DESTINED FOR FAILURE? AN ANALYSIS OF THE BIOLOGICS PRICE COMPETITION AND INNOVATION ACT OF 2009

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In 2010, Congress enacted the Biologics Price Competition and Innovation Act ("BPCIA") as part of the large health care reform bill. The BPCIA creates a statutory pathway for FDA approval of "biosimilars"—which are generic versions of biologic drugs. Congress expects this new approval pathway for biosimilars to help lower biologics prices, just as generic drugs have significantly lowered pharmaceutical prices.

This Note argues that, for three main reasons, the BPCIA will not succeed in lowering drug prices to the same degree that generic pharmaceuticals have. First, biosimilars are more expensive to develop than generic pharmaceutical drugs. Manufacturers will be hesitant to enter the biosimilars market, leading to less competition. Second, biosimilars will struggle more than generics to capture market share from the branded drug. Third, lengthy exclusivity periods awarded to the branded biologic and the first interchangeable biosimilar will substantially delay biosimilar market entry. This Note then concludes with suggestions for improving the BPCIA, both through potential amendments and regulatory process.

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I. INTRODUCTION

In 2002, after years of suffering from debilitating arthritis, Bonnie Cramer began to take a new drug called Enbrel.[1] Unlike a traditional pharmaceutical, Enbrel is a biologic: a large, complex molecule derived from cell cultures.[2] According to the Food and Drug Administration ("FDA"), biologics often represent the cutting edge of medical science and research.[3] Biologics are "may make it possible to treat a variety of medical conditions, including illnesses for which no other treatments are available."[4] In recent years, biologics have provided breakthroughs in treating various cancers, multiple sclerosis and rheumatoid arthritis.[5]

The day after Mrs. Cramer's first injection with Enbrel, she climbed out of bed without help.[6] During the six years Mrs. Cramer took Enbrel, she felt as though her arthritis

1 Barbara Barrett, *Health Care Bill Includes Generic Path for Biologic Drugs*, MCCLATCHY WASH., Nov. 30, 2009, http://www.mcclatchydc.com/2009/11/29/v-print/79540/health-care-bill-includes-generic.html.

2 *See* Henry G. Grabowski, *Data Exclusivity for Biologics: What Is the Appropriate Period of Protection?*, AEI ONLINE Sept. 2009 at 1, http://www.aei.org/files/2009/09/08/10-HPO-Grabowski-Sep08-g.pdf.

3 *FDA 101: Regulating Biological Products*, FDA, http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048341.htm (last visited Feb. 19, 2013).

4 *Id.*

5 *See* Grabowski, *supra* note 2, at 1.

6 Barrett, *supra* note 1.

had disappeared.[7] However, Enbrel costs approximately $48,000 per year.[8] Other biologics are just as expensive.[9] Lawmakers and doctors alike have often acknowledged that biologic drugs are too expensive for many patients to afford.[10] Helping drive these astronomical prices is the fact that until 2010, the FDA was not permitted to approve generic versions of biologics like Enbrel.

In 2010, Congress enacted the Biologics Price Competition and Innovation Act ("BPCIA")[11] as part of the Patient Protection and Affordable Care Act ("ACA"). The BPCIA will restructure the biotechnology industry by creating a statutory pathway for FDA approval of "biosimilars," which are generic versions of biologic drugs.[12] Congress enacted the BPCIA in an attempt to tackle the problem of rising biologics prices. Congress expects the new approval pathway for biosimilars to help lower biologics

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7 Barrett, *supra* note 1.

8 JUDITH A. JOHNSON, CONG. RESEARCH SERV., RL34045, FDA REGULATION OF FOLLOW-ON BIOLOGICS 1 (2010), *available at* http://primaryimmune.org/advocacy_center/pdfs/health_care_reform/Biosimilars_Congressional_Research_Service_Report.pdf.

9 The Congressional Research Service reports that "the cost of therapeutic biologics is often prohibitively high for individual patients." *Id.* Treatment for breast cancer with Herceptin costs up to $48,000 annually, treatment for Crohn's disease with Humira costs $51,000, and treatment for Gaucher's disease with Cerezyme costs $200,000. *Id.* Biologics cost, on average, twenty-two times as much as traditional pharmaceutical drugs. Anthony D. So & Samuel L. Katz, Op-Ed, *Biologics Boondoggle*, N.Y. TIMES, Mar. 10, 2010, at A23.

10 *See* Letter from Rep. Anna Eshoo et al. to President Barack Obama (Oct. 14, 2011), *available at* http://patentdocs.typepad.com/files/house-letter.pdf (stating that "many of these remarkable drugs are out of reach for patients"); *see also* Barrett, *supra* note 1 (recounting that doctors and patient advocates alike "say they've seen heartbreaking stories about patients who can't afford the pricey medicines").

11 Patient Protection and Affordable Care Act, Pub. L. No. 111-148, §§ 7001–03, 124 Stat. 119, §§ 804–21 (2010) (codified at 42 U.S.C. §262).

12 Richard A. Epstein, *The Constitutional Protection of Trade Secrets and Patents Under the Biologics Price Competition and Innovation Act of 2009*, 66 FOOD & DRUG L.J. 285, 286 (2011).

prices, just as generic drugs have significantly lowered pharmaceutical prices.[13]

Generic pharmaceuticals have been available since 1984, when Congress passed the Hatch-Waxman Act. In the quarter of a century since the passage of the law, Hatch-Waxman has had significant success in controlling the costs of pharmaceuticals. According to the Federal Trade Commission ("FTC"), "the first generic entrant generally offers a price that is 25 percent lower than the branded drug's price. The price discount can rise to 80 percent with multiple generic entrants."[14] Proponents of the BPCIA hope that biosimilars will spur an analogous price discount.

However, biologics and pharmaceuticals differ in many important ways. This Note will argue that the BPCIA, as written, will not be as successful in reducing drug prices as Hatch-Waxman. Part II will provide a brief background on both biologics and the BPCIA. Biologics and pharmaceuticals are regulated under different federal statutes, and the Hatch-Waxman Act only amended the statute regulating pharmaceuticals. Biosimilars, therefore, could not be approved under federal law until the BPCIA was passed.

Part III will argue that the BPCIA will not be as successful in bringing down drug prices as Hatch-Waxman. Biosimilars are more expensive to develop than generic pharmaceutical drugs, which will lead to less competition in the market because fewer biosimilars will be produced. Additionally, biosimilars will struggle more than generics to capture market share from the branded drug. Finally, lengthy exclusivity periods awarded to the branded drug and the first interchangeable biosimilar will ensure that biologic

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13 Letter from Rep. Anna Eshoo et al. to Barack Obama, *supra* note 9, at 1 ("Following in the footsteps of the earlier Hatch-Waxman Act, which ushered in a new era of competition and affordable drugs, the [BPCIA] would for the very first time allow patients access to generic, cheaper versions of biologic drugs.").

14 FTC, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION 12 (2009) [hereinafter FTC REPORT], *available at* www.ftc.gov/os/2009/06/po83901biologicsreport.pdf.

prices will not drop as quickly as pharmaceutical prices under Hatch-Waxman.

Part IV will recommend that Congress and the FDA act to improve the BPCIA. First, Congress can create a tax structure that incentivizes the manufacture of biosimilars. Having more biosimilars on the market will lead to lower prices. Second, the FDA can issue guidance documents to ensure that biosimilar manufacturers understand the regulatory approval process. Regulatory predictability and transparency will help entice more firms into the biosimilars arena. Third, Congress can reduce the exclusivity period for branded drugs from twelve to seven years. Biosimilars will be able to enter the market more quickly, and prices will fall as a result.

II. BACKGROUND ON BIOLOGICS AND THE BPCIA

A. Regulation of Biologics

Biologics are "medical products derived from living sources (animals, humans, and microorganisms) and include viruses, therapeutic serums, toxins and antitoxins, vaccines, blood and blood products, and cells, tissues and gene therapy products."[15] Biologics differ from traditional pharmaceutical drugs in a number of ways. First, biologics originate from living sources, while pharmaceuticals originate from chemically synthesized sources.[16] Second, biologics are more complex macromolecular entities, consisting of proteins

15 *See* Jordan Paradise, *Follow-On Biologics: Implementation Challenges and Opportunities*, 41 SETON HALL L. REV. 501, 502 (2011). Under federal law, a biologic is defined as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide) or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C.A. § 262(i) (West 2012).

16 Paradise, *supra* note 15, at 503.

whose structure is determined by four organizational levels: the sequence of amino acids in the protein chain, the spatial configuration of the amino acids within the chain, any three dimensional folding that occurs, and the interactions between different chains.[17] Third, biologics are typically manufactured using more sophisticated techniques, and due to the complexity of protein structure—the final biologic product is extremely susceptible to even the slightest changes in the manufacturing process.[18]

Due to a complicated legislative history, biologics and pharmaceuticals are regulated under different federal statutes. In 1938, Congress passed the Federal Food, Drug and Cosmetic Act ("FDCA")[19] to strengthen federal oversight of drugs.[20] The FDCA's definition of drug was broad enough to capture both pharmaceuticals and biologics.[21] Under the FDCA, a new drug[22] must be tested for safety in humans before the drug is released to the market.[23] The sponsor of the drug must submit a New Drug Application ("NDA"),

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17 *See generally* JOHNSON, *supra* note 8, at 10 ("A protein is a large organic molecule composed of a long chain of component parts, called amino acids, which are linked by chemical bonds. This amino acid chain folds into a complex three-dimensional structure").

18 Paradise, *supra* note 15, at 503.

19 Food, Drug and Cosmetic Act ("FDCA"), Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended in scattered sections of 21 U.S.C.).

20 Krista H. Carver, Jeffrey Elikan & Erika Lietzan, *An Unofficial Legislative History of the Biologics Price Competition and Innovation Act of 2009*, 65 FOOD & DRUG L.J. 671, 673 (2010).

21 *Id.*

22 The FDCA defined "new drug" as

> [A]ny drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the condition prescribed, recommended, or suggested in the labeling thereof . . . .

Food, Drug, and Cosmetic Act, § 201(p), 21 U.S.C.A. § 321 (West 2012).

23 Carver et al., *supra* note 20, at 673.

which is reviewed for approval by the Center for Drug Evaluation and Research ("CDER").[24]

However, six years after passing the FDCA, Congress passed the Public Health Service Act ("PSHA").[25] The PHSA specified that biologic drugs would from then on be approved under Section 351 of the PHSA while pharmaceuticals continued to be approved under the FDCA.[26] In 1997, Congress passed the Food and Drug Administration Modernization Act ("FDAMA"), which amended the PHSA to require sponsors to submit a Biologics License Application ("BLA") when seeking FDA approval of a biologic.[27] BLAs are reviewed either by the Center for Biologics Evaluation and Research ("CBER") or by CDER, depending on the product type.[28] The BLA approval process for biologics closely parallels the NDA approval process for pharmaceuticals; however, these processes remain under separate statutory authority.[29]

B. Abbreviated Routes to Market Under the FDCA

Before the BPCIA was passed, this bifurcated statutory authority led to the existence of an abbreviated route to market for generic pharmaceuticals without a similar pathway for biosimilars. The Drug Price Competition and Patent Term Restoration Act,[30] often referred to as the Hatch-Waxman Act, created abbreviated routes to market for generic versions of drugs under the FDCA but not under

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24 *See* Paradise, *supra* note 15, at 503 (citing *New Drug Application ("NDA")*, FDA, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.htm (last visited Mar. 19, 2013)).

25 Public Health Service Act, Pub. L. No. 78-410, 58 Stat. 682 (1944) (codified as amended in scattered sections of 42 U.S.C.).

26 *See* JOHNSON, *supra* note 8, at 6.

27 *Id.*

28 Paradise, *supra* note 15, at 503.

29 *Id.* at 504.

30 Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended in scattered sections of 15, 21, 35, and 42 U.S.C.).

the PHSA.[31] The Hatch-Waxman Act established two new sections of the FDCA under which generic versions of brand-name pharmaceutical drugs could be approved.[32]

The first pathway is through an Abbreviated New Drug Application ("ANDA"), established in FDCA section 505(j).[33] Under the ANDA pathway, the generic drug sponsor must prove bioequivalence with the brand-name reference drug through comparison studies.[34] To prove bioequivalence, comparison studies must show that "the product has the same active ingredient(s) as the reference product and the same route of administration, dosage form, and strength."[35] The FDA is not permitted to request preclinical or clinical data to support the generic drug's approval.[36] Proving bioequivalence permits the generic drug sponsor to rely on the FDA's previous findings of safety and efficacy of the reference product in the ANDA.[37] Therefore, the sponsor of the generic drug does not have to engage in the lengthy and expensive clinical trial process. It is typically not difficult to show bioequivalence because the structure of traditional pharmaceutical drugs can be verified analytically and copied by the generic manufacturer.[38] Most of the generics that are

31 JOHNSON, *supra* note 8, at 7.

32 *Id.*

33 21 U.S.C. § 355(j) (2011).

34 Paradise, *supra* note 15, at 504. *See also* FTC REPORT, *supra* note 14, at 7 n.15 ("Bioequivalence means that the rate and extent of the absorption of the generic drug is not significantly different from the rate and extent of absorption of the reference listed drug when administered at the same dosage.").

35 Carver, *supra* note 20, at 677 (citing 21 U.S.C. § 505(j)(2)(A)(ii)-(iii) (2011)).

36 21 U.S.C. § 505(j)(2)(A) (2011).

37 JOHNSON, *supra* note 8, at 7.

38 *See generally* Janet Woodcock et al., *The FDA's Assessment of Follow-On Protein Products: A Historical Perspective*, 6 NATURE REVS. DRUG DISCOVERY 437, 437 (2007) ("Non-protein, small-molecule drugs are typically organic molecules of low molecular mass and known structure. Because the molecular structure of such a drug can usually be verified analytically, it is fairly easy for a generic-drug manufacturer to produce a duplicate product containing an active ingredient that is the same as the active ingredient in an innovator's approved drug product.").

found on the shelves of pharmacies have been approved under Section 505(j).[39]

The second pathway, Section 505(b)(2),[40] allows for the approval of "a drug that has a significant difference from an innovator drug, but is still sufficiently *similar* to [the innovator] drug."[41] A sponsor files under 505(b)(2) when the new drug application "contains full reports of investigations of safety and effectiveness but where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference."[42] A 505(b)(2) application is permitted to rely upon published literature and the FDA's previous findings of safety and effectiveness for an approved drug.[43] However, the FDA may also require the sponsor to provide additional non-clinical and clinical data.[44]

The 505(b)(2) application pathway may have acted as a framework for the BPCIA. Due to a regulatory irregularity, a small set of biologic products (mostly hormones) are regulated as drugs under the FDCA rather than as biologics under the PHSA.[45] In 2003, the biologic manufacturer Sandoz filed a 505(b)(2) application for Omnitrope, a biologic human growth hormone, citing the previously approved Genotropin as the reference product.[46] When the FDA did not act on the application for two years, Sandoz filed suit in federal court, claiming that the FDA had violated its

39 *See generally* JOHNSON, *supra* note 8, at 7 (stating that the 505(j) pathway is used for the approval of most generic pharmaceutical drugs).

40 21 U.S.C. § 355(b)(2) (2011).

41 JOHNSON, *supra* note 8, at 7.

42 CTR. FOR DRUG EVALUATION AND RESEARCH, FDA, GUIDANCE FOR INDUSTRY: APPLICATIONS COVERED BY SECTION 505(b)(2), at 1 (1999), *available at* http://www.fda.gov/downloads/Drugs/GuidanceCompliance RegulatoryInformation/Guidances/ucm079345.pdf (quoting 21 U.S.C. § 505(b)(2)).

43 *Id.* at 2.

44 JOHNSON, *supra* note 8, at 7.

45 *Id.*

46 Sandoz, Inc. v. Leavitt, 427 F. Supp. 2d 29, 32 (D.D.C. 2006).

statutory obligation to act on applications within 180 days.[47] The court ruled that the FDA must consider Sandoz's 505(b)(2) application,[48] and in 2006, the FDA approved the 505(b)(2) application for Omnitrope.[49] However, in its decision letter, the FDA emphasized that the Omnitrope review process was simplified because human growth hormones can be more easily compared to one another than most biologics.[50] Although the FDA drafted the decision letter narrowly, "limiting its scientific and legal conclusions to the product and application before it, many believed that [this decision] signaled to Congress that the agency was prepared to begin approvals of biosimilars."[51]

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47 JOHNSON, *supra* note 8, at 3.

48 *Sandoz*, 427 F. Supp. 2d at 33.

49 COVINGTON & BURLING, FDA APPROVAL OF SANDOZ'S 505(b)(2) APPLICATION FOR A FOLLOW-ON RECOMBINANT HUMAN GROWTH HORMONE PRODUCT 2 (2006), *available at* http://www.cov.com/files/Publication/8405cdb8-b5ca-4050-a2a784ea54b23aac/Presentation/Publication Attachment/356e78e0-06fc-45e3-b0b8-9385b2b205b0/oid20985.pdf.

50 *See* Letter from FDA to Kathleen M. Sanzo, Stephan E. Lawton & Stephen G. Juelsgaard 7 (May 30, 2006) [hereinafter FDA Decision Letter], *available at* http://www.fda.gov/ohrms/dockets/dockets/04p0231/04p-0231-pdn0001.pdf. The FDA Decision Letter lists four characteristics of human growth hormone ("hGH") that facilitate comparisons:

> 1) hGH is a single-chain, 191 amino acid, non-glycosylated protein with two intramolecular disulfide bonds.
>
> 2) hGH is readily purified for structural assessments. The primary structure of hGH is known, and physicochemical tests exist for the determination of an hGH product's secondary and tertiary structures . . . .
>
> 3) Clinically relevant bioassays and qualified biomarkers are available for hGH. The mechanism of drug action is known and the human toxicity profile is well understood . . . .
>
> 4) hGH has a long history of clinical use as replacement therapy for endogenous GHD and its safety and efficacy profile is thoroughly described in the literature and well understood.

Id.

51 Carver et al., *supra* note 20, at 706.

C. The BPCIA

In 2006, Representative Henry Waxman introduced the first biosimilars bill in the House of Representatives.[52] Senator Charles Schumer introduced a similar bill in the Senate.[53] These bills "would have permitted a case-by-case approach with respect to clinical and other data supporting licensure of the biosimilar."[54] Such an approach contrasts sharply with the ANDA process, which specifies the data and information that the FDA is permitted to request in evaluating an ANDA.[55] The bills also did not provide a data exclusivity period for brand-name products.[56]

Biosimilars bills were introduced in every congressional session after 2006, but no such bill passed in either the House or the Senate until the BPCIA was included in the recent health care reform legislation.[57] The BPCIA "amends certain existing provisions of Section 351 [of the PHSA] and adds . . . new subsections at the end of Section 351: new Subsection (k) sets forth the regulatory pathway for the approval of [biosimilar] products; new subsection (l) sets forth the rules for identifying and resolving patent disputes."[58]

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52 *See* H.R. 6257, 109th Cong. (2006).

53 *See* S. 4016, 109th Cong. (2006).

54 Carver et al., *supra* note 20, at 716.

55 *Id.*

56 *Id.* at 717.

57 *Id.* at 716–806 (describing—before the passage of the BPCIA—the introduction of biosimilar bills in every session of Congress beginning in 2006). *See also* Martha M. Rumore, *The Hatch-Waxman Act—25 Years Later: Keeping the Pharmaceutical Scales Balanced*, PHARMACY TIMES, Aug. 15, 2009, *available at* http://www.pharmacytimes.com/publications/supplement/2009/genericsupplement0809/generic-hatchwaxman-0809 (stating that Congress failed to pass biosimilars initiatives because an agreement could not be reached on the data exclusivity period innovative biologics would enjoy).

58 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, 231–32 (2010).

Subsection (k) creates approval pathways for submission of a BLA that is either "biosimilar" to or "interchangeable" with the reference product.[59] In order to support a determination of biosimilarity, sponsors of biosimilars must meet five requirements. First, the sponsor must show that the product is biosimilar to the reference product.[60] A product is biosimilar if it is highly similar to the reference product, notwithstanding minor differences in clinically inactive components.[61] The sponsor must provide data from analytical studies, animal studies (including the assessment of toxicology), and clinical studies that demonstrate safety, purity, and potency.[62] Second, the sponsor must show that the biosimilar and reference product utilize the same mechanism of action for the condition or conditions of use prescribed in the proposed labeling, but only to the extent that the mechanism of action is known.[63] Third, the sponsor must demonstrate that reference product has been approved for the condition or conditions of use prescribed in the proposed labeling.[64] Fourth, the sponsor must provide evidence that the biosimilar and reference product possess the same route of administration, dosage form, and strength.[65] Finally, the sponsor must show that the facility in which the biosimilar is manufactured, processed, packed, or held meets standards designed to assure that the biosimilar continues to be safe, pure, and potent.[66] However, the bill gives the FDA broad authority to deem any of the above five requirements unnecessary for a particular biosimilar application.[67]

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59 Biosimilarity requirements are laid out under 42 U.S.C. § 262(k)(2)(A)(i) (2011), while interchangeability requirements are laid out under § 262(k)(4).

60 42 U.S.C.A. § 262(k)(2)(A)(i)(I) (West 2012).

61 *Id.*

62 *Id.*

63 *See id.* § 262(k)(2)(A)(i)(II).

64 *See id.* § 262(k)(2)(A)(i)(III).

65 *See id.* § 262(k)(2)(A)(i)(IV).

66 42 U.S.C.A. § 262(k)(2)(A)(i)(V) (West 2012).

67 *See id.* § 262(k)(2)(A)(ii).

A showing of interchangeability requires the sponsor to clear a higher hurdle. First, the sponsor must show biosimilarity.[68] Second, the sponsor must show that the biosimilar can be expected to produce the same clinical result as the reference product in any given patient.[69] Third, the sponsor must show that for a biologic administered more than once to a patient, the "risk in terms of safety or diminished efficacy of alternating or switching between use of the [biosimilar] and the reference product is not greater than the risk of using the reference product without such alteration or switch."[70]

Subsection (k) also describes exclusivity provisions for both the reference product and the first biosimilar to reach the market.[71] The BPCIA grants twelve years of exclusivity to reference products; no biosimilar may be approved until twelve years after the reference product was first licensed.[72] However, scholars have noted that the BPCIA does not specify the type of exclusivity it provides.[73] The FDA has tentatively "interpreted the language of the BPCIA to provide twelve years of market exclusivity, while some members of Congress and industry argue that it provides either twelve years of data exclusivity or four years of data exclusivity followed by eight years of market exclusivity."[74] The difference is significant; if biosimilar manufacturers are forced to wait twelve years to get access to the reference product's data, the reference product will likely be alone on the market for far longer than twelve years.[75] The BPCIA

68 42 U.S.C.A. § 262(k)(4)(A)(i) (West 2012).

69 *See id.* § 262(k)(4)(A)(ii).

70 *See id.* § 262(k)(4)(B).

71 *See id.* § 262(k)(7).

72 *See id.* § 262(k)(7)(A).

73 Paradise, *supra* note 15, at 507.

74 *Id.*

75 *See generally* Alicia Mundy, *Firms Push for Biotech Generics*, WALL ST. J., Jan. 26, 2011, at B1 ("The question [surrounding exclusivity] is whether makers of generics have to wait the whole period before even beginning to seek approval—or can get a head start with regulators so their copies can hit the shelves as soon as the 12 years are up.").

also provides a shorter period of market exclusivity for the first interchangeable biosimilar approved for each reference drug.[76]

Subsection (l) establishes the rules related to the exchange of patented information between the sponsor of the biosimilar and the sponsor of the reference product.[77] The full patent provisions are outside the scope of this Note; however, it is important to note significant areas of departure from the Hatch-Waxman Act. First, the scope of patents the sponsor must identify under the BPCIA is broader than under Hatch-Waxman.[78] The BPCIA patent provisions include not only patents that relate to the biosimilar and methods of use, but also "patents relevant to the product's manufacturing process."[79] Second, under the Hatch-Waxman Act, the approval of a generic is automatically stayed upon the filing of a patent infringement suit.[80] Under the BPCIA, however, the patentee must obtain a final judgment of infringement before approval is stayed, requiring that no appeal other than a petition for certiorari is available.[81] Further, even a final judgment does not result in an automatic stay of approval, but instead, an injunction against infringement of the patent.[82]

III. WILL THE BPCIA PROVE AS SUCCESSFUL AS HATCH-WAXMAN?

The Hatch-Waxman Act has had significant success in lowering the prices of pharmaceutical drugs. As previously noted, "the first generic entrant generally offers a price that is 25 percent lower than the branded drug's price. The price discount can rise to 80 percent with multiple generic

76 Public Health Service Act § 351(k)(6), 42 U.S.C.A. § 262(k)(6) (West 2012).

77 *See id.* § 351(l), 42 U.S.C.A § 262(l) (West 2012).

78 Dougherty, *supra* note 58, at 234.

79 *Id.*

80 *See id.*

81 *Id.*

82 *Id.*

entrants."[83] More than seventy percent of pharmaceutical prescriptions are written for generic drugs, creating substantial cost savings for consumers and insurers.[84] However, as currently written, the BPCIA is unlikely to have as much success in lowering drug prices as the Hatch-Waxman Act.

Three main factors suggest that the BPCIA will not be as successful in bringing down prices as Hatch-Waxman. First, biosimilars are more expensive to develop than generic pharmaceuticals, which will lead to fewer entrants into the biosimilar market and thus less competition. Less competition will lead to stagnant prices. Second, biosimilars will not capture market share from the branded drug as quickly as generic pharmaceuticals do. Third, lengthy exclusivity periods awarded to both the innovative biologic and the first interchangeable biosimilar will marginalize the BPCIA's ability to quickly reduce costs.

A. Biosimilars Are More Expensive to Develop

The cost of developing a biologic is roughly equal to the cost of developing a pharmaceutical.[85] However, this equivalence in cost does not extend to biosimilars and generics.[86] Experts have estimated that biosimilars will take eight to ten years to develop, and will cost between $100 and $200 million.[87] In contrast, the cost to develop a generic pharmaceutical typically ranges from $1 to $5 million, a difference of two orders of magnitude.[88] This difference in manufacturing cost stems from two major factors. First,

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83 FTC REPORT, *supra* note 14, at 12.

84 Rumore, *supra* note 57.

85 Henry G. Grabowski, Genia Long & Richard Mortimer, *Implementation of the Biosimilar Pathway: Economic and Policy Issues*, 41 SETON HALL L. REV. 511, 550 (2011).

86 FTC REPORT, *supra* note 14, at 14.

87 *The European Biosimilars Market: Trends and Key Success Factors*, SCICASTS (Oct. 27, 2008), http://scicasts.com/specialreports/20-biopharmaceuticals/2152-the-european-biosimilars-market-trends-and-key-success-factors.

88 FTC REPORT, *supra* note 14, at 14.

biosimilar sponsors will incur increased costs due to the complexity of manufacturing a large-molecule protein.[89] Even the slightest differences in temperature, media, and storage conditions in the manufacturing process will have a significant impact on the final biological product.[90] Experts have posited that manufacturing costs for biosimilars will be higher than manufacturing costs for the reference product because the biosimilar manufacturer must "modify[] [its] production process to achieve a very specific profile that closely approximates the reference product."[91]

Second, biosimilar sponsors will likely face increased data requirements imposed by the FDA. Under Hatch-Waxman, the FDA is not permitted to request additional preclinical or clinical data from ANDA applicants to support a finding of bioequivalence.[92] However, under the BPCIA, for any given biosimilar application, the FDA determines on a case-by-case basis the information the sponsor must submit to support a finding of biosimilarity. At one end of the spectrum, the FDA could simply require a bioequivalence study. However, at the other end of the spectrum, the FDA could require a full program of clinical studies, similar to what is required for a BLA.[93] The European Union ("EU") regulatory agency charged with overseeing the approval of biosimilars in Europe has required at least one Phase II or Phase III clinical trial per biosimilar to show similar safety and

89 *See supra* notes 16–18 and accompanying text.

90 *See generally* Jordan Paradise, *The Devil Is in the Details: Health-Care Reform, Biosimilars, and Implementation Challenges for the Food and Drug Administration*, 51 JURIMETRICS J. 279, 281 (2011) ("Biologics are complex macromolecular entities that are more susceptible to variations in biological activity of the final product given manufacturing procedures; temperature, media, and storage conditions; and interaction of the final product with the human body.").

91 Grabowski et al., *supra* note 85, at 522 (citing Interview with Mark McCamish, Global Head of Biopharmaceutical Dev., Sandoz Int'l, *available at* http://www.iirusa.com/upload/wysiwyg/2010-P-Div/P1586/Podcast/PodcastScript_MarkMcCamish.pdf).

92 Food, Drug, and Cosmetic Act § 505(j)(2)(A), 21 U.S.C. § 355(j)(2)(A) (2012).

93 *See* Grabowski et al., *supra* note 85, at 518–19.

efficacy to the reference drug.[94] In the United States, a reference product manufacturer submitting a BLA is typically required to produce data from at least two Phase III clinical trials.[95] If the FDA follows the EU and requires at least one large scale clinical trial, the clinical cost to manufacturers producing a biosimilar may total almost half the clinical cost of producing an innovative biologic.

In addition to the $100-200 million investment per biosimilar, biosimilar manufacturers will have to build and equip their own manufacturing facilities in order for the FDA to consider a product biosimilar.[96] According to the FTC, this is likely to cost a manufacturer between $250 million and $1 billion.[97] This cost alone will likely persuade some would-be biologics manufacturers that the cost of entrance into the biosimilars market is too high.[98]

Finally, biosimilar manufacturers will likely need to engage in post-approval surveillance of the biosimilar to ensure that initial dissimilarities between the biosimilar and the reference product do not increase over time.[99] Post-approval drift occurs when slight changes in the manufacturing process cause changes in the biologic. Drift "will result in both the reference product and the biosimilar changing separately over time following biosimilar

94 *See* Grabowski et al., *supra* note 85, at 521.

95 Lisa M. Schwartz & Steven Woloshin, *Lost in Translation—FDA Drug Information that Never Reaches Clinicians*, 361 NEW ENG. J. MED. 1717, 1717 (2009).

96 Public Health Service Act § 351(k)(2)(A)(i)(V), 42 U.S.C. § 262(k)(2)(A)(i)(V) (2011).

97 FTC REPORT, *supra* note 14, at 14.

98 *See generally* Henry G. Grabowski, David B. Ridley & Kevin A. Schulman, *Entry and Competition in Generic Biologics*, 28 MANAGERIAL & DECISION ECON. 439, 447 (2007) (arguing that because of high fixed costs for biologic manufacturing facilities, for the foreseeable future, the number of biosimilar entrants is likely to be smaller than that predicted for generic pharmaceutical markets).

99 *See generally* Grabowski et al., *supra* note 85, at 518 (explaining that one proposal for dealing with the phenomenon of drift is establishing a post-marketing system to monitor interchangeability).

approval."[100] To protect against complications from drift, the FDA could impose strong pharmacovigilence and reporting standards on the biosimilar manufacturer.[101] There is no comparable cost for generic manufacturers, as drift does not occur in traditional pharmaceutical drugs.

In light of these seemingly staggering entry costs, the FTC estimates that biosimilars will only develop for markets with sales in excess of $250 million per year.[102] Only large companies with substantial resources are likely to be able to produce a biosimilar.[103] Further, even when biosimilars do enter the market, high costs will result in fewer entrants than would be expected for the generic pharmaceutical market.[104] One study estimates that for a $500 million market, only two biosimilars would enter, as compared to nine generic pharmaceuticals.[105] With fewer biosimilar competitors, biosimilars will likely be relatively close in price to branded biologics.[106]

B. Interchangeability vs. Bioequivalence

In order to achieve an interchangeability rating, a biosimilar sponsor must show that safety and efficacy risks do not increase when switching between the reference

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100 Grabowski et al., *supra* note 85, at 518 (citing Approval Pathway for Biosimilar and Interchangeable Biological products; Public Hearing; Request for Comments, 75 Fed. Reg. 61,497, 61,499 (FDA, Dep't Health & Human Servs. Oct. 5, 2010)).

101 *Id.*

102 FTC REPORT, *supra* note 14, at 15 (citing Janet Woodcock et al., *supra* note 38, at 446).

103 *Id.* (listing the companies that are likely to enter the biosimilars market: Abbott, AstraZeneca, Biogen/IDEC, Eli Lilly, Johnson & Johnson, Pfizer, Roche, Novo Nordisk and Sanofi-Aventis).

104 Grabowski et al., *supra* note 98, at 440.

105 *Id.* This study, conducted before the BPCIA was passed, is based on the assumption that fixed costs of developing a biosimilar will be 150% greater than fixed costs of developing a generic pharmaceutical. Based on analyses of the BPCIA, this estimate seems quite conservative. Thus, even fewer biosimilars may enter the market than predicted by this study.

106 *Id.*

product and the biosimilar.[107] The FDA has not explained the process it will use to determine whether a biosimilar receives an interchangeability rating.[108] However, experts anticipate that achieving an interchangeability rating will be quite difficult. The FDA may initially limit interchangeability ratings to biologics (such as hGH, discussed above), "where molecules meet certain tests for establishing 'sameness' through differentiated characterization or other technology."[109] The FDA may also require "crossover trial designs in which patients in clinical trials switch between the products over time."[110] However, patients are often leery of participating in crossover trials, and crossover trials are often even more expensive than more typical trials.[111] Further, the trade association for biotechnology companies, the Biotechnology Industry Organization, has argued that an interchangeability rating should not be granted upon first marketing approval, "absent compelling data."[112] Many biosimilars are therefore unlikely to have an interchangeability rating.

The lack of interchangeability is "likely to dampen how quickly a [biosimilar] manufacturer acquires market share compared to generic drug entry."[113] When a generic is deemed bioequivalent to a reference product, pharmacies can automatically substitute the generic product without physician approval.[114] This drives rapid market share loss by the reference product as soon as the first generic enters

107 *See supra* notes 68–70 and accompanying text.

108 *See generally* Paradise, *supra* note 90, at 291 (stating that the industry is "eagerly awaiting" news regarding how the FDA will interpret the interchangeability provisions of the BPCIA).

109 Grabowski et al., *supra* note 85, at 519.

110 *Id.* at 524.

111 *Id.*

112 Letter from the Biotech. Indus. Org. to the FDA (Dec. 23, 2010), *available at* http://www.bio.org/advocacy/letters/bio-comments-food-and-drug-administration-approval-pathway-biosimilar-and-interchan.

113 FTC REPORT, *supra* note 14, at 16.

114 Grabowski et al., *supra* note 85, at 524.

the market.[115] Products deemed bioequivalent "achieve upwards of a 90–95% substitution rate in as little as one month following introduction."[116] Then, as subsequent generics are licensed, the generics compete for market share among themselves, quickly decreasing the price of obtaining the drug.[117]

However, the lack of an interchangeability rating will prevent biosimilars from being automatically substituted by pharmacists without physician approval.[118] Physicians often exhibit high levels of brand loyalty;[119] therefore, it will take longer for biosimilars to "significant market share."[120] Brand manufacturers will have less incentive to compete based on price, and instead will likely "try to out-market the biosimilar."[121] The introduction of a non-interchangeable biosimilar is thus unlikely to decrease prices as significantly as the introduction of a bioequivalent generic.

Further, biosimilars that are not rated as interchangeable may be viewed skeptically by both physicians and

115 Grabowski et al., *supra* note 85, at 524.

116 Letter from the Coalition for a Competitive Pharmaceutical Mkt. ("CCPM") to the FTC (Sept. 30, 2008), *available at* http://www.ftc.gov/os/comments/healthcarecompissues/537778-00012.pdf.

117 FTC REPORT, *supra* note 14, at 16.

118 *Id.*

119 Grabowski et al., *supra* note 85, at 527 (explaining that rates of biosimilar acceptance may vary according to whether the physician's specialty exhibits high levels of brand loyalty).

120 Letter from the CCPM to the FTC, *supra* note 116, at 3.

121 *Id.* *See also* Letter from Kelsey I. Nix, Partner, Willkie Farr & Gallagher LLP, to the FTC 5 (Dec. 22, 2008), *available at* http://www.ftc.gov/os/comments/healthcarecompissues/537778-00036.pdf ("Without an 'interchangeable' designation, biosimilar companies would be compelled to invest significant sums to market and promote biosimilars, thus driving up the cost to the consumer. Reference companies also would have less incentive to compete on price. Reference drug companies would more likely try to out-market the biosimilar companies, further driving up the costs of both the reference drug and market entry by the biosimilar.").

patients.[122] Physicians and patients are both quite familiar with generic pharmaceuticals, but may be more reluctant to substitute a biosimilar until "sufficient experience has accumulated in clinical practice settings, as opposed to clinical trials."[123] This reluctance may be even greater if the biosimilar and reference product do not share the same name.[124] The FDA typically permits a generic pharmaceutical to use the same name as the reference branded drug because both products possess the same active ingredient.[125] However, many experts believe that biosimilars should not be allowed to share the same name as the reference product.[126] The FDA has not specified the manner in which names will be assigned to biosimilars approved under the BPCIA,[127] although many interest groups have lobbied for unique names for biologic and biosimilar therapeutics.[128] Especially if names are different, "physicians and their patients who have safely been taking a pioneer biologic drug may be reluctant to switch to a [biosimilar] because of the risk that the patient will react differently to the new drug."[129] Thus, biosimilar substitution will likely be concentrated among new patients,[130] or those

122 *See generally* Grabowski et al., supra note 85, at 527–28 (arguing that physician acceptance of biosimilars is expected to be lower when the biosimilar lacks an interchangeability rating).

123 *Id.* at 528.

124 FTC REPORT, *supra* note 14, at 16.

125 *Id.* at 16 n.55.

126 *See generally* WORLD HEALTH ORG. ["WHO"], WHO INFORMAL CONSULTATION ON INTERNATIONAL NONPROPRIETARY NAMES (INN) POLICY FOR BIOSIMILAR PRODUCTS, INN Working Doc. 07.211 (Sept. 4-5, 2006), *available at* www.who.int/medicines/services/inn/BiosimilarsINN_Report.pdf. (discussing the challenges associated with naming biosimilar products and questioning whether a biosimilar should be assigned the same name as the reference product).

127 FTC REPORT, *supra* note 14, at 16 n.55.

128 Richard Dolinar, *It's All About the Name: What Is the Imperative of Adopting Unique Names for Biologic and Biosimilar Therapeutics?*, FDLI'S FOOD AND DRUG POL'Y F., Nov. 28, 2012, at 1, *available at* http://safebiologics.org/pdf/fdli-asbm-its-all-about-the-name.pdf.

129 FTC REPORT, *supra* note 14, at 16–17.

130 Grabowski et al., *supra* note 85, at 527.

whose symptoms have not improved using the reference biologic.[131]

The hGH market provides an example of the lack of market share commanded by biosimilars. When Omnitrope entered the hGH market in 2006, it struggled to gain any market share despite a thirty percent price discount.[132] In 2008, Omnitrope provided a forty percent discount, but still only received a two percent market share.[133] Omnitrope's experience might not be typical of the larger biosimilars market, since an important factor in the success of an hGH product is its delivery system.[134] The established brands have "invested in more sophisticated pen- or needle-free delivery systems compared to the delivery systems used by recent lower-priced entrants."[135] However, Omnitrope's experience is still instructive; it shows that a significantly lower price will not always lead to a high market share.

Overall, the FTC estimates that the market share for biosimilars will range from ten to thirty percent.[136] This small market share does not pose a significant threat to reference drug manufacturers, providing them with little incentive to compete based on price.

C. Exclusivity Periods

The BPCIA creates two periods of exclusivity: one for the reference biologic, and one for the first interchangeable biosimilar to be licensed.[137] The reference biologic gets

131 FTC REPORT, *supra* note 14, at 17.

132 Grabowski et al., *supra* note 85, at 538.

133 *Id.*

134 *Id.*

135 *Id.*

136 FTC REPORT, *supra* note 14, at 19. *See also* Henry G. Grabowski et al., The Effect on Federal Spending of Legislation Creating a Regulatory Framework for Follow-On Biologics: Key Issues and Assumptions 48 (Aug. 2007) (unpublished white paper), http://www.bio.org/sites/default/files/Federal_Spending_of_followonbkg200709.pdf (estimating that market share for biosimilars will be between ten and forty-five percent).

137 Public Health Service Act § 351, 42 U.S.C.A. § 262(k)(6–7) (West 2012).

twelve years of exclusivity under the statute, while the first biosimilar gets between twelve and forty-two months of exclusivity.[138] Both exclusivity periods undermine the BPCIA's ability to create drug price reduction.

1. Exclusivity Period for Reference Biologics

The Hatch-Waxman Act does not provide an exclusivity period for each branded pharmaceutical. Instead, Hatch-Waxman provides for exclusivity only "when market-based pricing has not provided sufficient incentive" to spur further innovation.[139] This may occur when the molecule is already in the public domain and therefore not patentable, or when the target patient population is too small to make research and development of a drug commercially viable.[140]

The BPCIA departs from the Hatch-Waxman model, choosing to provide a twelve-year exclusivity period to each reference product.[141] Such a lengthy exclusivity period will ensure that biologic prices remain higher for longer, and is unnecessary to spur innovation.

Innovative biologics manufacturers can rely on the patent system to safeguard innovation and prevent rival manufacturers from free-riding on discoveries.[142] Patent law exists in order to incentivize innovation.[143] Thus, biosimilar manufacturers will not be permitted to infringe patents when attempting to develop a biosimilar.[144] Moreover,

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138 Public Health Service Act § 351, 42 U.S.C.A. § 262(k)(6)–(7) (West 2012).

139 FTC REPORT, *supra* note 14, at 27.

140 *Id.*

141 Public Health Service Act § 351, 42 U.S.C.A. § 262(k)(7) (West 2012).

142 FTC REPORT, *supra* note 14, at 26.

143 *See, e.g.*, Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 146 (1989) ("[T]he federal patent laws have embodied a careful balance between the need to promote innovation and the recognition that imitation and refinement through imitation are both necessary to invention itself and the very lifeblood of a competitive economy.").

144 *See generally* FTC REPORT, *supra* note 14, at 26 ("Nothing about the introduction of [biosimilar] drug products changes the relationship of

innovative biologics are covered by higher numbers of patents than innovative pharmaceuticals.[145]

In fact, there is evidence to suggest that competitors will have a more difficult time designing around patents covering biologics. Biologics and pharmaceuticals are covered by the same types of patents with one exception: process patents and technology platform patents are more significant for biologics.[146] Process patents are important because "the 'processes by which biologics are made are highly specific, complex, and determine many of the biologic's functional and structural characteristics . . . [that] can often be expected to affect the product's safety, purity, and efficacy profile, and thus are integral to the approval of the product itself.'"[147] Process patents likely provide additional protection against infringing patents, which will make it more difficult for biosimilar manufacturers to design around patents.[148]

Pioneer biologic manufacturers argue that a biologic firm can never be certain whether its patent estate will cover the exact molecule that the biosimilar manufacturer produces.[149] Since generic drugs are made from the exact same molecule as the pioneer pharmaceutical, the pioneer pharmaceutical manufacturer can rest assured that its patents, while in force, will prevent a generic manufacturer from bringing a generic to market. However, pioneer biologic manufacturers worry that the "uncertain 'similarity' standard for approval of [biosimilars] creates a greater potential for the biologic patents to be designed around."[150]

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the pioneer biologic drug products to the patents protecting them. As a result, patent protection should continue to incentivize biotechnology innovation.").

145 FTC REPORT, *supra* note 14, at 26

146 *Id.* at 31.

147 *Id.* (alteration in original) (quoting Letter from the Biotech. Indus. Org. to the FDA 12 (Dec. 23, 2010), *available at* http://www.bio.org/advocacy/letters/bio-comments-food-and-drug-administration-approval-pathway-biosimilar-and-interchan).

148 *See* Letter from Kelsey I. Nix to the FTC, *supra* note 121, at 3.

149 *See* Letter from the Biotech. Indus. Org. *supra* note 147, at 5–6.

150 FTC REPORT, *supra* note 14, at 33.

However, this fear appears largely unfounded. The FTC argues that there is no reason to believe that patents for innovative biologics have been designed around more frequently than patents for innovative pharmaceuticals.[151] Further, the Patent and Trademark Office's written guidelines acknowledge the "percent identity" doctrine, allowing pioneer biologics manufacturers to claim their patent has been infringed if another molecule shares at least seventy percent identity with the patented amino acid sequence.[152] Thus, a molecule could differ by thirty percent from the pioneer biologic and still be covered by the pioneer biologic's patent estate. It will likely be difficult for a product to differ by thirty percent and still be found biosimilar, no matter how the FDA interprets the biosimilarity language in the BPCIA.

Under the rare circumstance that a patent estate could be designed around, a twelve-year exclusivity period is unnecessarily long. The twelve-year exclusivity period is based on a study, published in *Nature Reviews Drug Discovery*, which found that biologics manufacturers break even between 12.9 and 16.2 years after launch.[153] However, the FTC has contested the results of that study, finding that even the methodology used by the study supports the finding that pioneer biologics manufacturers break even just seven years after launch.[154] Other independent researchers have sided with the FTC, arguing that a seven-year exclusivity period is sufficient to promote innovation.[155]

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151 FTC REPORT, *supra* note 14, at 26.

152 *See* PATENT & TRADEMARK OFFICE, WRITTEN DESCRIPTION TRAINING MATERIALS (rev. 1 2008), *available at* http://www.uspto.gov/web/menu/written.pdf.

153 Henry G. Grabowski, *Follow-On Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, 7 NATURE REVS. DRUG DISCOVERY 479, 486 (2008).

154 FTC REPORT, *supra* note 14, at app. A (finding that with an exclusivity period of seven years, there is only one set of assumptions (of those most commonly used) that does not result in the branded manufacturer breaking even).

155 Alex Brill, a research fellow at the American Enterprise Institute, supports a seven-year exclusivity period. He argues that "seven years is

If the majority of pioneer biologics manufacturers break even seven years after launch, a twelve-year exclusivity period provides a windfall to these firms. As discussed above, unlike in the pharmaceutical industry, neither the price of the drug nor reference product market share drop substantially when biosimilars begin to enter the market.[156] Thus, the biologic manufacturer continues to make a profit long after the exclusivity period expires. A twelve-year exclusivity period is therefore unnecessary to incentivize biologics manufacturers to create new drugs. Further, such a long exclusivity period detracts from the cost savings that the BPCIA is trying to create.

2. Exclusivity Period for the First Interchangeable Biosimilar

The Hatch-Waxman Act provides a 180-day marketing exclusivity period to the first generic drug applicant that challenges the patents relating to the branded drug.[157] The D.C. Circuit explains that the 180-day exclusivity period rewards the first generic applicant for the expense and effort involved in challenging the branded drug's patents.[158] The first generic sponsor can sell its product at seventy-five percent of the price of the reference pharmaceutical.[159] However, once the first generic sponsor makes a successful challenge, subsequent generic sponsors do not have to relitigate the patents and can quickly enter the market.[160]

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sufficient to ensure that innovator drug companies continue to earn the necessary economic rents, but that a long period would lead to unreasonably large rent[s] . . . and provide no additional benefit to consumers." Carver et al., *supra* note 20, at 797 (alteration in original) (internal quotation marks omitted).

156 *See supra* Part III.A–B.

157 FTC REPORT, *supra* note 14, at 65.

158 Mova Pharmaceutical Corp. v. Shalala, 140 F.3d 1060, 1074 (D.C. Cir. 1998).

159 *See generally* FTC REPORT, *supra* note 14, at 12 (noting that the first generic entrant generally offers a price that is twenty-five percent lower than the reference drug price).

160 *Id.* at 65.

Once multiple generics have entered the market, the price will decrease to around twenty percent of the original price.[161] The 180-day exclusivity period allows "the first generic entrant to recoup its patent litigation costs before the substantial price drop caused by multiple generic entrants [occurs]."[162]

The BPCIA provides that the FDA may not designate a second product as biosimilar until the earlier of (1) one year after commercial marketing of the first interchangeable biosimilar; (2) eighteen months after a final court decision or dismissal on all patents in suit brought against the first approved interchangeable biosimilar; (3) forty-two months after approval of the first interchangeable biosimilar if litigation is still ongoing; or (4) eighteen months after approval of the first interchangeable biosimilar if the sponsor has not been sued.[163] The exclusivity period thus ranges from one year to forty-two months.

An exclusivity period for the first interchangeable biosimilar is unnecessary. The entrance of the first interchangeable biosimilar will not lead to a flood of subsequent interchangeable biosimilars on the market because demonstrating interchangeability will almost certainly require clinical trials.[164] Unlike sponsors of subsequent generics, sponsors of subsequent interchangeable biologics will be unable to simply begin production as soon as patent challenges are cleared. Thus, the price for the biologic will not drop as substantially as when the first generic enters the market; the sponsor of the first interchangeable biosimilar will not need the period of higher pricing to recoup its investment. Indeed, in comments to the FDA, a potential biosimilar sponsor argued that companies "will not likely rely on winning exclusivity to invest in the

161 *See generally* FTC REPORT, *supra* note 14, at 12 (noting that the price discount increases to eighty percent once multiple generics have entered the market).

162 *Id.*

163 42 U.S.C.A. § 262(k)(6)(A)–(C) (West 2012).

164 *See supra* notes 107–11 and accompanying text.

products because the development time and investment for [biosimilars] is so great."[165]

Not only is this exclusivity period unnecessary to spur the first interchangeable biosimilar to market, it is also antithetical to the BPCIA's goal of reducing biologic prices. Even the shortest exclusivity period of one year is significantly longer than the 180-day exclusivity period under Hatch-Waxman. The exclusivity period "blocks entry of a subsequent interchangeable product for a period of time and thereby denies consumers price competition."[166]

IV. RECOMMENDATIONS AND CONCLUSION

The BPCIA represents an important first step toward reducing biologics prices. However, for the reasons discussed above, the BPCIA is unlikely to be as successful at controlling costs as the Hatch-Waxman Act. Congress and the FDA must take further steps to help incentivize a vibrant and successful biosimilars market.

First, Congress should create tax credits to incentivize the manufacture of biosimilars. Such credits, including bonus depreciation, already exist to incentivize businesses to invest in tangible property. Bonus depreciation allows companies to write off a percentage of their investment in qualified property, such as tractors and computers.[167] A

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165 FTC REPORT, *supra* note 14, at 68.

166 *Id.* at 71.

167 *See, e.g.*, *Quick Facts: Bonus Depreciation and 100 Percent Expensing*, TAX POL'Y CTR., *available at* http://www.taxpolicycenter.org/taxtopics/Bonus-Depreciation-and-100-Percent-Expensing.cfm#2 (last visited Mar. 22, 2013); The Tax Policy Center explains bonus depreciation as follows:

> To determine taxable income, businesses subtract expenses from their receipts. Some business expenses are for items that are entirely used up during the year (e.g., materials and labor), but other expenses are for durable goods that last for many years. The expense for investment in capital equipment (e.g., tractors, computers, and wind turbines) occurs over many years as the value of that investment is used up or depreciated. Under current law,

biosimilar manufacturer could use bonus depreciation as a tax credit for the purchase of equipment, such as a centrifuge, to be used in a manufacturing facility.

However, manufacturing facilities for biosimilars will likely cost between $250 million and $1 billion to create.[168] Bonus depreciation for equipment alone will likely not incentivize companies to build such a factory. Instead, Congress should create a new tax credit, similar to bonus depreciation, which would allow biosimilar manufacturers to deduct from their income some percentage of an FDA-approved biosimilars manufacturing facility.

The BPCIA will function at its best as more biosimilars enter the market, increasing competition and forcing all firms to price their products competitively to fight for market share. Without incentives to build manufacturing facilities, biosimilars will not be economically feasible in many markets. By creating a tax incentive similar to bonus depreciation, Congress could help ensure that the BPCIA is successful in creating savings for consumers and insurers.

Second, the FDA should create as much predictability as possible in the licensing of biosimilars. The FDA has already begun this process. In February 2012, the FDA released draft guidance providing a high-level overview of the process through which the agency will determine biosimilarity.[169]

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businesses calculate taxable income by deducting capital costs over time according to fixed depreciation schedules.

Bonus depreciation allows for an additional deduction when the asset is first purchased. For example, a 50 percent bonus depreciation allowance would mean that businesses could immediately deduct 50 cents of every dollar spent on qualifying investment purchases. The remaining 50 cents would be deducted according to regular depreciation schedules.

Id.

168 *See supra* notes 92–94 and accompanying text.

169 *See* CTR. FOR DRUG EVALUATION AND RESEARCH, FDA, GUIDANCE FOR INDUSTRY: SCIENTIFIC CONSIDERATIONS IN DEMONSTRATING BIOSIMILARITY TO A REFERENCE PRODUCT 2 (2012) [hereinafter BIOSIMILARITY GUIDANCE], *available at* http://www.fda.gov/downloads/

The draft guidance reminds sponsors that applications must include "data derived from analytical studies, animal studies, or a clinical study or studies" unless the FDA determines one of these elements is unnecessary.[170] The FDA specifies that it will take a "risk-based, totality-of-the-evidence approach" in evaluating biosimilarity.[171]

Additionally, the FDA advises sponsors to take a stepwise approach to showing biosimilarity.[172] This approach should begin with "extensive structural and functional characterization of both the proposed product and the reference product."[173] Next, the sponsor should consider the role of animal data in assessing toxicity and providing additional support for biosimilarity.[174] The sponsor should "conduct comparative human [pharmacokinetics] studies, and [pharmacodynamic] studies if there is a clinically relevant [pharmacodynamic] measure."[175] Finally, sponsors should compare the clinical immunogenicity of biosimilar and the reference product.[176] If there are residual uncertainties, the FDA then specifies that the sponsor should consider what other types of clinical data "may be adequate."[177]

Although this guidance is a good first step, sponsors would benefit from information containing a greater degree of specificity. For each of the most common protein classes, the FDA should release additional guidance documents specifying exactly which types of data will be required to prove biosimilarity and/or interchangeability for each class of

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Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291128.pdf.

170 *See* BIOSIMILARITY GUIDANCE, *supra* note 169, at 5.

171 *Id.* at 8.

172 *Id.* at 5.

173 *Id.* at 7.

174 *Id.*

175 *Id.*

176 BIOSIMILARITY GUIDANCE, *supra* note 169, at 7.

177 *Id.* at 12 ("The scope and magnitude of clinical studies will depend on the extent of residual uncertainty about the biosimilarity of the two products after conducting structural and functional characterization and possible animal studies.").

protein. In Europe, the European Medicines Agency ("EMA") has released guidance for six different protein classes.[178] EMA guidance helps biosimilar manufacturers estimate costs and obtain EMA approval the first time the product is reviewed. The FDA should follow the EMA's lead and issue similar guidance as quickly as feasible.

Additionally, the EMA issues a detailed scientific document shortly after a biosimilar application is approved, rejected, or withdrawn.[179] These reports have been "helpful in elucidating how the guidelines and standards have been applied to regulatory decision-making."[180] Transparency in the approval process will aid biosimilar manufacturers in understanding what is needed to achieve biosimilarity and/or interchangeability. This understanding will lead to increased consistency and predictability, which may help convince manufacturers to take the risk of developing a biosimilar. Therefore, the FDA should adopt the EMA's practice of issuing detailed decision letters for each biosimilar application.

Third, Congress should reduce the exclusivity period for reference biologics from twelve to seven years. President Obama has taken a step in this direction, by including a recommendation for a seven-year exclusivity period in his fiscal year 2012 budget.[181] The budget states:

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178 *See Product-Specific Biosimilar Guidelines*, EUR. MED. AGENCY, http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000408.jsp&mid=WC0b01ac058002958c&jsenabled=true#Productspecificbiosimilarguidelines (last visited Mar. 19, 2013). Product-specific guidelines have been released for insulin, somatropin, granulocyte-colony stimulating factor, alpha interferon, low-weight molecular heparins, and erythropoietins. *Id.* At least four more product-specific guidelines are at the concept or draft stage. *Id.*

179 Barbara Mounho et al., *Global Regulatory Standards for the Approval of Biosimilars*, 65 FOOD & DRUG L.J. 819, 823 (2010).

180 *Id.*

181 OFFICE OF MGMT. & BUDGET, EXEC. OFFICE OF THE PRESIDENT, BUDGET OF THE U.S. GOVERNMENT, FISCAL YEAR 2012 TERMINATIONS, REDUCTIONS, AND SAVINGS 119 (2012) [hereinafter OMB 2012 REPORT], *available at* http://www.whitehouse.gov/sites/default/files/omb/budget/fy2012/assets/trs.pdf.

> 12-year exclusivity is unnecessary to promote innovation by brand biologic drug manufacturers and can potentially harm consumers by directing scarce research and development funding toward developing low-risk clinical data for drug products with proven mechanisms of action rather than toward new products to address unmet medical needs.[182]

The budget document estimates that changing the exclusivity period from twelve to seven years would result in savings of $2.34 billion by 2021.[183] However, President Obama's proposal has already encountered significant resistance from Congress. Fifty-one members of the House, from both sides of the aisle, sent a letter to President Obama reminding him that the twelve-year exclusivity provision was passed with significant bipartisan support.[184] The letter warned that reducing the exclusivity period would undermine the BPCIA's attempt to protect innovation, causing biotechnology firms to move their businesses to more hospitable countries such as India or China.[185]

However, a twelve-year exclusivity period is unnecessary to promote innovation. As noted above, the patent system provides adequate protection for innovative biologics manufacturers.[186] Additionally, most biosimilars will not be automatically substituted for their reference products. The reference biologic manufacturer will therefore continue to reap substantial profits even after the introduction of one or more biosimilars.[187]

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182 OMB 2012 REPORT, *supra* note 181.

183 *Id.*

184 Letter from Anna Eshoo et al. to Barack Obama, *supra* note 10, at 1 ("The Kennedy-Eshoo legislation to create a new pathway for biosimilars at the FDA had overwhelming bipartisan and bicameral support. The bill had 149 cosponsors [sic] in the House and passed by a vote of 47–11 in the Energy and Commerce Committee. The Senate version was introduced as an amendment in the [Health, Education, Labor & Pensions] HELP Committee and passed by a vote of 16–7.").

185 *Id.* at 2.

186 *See supra* notes 142–52 and accompanying text.

187 *See supra* notes 118–30 and accompanying text.

Still, the twelve-year exclusivity period is law, and President Obama cannot unilaterally change the law. For a seven-year exclusivity period to take effect, Congress will have to amend the BPCIA and should do so as soon as possible.

However, debates over the efficacy of the BPCIA as written should not prevent implementation of the BPCIA in its current form. The astronomical prices of biologics warrant an immediate solution. Until reform is implemented, high biologics prices will continue to weaken the economy by consuming more and more of the budgets of consumers and government insurers. And just as significantly, high biologics prices result in a social cost that is borne by vulnerable patients. Mrs. Cramer, the arthritis patient taking Enbrel, recounts leaving her doctor's office in tears after meeting other patients in her situation who could not afford Enbrel.[188] The BPCIA is important legislation. With a few tweaks, it has the potential to improve the economy and enhance patients' lives. Congress and the FDA must act to make the BPCIA as strong as possible so that these important goals can be achieved.

188 Barrett, *supra* note 1.