due to gaps in the regulatory landscape — namely, the absence of a patent listing requirement for biologics and the failure of the BPCIA to streamline patent litigation — patent thickets effectively deter competition from biosimilars and enlarge the intellectual property rights of branded biologics.

This Note analyzes these regulatory gaps and recommends both legislative and administrative solutions. Part II examines the market landscape for biologic drugs in the U.S. and concludes that patent thickets present the most significant barrier to biosimilar market entry. Part III evaluates the BPCIA framework and identifies features of the statute that allow patent thickets to block biosimilar competition. Part IV assesses recent legislative proposals to address the problem of patent thickets, and recommends

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https://www.i-mak.org/wp-content/uploads/2018/08/I-MAK-Overpatented-Overpriced-Report.pdf [https://perma.cc/JDR6-DCFZ] [hereinafter "I-MAK, OVERPATENTED, OVERPRICED"].

16. Yang et al., *supra* note 14, at 1468 ("The European Union countries have experienced greater savings from the development and marketing of biosimilars than the United States.").

17. *See* BIOSIMILARS COUNCIL, ASS'N. ACCESSIBLE MED., FAILURE TO LAUNCH: PATENT ABUSE BLOCKS ACCESS TO BIOSIMILARS FOR AMERICA'S PATIENTS (2019), https://www.biosimilarscouncil.org/wp-content/uploads/2019/06/Biosimilars-Council-White-Paper-Failure-to-Launch-June-2019.pdf [https://perma.cc/PH57-TXGA] (estimating $7.6 billion in lost savings as a result of patent abuse); BIOSIMILARS COUNCIL, ASS'N. ACCESSIBLE MED., BIOSIMILARS IN THE UNITED STATES: PROVIDING MORE PATIENTS GREATER ACCESS TO LIFESAVING MEDICINES 4 (2017), http://biosimilarscouncil.org/wp-content/uploads/2019/03/Biosimilars-Council-Patient-Access-Study.pdf [https://perma.cc/C52U-D99Y] (concluding that biosimilar access will benefit women, seniors, and low-income patients).

18. *See* 35 U.S.C. §§ 154(a)(1), (2).

19. *See* W. Nicholson Price II & Arti K. Rai, *How Logically Impossible Patents Block Biosimilars*, 37 NATURE BIOTECHNOLOGY 862 (2019).

administrative changes to strike a better balance between innovation and competition in the field of biologics.

II. THE BIOLOGICS MARKET FAILURE

The BPCIA, enacted as part of the Affordable Care Act in 2010, aimed to spur biosimilar competition while preserving the incentives for biologic innovation.[20] To achieve this end, it established an abbreviated licensure pathway for biosimilars. Prior to the BPCIA, a biosimilar had to receive licensure as a new drug, which required biosimilar manufacturers to perform the whole gamut of pre-clinical and clinical studies. The BPCIA's abbreviated pathway allowed for greater reliance on the FDA's previous finding of safety, purity, and potency for the biologic reference product. But despite this streamlined pathway for biosimilars, biosimilar competition in the U.S. remains "anemic."[21] The failure of biosimilars to launch and compete effectively in the market is due to both structural barriers and constructed barriers. This Part first analyzes, in Section A, the structural barriers that biosimilars face on their path to market. These structural barriers include barriers that are inherent in the nature of the biologics market and those that result from features of the statutory scheme. Section B concludes that despite high structural barriers to entry, competition is not an unrealistic goal. Section C then turns to the constructed barriers to biosimilar market entry, which are barriers intentionally established by market participants in order to block competition. Chief among these constructed barriers are patent thickets. Section C concludes that patent thickets present the greatest obstacle to robust and thriving competition in the biologics field.

A. STRUCTURAL BARRIERS TO BIOSIMILAR MARKET ENTRY AND PENETRATION

A competitor hoping to enter the biologics market faces a number of obstacles in successfully launching a biosimilar. The most

20. *Biologics and Biosimilars Hearing*, *supra* note 12, at 2 (statement of Rep. Henry C. "Hank" Johnson).

21. Scott Gottlieb, Comm'r, Food & Drug Admin., Dynamic Regulation: Key to Maintaining Balance between Biosimilars Innovation and Competition, Speech at the Brookings Institution (July 18, 2018), https://www.fda.gov/news-events/speeches-fda-officials/dynamic-regulation-key-maintaining-balance-between-biosimilars-innovation-and-competition-07182018 [https://perma.cc/SCJ5-8BU7] [hereinafter "Gottlieb Speech"].

obvious is the sheer cost: it is much more expensive to develop a biosimilar than it is to develop a generic small-molecule drug. While generics generally require one to three years to reach market, at a cost of approximately $1 million to $2 million, biosimilars require seven to eight years and expenditures of $100 million to $250 million.[22]

The unique demands of the biologic manufacturing process contribute to some of this cost. While small-molecules are manufactured through chemical synthesis, biologics are synthesized in living cells. Synthesis in living cells involves genetically engineering cells to express a gene that will drive production of the desired biologic molecule.[23] These genetically-engineered cells are cultured (or grown) in cell medium for some period of time, after which the molecule of interest is isolated and purified from the surrounding medium and other cell contents.[24] Organic synthesis is inherently more complicated and less readily controllable than chemical synthesis. The process necessarily generates some level of heterogeneity in the product, such that biologic molecules may vary between batches.[25] Moreover, the molecules are often sensitive to heat and bacterial contamination.[26] These characteristics of biologic drugs make the manufacturing process particularly challenging. Biosimilar manufacturers must either establish a specialized manufacturing facility or contract with an existing one; adhere to FDA requirements for "good manufacturing practices"; and invest

22. *See* OFF. OF THE ASSISTANT SEC'Y FOR PLAN. & EVALUATION, U.S. DEP'T OF HEALTH & HUM. SERVS., EXPANDING THE USE OF GENERIC DRUGS 4–5 (2010), https://aspe.hhs.gov/system/files/pdf/76151/ib.pdf [https://perma.cc/59GD-U9GH]; *see also* Gary Walsh, *Biopharmaceutical Benchmarks*, 32 NATURE BIOTECHNOLOGY 992, 995 (2014).

23. *See Building Biologics*, GENENTECH (Feb. 8, 2016), https://www.gene.com/stories/building-biologics [https://perma.cc/G2BK-VHFQ].

24. *Id.*

25. *See* Arnold G. Vulto & Orlando A. Jaquez, *The Process Defines the Product: What Really Matters in Biosimilar Design and Production?*, 56 RHEUMATOLOGY iv14, iv15 (2017) (noting that "biochemical variability [from cellular modifications] . . . is inherent to all biological therapies," and describing in greater detail the biological mechanisms of these modifications). Sources of variability may include the use of a different vector; a different cell line expression system; different cell growth media, pH, or temperature; and different methods of purification. Justin Daller, *Biosimilars: A Consideration of the Regulations in the United States and European Union*, 76 REGUL. TOXICOLOGY & PHARMACOLOGY 199, 200 fig.1 (2016).

26. CTR. FOR DRUG EVALUATION AND RSCH. & CTR. FOR BIOLOGICS EVALUATION AND RSCH., CONSIDERATIONS IN DEMONSTRATING INTERCHANGEABILITY WITH A REFERENCE PRODUCT: GUIDANCE FOR INDUSTRY 10–14 (2019), https://www.fda.gov/media/124907/download [https://perma.cc/Q9B6-Z47B] [hereinafter "*FDA Interchangeability Guidance*"].

in analytical tools and tests to characterize the product.[27] These requirements amount to significant expenses in terms of upfront investments and ongoing costs.

The cost of biosimilar development is also attributable to the need to reverse-engineer the branded product. Even knowing the structure of a biologic drug, it is very difficult, if not impossible, to know the precise manufacturing steps that a branded biologic manufacturer took to synthesize the end product.[28] Biologic products are purified from the cells in which they are synthesized. As such, the structure of the end product contains minimal clues as to the type of cell in which they were made; the medium in which the cells grew; the method used to "transfect," or drive production of the molecule in those cells; the exact processes of culturing those cells; and the method used to purify the biologic molecule from the other cell contents. Branded biologic manufacturers often keep the details of their manufacturing a trade secret, and carefully craft their process patents and composition-of-matter patents so as to avoid revealing manufacturing details.[29] The processes used to manufacture biologics are therefore not adequately disclosed, and biosimilar manufacturers must struggle to reverse-engineer the manufacturing process of the branded product. This reverse-engineering effort is expensive and difficult, especially because slight differences in manufacturing can have downstream effects on the efficacy or immunogenicity of the product.[30]

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27. Characterization means showing the molecular structure, properties, and biological function or activity of the molecule of interest (e.g., binding affinity in the case of an antibody protein). *Id.*; *see also* Erwin A. Blackstone & Joseph P. Fuhr, *Innovation, Patents and Biologics: The Road to Biosimilar Competition: Factors Influencing Investment, Business Decisions and Marketing of Biosimilars*, *in* BIOSIMILARS: REGULATORY, CLINICAL, AND BIOPHARMACEUTICAL DEVELOPMENT 23, 26 (Hiten J. Gutka et al. eds., 2018) (discussing the challenges of biosimilar manufacturing from an investment perspective); Daniel Galbraith, *Early Product Characterization Mitigates Risks in Biologics Development*, GENETIC ENG'G & BIOTECHNOLOGY NEWS (Sept. 3, 2019), https://www.genengnews.com/sponsored/early-product-characterization-mitigates-risks-in-biologics-development/ [https://perma.cc/L9K2-FN6H].

28. W. Nicholson Price II & Arti K. Rai, *Manufacturing Barriers to Biologics Competition and Innovation*, 101 IOWA L. REV. 1023, 1028 (2016).

29. *Id.* at 1046. Process patents are patents that claim a method of treating materials in order to produce a certain result or functionality. Composition-of-matter patents are patents that claim a composition of two or more substances that are chemically or mechanically joined. *See General Information Concerning Patents*, U.S. PAT. & TRADEMARK OFFICE (Oct. 2015), https://www.uspto.gov/patents/basics#heading-4 [https://perma.cc/WKD6-9LFC].

30. *Id.* at 1048; *see also* Gary H. Lyman et al., *Rationale, Opportunities, and Reality of Biosimilar Medicines*, 378 NEW ENG. J. MED. 2036, 2037 (2018) ("Minor modifications in manufacturing, processing, and packaging may result in lot-to-lot differences in both

The high cost of biosimilar development also stems from the relatively difficult process of achieving FDA licensure under the BPCIA. To gain approval as a generic drug under the Hatch-Waxman Act, a generic applicant need only show that its product is "bioequivalent" to the branded small-molecule drug.[31] A showing of bioequivalence requires the applicant to submit evidence that its product has the same active ingredient, route of administration, dosage form, and strength as the branded product, and is expected to have the same therapeutic effect when administered for the conditions of use prescribed.[32] Under the Hatch-Waxman Act, a generic applicant does not need to submit its own safety and efficacy studies in order to gain approval.[33]

In contrast, the BPCIA biosimilar licensure pathway demands more of biosimilar applicants. FDA designation as a biosimilar requires the biosimilar applicant to show that its product is "highly similar" to the reference product such that there are "no clinically meaningful differences in terms of safety, purity, and potency."[34] This showing requires the applicant to submit supporting data from analytical, animal, and clinical studies.[35] The biosimilar applicant must also demonstrate to the FDA that the biosimilar product uses the same mechanism(s) of action for the condition(s) of use prescribed, and has the same route of administration, dosage form, and strength as the branded reference product.[36] The FDA may designate the product as a "biosimilar" only if an applicant meets these requirements. While this does make licensure more difficult for biosimilars, the extra demands of the statute are scientifically justified: biologics are difficult to manufacture and characterize, and the health risks of improper manufacture or characterization can be dire.[37]

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biosimilars and originator products, which could potentially lead to a small but real risk of differences in immunogenicity and adverse-event profiles appearing over time."). Immunogenicity refers to the likelihood that a drug will trigger an adverse immune reaction when administered to a patient. *FDA Interchangeability Guidance*, *supra* note 26, at 19.

31. 21 U.S.C. § 355(j)(2)(A)(iv).

32. *Id.* §§ 355(j)(2)(A)(ii)–(iv).

33. Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and its Impact on the Drug Development Process*, 54 FOOD & DRUG L.J. 187, 189 (1999) ("[The Hatch-Waxman Act] is a unique piece of legislation because it actually ties the hands of a regulatory agency — in the area of public health — by providing specifically that FDA can require only bioavailability studies for ANDAs.").

34. 42 U.S.C. §§ 262(i)(2)(A), (B).

35. *Id.* § 262(k)(2)(A)(i)(I).

36. *Id.* §§ 262(k)(2)(A)(i)(II), (IV).

37. *FDA Interchangeability Guidance*, *supra* note 26, at 19.

Even after a biosimilar is licensed and reaches the market, it faces an uphill battle in gaining market share. Much of this struggle can be attributed to the lack of automatic substitution for biosimilars. Automatic substitution allows for the substitution of a generic for a branded product at the pharmacy level without the need for prescriber approval.[38] Automatic substitution under Hatch-Waxman played a key role in the creation of a robust generics market in the U.S.[39] Automatic substitution is a matter of state law, but states tether their automatic substitution laws to FDA determinations of therapeutic equivalence.[40] The Hatch-Waxman Act facilitated automatic substitution of generics by using "bioequivalence" as the sole standard for generic approval.[41] Once the FDA has designated a generic drug as "bioequivalent" to the branded small-molecule drug, state laws generally encourage pharmacy-level substitution of the generic for the branded drug by either permitting or requiring substitution.[42] The simplicity of Hatch-Waxman's bioequivalence framework dovetailed with state laws friendly to automatic substitution to drive generic market penetration.

In contrast, the BPCIA established two standards for biosimilar approval: a biosimilar may be approved as either a "biosimilar" product, as discussed above, or as an "interchangeable" product, or one which can be substituted for the reference product at the pharmacy level without the intervention of the prescriber.[43] As of 2019, forty-five states and Puerto Rico only allow automatic substitution of biosimilars designated as interchangeable by the FDA.[44] FDA

38. In some states, this substitution is mandatory, while in others it may require patient consent. *See* Yan Song & Douglas Barthold, *The Effects of State-Level Pharmacist Regulations on Generic Substitution of Prescription Drugs*, 27 HEALTH ECON. 1717, 1718 (2019) (modeling the effects of mandatory switching laws and presumed consent laws on consumer drug-purchasing behavior).

39. *See* Aaron S. Kesselheim & Jonathan J. Darrow, *Hatch-Waxman Turns 30: Do We Need a New Approach for the Modern Era?*, 15 YALE J. HEALTH POL'Y L. & ETHICS 293, 309, 312–13 (2015) (identifying automatic substitution as a key factor in Hatch-Waxman's creation of a robust generics market).

40. *Id.* at 311–12.

41. *See* 21 U.S.C. § 355(j)(2)(A)(iv) (bioequivalence standard).

42. Kesselheim & Darrow, *supra* note 39, at 312–13.

43. 42 U.S.C. §§ 262(i)(2)(A), (B) (biosimilarity standard); 262(k)(4) (interchangeability standard); *see also 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 [https://perma.cc/F5QF-LHCZ].

44. 42 U.S.C. § 262(i)(3); *see* Zachary Brennan, *Where are the Interchangeable Biosimilars?*, REGUL. AFFS. PROS. SOC'Y (Oct. 21, 2019), http://www.raps.org/news-and-articles/

guidance describes interchangeability as a more stringent standard than biosimilarity: for a biosimilar to be deemed interchangeable, the applicant must provide data and information "beyond that needed to demonstrate biosimilarity" to show that the biosimilar produces the same clinical result as the reference product in any given patient.[45] If the drug is to be administered to a patient more than once, which is the case for most biologics, the applicant must also evaluate the risk in terms of safety and reduced efficacy of switching between the biosimilar and the reference product.[46] Agency guidance has clarified that evaluating this risk will generally require data from a switching study, which can cost more than $50,000 per patient.[47] The FDA's bar for interchangeability has been criticized as prohibitively high, without scientific justification.[48] Tellingly, to date, the FDA has only deemed one biosimilar interchangeable.[49] Non-interchangeable biosimilars could be automatically substituted at the pharmacy level if states passed legislation to this effect, but the vast majority of states have not done so.[50] Thus, no biosimilars currently on the market are eligible for automatic substitution in these jurisdictions. Automatic substitution under Hatch-Waxman was instrumental in driving generics' market penetration. The low likelihood of automatic substitution under the BPCIA means that biosimilars may struggle to gain similar market share.

A biosimilar may also have to contend with reluctant physician adoption.[51] The main deterrents to biosimilar adoption include

news-articles/2019/10/where-are-the-interchangeable-biosimilars [https://perma.cc/E5K6-DGC8].

45. 42 U.S.C. § 262(k)(4)(A)(ii); *FDA Interchangeability Guidance*, *supra* note 26, at 5.

46. 42 U.S.C. § 262(k)(4)(B).

47. *FDA Interchangeability Guidance*, *supra* note 26, at 5; *see also* Benjamin P. Falit et al., *Biosimilar Competition in the United States: Statutory Incentives, Payers, and Pharmacy Benefit Managers*, 34 HEALTH AFFS. 294, 296 (2015).

48. *See, e.g.*, Carrier & Minniti, *supra* note 9, at 16 (predicting that few applicants will pursue interchangeability status due to cost); *see also* Hans C. Ebbers & Huub Schellekens, *Are We Ready to Close the Discussion on the Interchangeability of Biosimilars?*, 24 DRUG DISCOVERY TODAY 1963, 1966 (2019) (concluding that the high bar for interchangeability is not scientifically necessary, because the immunogenicity risk of switching to a biosimilar is no greater than switching between two batches of any biologic).

49. *See FDA Approves First Interchangeable Biosimilar Insulin Product for Treatment of Diabetes*, U.S. FOOD & DRUG ADMIN. (July 28, 2021), https://www.fda.gov/news-events/press-announcements/fda-approves-first-interchangeable-biosimilar-insulin-product-treatment-diabetes.

50. 42 U.S.C. § 262(i)(3); *see* Brennan, *supra* note 44.

51. Hillel Cohen et al., *Awareness, Knowledge, and Perceptions of Biosimilars Among Specialty Physicians*, 33 ADVANCES IN THERAPY 2160 (2016) (finding that a sizable minority of physicians surveyed were unsure or concerned about the safety of biosimilars).

limited knowledge of biosimilars, low prescribing comfort, and safety and efficacy concerns.[52] These concerns arise from the fact that biologic drugs are synthesized in living cells, which is an inherently less controllable process than chemical synthesis.[53] The heterogeneity of the product and the risk of contamination raise the potential that a biosimilar could differ from the branded drug in ways that increase its immunogenicity or decreases its effectiveness.[54] To date, there is little clinical evidence that biosimilars are more immunogenic or less effective than their branded counterparts.[55] Skepticism may therefore decrease over time as it has for small-molecule generics.[56] Until then, physician skepticism of biosimilars present an additional barrier to their adoption. For this reason, competing with an entrenched reference product will likely entail substantial marketing effort and expense for the biosimilar, adding to the already considerable costs of development and licensure.

B. AN UNNATURAL MONOPOLY

Because the biologic market maintains high barriers to entry and currently permits no automatic substitution, each biologic product market might be considered a "natural monopoly."[57] A

52. Emily Leonard et al., *Factors Affecting Health Care Provider Knowledge and Acceptance of Biosimilar Medicines: A Systematic Review*, 25 J. MANAGED CARE & SPECIALTY PHARM. 102 (2019).

53. *See* Vulto & Jaquez, *supra* note 25.

54. Asterios S. Tsiftsoglou, *Biosimilars: The Impact of Their Heterogeneity on Regulatory Approval*, 6 NATURE REVS. DRUG DISCOVERY 252 (2007) (noting that "heterogeneity in biosimilars might affect the quality of the active substance as well as the drug product in terms of biological activity, stability, pharmacokinetics, immogenicity and clinical efficacy.").

55. *See* Valderilio Azevedo et al., *Biosimilars: Considerations for Clinical Practice*, 1 CONSIDERATIONS IN MED. 13, 15 (2017) (reviewing clinical studies and concluding that there is minimal evidence of increased immunogenicity or reduced efficacy of biosimilars); *see also* Piotr Wiland et al., *Biosimilar Switching — Current State of Knowledge*, 56 REUMATOLOGIA 234 (2018) (concluding that there is no clinical evidence that a single switch from an originator to a biosimilar medicine is associated with any significant risk for patient safety or reduction in therapeutic efficacy).

56. *See* Ameet Sarpatwari et al., *The US Biosimilar Market: Stunted Growth and Possible Reforms*, 105 CLINICAL PHARM. & THERAPEUTICS 92, 97 (2019) (noting that skepticism about small-molecule generic safety and effectiveness has decreased over time); *see also* Nancy L. Keating et al., *Association of Physician Peer Influence with Subsequent Physician Adoption and Use of Bevacizumab*, 3 JAMA NETWORK OPEN (2020) (finding that peer influence drove physician uptake of Avastin biosimilar).

57. *See* Preston Atteberry et al., *Biologics are Natural Monopolies (Part 1): Why Biosimilars do not Create Effective Competition*, HEALTH AFFS. BLOG (Apr. 15, 2019), https://www.healthaffairs.org/do/10.1377/hblog20190405.396631/full/ [https://perma.cc/

natural monopoly is a market "unsuitable for competition," where "a single firm . . . naturally emerge[s] in equilibrium."[58] This circumstance arises where barriers to entry are prohibitively high or where economies of scale are particularly powerful.[59] In such a market, competition necessarily fails, and direct controls, such as price caps or nationalization, are necessary to avoid monopoly pricing.[60]

Recent additions to the biologics market, however, demonstrate that competition is not an entirely unrealistic goal.[61] The few biosimilars that have been launched successfully in the U.S. spurred significant price reductions for their corresponding reference products. For example, after the U.S. launch of biosimilars for Neupogen (filgrastim), Neulasta (pegfilgrastim), Remicade (infliximab), and Lantus (insulin glargine), the net prices of each branded drug either began to decrease or decreased at a significantly higher rate in response to the added competition.[62] While biologics still face little competition from biosimilars, these changes provide encouraging evidence that competition is nevertheless feasible. The success of some biosimilars shows that it is possible for biosimilar manufacturers to clear structural barriers, such as funding the cost of biosimilar development, reverse-engineering the reference product, and navigating the FDA licensure pathway, and that the weak state of biosimilar competition in the U.S. is not inevitable or an inherent feature of the biologics market.[63] Rather, as this Note will show, it is the outcome of constructed barriers: patent thickets and gaps in the biologics

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5VFN-6D93]; Mark Trusheim et al., *Biologics are Natural Monopolies (Part 2): A Proposal for Post-Exclusivity Price Regulation of Biologics*, HEALTH AFFS. BLOG (Apr. 15, 2019), https://www.healthaffairs.org/do/10.1377/hblog20190405.839549/full/ [https://perma.cc/GK3A-GBAC].

58. Paul J. Joskow, *Regulation of Natural Monopoly*, *in* 2 HANDBOOK OF LAW AND ECONOMICS 1227, 1239–40 (A. Mitchell Polinsky & Steven Shavell eds., 2007).

59. Richard A. Posner, *Natural Monopoly and Its Regulation*, 21 STAN. L. REV. 548, 612–13 (1968).

60. *Id.* at 548.

61. Though the high cost of biosimilar development may mean that only experienced and well-funded firms will be able to enter and compete effectively in the market. *See* Yaniv Heled, *Follow-On Biologics Are Set up to Fail*, 2018 U. ILL. L. REV. ONLINE 113.

62. *See* Alvaro San Juan Rodriguez et al., *Trends in List Prices, Net Prices, and Discounts for Originator Biologics Facing Biosimilar Competition*, 2 JAMA NETWORK OPEN *1 (2019); *see also* Alex Brill & Benedic Ippolito, *Biologics are Not Natural Monopolies*, HEALTH AFFS. BLOG (July 2, 2019), https://www.healthaffairs.org/do/10.1377/hblog20190701.349559/full/ [https://perma.cc/VKX5-B7UZ] (finding the same result for Neupogen and Remicade using wholesale acquisition cost rather than net price).

63. Gottlieb Speech, *supra* note 21.

regulatory scheme that leave biosimilars embroiled in patent litigation for years before they reach the market, if they reach the market at all.

C. CONSTRUCTED BARRIERS: PATENT THICKETS

Branded biologic manufacturers use the patent system to block biosimilar competition and secure longer monopoly periods than those provided for by the patent statute.[64] Specifically, branded manufacturers protect their products with patent thickets — "dense web[s] of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology."[65] One way to create a patent thicket is through "overpatenting" (or more colorfully, "evergreening"), a practice that extends monopoly protection through the patenting of minor variations in the manufacturing process or product.[66] The practice of overpatenting and the creation of patent thickets both use the patent system to stifle rather than stimulate innovation.

Patent thickets and overpatenting are rampant in the biologics field. Branded biologic manufacturers capitalize on the complexity of biologics' structure and manufacturing process by filing dozens or sometimes hundreds of patents on a single drug.[67] To illustrate:

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64. The patent statute grants patents for twenty-year term, which begins when the date on which the patent is filed with the USPTO. 35 U.S.C. § 154(a)(2). During this period, the owner of the patent can exclude others from making and using the invention. The BPCIA provides another form of protection for reference products in the form of a 12-year marketing exclusivity period, during which the FDA cannot license a competitor product (a biosimilar). 42 U.S.C. § 262(k)(7). However, branded biologic products almost always have more than twelve years of guaranteed patent term left by the time they reach the market, so the 12-year period does not matter that much in practice. Kesselheim & Darrow, *supra* note 39, at 861.

65. Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting*, *in* 1 INNOVATION POLICY AND THE ECONOMY 119 (Adam B. Jaffe et al. eds. 2000).

66. *See* C. Scott Hemphill & Bhaven N. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 31 J. HEALTH ECON. 327 (2012) (empirical study of evergreening in the small-molecule context).

67. *See* Paul Calvo, *Post-Grant Proceedings Are Important for Biosimilars*, LAW360 (Mar. 19, 2015, 9:12 AM), https://www.sternekessler.com/sites/default/files/2017-11/Post-Grant_Proceedings_Are_Important_For_Biosimilars0.pdf [https://perma.cc/5LHT-XYUX] ("[B]iosimilar developers potentially face a much more complicated patent thicket because of the complexity of producing a biologic drug."); *see also* Sy Mukherjee, *Protect at All Costs: How the Maker of the World's Bestselling Drug Keeps Prices Sky-High*, FORTUNE (July 18, 2019, 6:30 AM), https://fortune.com/longform/abbvie-humira-drug-costs-innovation/ [https://perma.cc/7N6H-V5QG] ("Amid all these [manufacturing] procedures . . . branded [biologic] product sponsors like AbbVie have found many more opportunities to conclude

the top seven biologics of 2018 each filed an average of 158 patent applications, and, on average, 83 were issued.[68] The average number of Orange Book patents[69] per small-molecule drug, by contrast, is 3.9.[70] In order for a patent to be valid, it must claim subject matter that is useful, novel, and nonobvious.[71] The number and density of patents on the top-selling biologic drugs suggest substantial overlap and dubious novelty. AbbVie's Humira, for example, is the world's best-selling drug and also its most-patented drug. AbbVie's own marketing material describes its "Broad U.S. Humira Patent Estate," consisting of one composition-of-matter patent on the active compound adalimumab, fourteen patents on its formulation, twenty-four patents on its method of manufacture, twenty-two patents on its seven therapeutic indications, and fifteen patents on "other" components, such as associated devices and diagnostics.[72] AbbVie's "patent estate" forms a patent thicket that makes it nearly impossible for a biosimilar to enter the market without risking massive infringement liability.

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that little wrinkles in the manufacturing process are innovative and can be protected by patents.").

68. As of 2018, an average of 158 patent applications (range of 57 to 247) have been filed on Humira, Rituxan, Enbrel, Herceptin, Remicade, Avastin, and Eylea; on average, 83 patents issued (range of 41 to 132). These seven drugs each stand to block biosimilar competition for an average of 40.1 years (range of 32 to 48 years). *See* I-MAK, OVERPATENTED, OVERPRICED, *supra* note 15, at 7.

69. Orange Book patents are patents on small-molecule drugs that claim the drug, its formulation, or its method of use, and for which a claim of infringement "could reasonably be asserted" in patent litigation. *See* 21 U.S.C. § 355(b)(1)(G); 21 C.F.R. § 314.53(b) (2021).

70. While certain blockbuster small-molecule drugs, such as Eliquis, Xarelto, and Lyrica, have patent portfolios that rival those of biologics, small-molecule drugs on average have far fewer patents. *See* C. Scott Hemphill & Bhaven N. Sampat, *When Do Generics Challenge Drug Patents?*, 8 J. EMPIRICAL LEGAL STUD. 613 (2011) (finding that branded small-molecule drugs have an average of 3.9 Orange Book patents). The Hatch-Waxman Act requires branded manufacturers to disclose these patents, which the FDA then publishes in the Orange Book. Unfortunately, there is no empirical data currently available on the average number of patents that correspond to a biologic drug; empirical studies of biologics have been limited to case studies. *See* Jeffrey Wu & Claire W. Cheng, *Into the Woods: A Biologic Patent Thicket Analysis*, 19 CHI.-KENT J. INTELL. PROP. 93, 122 (2020) (quantitative case study of three biologic patent thickets corresponding to Humira, Enbrel, and Rituxan).

71. *See* 35 U.S.C. § 101 ("Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor . . . "); *id.* § 102 (novelty requirement); *id.* § 103 (nonobvious requirement).

72. *See* RICHARD GONZALEZ, ABBVIE LONG-TERM STRATEGY 14 (2020), http://www.biotechduediligence.com/uploads/6/3/6/7/6367956/abbvie_strategy_presentation__1_.pdf [https://perma.cc/ART8-9GPG]. A therapeutic indication refers to the approved application of a drug to a specific condition or disease (*e.g.*, insulin is indicated for the treatment of diabetes).

Moreover, many of the patents that make up these patent thickets are filed years after the product's launch date. The timing of later-filed patents often coincides with the expiration of the principal patents on the branded drug, suggesting an intentional effort to secure a longer monopoly period.[73] Fifty of the patents in Humira's "patent estate," for instance, were granted just before its primary patent on adalimumab expired in 2016. AbbVie is not alone in this effort. Each of the top seven biologics stands to block biosimilar competition for an average of 40.1 years, more than twice the term granted by the patent statute.[74]

In fact, a pending antitrust suit in the Northern District of Illinois alleges that AbbVie specifically engineered a scheme to accumulate overlapping and non-inventive patents as a means to block competition.[75] On a motion to dismiss, the district court recognized this as a new theory of antitrust liability, but held that AbbVie's conduct was not subject to antitrust scrutiny unless its petitions to the United States Patent and Trademark Office (USPTO) and the FDA were objectively baseless.[76] The court considered AbbVie's behavior in USPTO proceedings and patent litigation, and held that "the vast majority of the alleged scheme" constitutes AbbVie's lawful petitioning and objectively reasonable assertions of rights.[77] Plaintiffs have appealed to the Seventh Circuit Court of Appeals, and a number of states have filed amici briefs on their behalf.[78]

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73. *See* Amended Complaint & Demand for Jury Trial at ¶ 4, Mayor & City Council of Baltimore v. AbbVie Inc., 465 F. Supp. 3d 811 (N.D. Ill. 2020), *sub nom. In re* Humira (Adalimumab) Antitr. Litig., 465 F. Supp. 3d 811 (N.D. Ill. 2020) (No. 1:19-cv-01873), https://www.courtlistener.com/recap/gov.uscourts.ilnd.362729/gov.uscourts.ilnd.362729.109.0.pdf [https://perma.cc/PR4Q-CWZE] [hereinafter "Amended *Humira* Complaint"].

74. I-MAK, OVERPATENTED, OVERPRICED, *supra* note 15, at 7; *see also* 35 U.S.C. § 154(a)(2) (patent term is twenty years).

75. *See* Amended *Humira* Complaint, *supra* note 73, ¶¶ 16–27; *see also* Morgan Marmaro, Note, *Molecule Size Doesn't Matter: The Case for Harmonizing Antitrust Treatment of Pay-for-Delay Agreements*, 54 COLUM. J.L. & SOC. PROBS. 169 (2021) (arguing for harmonization of antitrust treatment of small-molecule and biologic drugs with respect to reverse payment settlements).

76. *In re* Humira (Adalimumab) Antitr. Litig., 465 F. Supp. 3d 811, 830 (N.D. Ill. 2020).

77. *Id.* at 834 (noting that "the vast majority of the alleged scheme is immunized from antitrust scrutiny, and what's left are a few sharp elbows thrown at sophisticated competitors participating in regulated patent and biologic-drug regimes.").

78. *See* Brief for Amici Curiae States of Washington et al. Supporting Plaintiffs-Appellants and Reversal, UFCW Local 1500 Welfare Fund v. AbbVie, Inc., No. 20-2402 (7th Cir. Oct. 13, 2020), https://oag.ca.gov/sites/default/files/Humira_States_Amicus.pdf [https://perma.cc/UGF3-79TY]. The FTC has also filed an amicus brief (in support of neither party) to address the separate issue of anticompetitive patent settlements. *See* Brief of Amicus Curiae the Federal Trade Commission in Support of No Party, UFCW Local 1500 Welfare Fund v. AbbVie, Inc., No. 20-2402 (7th Cir. Oct. 13, 2020), https://www.ftc.gov/

Branded biologic manufacturers commonly defend their patent portfolios by claiming that later-filed patents reflect incremental innovation and improvement in the product over time.[79] But the timing and sheer number of patents, as described, suggest otherwise. For example, many of the method-of-manufacture patents asserted against biosimilars in litigation were filed more than a year after the branded product launched. Scholars Arti Rai and Nicholson Price have dubbed these "impossible patents" — impossible because they cannot logically be used to block biosimilar competition, and yet they are asserted in litigation against biosimilars.[80] Such patents cannot block biosimilar competition by virtue of their filing date: by statute, if the patents claim a method used to make the drug at its launch, those patent claims are invalid where the method was in "public use" for more than a year prior to filing.[81] If, on the other hand, the patents claim a method *not* used to make the drug at its launch, that method would not be necessary to make the drug, and therefore the patent could not be used in

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system/files/documents/amicus_briefs/ufcw-local-1500-welfare-fund-et-al-v-abbievie-inc-et-al/ufcw_local_1500_welfare_fund_amicus_brief.pdf [https://perma.cc/ZJN4-FSQP] [hereinafter FTC Brief].

79. *See, e.g.*, *Drug Pricing in America: A Prescription for Change, Part II: Hearing before the S. Comm. on Fin.*, 116th Cong. 24–25 (2019):

> Senator STABENOW. So, Mr. Gonzales, your primary patent expired in the U.S. in 2016. Is that correct?
>
> Mr. GONZALEZ. That is correct.
>
> Senator STABENOW. And you have more than a hundred other kinds of patents for processes and techniques and so on. In fact, according to a report, 'Broad U.S. Humira Patent Estate,' some of the patents go up to 2034, which gives you about 31 years of patent protection. That is a pretty good deal on this successful drug. When we look at what is happening around — well, let me first ask this. Has the drug itself gotten any better with all the new patents?
>
> Mr. GONZALEZ. I think as you look at the evolution of the patent portfolio that is around Humira, it is important to keep in perspective that that patent portfolio evolved as we discovered and learned new things about Humira, in particular, as we discovered that this particular molecule could be utilized across a large number of different disease states.
>
> Senator STABENOW. And I am going to, unfortunately, in the interest of time — I appreciate that and would want to follow up in writing, but as I understand it, the chemical formula is the same. And so it is a question of how we use the patent system.

80. *Id.*

81. *See* 35 U.S.C. § 102(b) (2006) (pre-America Invents Act, patents claiming inventions that were "in public use or on sale in this country more than one year prior to the date of the application for patent" fail the novelty requirement); *see also* 35 U.S.C. § 102(a) (post-America Invents Act, patents filed on or after March 16, 2013 claiming inventions that were in "public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention" fail the novelty requirement).

litigation to block a biosimilar from entering the market.[82] The potential invalidity of many biologic patents would seem to be a boon to biosimilars hoping to enter the market.[83] Even weak patents, however, can shore up a patent portfolio by presenting an additional hurdle in litigation or by extending a period of exclusivity.[84]

The problem of "impossible patents" is particularly egregious in the case of AbbVie's Humira: 89% of AbbVie's 247 patent applications on Humira were filed after the drug's market entry in 2002, and 49% were filed after its first patent expired in 2014.[85] At least twenty of these were "impossible patents" and yet were asserted by AbbVie in litigation to block biosimilars.[86] Four Humira biosimilars ultimately executed settlement agreements with AbbVie, agreeing to postpone market entry in the United States until 2023 in exchange for earlier market entry in Europe.[87] While Humira is an extreme example, preliminary evidence suggests that it is not the only drug with impossible patents.[88] Together, these observations cast doubt on the value and validity of later-filed patents that claim biologic products. Though many of the patents may be weak individually, such sprawling patent portfolios are a significant impediment to biosimilars hoping to reach the market, and a strong deterrent to biosimilar investment in the first place. Indeed, ongoing patent litigation and deferred market entry agreements have

82. Price & Rai, *supra* note 19, at 862.

83. The granting of low-value patents results in part from certain features of the patent filing process, such as a limited patent examination process, presumptions in favor of patent approval, and structural limitations of the USPTO. *See* Michael R. Herman, *Note: The Stay Dilemma: Examining Brand and Generic Incentives for Delaying the Resolution of Pharmaceutical Patent Litigation*, 111 Colum. L. Rev. 1788, 1798 (2011).

84. *See* Hemphill & Sampat, *supra* note 70, at 621 ("[Weak patents] nevertheless have the effect of making the patent portfolio stronger. If they overlap in duration with a strong composition of matter patent, they provide an additional barrier to generic entry prior to expiration of the strong patent, since the generic firm must defeat the weak patent in addition to the strong one. Indeed, the prospect of having to defeat both patents might cause a generic firm to decline or delay a challenge. Moreover, the additional patent strengthens the portfolio in a second way. A patent that expires later than the strong patent potentially provides a substantial temporal extension in a brand-name drug maker's effective exclusivity.").

85. I-MAK, OVERPATENTED, OVERPRICED: SPECIAL HUMIRA EDITION 4 (2018).

86. Price & Rai, *supra* note 19, at 862. All but one of these cases have settled, with the result that at least four of five Humira biosimilars licensed by the FDA will not reach the market until 2023. The last case is ongoing. *See* Mike Z. Zhai et al., *Why Are Biosimilars Not Living Up to Their Promise in the US?*, 21 A.M.A. J. ETHICS 668, 671 (2019).

87. *See* FTC Brief, *supra* note 78, at 2.

88. Price & Rai, *supra* note 19, at 863.

been identified as the main reasons for delayed or failed biosimilar market entry in the U.S.[89]

In sum, patent thickets are the reason that most biosimilars approved by the FDA are not marketed, and the reason that biologic prices remain so high. Biosimilars face multiple structural barriers in their path to market, such as the high cost of biosimilar development, the difficulty of the FDA licensure pathway, and the lack of automatic substitution at the pharmacy level. These structural barriers are significant, but not insurmountable. Patent thickets, in contrast, often are insurmountable due to the cost and uncertainty of patent litigation. The problem of patent thickets implicates the regulatory framework of the BPCIA, and in particular its patent provisions, which Part III explores in greater depth.

III. A SKEWED BALANCE: REGULATORY GAPS IN THE BPCIA

A central concern of BPCIA drafters was finding a way "to frame the intellectual property protections in a pathway for biosimilars that incentivizes the extraordinary investment required to develop new biologics but does not discourage biosimilar introduction."[90] The statute has been successful with respect to incentivizing the investment required to develop new biologics. Since its passage, the FDA has approved new biologic products at increasing rates.[91] Biologics also represent an increasing share of the total drug market.[92] The growth of biologic medicines is a testament to the robust incentives for innovation in this field.

The BPCIA, however, fails to foster competition. It has not created a robust and functioning biosimilars market in the way Hatch-Waxman did for generics. Although modeled on the Hatch-Waxman Act, the BPCIA differs from Hatch-Waxman in certain important respects. This Part identifies two main features of the BPCIA that allow patent thickets to block biosimilars. Section A first describes the structure of the Hatch-Waxman Act. Section B explains one of the BPCIA's notable departures from the Hatch-

89. *See* Zhai et al., *supra* note 86, at 669, 671.

90. *Biologics and Biosimilars Hearing*, *supra* note 12, at 2 (statement of Rep. Henry C. "Hank" Johnson).

91. *See* Jonathan J. Darrow et al., *FDA Approval and Regulation of Pharmaceuticals, 1983–2018*, 323 JAMA 164, 171 fig.6 (2020).

92. *Id.* at 170 (showing that biologics represented 29% of new drug approvals in 2018); *see also* AITKEN & KLEINROCK, *supra* note 3, at 26 (showing that net spending on biologics totaled $125.5 billion in 2018, up 9.5 percent since 2017).

Waxman framework: the lack of a public patent listing requirement. It argues that the lack of public patent listing under the BPCIA allows patent thickets to thrive and makes it overly difficult for biosimilars to navigate the path to market. Section C turns to the BPCIA's other major departure from Hatch-Waxman: its scheme for the resolution of patent disputes, known as "the patent dance." Section C argues that although the BPCIA was designed to give the biosimilar applicant substantial control over the patent dance, the complexity and protracted nature of the dispute resolution process ultimately work to biosimilars' disadvantage.

A. THE HATCH-WAXMAN ACT: THE MODEL FOR THE BPCIA

The Hatch-Waxman Act was enacted to both spur competition from generics and strengthen the incentives for small-molecule drug innovation.[93] To achieve the first aim, the Act established an abbreviated approval pathway for generic drugs using "bioequivalence" as the standard for approval.[94] Embedded within this approval pathway is a notice-and-litigation scheme designed to streamline patent litigation. The Hatch-Waxman scheme proceeds as follows: the generic applicant can challenge active patents on the branded drug by filing a "Paragraph IV certification" with its application for approval, in which it asserts either that the generic product does not infringe the relevant patents, or that the relevant patents are invalid.[95] Paragraph IV certification is considered a statutory act of patent infringement, because it signals that the generic manufacturer intends to market its drug before the relevant patents expire.[96] The generic manufacturer must then give notice to the branded manufacturer and patent owner(s) of the

93. *See* H.R. REP. NO. 98-857, pt. 1, at 14–18 (1984), *as reprinted in* 1984 U.S.C.C.A.N. 2647, 2647–51.

94. 21 U.S.C. § 355(j)(2)(A)(iv).

95. The generic applicant must certify either that the active patents on the branded product are either "invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted." *Id.* § 355(b)(2)(A)(iv).

96. Stephanie M. Greene, *A Prescription for Change: How the Medicare Act Revises Hatch-Waxman to Speed Market Entry of Generic Drugs*, 30 IOWA J. CORP. LAW 309, 317 (2005); *see* 35 U.S.C. § 271(e)(2)(C) ("It shall be an act of infringement to submit . . . [an ANDA] if the purpose of such submission is to obtain approval to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.").

certification, after which the branded manufacturer has forty-five days to file an infringement suit.[97]

Central to this notice-and-litigation scheme is the public listing of patents in the Orange Book. The Act requires manufacturers of branded small-molecule drugs to name all patents which claim the drug, its formulation, or its method of use, and which contain claims that "could reasonably be asserted" in patent litigation.[98] These patents are compiled in the Orange Book, which the FDA publishes and updates on a monthly basis.[99] As a reward for the time and cost of litigation, the first generic challenger enjoys a 180-day exclusivity period in which it is the only generic competing with the branded product.[100] Hatch-Waxman's generic approval pathway, notice-and-litigation scheme, requirement for public patent listing, and generic exclusivity period are all provisions aimed at accelerating generic market entry and increasing competition.

To strengthen incentives for innovation, the Hatch-Waxman Act grants a five-year period of exclusivity to new chemical entities, or drugs whose active ingredient had not been previously approved by the FDA.[101] During this period, the FDA cannot accept generic applications for drugs with the same active ingredient.[102] In addition to the five-year exclusivity period, Hatch-Waxman also established patent term restoration for innovators of new small-molecule drugs.[103] This provision extends the term of a branded manufacturer's patent so as to restore the time lost to the clinical trial and FDA review process.[104]

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97. 21 U.S.C. §§ 355(b)(3), (c)(3)(C).

98. *Id.* §§ 355(b)(1)(G); 21 C.F.R. § 314.53(b) (2021).

99. *See Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, FOOD & DRUG ADMIN. (Jan. 4, 2021), https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm [https://perma.cc/YQ5S-E6KP] [hereinafter "*Orange Book*"].

100. 21 U.S.C. § 355(j)(5)(B)(iv).

101. *Id.* § 355(j)(5)(F)(ii); 21 C.F.R. § 314.108(a) (2021) ("*New chemical entity* means a drug that contains no active moiety that has been approved by FDA in any other NDA submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act." (emphasis added)).

102. This bar is in place for five years unless a generic manufacturer submits a Paragraph IV certification (a patent challenge), in which case the FDA may accept the generic application one year early (e.g., four years after the approval of the new chemical entity). *See* 21 U.S.C. § 355(j)(5)(F)(ii).

103. 35 U.S.C. § 156.

104. The maximum extension is 5 additional years of patent life. *Id.* § 156(g)(6)(A). The total market exclusivity time cannot exceed 14 years. *Id.* § 156(c)(3); *see also* Robert A. Armitage, *The Hatch-Waxman Act: A Path Forward for Making It More Modern*, 40 WM. MITCHELL L. REV. 1200, 1246 n.100 (2014) (elaborating the complexities of the statutory calculation). This applies only to the product's first approval and can only extend the term

Altogether, policymakers and other experts have considered the Hatch-Waxman Act a success.[105] It was an ambitious and innovative piece of legislation, and it enabled the growth of a robust generics market in the U.S. without compromising rates of small-molecule innovation.[106] For this reason, legislators consciously modeled the BPCIA after the Hatch-Waxman Act. The general structure of the BPCIA is analogous to that of Hatch-Waxman: an abbreviated pathway for biosimilars, a period of exclusivity for biologic innovators, a mechanism for resolution of patent disputes, and a period of exclusivity for certain biosimilars. However, the BPCIA ultimately diverges from the Hatch-Waxman Act in several significant ways, especially with respect to its patent provisions. These differences have important repercussions for the cost and accessibility of biologic medications for patients.

B. LACK OF PUBLIC PATENT LISTING UNDER THE BPCIA

The BPCIA's most notable departure from the Hatch-Waxman framework is its treatment of public patent listing. The BPCIA only requires the listing of certain patents, but not all patents, that protect the branded product.[107] As described, the Hatch-Waxman Act requires small-molecule manufacturers to disclose patents which claim the drug, its formulation, or its method of use, and lists these patents in the Orange Book. Public patent listing under Hatch-Waxman has increased transparency for generic entrants, facilitated challenges to weak secondary patents, and thereby

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of a single patent, but it ensures innovators that clinical trials will not entirely consume the life of their patents. 35 U.S.C. §§ 156(a)(2), (c)(4).

105. Kesselheim & Darrow, *supra* note 39, at 295–96.

106. The percentage of prescriptions that are filled with generics has risen steadily since 1984, and generics are now dispensed 97 percent of the time when available. *See* AITKEN & KLEINROCK, *supra* note 3, at 5; Kesselheim & Darrow, *supra* note 39, at 310. Likewise, rates of innovation increased significantly in the twenty years after the enactment of the Hatch-Waxman Act: the FDA approved 79 percent more new chemical entities in the two decades following Hatch-Waxman than in the two decades prior. *See* Kesselheim & Darrow, *supra* note 39, at 308 n.77.

107. The BPCIA, as amended in December 2020 by the Purple Book Continuity Act, only requires branded biologic manufacturers to disclose patents that have been already been exchanged in the "patent dance," or the series of exchanges that may occur between the branded manufacturer and a biosimilar applicant prior to litigation under the BPCIA. *See* 42 U.S.C. § 262(k)(9)(A)(iii); *see also id.* § 262(*l*). The amendments to the BPCIA's patent listing provision are discussed in greater detail *infra* Part IV.

allowed for "pruning" of patent thickets.[108] It also has enabled empirical analysis of the relationship between patent rights and pharmaceutical market features, which in turn informs innovation policy.[109]

In contrast, the BPCIA's patent listing requirement is much more circumscribed.[110] As a result, the complete portfolio of patents protecting a branded biologic drug is not easily retrievable in a centralized location. The FDA publishes the Purple Book, which lists all biologic products licensed by the FDA, along with their dates of licensure, exclusivity expiration dates, and status as a reference, biosimilar, or interchangeable product.[111] But the patents on the vast majority of products remain undisclosed. And although patents are publicly searchable, it may not be clear what to search *for*.[112] Biologic patents often claim broad categories of agents and processes, the exact scope of which can be unclear.[113] Moreover, aspects of the manufacturing process, such as methods of driving gene expression in specific cell lines; methods of purification;

108. *See generally* Hemphill & Sampat, *supra* note 66 (finding that patent challenges serve to keep evergreening of small-molecules in check, and serve to restore effective market exclusivity to about 12 years).

109. *See, e.g.*, *id.* at 329 (empirical study of evergreening using Orange Book data); Amy Kapczynski et al., Abstract, *Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of "Secondary" Pharmaceutical Patents*, 7 PLoS ONE 1, 1 (2012) (empirical study of secondary patenting using Orange Book data); Hemphill & Sampat, *supra* note 70, at 619 (using Orange Book data to assess changes in brand-name patenting and generic challenges over time); Reed F. Beall et al., *Pre-Market Development Times for Biologic Versus Small-Molecule Drugs*, 37 NATURE BIOTECHNOLOGY 708, 710 (2019) (using Orange Book data to analyze patent term restoration granted under the pediatric exclusivity program); Tulip Mahaseth, Maintaining the Balance: An Empirical Study on Inter Partes Review Outcomes of Orange Book Patents and its Effect on Hatch-Waxman Litigation 1 (Nov. 29, 2018) (unpublished manuscript) (on file with author) (empirical study of challenges to Orange Book patents leveraged in inter partes review proceedings).

110. The Purple Book Continuity Act only requires disclosure of patents that have already been exchanged in the "patent dance," as explained further *infra* Part IV. *See* 42 U.S.C. § 262(k)(9)(A)(iii); *see also id.* § 262(*l*).

111. *See Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*, FOOD & DRUG ADMIN. (Jan. 8, 2020), https://purplebooksearch.fda.gov/ [https://perma.cc/PPC9-3AUR].

112. *See USPTO Patent Full-Text and Image Database*, U.S. PATENT & TRADEMARK OFF., http://patft.uspto.gov/netahtml/PTO/search-bool.html [https://perma.cc/WME3-FVY3].

113. *See* Falit et al., *supra* note 47, at 297 ("[Biologic] patents are publicly searchable but can be difficult to assess since they often govern broad groups of agents[.]"); *accord* Price & Rai, *supra* note 28, at 1050–51 (noting that broadness of biologic patents does not provide useful disclosure for biosimilars, especially with respect to manufacturing processes); *see, e.g.*, DNA Encoding a Chimeric Polypeptide Comprising the Extracellular Domain of TNF Receptor Fused to IGG, Vectors, and Host Cells, U.S. Patent No. 5,447,851 (filed Apr. 2, 1992) (Amgen's principal patent on the biologic drug Enbrel, notably broad in the scope of its claims).

methods of assaying and characterizing the molecules; or other aspects of the biotechnology may be patented without direct reference to the specific biologic molecule itself. Thus, even with the USPTO patent database, it can be very difficult to identify the entire portfolio of patents that a branded biologic manufacturer may assert against a biosimilar in litigation.

This lack of patent transparency makes it exceedingly difficult for a biosimilar competitor to assess the patent thicket that surrounds the branded product.[114] A competitor eyeing market entry has no straightforward way to predict the number, nature, and scope of the patents it may face in litigation. The lack of transparency also insulates weaker patents from invalidity challenges made via post-grant proceedings at the USPTO. Post-grant proceedings are administrative proceedings for challenging the validity of granted patents. They include *ex parte* reexamination, inter partes review (IPR), and post grant review, and may take place prior to or in parallel with patent litigation.[115] These mechanisms enable generic and biosimilar applicants to invalidate or weaken the branded manufacturer's patents without the time and cost of patent litigation. Taking advantage of these proceedings, however, requires first identifying the patents that block the applicant's path to market. Lack of patent transparency makes this effort difficult. Finally, lack of patent transparency under the BPCIA makes it impossible for researchers, policymakers, and the public to fully grasp the extent of the problem. In short, biologic patent thickets thrive in the dark.

C. THE PATENT DANCE

Under the Hatch-Waxman Act, patent litigation is relatively straightforward, comprised of "Paragraph IV certification," notice to the branded manufacturer, and a window of time for the branded manufacturer to file suit. In contrast to Hatch-Waxman's public and relatively simple mechanism for patent litigation, the BPCIA sets up a private, confidential, and complex information

114. *See* Price & Rai, *supra* note 19, at 863 ("[F]or now, it is very difficult to know how many and which patents cover any particular biologic, and correspondingly to know how dense or valid the relevant patent thickets might be.").

115. *See* 35 U.S.C. § 301 (*ex parte* reexamination); *id.* § 311 (inter partes review); *id.* § 321 (post-grant review).

exchange known as "the patent dance."[116] The patent dance takes place between a biosimilar applicant and branded biologic manufacturer, and involves a complex series of disclosures and negotiations designed to identify and narrow down the patents at issue.

The patent dance proceeds as follows. First, a biosimilar applicant submits its application to the FDA for licensure. When the FDA notifies the applicant that its application has been accepted for review, the applicant has twenty days to provide a copy of its application and information about its manufacturing process to the manufacturer of the branded product.[117] The branded manufacturer then evaluates the information provided for possible infringement of its own patents, and within sixty days, provides the applicant with a list of patents for which the manufacturer believes it could reasonably assert a claim of infringement.[118] The branded manufacturer is prevented from bringing infringement claims on patents not included in the initial lists nor provided as a supplement to the list within thirty days of a newly issued or licensed patent.[119]

After receiving the branded manufacturer's list, the applicant then has sixty days to reply with a "detailed statement" as to each patent listed; for each patent, the applicant may argue that the patent is invalid, unenforceable, or not infringed, or alternatively, state that it will not market its biosimilar until after that patent expires.[120] It must respond to any licensing offers, and may also provide its own list of patents that it believes are at issue.[121] The branded manufacturer then has sixty days to return with its own "detailed statements" as to the invalidity, unenforceability, or noninfringement of each patent listed by the applicant.[122] The goal of these exchanges is to identify all relevant patents and to allow the

116. *See generally* 42 U.S.C. § 262(*l*); *see* Sarpatwari, *supra* note 56, at 95–96 (discussion of the patent dance).

117. 42 U.S.C. § 262(*l*)(2). The information provided by the biosimilar applicant is governed by certain confidentiality restrictions which are enforceable by injunction. *See id.* § 262(*l*)(1).

118. *Id.* § 262(*l*)(3)(A). This also includes an identification of any patents which the branded manufacturer is open to licensing. *See id.* § 262(*l*)(3)(A)(ii).

119. *Id.* § 262(*l*)(7); 35 U.S.C. § 271(e)(6)(C); Amgen Inc. v. Apotex Inc., 827 F.3d 1052, 1058 (Fed. Cir. 2016) ("If a patent that the reference product sponsor should have included on its (3)(A) list or its (7) supplement 'was not timely included,' then the owner of that patent may not sue for infringement under 35 U.S.C. § 271 with respect to the biological product at issue." (citing 35 U.S.C. § 271(e)(6)(C)).

120. 42 U.S.C. § 262(*l*)(3)(B).

121. *Id.* §§ 262(*l*)(3)(B)(i), (iii).

122. *Id.* § 262(*l*)(3)(C).

parties to evaluate the strength of their positions in advance of litigation. It also encourages the parties to negotiate licensing agreements.

Having completed the first round of exchanges, the parties may enter into the first of two phases of patent litigation.[123] The first phase requires the parties to "engage in good faith negotiations" to agree on a list of patents to litigate immediately.[124] If they reach an agreement, the branded biologic manufacturer has thirty days to initiate suit on the agreed-upon list.[125] If they fail to reach an agreement, they again exchange lists of patents that each would like to litigate, with the ultimate number of patents on the list controlled by the biosimilar applicant.[126] Notably, the biosimilar applicant can restrict this first phase of litigation to a single patent, postponing the litigation of all other relevant patents to the second phase of litigation.[127] The second phase of litigation begins when the biosimilar applicant gives the branded manufacturer its notice of commercial marketing, which it must do at least 180 days before its biosimilar launches on the market.[128] The branded manufacturer may then seek a preliminary injunction to enjoin marketing of the biosimilar pending judicial resolution of the remaining

123. *See* Sandoz Inc. v. Amgen Inc., 137 S. Ct. 1664, 1671 (2017) ("Following this exchange, the BPCIA channels the parties into two phases of patent litigation."). This two-phase structure has been called "a radical departure from traditional patent litigation," but its rationale is unclear. Erika Lietzan et al., *An Unofficial Legislative History of the Biologics Price Competition and Innovation Act 2009*, 65 FOOD & DRUG L.J. 671, 814 (2010). Separation of the litigation into two phases may encourage the parties to execute licensing agreements or reach settlement earlier in the process. It may also give the biosimilar applicant some flexibility in choosing when it wants to attack which patents. For example, it may choose to narrow the first phase of litigation to only the weaker patents and then attack the stronger patents later, once it has progressed further on the path toward FDA approval and presumably has more resources and ability to litigate. Essentially, the two-phase structure of litigation under the BPCIA may operate to give biosimilars flexibility in deciding when, and in what manner, they allocate resources to the litigation.

124. 42 U.S.C. §§ 262(*l*)(4)(A), (B).

125. *Id.* § 262(*l*)(6)(A). If the branded manufacturer fails to file suit within 30 days, or fails to prosecute a filed suit in good faith, its remedies for infringement will be limited to a reasonable royalty. 35 U.S.C. §§ 271(e)(6)(A), (B).

126. *See* 42 U.S.C. § 262(*l*)(5); *see also Sandoz*, 137 S. Ct. at 1671 ("This process gives the applicant substantial control over the scope of the first phase of litigation: The number of patents on the sponsor's list is limited to the number contained in the applicant's list, though the sponsor always has the right to list at least one patent.").

127. *See* Michael P. Dougherty, *The New Follow-On-Biologics Law: A Section by Section Analysis of the Patent Litigation Provisions in the Biologics Price Competition and Innovation Act of 2009*, 65 FOOD & DRUG L.J. 231, 238 (2010).

128. 42 U.S.C. § 262(*l*)(8)(A). Note that under *Sandoz v. Amgen*, the applicant need not wait for FDA licensure to give its notice. *See Sandoz*, 137 S. Ct. at 1677 ("Accordingly, the applicant may provide notice either before or after receiving FDA approval.").

patents.[129] The biosimilar applicant may also seek declaratory judgment on the invalidity, unenforceability, and/or non-infringement of any of these patents.[130]

The patent dance was intended "to help ensure that litigation surrounding relevant patents will be resolved expeditiously and prior to the launch of the biosimilar product, providing certainty to the applicant, the reference product manufacturer, and the public at large."[131] Yet the BPCIA's patent provisions are elaborate, cumbersome, and plagued with uncertainty. The dance demands a high degree of sophistication and strategy from both sides. Some have argued that the complexity of the BPCIA's patent framework disadvantages biosimilar applicants by creating opportunities for gamesmanship.[132] It also requires the biosimilar to reveal its manufacturing information without requiring the same of the branded manufacturer, and involves two phases of litigation prior to market launch.[133] The complexity and information asymmetry of the patent dance make the path to commercial marketing more precarious for biosimilar applicants.

The BPCIA does give the biosimilar applicant substantial control over the patent dance.[134] It allows the biosimilar to dictate the scope of the first phase of litigation and the timing of the second (by deciding when it will give pre-marketing notice).[135] The

129. 42 U.S.C. § 262(*l*)(8)(B).

130. *Id*. § 262(*l*)(9)(B).

131. *Biologics and Biosimilars Hearing*, *supra* note 12, at 9 (statement of Rep. Anna Eshoo).

132. *See, e.g.*, Heled, *supra* note 61, at 118 n.32; Sarpatwari, *supra* note 56, at 95–96; Brian F. McMahon, *The Biologics Price Competition and Innovation Act of 2009: Legislative Imprudence, Patent Devaluation, and the False Start of A Multi-Billion Dollar Industry*, 100 KY. L.J. 635, 675–77 (2012).

133. Heled, *supra* note 61, at 118–19; *see also* Falit, *supra* note 47, at 297–98 ("Unfortunately, this requirement may make the 351(k) pathway less attractive. Applicants may have developed improvements to the manufacturing process that they do not want to disclose. Moreover, information contained in the dossier might allow the innovator to identify aspects of the biosimilar's manufacturing process that infringe on the originator's patents and would otherwise have been undiscoverable.").

134. *See Biologics and Biosimilars Hearing*, *supra* note 12, at 209–10 (statement of Teresa Stanek Rea, President of the American Intellectual Property Law Ass'n) ("Under H.R. 1427, pre-launch litigation of any patent is entirely within the control of the follow-on applicant. . . ."); *see also* Amgen Inc. v. Apotex Inc., 827 F.3d 1052, 1062 n.3 (Fed. Cir. 2016) ("Such applicant control is part of the design [of section 262(*l*)].").

135. *See, e.g.*, Sandoz, Inc. v. Amgen, Inc., 137 S. Ct. 1664, 1671–72 (2017) (explaining that, under the BPCIA, "the applicant [has] substantial control over the scope of the first phase of litigation" and "substantial control over the timing of the second phase of litigation"); *accord Apotex*, 827 F.3d at 1062 ("[Section 262(*l*)] gives the applicant substantial authority to force such a limitation on the scope of the first-stage litigation."); *id*. at 1062 n.3 ("Such applicant control is part of the design.").

biosimilar applicant is also free to opt out of the patent dance entirely and withhold its manufacturing information, as the Supreme Court held in *Sandoz, Inc. v. Amgen, Inc.*, 137 S. Ct. 1664 (2017).[136] However, if the biosimilar applicant opts out of the patent dance, the branded manufacturer can bring an immediate action for declaratory judgment on any and all patents it believes the biosimilar applicant infringed.[137] The lack of a public patent listing requirement means that the biosimilar applicant has limited knowledge about the number, nature, and scope of patents that may be asserted against it in this action. Declining to engage in the patent dance cedes all control the biosimilar applicant would otherwise have had, and, in the words of Justice Thomas, "deprives the applicant of the certainty that it could have obtained by bringing a declaratory-judgment action prior to marketing its product."[138] The biosimilar applicant is therefore caught between a rock and a hard place. It must either navigate the stratagems of the patent dance or risk infringement liability of unknown proportions. So far, most applicants have opted to dance.[139]

The BPCIA's patent litigation framework leaves many biosimilars mired in litigation for years before they reach the market.[140] Given the steep costs of patent litigation,[141] the lack of patent transparency, and the high degree of unpredictability in biologic

136. *Sandoz*, 137 S. Ct. at 1674 (holding that a biosimilar applicant who fails to disclose its application and manufacturing information cannot be forced by injunction to follow 42 U.S.C. § 262(*l*)(2)(A)).

137. 42 U.S.C. § 262(*l*)(9)(B).

138. *Sandoz*, 137 S. Ct. at 1675.

139. *See* Limin Zheng, *The Biosimilar Patent Dance: What Can We Learn From Recent BPCIA Litigation?*, Biosimilar Development (Mar. 6, 2018), https://www.biosimilardevelopment.com/doc/the-biosimilar-patent-dance-what-can-we-learn-from-recent-bpcia-litigation-0001 [https://perma.cc/J77R-ZG8C] (noting that, of the 17 biosimilar products litigated under the BPCIA as of March 2018, about 70 percent of the applicants engaged in and completed the patent dance before onset of litigation, and only in three instances did the applicant "decline[ ] to dance outright.").

140. Zhai et al., *supra* note 86, at 670 (identifying ongoing patent litigation or settlement agreements to defer entry as the primary reason for delayed market entry of biosimilars).

141. Anne S. Layne-Farrar, *The Cost of Doubling Up: An Economic Assessment of Duplication in PTAB Proceedings and Patent Infringement Litigation*, LANDSLIDE, May–June 2018, at 1 ("For $10–$25 million at risk, median costs [of patent infringement litigation] through discovery are $1.9 million and over $3 million through final disposition. If more than $25 million is at risk, taking the case through discovery typically costs $3 million, with a median cost of $5 million to reach final disposition."), https://www.americanbar.org/groups/intellectual_property_law/publications/landslide/2017-18/may-june/cost-doubling-up/ [https://perma.cc/J4E3-MBCW].

patent litigation,[142] many would-be competitors agree to defer market entry to a certain date and settle the litigation rather than sink resources into a long and costly defense.[143] For a biosimilar competitor already facing high barriers to entry, the steep and unpredictable costs of patent litigation under the BPCIA may discourage entry altogether.

In sum, while the BPCIA has effectively maintained the incentives for biologic innovation, it has resulted in a market with woefully inadequate competition from biosimilars. The BPCIA's lack of a public patent listing requirement allows patent thickets to flourish and makes it difficult for the applicant to prune the field of low-value patents, or even to predict the number, nature, and scope of the patents it may come up against in litigation. Moreover, the BPCIA's patent dispute resolution scheme is unwieldy and difficult. Far from streamlining biosimilar market entry, the patent dance compels a highly complex and demanding back-and-forth between the applicant and the branded manufacturer. As a result, biosimilar applicants commonly remain stuck in litigation for years, or settle to delay market entry for a comparable amount of time. The overgrowth of patent thickets and the difficulty of the patent dance operate to block biosimilars that have gained FDA approval from marketing, and also disincentivize initial investment in biosimilar ventures. The result is an overgrown patent landscape, a stunted biosimilars market, and a lack of transparency for biosimilar applicants, researchers, policymakers, and the public.

IV. PROPOSALS FOR CHANGE

The biologics regulatory landscape desperately needs reform. This Part offers both legislative and administrative solutions to the problem of biologic patent thickets. Section A evaluates a recent legislative proposal, the Biologic Patent Transparency Act (BPTA), and concludes that the bill would bring much-needed transparency to the biologic patent landscape, but contains

142. *See generally* D. Alan White, *The Doctrine of Equivalents: Fairness and Uncertainty in an Era of Biologic Pharmaceuticals*, 60 EMORY L.J. 751 (2011) (arguing that the complexity of biologic drugs creates uncertainty surrounding the scope of biologic patents, and that this uncertainty is magnified under certain doctrines in patent law).

143. *See* Zhai et al., *supra* note 86, at 670; *see also* Marmaro, *supra* note 75, at 169 (discussion of antitrust treatment of reverse payment settlements between biologic manufacturers).

problematic language that could undermine this purpose if not corrected. Section B recommends administrative changes to facilitate challenges to low-value patents, spur biosimilar market penetration, and curtail anti-competitive tactics in the biologics market. These administrative changes include lowering the FDA's bar for interchangeability of biosimilars; preserving the institution of inter partes review at the USPTO; and promoting inter-agency coordination between the FDA, USPTO, and Federal Trade Commission (FTC). Together, the legislative and administrative solutions recommended here have the power to combat patent thickets, stimulate biosimilar competition, and ultimately make life-saving biologic medicines more affordable for patients.

A. LEGISLATIVE PROPOSALS

The BPTA, a bipartisan bill introduced in the Senate in March 2019, promises to address the transparency problem in the biologics field. The BPTA aims "to provide for additional requirements with respect to patent disclosures."[144] Specifically, it requires manufacturers of branded biologics to submit to the FDA "a list of each patent required to be disclosed."[145] The bill defines "patents required to be disclosed" as "any patent for which the holder believes a claim of infringement could reasonably be asserted by the holder . . . if a person not licensed by the holder engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product."[146] The FDA must publish this information in the Purple Book.[147] Manufacturers must also notify the FDA within thirty days if any listed patent or claim is determined to be invalid or unenforceable.[148] As a strong incentive to comply with the listing requirement, the BPTA includes a "list-it-or-lose-

144. Biologic Patent Transparency Act, S. 659, 116th Cong. (2019), https://www.congress.gov/116/bills/s659/BILLS-116s659is.pdf [https://perma.cc/96UC-TSQF] [hereinafter "BPTA"].

145. *Id.* § 2 (Patent Disclosure Requirements).

146. *Id.*

147. *Id.*

148. *Id.* ("The holder of a biological product license . . . shall submit to the Secretary a list that includes . . . any patent, or any claim with respect to a patent, included on the list . . . subsequently determined to be invalid or unenforceable, within 30 days of a determination of patent invalidity.").

it" provision, making patents not listed in the Purple Book unenforceable in subsequent litigation under the BPCIA.[149]

The BPTA promises to bring much-needed transparency to the biologics patent landscape. By requiring biologic manufacturers to disclose their patents, the BPTA would enable biosimilars to assess the patent landscape much earlier in the market entry process, and strategize accordingly. The disclosure requirements of the BPTA would outline the maximal extent of patents that a biosimilar may contend with in downstream BPCIA litigation. It would also facilitate challenges to weaker secondary patents on the reference product via post grant challenges and IPR proceedings at the USPTO.[150] These are all advantages for biosimilars, and would help to re-calibrate the BPCIA's skewed balance between innovation and competition.

In many ways, the BPTA would bring the BPCIA in line with the Hatch-Waxman Act. The reporting of biologic patents in the Purple Book nicely mirrors the reporting of small-molecule patents in the Orange Book. However, the list-it-or-lose-it provision in the BPTA would go further than the Hatch-Waxman Act, which imposes consequences for untimely listing of a patent but does not altogether bar infringement claims for such patents.[151] By restricting enforcement of non-listed patents, the BPTA would create a strong incentive for disclosure. The scope of patents that must be listed under the BPTA is also broader than that under Hatch-Waxman, as it includes method-of-manufacture patents, which the Hatch-Waxman Act excludes.[152] This is necessary for biologic products, due to the complexity of biologics' structure and manufacture, and the diverse nature of the patents at play.

While the BPTA has many advantages, certain language in the bill creates unnecessary ambiguities. The BPTA defines "patents required to be disclosed" as "any patent for which the holder . . . *believes* a claim of patent infringement could reasonably be asserted by the holder . . . if a person not licensed by the holder

149. *See id.* ("The owner of a patent that should have been included in the list . . ., but was not timely included in such list, *may not bring an action under this section for infringement of the patent*." (emphasis added)).

150. *See* discussion *infra*, Part IV.B.2 for description of IPR proceedings.

151. *See* 21 C.F.R. § 314.53(d)(3) (2021) ("If the required patent information is not submitted within 30 days of the issuance of the patent, FDA will list the patent, but patent certifications . . . will be governed by the provisions regarding untimely filed patent information."). The BPCIA does contain a list-it-or-lose-it provision, but in the context of the patent dance list exchanges. *See* 35 U.S.C. § 271(e)(6)(C).

152. Whereas method-of-manufacture patents are not listed in the Orange Book. *See* 21 U.S.C. § 355(b)(1)(G); 21 C.F.R. 314.53(b) (2021).

engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product."[153] The operative word "believes" is not found in the analogous Hatch-Waxman provision.[154] Does the BPTA, by inclusion of this modifier, entail an inquiry into the state-of-mind of the biologic license holder? If so, is it a subjective or objective inquiry? These questions would require litigation and resolution by the federal courts if the language is not clarified by changes to the Bill. If the language is clarified or interpreted to mean a subjective state-of-mind inquiry, this approach would likely entail greater litigation costs for biologic manufacturers and biosimilar applicants alike. BPCIA litigation is already long and costly. To avoid these substantial uncertainties, the language of the BPTA should mirror that of the Hatch-Waxman Act as to the definition of a "patent required to be disclosed."[155]

The BPTA's companion bill, the Purple Book Continuity Act, became law on December 22, 2020.[156] Although it was the BPTA's companion bill, it differs significantly from the BPTA.[157] The Purple Book Continuity Act aims "to provide for the publication of a list of licensed biological products, and for other purposes."[158] Transparency is not its articulated aim. It requires the FDA to publish a list of all licensed biologics (reference products and biosimilars), including their dates of approval and marketing or licensure status, in "a searchable, electronic format."[159] The Act also

153. *See* BPTA, *supra* note 144, § 2 (emphasis added).

154. *See* 21 U.S.C. § 355(b)(1) (requiring disclosure of "any patent which claims the [small-molecule] drug . . . or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.").

155. *Id.*

156. *See* Consolidated Appropriations Act of 2021, Pub. L. No. 116-246, div. BB, tit. III, § 325, 134 Stat. 1182, 2936–38 (2020). This portion of the appropriations statute is textually identical to the Senate version of the Purple Book Continuity Act of 2020, which the Senate passed by unanimous consent on December 10, 2020. *See* 166 CONG. REC. S7396–97 (daily ed. Dec. 10, 2020).

157. A companion bill is a piece of legislation introduced in the House that is similar or identical to a bill introduced in the Senate. Companion bills are introduced to promote consideration of the legislative measures in both chambers of Congress. The Purple Book Continuity Act differs significantly from the BPTA, as discussed, which is not usually the case. *See* Justin H. Kirkland & Mary A. Kroeger, *Companion Bills and Cross-Chamber Collaboration in the U.S. Congress*, 46 AM. POL. RSCH. 629 (2017) (empirical model of companion bills with respect to their likelihood of surviving the legislative process).

158. *See* Purple Book Continuity Act of 2019, H.R. 1520, 116th Cong. pmbl. (as passed by House, May 8, 2019), https://www.congress.gov/116/bills/hr1520/BILLS-116hr1520eh.pdf [https://perma.cc/VA54-W56M].

159. 42 U.S.C. §§ 262(k)(9)(A)(i)(I)–(III).

requires patent listing in the Purple Book.[160] However, its listing requirement only comes into effect once a patent dance has already begun, and is restricted to the list exchanged in the patent dance, rather than the full list of patents on the reference product.[161] There is also no list-it-or-lose-it provision like that found in the BPTA.

The Purple Book Continuity Act does not serve to adequately increase transparency in the biologics field, for four main reasons. *First*, it delays patent disclosure until after the first biosimilar applicant initiates the patent dance. Under this regime, the first applicant does not have access to the list of patents that protect the reference product. Instead, the first applicant proceeds much as it did before: it submits its application blindly, and only gains access to the patent information if it initiates the patent dance. Market entry for biosimilar applicants who are first-to-file will therefore be just as difficult as it is now, and only those biosimilars who file *after* the first will enjoy the benefits of public patent listing. *Second*, because the disclosure is limited to the list exchanged in the patent dance between the first applicant and the branded manufacturer, subsequent applicants may still need to go through the patent dance process all over again to get disclosure of the patents relevant to them. Subsequent applicants may infringe upon a slightly different set of patents than the first applicant if they use a different method of manufacture, administration device, or method to determine patient suitability for the treatment.[162] For such applicants, the disclosure required by the Purple Book Continuity Act would be inadequate. *Third*, the Purple Book Continuity Act fails to address the possibility that the first biosimilar applicant opts out of the patent dance entirely. In this scenario, no patents would be exchanged, and the branded product would not be compelled to disclose any patents whatsoever. *Fourth*, the Purple Book Continuity Act lacks a list-it-or-lose-it provision, and so does not provide a strong incentive to comply with its disclosure

160. *Id.* § 262(k)(9)(A)(iii).

161. *See id.* ("Not later than 30 days after a list of patents under subsection (*l*)(3)(A), or a supplement to such list under subsection (*l*)(7), has been provided by the reference product sponsor to the subsection (k) applicant . . . the reference product sponsor shall provide such list of patents . . . and their corresponding expiry dates to the Secretary, and the Secretary shall . . . include such information for such biological product.").

162. Wu & Cheng, *supra* note 70, at 121–22 (quantitative case study of three biologic patent thickets with discussion of peripheral patents, and how different biosimilars might infringe a different subset of peripheral patents).

requirements. These features of the Purple Book Continuity Act significantly undermine the purpose of public patent listing, and may well disincentivize biosimilars from being the first to file.

Despite the weaknesses of the Purple Book Continuity Act of 2020 and the BPTA, both indicate a bipartisan push for greater transparency in the biologic patent realm. The BPTA would be an important first step in the greater effort for better biosimilar competition and more affordable biologic drugs.

B. ADMINISTRATIVE PROPOSALS

Reform in the field of biologics need not be solely legislative in nature. Administrative solutions also have significant potential to enhance biosimilar competition and combat patent thickets. Three administrative solutions in particular hold the most promise for biosimilars: lowering the FDA's bar for interchangeability of biosimilars; preserving the institution of inter partes review at the USPTO; and facilitating coordination between agencies charged with the regulation of biologics.

1. *Lowering the Bar for Interchangeability*

First, the FDA should lower the bar for interchangeability. State automatic substitution laws determine to a large extent how easy or difficult it will be for a biosimilar to penetrate the market.[163] Because these laws are tethered to FDA interchangeability determinations, the FDA's standard for this determination is critical to the success or failure biosimilars. The BPCIA gives the FDA considerable discretion as to the type and amount of data necessary to demonstrate interchangeability.[164] This level of discretion is a departure from the Hatch-Waxman Act, which expressly prohibits the FDA from requesting data from a generic applicant beyond that needed to demonstrate bioequivalence.[165] Unfortunately, the FDA has set the bar unnecessarily high for biosimilars

163. *See supra* Part II.A.

164. 42 U.S.C. § 262(k)(4) ("[T]he Secretary shall determine the biological product to be interchangeable with the reference product if the Secretary determines that the information submitted in the application . . . is sufficient to show that [the two requirements for interchangeability are met].").

165. *See* 21 U.S.C. § 355(j)(2)(A)(viii) ("The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii)."); *see also* Mossinghoff, *supra* note 33, at 189 ("[The Hatch-Waxman Act] is a unique piece of legislation because it actually ties the hands of a regulatory agency — in the area of public health — by providing specifically that FDA can require only bioavailability studies for ANDAs.").

by requiring applicants to conduct a switching study to demonstrate that switching between the reference product and the biosimilar does not diminish the safety or efficacy of the drug.[166] Experts contend that this decision is not grounded in a sound public health rationale.[167] The European Medicines Agency and the European Commission have stated that evidence from the past ten years of biosimilar use in Europe "has not identified any relevant difference in the nature, severity or frequency of adverse effects between biosimilars and their reference medicines."[168]

The FDA's requirements for interchangeability only impede biosimilar market penetration, and thereby restrict the affordability and accessibility of biologic medicines for the patients who need them.[169] However, the BPCIA's grant of discretion also gives the FDA flexibility in regulating biologics. The FDA should leverage its statutory grant of discretion and issue new guidance to make interchangeability more attainable for biosimilars. For instance, the FDA could make all biosimilars eligible for automatic substitution by relaxing the interchangeability standard to the level of biosimilarity.[170] Alternatively, it could withdraw the requirement

166. *See FDA Interchangeability Guidance*, *supra* note 45, at 5.

167. *See* Wiland et al., *supra* note 55, at 240 (concluding that there is no clinical evidence that a single switch from an originator to a biosimilar medicine is associated with any significant risk for patient safety or reduction in therapeutic efficacy); Fernando de Mora et al., *Biosimilar and Interchangeable: Inseparable Scientific Concepts?*, BRIT. J. CLINICAL PHARMACOLOGY 2460, 2460 (2019) (arguing that interchangeability is inherent in the definition of biosimilarity, given that there is a "clinically acceptable range of structural heterogeneity for any biological product").

168. EUROPEAN MED. AGENCY & EUROPEAN COMM'N, BIOSIMILARS IN THE EU: INFORMATION GUIDE FOR HEALTHCARE PROFESSIONALS 4 (2019), https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf [https://perma.cc/2P34-3J5E]. The European Medicines Agency (EMA) defines "biosimilar" as "a biological medicine highly similar to another biological medicine already approved in the EU" in terms of "structure, biological activity and efficacy, safety and immunogenicity profile." *Id.* at 3. Biosimilar developers must demonstrate through studies that: (1) their product is highly similar to the reference medicine, and (2) there are no clinically meaningful differences between two in terms of safety, quality and efficacy. *Id.* at 8. In short, the European standard for biosimilarity is comparable to the U.S. standard. The E.U. has more years of experience with biosimilars and has significantly more biosimilars available on the market than does the U.S. *Id.* at 3. The experience with biosimilar safety and efficacy in the E.U. is therefore highly germane to the FDA's decision on the interchangeability standard.

169. As noted, biosimilar products lacking the interchangeability designation are not eligible for automatic substitution at the pharmacy level, and so will likely struggle to gain market share.

170. The BPCIA only requires that in order to be interchangeable, the biological product must be "biosimilar to the reference product," and "can be expected to produce the same clinical result as the reference product in any given patient." 42 U.S.C. §§ 262(k)(4)(A)(i)–(ii). If the FDA were to determine that "biosimilarity" as defined by the statute, *see id.* § 262(i)(2), necessarily means that the product can be expected to produce the same clinical

that biosimilar manufacturers (of drugs to be administered to a patient more than once) conduct a switching study. The FDA could also lower the interchangeability bar for certain classes of biologic products, which may be the preferable approach from a risk management perspective.[171]

In 2018, the FDA announced the Biosimilars Action Plan to spur competition from biosimilars.[172] The Plan involves four main goals: (1) to improve the efficiency of the biosimilar development and approval process; (2) to maximize scientific and regulatory clarity for biosimilar developers; (3) to improve understanding of biosimilars among patients, providers, and payers; and (4) to reduce "gaming of FDA requirements or other attempts to unfairly delay competition."[173] However, the FDA released its current interchangeability guidance after the Biosimilar Action Plan. Whether the agency will harness its full statutory grant of discretion in executing the Plan with respect to the interchangeability standard remains to be seen.[174] Any of the measures outlined in this subsection would make interchangeability a more feasible goal, allow for better market penetration, and encourage investment in biosimilar ventures.

2. *Preservation of IPR*

Second, the inter partes review (IPR) process must be upheld by the courts and legislators against likely challenges as a powerful mechanism for challenging the validity of low-value patents. Established in 2011 by the America Invents Act, IPR proceedings allow any third party to challenge the validity of a patent on novelty or obviousness grounds.[175] The usual presumption of patent validity does not apply in IPR, and challengers must only satisfy a preponderance standard in order to prevail.[176] Biosimilar competitors have eagerly issued patent challenges to biologic patents via

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result in any given patient, then all biosimilars would effectively be deemed "interchangeable."

171. *See id.* §§ 262(k)(8)(D)(i)–(ii).

172. *See generally* U.S. FOOD & DRUG ADMIN., BIOSIMILARS ACTION PLAN: BALANCING INNOVATION AND COMPETITION (2018), https://www.fda.gov/media/114574/download [perma.cc/67WP-7XQF].

173. *Id.* at 5.

174. *See* Gottlieb Speech, *supra* note 21 (announcing the FDA's Biosimilar Action Plan).

175. *See generally* 35 USC §§ 311–319 (inter partes review).

176. 35 U.S.C. § 316(e).

IPR.[177] However, such challenges are currently restrained by the lack of transparency as to the type and number of patents that exist on the reference product. If the BPTA is enacted and public patent listing becomes a requirement, industry stakeholders may mount legislative, regulatory, and legal challenges to the institution of IPR in attempts to insulate their disclosed patents from post grant review.[178] However, IPR should be upheld on all fronts. The ability to challenge patents via IPR will be instrumental in pruning the field of low-value patents and paving the way for more biosimilars.

3. *Inter-Agency Coordination*

Third, an effective regime for biologics requires coordination between agencies. Biologic drug regulation falls at the intersection of public health, innovation, and antitrust policy. The FDA possesses the chief authority to make and implement rules and regulations in this arena, but the USPTO and FTC also have important roles to play.[179]

The FTC in particular has played a crucial role in the small-molecule field by shaping the 2003 amendments to the Hatch-Waxman Act that made it less prone to regulatory abuses;[180] challenging anticompetitive patent litigation settlements;[181] weighing in on

177. *Robert Cerwinski: Recent Trends in PTAB Decisions on Biologics, Biosimilars*, AM. J. MANAGED CARE, CTR. FOR BIOSIMILARS (Aug. 29, 2017) https://www.centerforbiosimilars.com/view/robert-cerwinski-recent-trends-in-ptab-decisions-on-biologics-biosimilars [perma.cc/JJ6A-UGU9] (noting upward trends in the number of IPRs filed by biosimilar manufacturers prior to market launch).

178. For legal challenges, see Oil States Energy Servs., LLC v. Greene's Energy Grp., LLC, 138 S. Ct. 1365 (2018) (upholding IPR against constitutional challenge, and holding that IPRs violated neither Article III nor the Seventh Amendment); Celgene Corp. v. Peter, 931 F.3d 1342 (Fed. Cir. 2019) (upholding IPR against constitutional challenge claiming that retroactive application of IPR to pre-AIA patents violated the takings clause), *cert. denied*, 141 S. Ct. 132 (2020); Enzo Life Scis., Inc. v. Becton, Dickinson & Co., 780 F. App'x 903 (Fed. Cir. 2019) (following *Celgene*), *cert. denied*, 140 S. Ct. 2634 (2020); Collabo Innovations, Inc. v. Sony Corp., 778 F. App'x 954, 961 (Fed. Cir. 2019) (following *Celgene*); *see also* St. Regis Mohawk Tribe v. Mylan Pharms., Inc., 896 F.3d 1322 (Fed. Cir. 2018) (rejecting Allergan's attempt to shield patent from IPR by transferring patent rights to a tribal entity and invoking the doctrine of sovereign immunity), *cert. denied*, 139 S. Ct. 1547 (2019).

179. 21 U.S.C. § 371(a).

180. *See* FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY (2002), https://www.ftc.gov/sites/default/files/documents/reports/generic-drug-entry-prior-patent-expiration-ftc-study/genericdrugstudy_0.pdf [perma.cc/YGV5-DDFJ].

181. *See, e.g.*, FTC v. Actavis, Inc., 570 U.S. 136 (2013) (FTC suit alleging that pharmaceutical manufacturer's reverse payment agreements amounted to antitrust violations).

antitrust cases between branded and generic manufacturers;[182] and monitoring manufacturers' ongoing compliance with antitrust regulations.[183] In February 2020, the FTC and FDA released a joint statement announcing their intention to collaborate in regulating the biologics market.[184] The agencies identified four main goals: (1) "to promote greater competition in biologic markets" by developing materials to educate consumers and providers about biosimilars; (2) "to deter behavior that impedes access to samples needed for the development of biologics, including biosimilars"; (3) "to take appropriate action against false or misleading communications about biologics, including biosimilars"; and (4) for the FTC to "review patent settlement agreements involving biologics, including biosimilars, for antitrust violations."[185]

The agencies' intention to collaborate in this effort is good news for biosimilars, but the stated goals may not go far enough. To maximize its impact, the FTC should issue a report on the antitrust issues presented by biologic patent thickets. If the BPTA amends the BPCIA, a report from the FTC on this issue would greatly inform the drafting effort. The FTC should also uncover and prosecute other anti-competitive behaviors by biologic manufacturers, such as the practice of "rebate traps," or exclusionary contracts with insurers that offer discounts on the branded biologic in exchange for exclusive approval of the brand-name.[186]

Though the USPTO has historically been more limited than other agencies in its rulemaking authority, the 2011 America

182. *See* Brief for Fed. Trade Comm'n as Amicus Curiae at 6, Mylan Pharms., Inc. v. Warner Chilcott Pub. Ltd. Co., 2013 WL 5692880 (E.D. Pa. June 12, 2013) (No. 2:12-cv-03824), 2012 WL 7649225.

183. *See* FED. TRADE COMM'N, AGREEMENTS FILED WITH THE FEDERAL TRADE COMMISSION UNDER THE MEDICARE PRESCRIPTION DRUG, IMPROVEMENT, AND MODERNIZATION ACT OF 2003: OVERVIEW OF AGREEMENTS FILED IN FY 2016 (2019), https://www.ftc.gov/news-events/press-releases/2019/05/ftc-staff-issues-fy-2016-report-branded-drug-firms-patent [perma.cc/CEN7-5PWN].

184. Statement, Stephen M. Hahn, Comm'r, Food & Drug Admin., & Joseph J. Simons, Chair, Fed. Trade Comm'n, Joint Statement of the Food & Drug Administration and the Federal Trade Commission Regarding a Collaboration to Advance Competition in the Biologic Marketplace (Feb. 3, 2020), https://www.ftc.gov/system/files/documents/public_statements/1565273/v190003fdaftcbiologicsstatement.pdf [perma.cc/HF28-Q3P4].

185. *Id.* at 4–6.

186. *See* Zhai et al., *supra* note 86, at 671; *see also* James D. Chambers et al., *Coverage for Biosimilars vs Reference Products Among US Commercial Health Plans*, 323 JAMA 1972, 1972–73 (2020) (finding that U.S. health plans cover biosimilars as preferred in only 14 percent of coverage decisions, and identifying rebate agreements as a possible source of this disparity). This practice recently gave rise to an antitrust lawsuit against Johnson & Johnson in connection with its biologic drug Remicade. *See* Walgreen Co. v. Johnson & Johnson, 375 F. Supp. 3d 616 (E.D. Pa. 2019).

Invents Act empowered it to set standards of review and procedures for post-grant proceedings, along with other new procedural and quasi-substantive powers.[187] The policies, standards, and procedures of the USPTO have consequences for the regulation of drugs and drug markets. Specifically, the agency can set standards of review and make procedural choices in ways that facilitate patent challenges.[188] Furthermore, for IPR to take place, the challenger first has to file a petition to institute IPR; the USPTO then makes a decision whether to institute the proceeding or not.[189] To facilitate such challenges, the USPTO could increase the rate at which it institutes IPR, which has consistently declined over the past eight years.[190] These choices would help to invalidate patents of questionable validity before they are asserted against a biosimilar in BPCIA litigation.

Moreover, the FDA could coordinate with the USPTO to identify potentially invalid patents. If the FDA shared data from biologics license applications with the USPTO, the USPTO may be able to pick out those "impossible patents" discussed in Part II.C, and either strike the claims or cabin them to their appropriate scope.[191] Sharing of data between agencies could occur in the patent application process or at post grant review. In general, collaboration between agencies will leverage the combined expertise of the FDA, FTC, and USPTO, and allow for flexible, dynamic, and innovative modes of regulating the biologics market.

V. CONCLUSION

The field of biologics is in critical need of reform. Biologic drugs are transformative, and in many cases life-saving. But they come at an exponential cost. Robust competition from biosimilars would lower prices and expand access to treatment, but have so far failed to penetrate the U.S. market. Among the many barriers to market

187. *See* 35 U.S.C. §§ 2(b)(2)(A)–(G); *see generally* Sarah Tran, *Patent Powers*, 25 HARV. J.L. & TECH. 609 (2012) (describing the America Invents Act as marking a "new era in patent law" in terms of the extent and array of powers it grants to the USPTO).

188. *See* Jonathan Tamimi, *Breaking Bad Patents: The Formula for Quick, Inexpensive Resolution of Patent Validity*, 29 BERKELEY TECH. L.J. 587, 626–31 (2014) (discussing unsettled questions of IPR procedure).

189. *See* 35 U.S.C. §§ 311, 314.

190. PAT. TRIAL & APPEAL BD., U.S. PAT. & TRADEMARK OFF., TRIAL STATISTICS: IPR, PGR, CBM 6 (2020), https://www.uspto.gov/sites/default/files/documents/trial_statistics_20200131.pdf [perma.cc/Z5M7-JTVX].

191. *See* Price & Rai, *supra* note 19, at 862–63.

entry that biosimilars face, patent thickets are the most daunting. Patent thickets flourish thanks to the lack of public patent listing and the protracted nature of litigation under the BPCIA. In this regulatory landscape, branded biologic manufacturers are free to insulate their products from competition and thereby lock in the steep prices of these drugs for periods longer than contemplated by statute. Ultimately, the public bears the cost.

Yet the time is ripe for change. Legislative proposals combined with administrative solutions have the power to spur biosimilar competition, lower the prices of biologic drugs, and expand access to treatment. Public patent listing, as set forth in the BPTA, will expose the patent thickets and patenting strategies that stifle biosimilar competition. The joint efforts of the FDA, USPTO, and FTC will pave the way for more biosimilars to reach the market and compete successfully with branded products. The biologics market is currently a system that suffers from inadequate competition, but a better balance is within our grasp. The rising costs of drug spending in the United States, the rapid growth of the biologic drug sector, and the interests of the public demand it.