NOTE

Take Two and Call Congress in the Morning: How the Biologics Price Competition and Innovation Act May Fail to Prevent Systemic Abuses in the Follow-on Biologics Approval Process

*Charles Davis**

ABSTRACT

Biologics drugs present great promise for curing deadly diseases such as cancer or neurological disorders. These auspicious drugs are, however, inordinately expensive. The patents on many of these blockbuster biologics treatments will soon expire, creating high demand for cheap generic versions of biologics drugs. Yet until 2010, no FDA approval pathway for follow-on biologics existed in the United States.

As part of the Patient Protection and Affordable Care Act, Congress passed the Biologics Price Competition and Innovation Act. The BPCIA included an approval pathway for follow-on biologics modeled closely after the Hatch-Waxman approval process for generic small molecule drugs. Congress did not sufficiently consider the myriad of abuses that existed under the

* J.D., May 2013, The George Washington University Law School; Ph.D., Biochemistry & Biophysics, 2010, The University of North Carolina at Chapel Hill; B.S., Chemistry, 2005, The University of North Carolina at Chapel Hill. I would like to thank the staff of *The George Washington Law Review*, in particular Elizabeth Hagerty, Anna Crane, Patrice Hendrikson, Shane Huang, Courtney Murtha, Nicole Durkin, and James Gross, for their time spent in selecting and editing this note. I would also like to thank my parents, Chuck Davis and Gilda Hollar, for being willing ears for my ideas. Finally, and most importantly, I'd like to thank my wife, Erin Heenan, for her insightful comments and unyielding support.

Hatch-Waxman Act, leaving open multiple avenues for abuse in the BPCIA, particularly in the Act's novel patent dispute resolution procedures.

This Note analyzes several of the most serious issues with the BPCIA approval process. In particular, the BPCIA does not provide for any third-party input or public notification in the patent dispute provisions. Further, the BPCIA places no limit on abusive pay-to-delay settlements between pioneer and follow-on biologics manufacturers. This Note argues that Congress should amend the BPCIA to provide for greater public notification processes and opportunities for third-party intervention in patent disputes. Congress should also act to significantly limit pay-to-delay settlements by requiring the filing of such settlements with the FTC and DOJ for approval. Through such amendments, Congress will finally achieve a follow-on biologics process that provides significant avenues for both competition and innovation in the biologics industry.

TABLE OF CONTENTS

INTRODUCTION 1257
I. BACKGROUND: FDA APPROVAL PROCESSES FOR NEW DRUGS, SMALL-MOLECULE GENERIC DRUGS, AND BIOLOGICS DRUGS 1261
A. What Are Biologics? 1261
1. Differentiating Biologics from Small-Molecule Drugs 1262
2. Follow-on Biologics 1264
B. FDA Drug Approval Processes Prior to the BPCIA 1265
1. FDA Approval of New Drugs 1265
2. FDA Approval of Generic Small-Molecule Drugs 1267
a. Hatch-Waxman Approval Process for Generic Small-Molecule Drugs: ANDA 1268
b. Patent Concerns in ANDA Approval Under the Hatch-Waxman Act 1269
c. Abuses of the Hatch-Waxman Approval Process 1270
d. Congressional and Judicial Responses to Abuses of the Hatch-Waxman Approval Process 1271
C. Regulating Biologics Under the BPCIA 1273
1. Follow-on Biologics Licensure Provisions Under the BPCIA 1273
2. Patent Dispute Provisions Under the BPCIA ... 1275

a. *Patent Exchange Process Prior to Infringement Litigation* 1275
b. *Patent Negotiation Process Prior to Infringement Litigation* 1276
c. *Patent Infringement Litigation* 1277
d. *Postinfringement Procedures and Patent Rights Under the BPCIA* 1278
II. POTENTIAL ABUSES OF THE BPCIA PATENT DISPUTE SCHEME 1279
A. *The Legislative History of the BPCIA Demonstrates Widespread Concern over Abuses of the Approval Process* 1279
B. *Lack of Public Disclosure and Pay-to-Delay Settlements Represent Major Potential Sources of Abuse Under the BPCIA* 1281
1. Lack of Public Disclosure or Third-Party Input. 1281
2. Lack of Control over Pay-to-Delay Settlements 1283
III. SOLUTIONS TO THE POTENTIAL ABUSES OF THE PATENT DISPUTE PROCESS UNDER THE BPCIA 1285
A. *Congress Should Adopt Aspects of the 2011 House Bill to Cure Sources of Abuse Within the BPCIA* ... 1286
B. *Congress Should Require Disclosure of Patent Dispute Information and Pay-to-Delay Settlements* .. 1288
1. Congress Should Require Publication of Paragraph 3 Patent Lists 1288
2. Congress Should Directly Limit the Ease of Entering Pay-to-Delay Settlements 1290
CONCLUSION 1293

INTRODUCTION

The unsustainable cost of healthcare in the United States has become one of the defining debates of the early twenty-first century. A key aspect of this debate is the high cost of prescription medications.[1] In 2010, overall spending on medications in the United States was $307 billion,[2] which represents 2.1% of the U.S. gross domestic prod-

1 *See* IMS INST. FOR HEALTHCARE INFORMATICS, THE USE OF MEDICINES IN THE UNITED STATES: REVIEW OF 2010, at 3 (2011), http://www.imshealth.com/deployedfiles/imshealth/Global/Content/IMS%20Institute/Static%20File/IHII_UseOfMed_report.pdf.

2 *Id.* at 4.

uct for that year.[3] Of that $307 billion, $67 billion[4] (21%) was spent on biologics, a growing class of medications that are derived from biological sources and provide novel therapies for a host of disorders.[5] On an individual level, hundreds of millions of patients globally have been treated using biologics,[6] with costs of some medications reaching over $20,000 per year.[7]

Although biologics continue to grow in importance and biologics sales constitute an increasingly greater percentage of consumer spending, most biologics sold today are not generic drugs.[8] Global spending on less-expensive follow-on biologics[9] was only $311 million, which is minuscule compared to the billions of dollars spent on biologics annually.[10] Thus, in comparison to the traditional small-molecule drug[11] market that is replete with generic counterparts to blockbuster drugs, the follow-on biologics market is substantially underserved. This phenomenon is particularly striking given that biologics are inherently more expensive than traditional small-molecule drugs, costing consumers twenty-two times more on average.[12] There is also a great demand for follow-on biologics, as twenty-eight percent of sales of the pharmaceutical industries' top-100 products come from sales of bio-

---

3 *See* Eugene P. Seskin & Shelly Smith, Bureau of Econ. Analysis, *Annual Revision of the National Income and Products Accounts*, 91 SURV. CURRENT BUS. 6, 13 (2011), http://www.bea.gov/scb/pdf/2011/08%20August/0811_nipa_annual_article.pdf. This is a growth increase of almost eighty percent in spending on medications in only nine years. *See* IMS INST. FOR HEALTHCARE INFORMATICS, *supra* note 1, at 4.

4 IMS INST. FOR HEALTHCARE INFORMATICS, *supra* note 1, at 6. The $67 billion spent on biologics in 2010 was an almost seven percent increase in spending on biologics from the previous year, which represents the largest increase in any category of medications. *Id.*

5 For a more thorough description of biologics, see *infra* Part I.A.

6 Carl B. Feldbaum, President, Biotechnology Indus. Org., Address at BioIreland Conference: "It Was 20 Years Ago Today . . .": U.S. Biotechnology Trends, Fall 2002 (Nov. 14, 2002), *available at* http://test.bio.org/speeches/speeches/20021114.asp (estimating that over 325 million patients worldwide had received some sort of biologics therapy). This suggests that, as the availability of biologics has continued to rise, potentially billions of people around the world have received biologics therapy to date. *See id.*

7 *E.g.*, Alfred B. Engelberg, Aaron S. Kesselheim & Jerry Avorn, *Balancing Innovation, Access, and Profits—Market Exclusivity for Biologics*, 361 NEW ENG. J. MED. 1917, 1917–19 (2009); Anthony D. So & Samuel L. Katz, Op-Ed., *Biologics Boondoggle*, N.Y. TIMES, Mar. 8, 2010, at A23 (noting that Herceptin, a lifesaving treatment for breast cancer, costs $37,000 per year, and Humira, a novel treatment for rheumatoid arthritis, costs $50,000 per year).

8 *See* IMS INST. FOR HEALTHCARE INFORMATICS, *supra* note 1, at 14.

9 This Note will refer to generic biologics as "follow-on biologics" for consistency with the terminology most often used in the United States.

10 *See* IMS INSTITUTE FOR HEALTHCARE INFORMATICS, *supra* note 1, at 14.

11 See *infra* Part I.A.1 for a thorough definition of small-molecule drugs.

12 So & Katz, *supra* note 7, at A23.

logics.[13] As patent protection for blockbuster biologics begins to expire,[14] significant opportunities for a major expansion in the prevalence of follow-on biologic medications will soon be at hand.

Due to concerns about the safety of follow-on biologics[15] and disagreement among the pioneer pharmaceutical industry, the generic manufacturing industry, and members of Congress regarding the appropriate regulatory scheme for follow-on biologics,[16] no formal pathway for approval of follow-on biologics existed in the United States until 2010. To fill this regulatory gap, Congress, in 2010, enacted the Biologics Price Competition and Innovation Act of 2009 ("BPCIA")[17] as part of the Patient Protection and Affordable Care Act ("ACA")[18]. Based in part on the Hatch-Waxman Act,[19] which created a formal approval pathway for generic small-molecule drugs, Congress intended that the BPCIA would spur both an increase in the follow-on biologics industry in the United States and a subsequent decrease in biologics prices.[20]

Although the BPCIA is an important first step towards providing a formal approval pathway for follow-on biologics, the BPCIA still affords ample opportunity for abuse by both pioneer and follow-on manufacturers. One area especially ripe for abuse involves the method by which follow-on and pioneer manufacturers settle patent disputes during the follow-on biologic approval process. The complicated patent dispute process developed in the BPCIA is an intricate series of negotiations between the follow-on and pioneer manufactur-

---

13 *Id.*

14 *See, e.g.*, U.S. Patent No. 6,165,464 (filed Mar. 17, 1998) (Herceptin patent, expiring in 2016); U.S. Patent No. 5,756,349 (filed June 6, 1995) (Epogen patent, expiring in 2015); Andrew Pollack, *For Amgen, A Monopoly is Ending*, N.Y. TIMES, Mar. 28, 2012, at B1; *Patent Term Extensions*, U.S. PATENT & TRADEMARK OFFICE, http://www.uspto.gov/patents/resources/terms/156.jsp (last modified Apr. 4, 2012).

15 See *infra* Part I.A.1 for a thorough discussion of the safety concerns present in the development of follow-on biologics.

16 *See infra* Part II.A.

17 Biologics Price Competition and Innovation Act of 2009 § 7002, 42 U.S.C. § 262 (Supp. V 2012).

18 Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119 (2010) (codified as amended in scattered sections of 26 and 42 U.S.C.).

19 Drug Price Competition and Patent Term Restoration ("Hatch-Waxman") Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 21 U.S.C. § 355 (2006) and 35 U.S.C. § 271(e) (2006)).

20 Brenda Flores Gehani, *The Biologics Act: Hopes for Access to Generic Biologics May Instead Be a Catalyst for New Innovation*, 20 ANNALS HEALTH L. ADVANCE DIRECTIVE 170, 171 (2011), http://www.luc.edu/law/media/law/centers/healthlaw/pdfs/advancedirective/pdfs/issue6/flores.pdf.

ers.[21] This dispute process, which happens completely out of the public eye, is vulnerable to systemic abuse. In particular, due to the highly private nature of the dispute resolution process, the pioneer and follow-on biologics manufacturers are likely to collude against third parties[22] or enter pay-to-delay settlements.[23] This may be a favorable result for the parties involved but will harm the public by decreasing competition for a specific biologic drug.[24] By delaying the entry of much cheaper follow-on biologics to market, these abuses will perpetuate the increasingly out-of-reach costs for lifesaving medications.

This Note argues that Congress should amend the BPCIA to provide for greater public scrutiny of the early stages of the patent dispute process and to strongly discourage pay-to-delay settlements. By allowing for more public intervention in the earliest stages of the biologics approval process and by limiting pay-to-delay settlements, Congress can lessen the public harms associated with abuse of the approval process and incentivize the development of follow-on biologics.

Part I of this Note provides the relevant background for this analysis, first defining biologics in relation to small-molecule drugs, and then describing the Food and Drug Administration ("FDA") approval process for generic small-molecule drugs under the Hatch-Waxman Act and follow-on biologics under the BPCIA. Part II then compares the potential abuses that could arise under the BPCIA to those that existed—and some that continue to exist—under the Hatch-Waxman Act framework for small-molecule drugs. Finally, Part III proposes changes to the BPCIA that would mitigate these sources of abuse by limiting pay-to-delay settlements and requiring more public involvement in the follow-on biologics approval process.

---

21 *See infra* Part I.C.2.

22 Collusion refers to the practice of pioneer and follow-on biologics manufacturers coordinating to delay the entry into the market of other follow-on biologics made by a third-party manufacturer. *See infra* Part II.B.1.

23 A "pay-to-delay" settlement is a settlement between a pioneer and a follow-on biologics manufacturer in which the follow-on manufacturer agrees not to challenge the pioneer's patent or market their biologics product in exchange for payments by the pioneer. *See infra* Part I.B.2.c.

24 See *infra* Part II for a more detailed explanation of the public harm that such agreements can cause.

I. BACKGROUND: FDA APPROVAL PROCESSES FOR NEW DRUGS, SMALL-MOLECULE GENERIC DRUGS, AND BIOLOGICS DRUGS

The FDA drug approval processes are quite complex. The approval process differs for pioneer small-molecule drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA"),[25] generic small-molecule drugs under the Hatch-Waxman Act, and follow-on biologics under the BPCIA. Nevertheless, each separate approval process elucidates potential weaknesses that may be exploited in the context of follow-on biologics.

A. *What Are Biologics?*

Aside from the differences in approval pathways for small-molecule drugs and biologics, there are also important physical differences between these products. Early biologics contained purified extracts of animal or human blood, which is in part the reason these compounds are known as "biologics."[26] Although foundational research on biologics production had been ongoing for years,[27] the biologics revolution truly began with the founding of Genentech in 1976, and, by 1982, the U.S. biologics industry had become fully operational.[28] Since 1982, the United States has approved over 250 biologics.[29] Biologics show great promise in curing some of the more common and serious modern human afflictions such as cancer and multiple autoimmune disorders.[30]

---

25 Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301–399 (2006)).

26 *See* Robert N. Sahr, *The Biologics Price Competition and Innovation Act: Innovation Must Come Before Price Competition*, B.C. INTELL. PROP. & TECH. F. 2 (July 19, 2009), http://bciptf.org/wp-content/uploads/2011/07/7-THE-BIOLOGICS-PRICE-COMPETITION-AND-INNOVATION-ACT.pdf.

27 *See id.* This research included forms of recombinant technology, which remains the backbone of biologics production today. Recombinant technology involves the use of DNA encoding for a human protein that is inserted into modified cell lines, commonly derived from yeast and bacteria, which will mass-produce a specific protein that can later be harvested. *See id.*

28 *See A History of Firsts*, GENENTECH, http://www.gene.com/media/company-information/chronology (last visited May 9, 2013). By 1978, Genentech had cloned human insulin, and, shortly thereafter, licensed the technology to Eli Lilly. In 1982, Lilly began to market recombinant insulin. *Id.*

29 *See* Thijs J. Giezen et al., *Safety-Related Regulatory Actions for Biologicals Approved in the United States and the European Union*, 300 JAMA 1887, 1887 (2008).

30 *See* N. Lee Rucker, AARP Pub. Policy Inst., *Biologics in Perspective: Expanded Clinical Options Amid Greater Cost Scrutiny*, AARP (June 11, 2007), http://www.aarp.org/health/drugs-supplements/info-2007/fs136_biologics.html.

1. *Differentiating Biologics from Small-Molecule Drugs*

There is not one definition of a "biologic" broad enough to cover the entire class of such compounds. The legal definitions for biologics are highly formulaic.[31] The Public Health Service Act ("PHSA")[32] defines a "biological product" as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings."[33] The BPCIA amended this definition to include "protein (except any chemically synthesized polypeptide)."[34] These statutory definitions thus embrace the vast range of potential sources of biologics, including DNA/RNA,[35] protein,[36] cellular,[37] and bacterial.[38] These legislative definitions also link the definition of biologics to its "prevention, treatment, or cure of a disease."[39]

Nevertheless, the easiest method for defining biologics is by contrasting them with traditional small-molecule drugs. The FDA has differentiated small-molecule drugs and biologics based on the source of the drug and its physical characteristics.[40] Small-molecule drugs are comparatively small, simple chemical compounds.[41] Biologics, on the other hand, are normally large compounds characterized by a complex structure.[42] For example, acetaminophen, the small-molecule drug that is the active ingredient in Tylenol, has a molecular mass of 151

---

31 In contrast, the scientific definition of biologics covers almost any composition of matter that derives from animals or humans, such as stem cells and gene therapy. *See* Sahr, *supra* note 26, at 2.

32 Public Health Service Act ("PHSA") of 1944, Pub. L. No. 78-410, 58 Stat. 682, *amended by* Biologics Price Competition and Innovation Act ("BPCIA") of 2009, Pub. L. No. 111-148, § 7002, 124 Stat. 804 (2010) (codified at 42 U.S.C. § 262 (Supp. V 2012)).

33 PHSA § 351(a), 58 Stat. at 702.

34 42 U.S.C. § 262(i)(1) (Supp. V 2012).

35 E.g., gene therapy. *Id.* (referencing blood components or derivatives and therapeutic sera).

36 E.g., recombinant proteins. *Id.*

37 E.g., stem cells or blood components. *Id.*

38 E.g., toxins or antitoxins. *Id.*

39 *Id.*

40 *See What Are "Biologics" Questions and Answers*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133077.htm (last visited Apr. 14, 2013) [hereinafter *FDA Biologics Q&A*].

41 Scott Gottlieb, *Biosimilars: Policy, Clinical, and Regulatory Considerations*, 65 AM. J. HEALTH-SYS. PHARMACY (SUPP. 6) S2, S4 (2008).

42 *Id.*

Da.[43] By contrast, Procrit, a common biologic, has a molecular mass of 30.4 kDa—200 times larger than a small-molecule drug.[44]

Due to their small sizes, small-molecule drugs are synthesized using well-established, consistent mechanisms that produce uniform products.[45] Biologics, however, are not uniformly produced through traditional manufacturing. Biologics are largely manufactured within cells, not through simple chemical synthesis.[46] This manufacturing process can result in small alterations in a given biologic's chemical structure,[47] which can have a substantial impact on the biologic's efficacy.

The approval story of Eprex and Epogen presents an appropriate cautionary tale.[48] The biologics Eprex and Epogen were forms of the protein erythropoietin,[49] developed to treat anemia.[50] The only difference in manufacturing between Eprex and Epogen was the cell culture media used during the manufacturing process.[51] This small difference in manufacturing caused patients taking Eprex to develop antibodies against erythropoietin, leading their own immune system to start attacking both the Eprex and natural erythropoietin.[52] As a result, over a six-year span, Eprex produced 175 cases of severe anemia,

---

43 MCNEIL CONSUMER HEALTHCARE, TYLENOL PROFESSIONAL PRODUCT INFORMATION 7 (2010), *available at* http://www.tylenolprofessional.com/assets/TYL_PPI.pdf. A "dalton," abbreviated "Da," is a scientific unit of mass that corresponds to 1 gram per mole. *See* BUREAU INTERNATIONAL DES POIDS ET MESURES, THE INTERNATIONAL SYSTEM OF UNITS (SI) 126 (8th ed. 2006).

44 ORTHO BIOTECH, PROCRIT® EPOEIN ALFA 1 (1993), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/label/pre96/103234s1015_LBL.pdf.

45 *See FDA Biologics Q&A*, *supra* note 40.

46 Sahr, *supra* note 26, at 2–3. During complex manufacturing within a cell, proteins are heavily modified through processes known as post-translational modification that are replete with potential sources of error. *Id.*

47 Differences in manufacturing can cause differences in protein folding, which alter the protein function. Protein folding involves the conversion of a linear string of bonded amino acids into a final, three-dimensional structure, which converts the protein from an inactive to an active state. *See, e.g.*, Shawn Glidden, *The Generic Industry Going Biologic*, 20 BIOTECH. L. REP. 172, 172–73 (2001).

48 *See* Charles L. Bennett et al., *Pure Red-Cell Aplasia and Epoetin Therapy*, 351 NEW ENG. J. MED. 1403, 1404 (2004).

49 Jeanne Yang, Note, *A Pathway to Follow-on Biologics*, 3 HASTINGS SCI. & TECH. L.J. 217, 226 (2011). Erythropoetin helps to regulate blood cell production. Thus, increased erythropoietin helps to cure the low iron counts that are indicative of anemia. Bennett et al., *supra* note 48, at 1404.

50 Yang, *supra* note 49, at 226. Both Eprex and Epogen were manufactured using the same DNA sequence. *Id.*

51 *Id.* Epogen was manufactured in a human serum albumin media while Eprex was manufactured in a glycine and polysorbate-80 medium. *Id.*

52 *Id.*

known as red-cell aplasia,[53] in comparison to only five cases for patients taking Epogen.[54] Due to the sensitivity and inherent difficulty of biologics manufacturing, the standard biologics approval process requires approximately 250 safety tests, while the average small-molecule approval process only requires 40–50 tests.[55]

2. *Follow-on Biologics*

Much of the current regulatory interest in biologics involves "follow-on biologics."[56] When the patent and marketing exclusivity rights expire for a small-molecule drug, generic drug manufacturers attempt to create generic copies of the drug for marketing.[57] Such generic drugs are immensely important for patients, as the existence of competition in the marketplace drives down the cost of the drug.[58] Like small-molecule generic drugs, follow-on biologics attempt to mimic the structure of pioneer biologics. Unlike small-molecule generic drugs, however, a follow-on biologics manufacturer may use a different manufacturing process from the pioneer manufacturer.[59] Because different processes are used, the final product for the follow-on biologic may differ in comparison to the pioneer product.[60]

In addition to these inconsistent manufacturing processes, biologics manufacturing presents other challenges not present in small-molecule manufacturing that necessitate special considerations in developing a follow-on biologics approval pathway. Biologic medicines are exceptionally expensive compared to their small-molecule counterparts, greatly increasing the need for an efficient approval procedure for follow-on biologics.[61] Further, as evidenced by the Eprex/

---

53 In red-cell aplasia, the body no longer has sufficient erythropoietin to make red blood cells, leading to severe anemia. *See id.*

54 Bennett et al., *supra* note 48, at 1405.

55 *See* Ingrid Kaldre, Note, *The Future of Generic Biologics: Should the United States "Follow-on" the European Pathway?*, 2008 DUKE L. & TECH. REV. 0009 ¶ 14 (Nov. 6, 2008), http://scholarship.law.duke.edu/cgi/viewcontent.cgi?article=1184&context=dltr. As can be imagined, the requirement for more testing increases the cost of biologics approval in comparison to small-molecule approval. *Id.* There are also other, more subtle differences between biologics and small-molecule drugs. For example, small-molecule drugs are more stable and can be administered as pills, whereas biologics are less stable and must be administered by injection. Michał Nowicki, *Basic Facts About Biosimilars*, 30 KIDNEY & BLOOD PRESSURE RES. 267, 268 (2007).

56 Nowicki, *supra* note 55, at 268. Follow-on biologics are known as "biosimilars" in European terminology. *Id.*

57 *Id.*

58 *See id.* at 271.

59 *Id.* at 268.

60 *Id.*

61 *See* Yang, *supra* note 49, at 223–24.

Epogen example, there are immunogenicity and safety concerns for the approval of follow-on biologics that may only be discoverable in full clinical trials.[62] Additionally, for small-molecule drugs, if there is a showing of bioequivalence[63] between the generic and pioneer compounds during FDA approval, pharmacists can substitute the generic drug for the pioneer compound without permission from a physician.[64] With follow-on biologics, however, pharmacists will have to be much more careful in making such substitutions because follow-on biologics are not exact copies of the pioneer biologics.[65] Due to these significant concerns, the regulatory pathway developed under the BPCIA differs from the regulatory pathway for generic small-molecule drugs under the Hatch-Waxman Act.

B. FDA Drug Approval Processes Prior to the BPCIA[66]

Prior to congressional enactment of the BPCIA, the FDA approved the vast majority drugs under either the FDCA[67] or the PHSA.[68] Since 1984, most generic drugs have been reviewed under the Hatch-Waxman Act.[69] The FDA usually reviews pioneer small-molecule drugs under the FDCA and pioneer biologics under the PHSA.[70]

1. FDA Approval of New Drugs

Under the FDCA, a drug is defined in part as an "article[ ] intended for use in the diagnosis, cure, mitigation, treatment, or preven-

---

62 *See id.* at 226–27.

63 For a more detailed description of the statutory term "bioequivalence," see *infra* note 97 and accompanying text.

64 Nowicki, *supra* note 55, at 271. Such substitutions are permitted because there should be no safety concern in substituting the generic drug for the pioneer drug, as they are essentially the same compound. *Id.*

65 *Id.*

66 For a detailed history of the regulation of biologics and the influence of that regulation on the enactment of the BPCIA, see generally Krista Hessler 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 (2010).

67 Federal Food, Drug, and Cosmetic Act ("FDCA"), Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301–399 (2006)).

68 Public Health Service Act ("PHSA") of 1944, Pub. L. No. 78-410, 58 Stat. 682, *amended by* Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, 124 Stat. 804 (2010) (codified at 42 U.S.C. § 262 (Supp. V 2012)).

69 Drug Price Competition and Patent Term Restoration ("Hatch-Waxman") Act of 1984, Pub. L. No. 98-417, 98 Stat 1585.

70 *See* Donna M. Gitter, *Innovators and Imitators: An Analysis of Proposed Legislation Implementing an Abbreviated Approval Pathway for Follow-on Biologics in the United States*, 35 FLA. ST. U. L. REV. 555, 563 (2008).

tion of disease."[71] Any product that claims to have diagnostic, preventative, or therapeutic characteristics must be approved through a detailed process overseen by the FDA.[72]

The first step of the approval process involves a manufacturer submitting an Investigational New Drug Application ("IND") to the FDA.[73] Once the IND is approved, the applicant can begin a series of three stages of human clinical trials.[74] After the trials are completed, the applicant will submit either a New Drug Application ("NDA") or a Biologic License Application ("BLA") to the FDA.[75] Among other factors required by the FDCA,[76] an applicant must demonstrate the safety and efficacy of the drug through substantial evidence in order to receive approval of an NDA.[77] In contrast, the FDA approves a BLA based on the statutory directives of the PHSA.[78] For approval of a BLA, the compound must be "safe, pure, and potent."[79] Historically, there were more significant differences between the FDA's treatment of NDAs and BLAs,[80] but today the only significant difference between the NDA and BLA approval process is that BLA applicants must meet manufacturing facility quality and inspection requirements that are absent from the NDA approval process.[81]

After an NDA or BLA is approved, the FDA publishes the drug name and all patents associated with the drug in the *Approved Drug Products with Therapeutic Equivalence Evaluations*, otherwise known as the *Orange Book*.[82] These patents were exceedingly important for

---

71 21 U.S.C. § 321(g)(1)(B).

72 Gitter, *supra* note 70, at 565–68 (describing the FDA approval process).

73 *Id.* at 565.

74 *Id.*

75 Approximately sixty-four percent of drugs that reach Phase III testing will lead to submission of an NDA or BLA. *See id.* at 566.

76 21 U.S.C. § 355(b)(1).

77 *Id.* § 355(d).

78 Public Health Service Act ("PHSA") of 1944, Pub. L. No. 78-410, § 351, 58 Stat. 682 (codified at 42 U.S.C. § 262(a) (2006)).

79 42 U.S.C. § 262(a)(2)(c)(i)(I).

80 Prior to 2000, there were more significant differences between the NDA and BLA approval process. Gregory N. Mandel, *The Generic Biologics Debate: Industry's Unintended Admission That Biotech Patents Fail Enablement*, 11 VA. J.L. & TECH. no. 8, 2006, ¶ 38, http://www.vjolt.net/vol11/issue4/v11i4_a8-Mandel.pdf. In the Food and Drug Administration Modernization Act of 1997, however, Congress directed the FDA to "minimize differences in the review and approval of products" under BLAs and NDAs. Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 123(f), 111 Stat. 2296, 2324 (codified at 21 U.S.C. § 355 (2006)).

81 *See* Gitter, *supra* note 70, at 574.

82 OFFICE OF GENERIC DRUGS, U.S. FOOD & DRUG ADMIN., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (33d ed. 2013) [hereinafter ORANGE

the applicant prior to enactment of the Hatch-Waxman Act, as any competitor had to wait for the patent terms to expire before testing or developing a generic version of the drug.[83]

The average cost for bringing a small-molecule drug to market is between $800 million and $1.7 billion.[84] For a biologic, the cost to bring a drug to market is approximately $1.2 billion.[85] These costs include the early development of the drug, the clinical trials process, the application process, legal fees, early marketing, and, most significantly, the costs associated with failed attempts at approval for similar drugs.[86] The substantial costs necessary to bring a successful drug to market are a major cause of the high costs of pioneer drugs that are ultimately passed on to patients.[87]

2. *FDA Approval of Generic Small-Molecule Drugs*

Prior to 1984 and the enactment of the Hatch-Waxman Act, the generic drug market was almost nonexistent. At that time, a generic manufacturer of a small-molecule or biologic drug had to undergo the full NDA or BLA approval process to bring its drug to market, including performing the same clinical trials as the pioneer manufacturer.[88] Under this scheme, there was little incentive to produce generic drugs and the generic industry was therefore essentially irrelevant.[89]

BOOK]; *see also* 21 C.F.R. § 314.53(e) (2012). The *Orange Book* represents the key source of notice for all drug manufacturers regarding what patents could possibly be infringed upon by the marketing of a generic form of the approved drug. Under a BLA, submission of patent information is not required. *See* Gitter, *supra* note 70, at 574.

83 *See* Matthew J. Seamon, *Antitrust and the Biopharmaceutical Industry: Lessons from Hatch-Waxman and an Early Evaluation of the Biologics Price Competition and Innovation Act of 2009*, 34 NOVA L. REV. 629, 654 (2010). The Hatch-Waxman Act substantially altered this limit on testing and development of generic drugs. *See infra* Part I.B.2.b.

84 Pradeep Suresh & Prabir K. Basu, *Improving Pharmaceutical Product Development and Manufacturing: Impact on Cost of Drug Development and Cost of Goods Sold of Pharmaceuticals*, 3 J. PHARMACEUTICAL INNOVATION 175, 178–81 (2008).

85 BIOTECH. INDUS. ORG., THE DIFFERENCE WITH BIOLOGICS: THE SCIENTIFIC, LEGAL, AND REGULATORY CHALLENGES OF ANY FOLLOW-ON BIOLOGICS SCHEME 4 (2007), http://www.bio.org/sites/default/files/WhitePaper.pdf.

86 Gitter, *supra* note 70, at 565–67. Only twenty percent of small-molecule drugs and thirty percent of biologics that begin the IND process eventually receive marketing approval. *Id.* at 566–67.

87 *See id.*

88 George Fox, Note, Integra v. Merck*: Limiting the Scope of the § 271(e)(1) Exception to Patent Infringement*, 19 BERKELEY TECH. L.J. 193, 195 n.16 (2004). Another substantial barrier to generic entry to market was the Federal Circuit decision in *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858 (Fed. Cir. 1984), which held that the use of a patented drug in the development of a generic version constituted infringement under 35 U.S.C. § 271. *Id.* at 861–64.

89 *See* Seamon, *supra* note 83, at 654.

To remedy this lack of a robust generics market, Congress passed the Drug Price Competition and Patent Term Restoration Act of 1984, popularly known as the Hatch-Waxman Act.[90] Under the Hatch-Waxman Act, the generic applicant can use the pioneer applicant's clinical trials data—disclosed in the original NDA—to demonstrate the generic compound's safety and efficacy.[91] The Hatch-Waxman Act has decreased the cost of bringing a generic drug to market to only $2 million—as compared to the $1 billion necessary to complete a full NDA application—leading to a boom in the generic drug industry.[92] The Hatch-Waxman Act was very much the model for the BPCIA,[93] so an analysis of the approval process for small-molecule drugs highlights the differences adopted in the BPCIA.

a. Hatch-Waxman Approval Process for Generic Small-Molecule Drugs: ANDA.[94]

The most prominent pathway for generic small-molecule drug approval through the Hatch-Waxman Act is under section 505(j), known as the abbreviated new drug application ("ANDA").[95] Generic drugs that are identical or almost identical to the pioneer compound can follow the ANDA process for approval,[96] allowing the generic applicant to rely on the original NDA for proof of safety and efficacy.[97] In

---

90 Drug Price Competition and Patent Term Restoration ("Hatch-Waxman") Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585; *see also* Seamon, *supra* note 83, at 654.

91 *See* Yang, *supra* note 49, at 229.

92 Gitter, *supra* note 70, at 571.

93 The Hatch-Waxman approval process, particularly the abbreviated new drug application ("ANDA") process, does not apply to biologics in general, because the pioneer compound must have been approved under an NDA in order to use an ANDA, but most biologics are approved under a BLA. *See* John Alan Little, Jr., Note, *Taking from Trailblazers: Learning from Those Who Have Gone Before When Approving Biosimilars*, 44 GA. L. REV. 1097, 1106–08 (2010).

94 The Hatch-Waxman Act also provides another pathway for approval of generic drugs, known as the § 505(b)(2) or "Paper NDA" application. This pathway is used for compounds that are similar, but not identical, to the pioneer compound. While this process would appear to be available for follow-on biologics, which are not identical to the pioneer biologic, it has not been widely used as such. *See, e.g.*, Gitter, *supra* note 70, at 570–76; Sahr, *supra* note 26, at 5–6; Seamon, *supra* note 83, at 648; Janet Woodcock et al., Opinion, *The FDA's Assessment of Follow-on Protein Products: A Historical Perspective*, 6 NATURE REVS.: DRUG DISCOVERY 437, 438 (2007).

95 21 U.S.C. § 355(j) (2006); *see also* Gitter, *supra* note 70, at 568.

96 21 U.S.C. § 355(j); 21 C.F.R. § 314.92(a) (2012).

97 21 U.S.C. § 355(j)(2)(A)(iv); *see also* Sahr, *supra* note 26, at 5. The only additional requirement on the generic drug manufacturer is an abridged study to demonstrate bioequivalence. ORANGE BOOK, *supra* note 82, at viii–x. Bioequivalence is shown through pharmacokinetic experiments, which are much cheaper than full clinical trials. 21 C.F.R. § 320; *see also* Sahr, *supra* note 26, at 5.

exchange for allowing generic manufacturers to use the data from the pioneer drug's NDA, the Hatch-Waxman Act also prevents the generic manufacturer from gaining approval under an ANDA within five years of the pioneer drug's approval date.[98] This compromise strikes a balance between bringing the generic drugs to market and protecting the proprietary interests of pioneer manufacturers.

b. *Patent Concerns in ANDA Approval Under the Hatch-Waxman Act*

Under the ANDA approval pathway, the pioneer manufacturer's intellectual property is protected through a complicated process.[99] The Hatch-Waxman Act does not allow the generic manufacturer to begin marketing its product until either the pioneer's patents expire or those patents are found to be invalid.[100] The generic applicant must make one of four certification statements related to the relevant pioneer compound for each patent listed in the *Orange Book*.[101] Of particular importance, a Paragraph IV certification that the pioneer's patents are invalid or not infringed will almost certainly lead to litigation, as the pioneer manufacturer will likely assert that its patents are presumptively valid as issued.[102] Filing a Paragraph IV certification triggers a thirty-month stay that prevents the FDA from approving the ANDA pending completion of subsequent litigation.[103]

Filing a certification under Paragraph IV has several benefits for the generic applicant. First, if an ANDA includes a Paragraph IV certification, the applicant can submit the ANDA four years after the

---

98 This time period is known as "exclusivity." 21 U.S.C. § 355(j)(5)(F)(ii).

99 The Hatch-Waxman Act amended the patent infringement statute to allow use of a patented compound to obtain data for an ANDA, effectively overruling the Federal Circuit's holding in *Roche* that such activity constituted infringement. Drug Price Competition and Patent Term Restoration ("Hatch-Waxman") Act of 1984, Pub. L. No. 98-417, § 202, 98 Stat. 1585, 1603 (codified as amended at 35 U.S.C. § 271 (2006)); Roche Prods., Inc. v. Bolar Pharm. Co., 733 F.2d 858, 861–64 (Fed. Cir. 1984).

100 21 U.S.C. § 355(a) (noting that no drug can be marketed unless there is an approval of a paper NDA application, § 355(b), or an ANDA, which may not be approved until the patents expire or are found invalid per § 355(j)(5)(B)).

101 *See* 21 U.S.C. § 355(j)(2)(A)(vii) (describing the four kinds of certifications available to the generic applicant).

102 *See* Seamon, *supra* note 83, at 658.

103 *See* 21 U.S.C. § 355(j)(5)(B)(iii). After the filing of a Paragraph IV certification, the pioneer manufacturer has forty-five days to file an infringement suit. Otherwise, the thirty-month stay order is lifted and the FDA can approve the ANDA. *See id.* If the pioneer manufacturer files the suit, the FDA stays approval until either (1) the patents expire, (2) the thirty-month period is up, or (3) the infringement suit is complete. *See id.*; Seamon, *supra* note 83, at 658.

pioneer NDA is approved—one year sooner than the normal five-year exclusivity period would otherwise allow.[104] Additionally, if the first ANDA applicant for a specific drug files a Paragraph IV certification, that applicant generally will enjoy a 180-day exclusivity period against all other generic applicants beginning with the first commercial marketing of the approved generic drug.[105] For the pioneer manufacturer, the ANDA process provides at least four or five years of data exclusivity, a formulaic process for handling infringement suits, and, most importantly, patent term extensions for pioneer drugs approved through the NDA process.[106]

There is still some concern that the Hatch-Waxman Act has not fully accomplished the decrease in drug prices that Congress sought.[107] Nevertheless, the Hatch-Waxman Act has been extremely successful in fostering a booming generic drug industry in the United States.

c. *Abuses of the Hatch-Waxman Approval Process*

Certain abuses of the ANDA process have plagued generic drug approval and will likely be of substantial concern for follow-on biologic approval under the BPCIA.

First, pioneer manufacturers have removed patents from the *Orange Book* during potentially successful Paragraph IV challenges by generic manufacturers.[108] By removing the patent from the *Orange Book*, the generic applicant must amend their certification, which forces the generic applicant to lose the potential 180-day exclusivity period.[109]

Second, pioneer manufacturers have obtained a series of "sham" patents and listed these patents in the *Orange Book* after a Paragraph IV proceeding had begun.[110] Because the generic applicant could po-

---

104 21 U.S.C. § 355(j)(5)(F)(ii).

105 *Id.* § 355(j)(5)(B)(iv).

106 *See generally* 35 U.S.C. § 156 (2006). These patent term extension provisions compensate the NDA applicant for the time spent during the IND and NDA approval process. *See* Seamon, *supra* note 83, at 655.

107 *See* Seamon, *supra* note 83, at 656–67. The first generic to market is often priced at approximately ninety-four percent of the pioneer drug price, showing no real savings. It is only after seventeen generics come to market that competition drives the price of the drug down to ten percent of the original pioneer drug price. *Id.*

108 *See id.* at 660–61.

109 *See id.*

110 Sham patents are patents involving peripherally related aspects of the drug not at issue in the litigation but still potentially infringed by the applicant. *See* Matthew Avery, Note, *Continuing Abuse of the Hatch-Waxman Act by Pharmaceutical Patent Holders and the Failure of the 2003 Amendments*, 60 HASTINGS L.J. 171, 179–80 (2008).

tentially infringe these patents, the applicant must file a new Paragraph IV certification, which triggers another 30-month stay before approval.[111]

Finally, pioneer manufacturers have entered "pay-to-delay" agreements with generic manufacturers.[112] In these agreements, the pioneer manufacturer proposes a settlement wherein the ANDA is approved, but the generic applicant agrees not to enter the market in exchange for financial compensation.[113] Such agreements also bar the entry of other generic competitors to the market because competitors cannot begin marketing until the 180-day exclusivity period for the first generic applicant lapses[114] Through such agreements, the pioneer has de facto exclusivity until its patents expire.[115]

Although these are not the only potential abuses of the Hatch-Waxman Act approval process,[116] they are the abuses that have caused Congress the most concern. These abuses are particularly worrisome because similar problems may be present in the follow-on biologics approval process.

d. Congressional and Judicial Responses to Abuses of the Hatch-Waxman Approval Process

In response to these abuses, Congress included provisions in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA")[117] to prevent the most harmful abuses of the Hatch-Waxman Act. Under the MMA, a pioneer manufacturer can receive

---

111 *See id.*; *see also, e.g.*, Mylan Pharm., Inc. v. Thompson, 268 F.3d 1323, 1330–31 (Fed. Cir. 2001).

112 *E.g.*, Seamon, *supra* note 83, at 673, 674; *see also* Avery, *supra* note 110, at 181.

113 *See* Avery, *supra* note 110, at 181.

114 *See id.*

115 *See id.* The drafters of the Hatch-Waxman Act have roundly condemned this process. 148 CONG. REC. S15,353–54 (daily ed. July 30, 2002) (statement of Sen. Orrin Hatch) ("As a coauthor of the Drug Price Competition and Patent Term Restoration Act, I can tell you that I find these type of reverse payment collusive arrangements appalling.").

116 Another possible abuse receiving substantial publicity is "authorized generics" licensing. Under "authorized generics" licensing, a pioneer manufacturer will license their product, after losing a Paragraph IV challenge to a generic manufacturer, to a different generic manufacturer to distribute in exchange for royalties. This second generic manufacturer is not subject to the 180-day marketing exclusivity that the ANDA applicant receives for their successful Paragraph IV challenge. By licensing their product and receiving a royalty, the pioneer is able to hedge their losses after a Paragraph IV challenge. *See* Avery, *supra* note 110, at 182–83. The FDA has not yet condemned this practice because it appears to increase competition by adding a new generic manufacturer to the market. *Agency Views on Authorized Generics a Boon to Brands*, 36 WASH. DRUG LETTER, no. 40 (Oct. 11, 2004), http://www.fdanews.com/newsletter/article?articleId=66277&issueId=6931.

117 Medicare Prescription Drug, Improvement, and Modernization Act ("MMA") of 2003,

only a single thirty-month stay upon a Paragraph IV certification by an ANDA applicant, which removes any incentive to seek sham patents.[118] Further, the generic ANDA applicant only has to make a Paragraph IV certification against those patents that were listed in the *Orange Book* at the time the ANDA was filed.[119] The MMA also provides that the 180-day exclusivity provision starts when the applicant begins selling either its own generic or an authorized generic.[120]

Additionally, the MMA establishes a series of forfeiture provisions that prevent the pioneer from entering settlements or delaying any generic entry on the market.[121] To prevent abusive pay-to-delay agreements, the MMA requires that agreements between pioneer and generic manufacturers be filed with the Federal Trade Commission ("FTC") and the Department of Justice ("DOJ") for review of potential antitrust violations.[122]

Although the MMA does create reporting requirements for pay-to-delay agreements, the MMA does not ban such agreements.[123] Congress has not spoken directly to the validity of pay-to-delay agreements, so the courts are left to determine if these agreements are invalid as anticompetitive. The current rule appears to be that pay-to-delay agreements are legal if they do not artificially extend a patent's term, but the Supreme Court has not conclusively spoken on this issue.[124] Although Congress and the courts have attempted to limit the

---

Pub. L. No. 108-173, 117 Stat. 2066 (codified as amended in scattered sections of 21 and 42 U.S.C.).

118 Avery, *supra* note 110, at 184–85; *see also* 21 U.S.C. § 355(c)(3)(C) (2006).

119 21 U.S.C. § 355(j)(5)(B)(iii); Avery, *supra* note 110, at 184. Courts have also been fairly vigilant in protecting against abuses of the system through such sham patents. *See, e.g.*, Aventis Pharma S.A. v. Amphastar Pharm., Inc., 525 F.3d 1334, 1349 (Fed. Cir. 2008) (finding inequitable conduct when using sham patents to abuse a 30-month stay); *In re* Neurontin Antitrust Litig., No. 02-1390, 2011 WL 2357793, at *1 & n.1 (D.N.J. June 9, 2011) (alleging defendant used listing of sham patents to delay entry into the generic market).

120 21 U.S.C. § 355(j)(5)(B)(iv)(I).

121 *See* Avery, *supra* note 110, at 185–86.

122 21 U.S.C. § 355 note (Federal Trade Commission Review). This provision applies to agreements involving (1) the manufacture or sale of the patented drug or (2) the 180-day exclusivity period. Avery, *supra* note 110, at 187.

123 Avery, *supra* note 110, at 189–90.

124 Three circuits have held that such agreements are valid as long as they are not used to cover up clearly invalid patents. *In re* Ciprofloxacin Hydrochloride Antitrust Litig., 544 F.3d 1323, 1336 (Fed. Cir. 2008); *In re* Tamoxifen Citrate Antitrust Litig., 466 F.3d 187, 202–03 (2d Cir. 2006), *cert. denied sub nom.* Joblove v. Barr Labs, Inc., 551 U.S. 1144 (2007); Valley Drug Co. v. Geneva Pharm., Inc., 344 F.3d 1294, 1304 (11th Cir. 2003), *cert. denied*, 543 U.S. 939 (2004). The Sixth Circuit has held such agreements to be per se invalid. *In re* Cardizem CD Antitrust Litig., 332 F.3d 896, 908 (6th Cir. 2003), *cert. denied sub nom.* Andrx Pharm., Inc. v. Kroger Co., 543 U.S. 939 (2004). The D.C. Circuit has found one specific agreement to be an

abuses inherent in the Hatch-Waxman system, these abuses are still prevalent today and must be considered in light of the patent provisions under the BPCIA.

C. *Regulating Biologics Under the BPCIA*

Due to the lack of a formal approval process for follow-on biologics under the FDCA and the Hatch-Waxman Act, Congress developed a pathway for follow-on biologics approval, the BPCIA,[125] as part of the ACA.[126] The BPCIA made two major changes to the existing drug approval process under the PHSA. First, new § 262(k) establishes a formal process for licensure of follow-on biologics.[127] Second, new § 262(*l*) creates a mechanism for resolving patent disputes between a pioneer biologics manufacturer and a follow-on biologics manufacturer.[128] Through the BPCIA, Congress has solidified a pathway for development of generic biologics.

1. *Follow-on Biologics Licensure Provisions Under the BPCIA*

The licensure provisions for follow-on biologics share many similarities with the pre-existing generic approval process for small-molecule drugs, but with some key differences. The biologics applicant must demonstrate that its product is "biosimilar" to the approved pioneer product,[129] and that the follow-on biologic matches the pioneer

---

invalid restraint of trade. Andrx Pharm., Inc. v. Biovail Corp. Int'l, 256 F.3d 799, 815 (D.C. Cir. 2001), *cert. denied*, 535 U.S. 931 (2002). The Eleventh Circuit later applied a rule of reason approach to uphold such agreements. Schering-Plough Corp. v. FTC, 402 F.3d 1056, 1066 (11th Cir. 2005); *see also* Avery, *supra* note 110, at 190. The Supreme Court granted certiorari in 2012 to determine the level of scrutiny appropriate for pay-to-delay settlement agreements, and heard oral arguments in the case on March 25, 2013. FTC v. Watson Pharm., Inc., 677 F.3d 1298 (11th Cir. 2012), *cert. granted*, 133 S. Ct. 787 (2012); *Supreme Court of the United States October Term 2012: For the Session Beginning March 18, 2013*, SUPREME COURT OF THE U.S. (last revised Feb. 1, 2013), http://www.supremecourt.gov/oral_arguments/argument_calendars/MonthlyArgumentViewer.aspx?Filename=MonthyArgumentCalMar2013.htm. The case is now proceeding under the name *FTC v. Actavis*. *See id.*

125 Biologics Price Competition and Innovation Act of 2009 § 7002, 42 U.S.C. § 262 (Supp V. 2012).

126 Patient Protection and Affordable Care Act ("ACA"), Pub. L. No. 111-148, 124 Stat. 119 (2010) (codified as amended in scattered sections of 26 U.S.C. and 42 U.S.C.). The ACA was recently upheld as constitutional by the Supreme Court. Nat'l Fed'n. of Indep. Bus. v. Sebelius, 132 S. Ct. 2566 (2012).

127 42 U.S.C. § 262(k) (Supp. V 2012).

128 *Id.* § 262(*l*). The BPCIA refers to the pioneer manufacturer as the "reference product sponsor." *Id.* However, to maintain consistency, this Note replaces the term "reference product sponsor" with "pioneer manufacturer" throughout.

129 *Id.* § 262(k)(2)(A)(i)(I). The BPCIA definition of "biosimilar" requires that "the biological product is highly similar to the reference product notwithstanding minor differences in

compound in safety, purity, and potency.[130] On top of meeting the biosimilarity requirements,[131] the applicant can also attempt to prove that the follow-on biologic is interchangeable with the reference product.[132]

Section 262(k) also defines the extent of exclusivity granted to the pioneer manufacturer.[133] A follow-on biologics application cannot be filed until four years after the date on which the pioneer product was licensed.[134] Further, the FDA may not approve a follow-on biologics license until twelve years after the date the pioneer product was licensed.[135] This twelve-year exclusivity period is the main benefit provided to a pioneer biologics applicant, allowing the pioneer to recoup substantial development and licensing costs.[136] The follow-on biologics applicant may also receive exclusivity benefits under the BPCIA. The first follow-on biologics applicant that obtains interchangeability status receives one year of exclusivity against other generic manufacturers from the time of first marketing.[137]

The FDA has stated that it will soon issue comprehensive guidance documents to help clarify this complex follow-on biologics ap-

---

clinically inactive components" and that "there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product." *Id.* § 262(i)(2). This "biosimilarity" standard is more exacting than the "bioequivalence" standard of an ANDA. *See* Steven A. Nash & Rebecca Workman, *A New Pathway for Follow-on Biologics*, 20 FED. CIR. B.J. 193, 198 (2010). Nevertheless, biosimilarity can be shown through much less rigorous studies than those required for a BLA or NDA. *See* 42 U.S.C. § 262(k)(2)(A)(i)(I); *see also supra* Part II.B.

130 42 U.S.C. § 262(i)(2)(B).

131 Further requirements are listed in § 262(k)(2)(A)(i)(I).

132 "Interchangeable" status allows a pharmacist to exchange the pioneer drug for a generic drug because the generic drug "produc[es] the same clinical result as the reference product in any given patient." *Id.* § 262(k)(4).

133 *Id.* § 262(k)(6).

134 *Id.* § 262(k)(7)(B).

135 *Id.* § 262(k)(7)(A).

136 Nash & Workman, *supra* note 129, at 199–200.

137 42 U.S.C. § 262(k)(6). The provision only applies to applicants seeking interchangeable status, not just biosimilar status. *Id.* Only the first biologic applicant to achieve interchangeable status receives this exclusivity. *Id.* This is a subtle difference from the ANDA approach, which grants exclusivity to the first applicant to file for Paragraph IV regardless of the success of the Paragraph IV challenge, and may help prevent some abuses mentioned in Part II.B.2 of this Note. *See* Nash & Workman, *supra* note 129, at 202. This one-year exclusivity period can be altered by events during the patent dispute process. *See, e.g.*, 42 U.S.C. § 262(k)(6)(B) (allowing consideration of any application eighteen months after completion of patent litigation); *id.* § 262(k)(6)(C)(ii) (extending interchangeable exclusivity to eighteen months if no patent litigation ensues).

plication scheme, and will also begin to accept applications immediately.[138]

2. *Patent Dispute Provisions Under the BPCIA*

As with the patent resolution system developed under the Hatch-Waxman Act, the BPCIA includes complicated patent dispute provisions that allow the generic biologic manufacturer to prepare a follow-on biologics application without infringing the pioneer manufacturer's patents.[139] The patent provisions developed under the BPCIA, however, differ substantially from those found in the Hatch-Waxman Act.

a. Patent Exchange Process Prior to Infringement Litigation

The first steps in the patent dispute provisions involve the exchange of information regarding relevant patents ("patent exchange process"). In contrast to the patent disclosure requirements for small molecule drugs, the BPCIA does not require public listing of relevant patents for biologics.[140] As such, there is no equivalent of the *Orange Book* for biologics. Instead, the BPCIA provides for a patent exchange scheme that occurs almost completely in private between the pioneer manufacturer and the generic applicant, with strict confidentiality limitations placed on the parties involved.[141]

Shortly after the FDA accepts a § 262(k) application for review, the applicant must provide the pioneer manufacturer with a copy of the application.[142] In response, the pioneer manufacturer must then provide the applicant with a list of relevant patents at issue, known as

---

138 *See Implementation of the Biologics Price Competition and Innovation Act of 2009*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/ucm215089.htm (last updated Mar. 10, 2011). The FDA released its first series of proposed draft guidance regarding the BPCIA on February 9, 2012. Press Release, U.S. Food & Drug Admin., FDA Issues Draft Guidance on Biosimilar Product Development (Feb. 9, 2012), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm291232.htm. The FDA is prepared to accept § 262(k) applications, but although manufacturers have shown interest in imminent submissions, none appear to have been submitted as of May 2012. Rosemary Frei, *U.S. Prepares Groundwork for Biosimilar Approvals*, 7 CLINICAL ONCOLOGY NEWS, May 2012, at 1, 26, 28.

139 42 U.S.C. § 262(*l*).

140 42 U.S.C. § 262(*l*)(1).

141 Under these limitations, only the in-house and outside counsel for the follow-on biologic and pioneer manufacturers have access to lists of the relevant patents involved. *Id.* § 262(*l*)(1)(B)(ii).

142 *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, 234 (2010).

a Paragraph 3 list.[143] If the pioneer manufacturer fails to list a patent in its Paragraph 3 listing, it loses the ability to bring an infringement suit on that patent in later stages of the approval process.[144] The applicant will then provide the pioneer manufacturer with a rebuttal Paragraph 3 list of relevant patents at issue for the follow-on biologic, as well as a claim-by-claim analysis of the pioneer manufacturer's Paragraph 3 list.[145] In the last step of this process, the pioneer manufacturer provides a response to the applicant's claim-by-claim analysis, explaining why specific claims would be infringed or are valid.[146] In summary, this patent exchange process results in two Paragraph 3 lists of relevant patents, one for each party, and each party's analysis of the validity and scope of each patent.

b. Patent Negotiation Process Prior to Infringement Litigation

After the exchange of Paragraph 3 lists, the BPCIA requires a series of good faith negotiations between the applicant and pioneer manufacturer over which patents will be the subject of an infringement suit.[147] If the two parties fail to agree on the patents to be litigated, a series of "patent resolution" procedures are triggered.[148] First, the applicant notifies the pioneer manufacturer of the *number* of patents the applicant believes should be at issue.[149] Each side then develops a second list, known as a Paragraph 5 list, in which they identify the patents from their respective Paragraph 3 lists that will be subject to immediate litigation. The number of patents selected for each Paragraph 5 list is limited to the number of patents the applicant believes to be at issue.[150] For example, the applicant could state that it believes two patents should be at issue.[151] Both the applicant and pioneer manufacturer then each list two patents from their respective

143 Relevant patents include: (1) patents owned by either the pioneer manufacturer or exclusively licensed to the pioneer manufacturer, and (2) a list of patents the pioneer manufacturer would license to the applicant. 42 U.S.C. § 262(*l*)(3)(A). This is the only time when a third party licensor could assert their interest in the dispute process.

144 *See* Nash & Workman, *supra* note 129, at 217. If a newly issued, relevant patent becomes available to the pioneer manufacturer after the initial exchange of information, however, the pioneer manufacturer has thirty days after the issuance of the patent to notify the applicant of the new patent and preserve the patent for later litigation. 42 U.S.C. § 262(*l*)(7).

145 42 U.S.C. § 262(*l*)(3)(B).

146 *Id.* § 262(*l*)(3)(C).

147 *Id.* § 262(*l*)(4).

148 *Id.* § 262(*l*)(4)(B); *see also* Dougherty, *supra* note 142, at 237.

149 42 U.S.C. § 262(*l*)(5)(A). This is a novel procedure under the BPCIA scheme.

150 *Id.* § 262(*l*)(5)(B)(i). However, if the applicant lists zero patents, the pioneer manufacturer can propose one patent at issue. *Id.* § 262(*l*)(5)(B)(ii).

151 Dougherty, *supra* note 142, at 237–38.

Paragraph 3 lists that they believe to be at issue in a potential infringement suit.[152] These listed patents will be the basis of the infringement suit.[153]

c. Patent Infringement Litigation

Once the "patent exchange" and "patent resolution" procedures are completed, the "immediate patent infringement" action can occur.[154] The pioneer manufacturer has thirty days after the patent negotiation process ends[155] to bring an infringement suit on the listed patents.[156] Following the prior example, the pioneer manufacturer can only claim infringement of the four patents listed in the Paragraph 5 lists, and, at this time, cannot claim infringement on any patents not listed therein.[157] For any other potentially relevant patents,[158] the pioneer manufacturer must wait until receiving a statutorily required 180-day notice of marketing from the follow-on biologic applicant to claim any other infringement.[159] Unlike the Hatch-Waxman Act, the BPCIA does not include an automatic stay of approval for the § 262(k) application when a complaint is filed.[160] Once the complaint for the immediate patent infringement action has been filed, the Secretary of Health and Human Services ("HHS") must publish notice of the complaint in the Federal Register.[161] The matter will then proceed as a normal infringement suit with some slight modifications.[162] Namely, the BPCIA amends the damages and remedies provisions of

152 In this example, of the four total listed patents between the two sides, they could both propose the same patents (in which case two patents would be listed in the complaint), completely different patents (in which four patents would be listed in the complaint), or share one in common (in which three patents would be listed in the complaint). *Id.* at 237.

153 *Id.*

154 42 U.S.C. § 262(*l*)(6).

155 The patent negotiation process can end either through agreement between the two parties on the patents to litigate or once the Paragraph 5 lists are exchanged. *Id.* § 262(*l*)(6).

156 *Id.* § 262(*l*)(6)(B).

157 The language of the statute is somewhat unclear regarding the scope of the infringement action, as it is not obvious that the pioneer manufacturer cannot list Paragraph 5 patents that were not included in the Paragraph 3 lists. *See* Nash & Workman, *supra* note 129, at 209–10. However, such a reading would be inconsistent with the statutory scheme.

158 Other potentially relevant patents include patents listed in the Paragraph 3 exchange that were not included in the Paragraph 5 listing.

159 *See* Dougherty, *supra* note 142, at 238.

160 *See* Nash & Workman, *supra* note 129, at 210.

161 42 U.S.C. § 262(*l*)(6)(C). This is the first point at which the public is informed of the patent dispute procedure for a given product.

162 *See* 35 U.S.C. § 271(e)(2) (Supp. V 2012) (amending the Patent Act to include new § 271(e)(2), which makes it an act of infringement to submit an application for approval of a biosimilar product).

the Patent Act[163] to allow for preliminary[164] and permanent injunctive relief, a stay of FDA approval of the § 262(k) application, and damages[165] for infringement due to manufacture, use, or sale of a patented biological product.[166]

d. Postinfringement Procedures and Patent Rights Under the BPCIA

The BPCIA also alters other aspects of the follow-on biologics approval process. After the initial exchange and litigation process, the applicant must provide the pioneer manufacturer with written notice 180 days prior to the date when the applicant will begin to market the follow-on biologic product.[167] Once the pioneer manufacturer receives the notice, the pioneer manufacturer can seek a preliminary injunction against infringement of any patents listed in the initial Paragraph 3 exchange but not included in the Paragraph 5 lists.[168] This 180-day notice provision ensures that the pioneer manufacturer does not lose all patent rights for patents that are not included in the Paragraph 5 lists.

The BPCIA also creates a series of penalty default rules for noncompliance with the above-listed procedures.[169] If the applicant fails to provide the § 262(k) application to the pioneer manufacturer within statutory time limits, the pioneer manufacturer can seek a declaratory judgment of infringement at any time for any patent without following the patent exchange procedures.[170] Similarly, if the applicant fails to complete other steps in the patent dispute resolution process in a timely manner, the pioneer manufacturer can bring a declaratory judgment suit at any time for any Paragraph 3 patents.[171] If the pioneer manufacturer fails to timely identify patents during the "patent exchange" process, however, it permanently loses the ability to assert infringement of those patents as to that particular applica-

163 35 U.S.C. §§ 1–376 (2006).

164 A preliminary injunction is vitally important without an automatic stay of § 262(k) approval. *See* Nash & Workman, *supra* note 129, at 210.

165 Monetary damages are not available under the BPCIA patent litigation process until the biological product in question has been manufactured and sold. *See id.* at 214–16.

166 35 U.S.C. § 271(e)(4) (Supp. V 2012). A more thorough discussion of the litigation process under the BPCIA can be found in Nash & Workman, *supra* note 129, at 210–16.

167 *See* 42 U.S.C. § 262(*l*)(8) (Supp. V 2012).

168 *Id.*

169 *Id.* § 262(*l*)(9).

170 *Id.* § 262(*l*)(9)(C).

171 *Id.* § 262(*l*)(9)(B).

tion.[172] Finally, if the pioneer manufacturer fails to bring an infringement action within the thirty days after the "patent resolution" procedures, the pioneer manufacturer can no longer seek injunctive relief.[173] These strict penalties for failure to comply with the statutory time requirements of the BPCIA create substantial incentives for quick resolution of patent disputes.

II. Potential Abuses of the BPCIA Patent Dispute Scheme

The BPCIA patent dispute process provides substantial benefits to both follow-on biologics applicants and pioneer manufacturers. To the applicant, the BPCIA approval process grants control over the scope of the initial infringement suit, prevents third parties from intervening, provides for strong penalties against delay by the pioneer manufacturer, avoids immediate stays of FDA approval upon filing of an infringement suit, and limits the number of declaratory judgment actions a pioneer manufacturer can bring prior to marketing.[174] For the pioneer manufacturer, the entire patent dispute process is private until the infringement proceedings are initiated, giving the pioneer manufacturer more power to influence the patent dispute process.[175] In addition, the pioneer manufacturer retains essentially all of its patent rights prior to marketing for patents included in the Paragraph 3 lists.[176] Although Congress intended these benefits to spur development of the follow-on biologics industry, these provisions hide a substantial possibility for abuse of the system.

A. The Legislative History of the BPCIA Demonstrates Widespread Concern over Abuses of the Approval Process

During the congressional debate on the BPCIA, members of Congress, government agencies, and pharmaceutical companies identified several potential sources of abuse in the proposed patent dispute procedures.[177] The FTC argued that a pre-approval patent dispute resolution process would be essentially useless because biologics patents are so complex that a truncated dispute process could not adequately address infringement claims.[178] Further, the FTC

172 *See* Dougherty, *supra* note 142, at 244.

173 *See id.* at 243.

174 *Id.* at 244–45.

175 *Id.* at 235–38.

176 *Id.* at 238.

177 For a more thorough discussion of the full debate that took place prior to passage of the BPCIA, see generally Carver, Elikan & Lietzan, *supra* note 66.

178 *Id.* at 788–89.

noted that the patent provisions developed in the Hatch-Waxman Act were designed in part to protect small generic manufacturers from being forced to settle with large pioneer manufacturers to avoid expensive postmarketing litigation.[179] In contrast, large corporations will manufacture follow-on biologics in most cases, obviating the need for premarket patent dispute procedures to protect against abuse by pioneer manufacturers in this context.[180]

Members of the pharmaceutical industry expressed concern that the patent dispute procedures were too limited in only covering patents held by the pioneer manufacturer.[181] These procedures would not allow any third-party patent concerns to be heard until immediately prior to the marketing of the follow-on biologic.[182] Further, the pharmaceutical industry believed that the patent dispute provisions would give too much power to the follow-on applicant, as the applicant sets the number of patents that are immediately at issue.[183] Because the follow-on biologic manufacturer may want to litigate as little as possible upfront,[184] most patent disputes could be delayed until the 180-day notice period prior to marketing. As a result of this delay, district court judges will have to make rushed decisions on preliminary injunction requests for delays in marketing of approved follow-on biologics, which could affect the entire healthcare industry.[185]

Finally, during markup of the ACA, members of Congress noted that pay-to-delay settlements could result in abuses of the approval process for follow-on biologics.[186] Although the House version of the BPCIA included reporting requirements for any pay-to-delay settlement entered between the pioneer and follow-on biologics manufacturers,[187] the BPCIA as passed did not include any such requirements.[188]

---

179 *Id.*

180 *See id.*

181 *See id.* at 800.

182 *See id.*

183 *Id.*

184 This is especially true considering that the premarket litigation may predate approval of the follow-on biologic by the FDA. *See supra* Part I.C.1.

185 *See* Carver, Elikan & Lietzan, *supra* note 66, at 800.

186 *See id.* at 803–04.

187 *See id.*

188 *See* 42 U.S.C. § 262(k)–(*l*) (Supp. V 2012) (showing no reporting requirements regarding settlements entered during the patent dispute resolution process).

B. *Lack of Public Disclosure and Pay-to-Delay Settlements Represent Major Potential Sources of Abuse Under the BPCIA*

The concerns identified during congressional negotiations over the BPCIA demonstrate substantial potential sources of abuse in the patent dispute provisions. Among these possible sources of abuse, two are particularly problematic: (1) the lack of public disclosure or third-party input into the dispute process and (2) the lack of any external constraints on pay-to-delay settlements.

1. *Lack of Public Disclosure or Third-Party Input*

The extent of public disclosure in the biologics approval process was not seriously discussed prior to the enactment of the BPCIA. As a result, the BPCIA essentially provides no opportunity for public input or third-party intervention during the follow-on biologics approval process.[189] Prior to the filing of a complaint in the "initial infringement action," third parties can only assert their patent claims if a pioneer manufacturer has an exclusive license for use of that patent.[190] Further, the expansive privacy provisions of the BPCIA strictly limit third-party access to information exchanged between the pioneer manufacturer and the follow-on biologics applicant.[191] A third-party patent holder is entitled to review application materials,[192] but because there is no public notification requirement, it is unlikely that a third-party patent holder would be aware of its right to do so.

Although it might not appear that third-party interests would be particularly important in a typical patent dispute involving drug approval,[193] the BPCIA expanded the realm of relevant patents to include manufacturing patents.[194] Because manufacturing patents are often held by third parties, these third parties have a substantial interest in becoming involved in the patent dispute procedures. Further, the manufacturing processes used for different biologics are often very

---

189 *See supra* Part I.C.2.

190 42 U.S.C. § 262(*l*)(3)(A). This would presumably also include patents assigned by a third-party to the pioneer manufacturer.

191 *Id.* § 262(*l*)(1).

192 *Id.* § 262(*l*)(1)(B)(iii).

193 *See* 21 U.S.C. § 355(b)(1) (2006) (limiting contestations under the Hatch-Waxman Act to method and product patents, which were primarily held by the pioneer manufacturer); Dougherty, *supra* note 142, at 235.

194 *Compare* 42 U.S.C. § 262(*l*)(2)(A) (requiring details about manufacturing method patents under the BPCIA), *with* 21 U.S.C. § 355(b)(1) (lacking requirement for manufacturing information under the Hatch Waxman Act).

similar.[195] A third-party patent holder could often either license a manufacturing patent to several different biologics manufacturers or manufacture biologics on behalf of different biologics producers itself. In either case, however, the party holding the manufacturing patent has no rights under the BPCIA to initiate litigation until immediately prior to marketing.[196] Preventing third parties from asserting their rights prior to market entry increases the likelihood that approved follow-on products will have to be removed from the market during subsequent litigation, raising concerns about expensive postmarket litigation and a lack of settled expectations for manufacturers.

Along with the absence of third parties in the patent dispute process, there is no public notification of the patent dispute until the complaint is listed in the *Federal Register*.[197] Because there is no *Orange Book* for biologics,[198] the follow-on manufacturer can only guess as to the relevant patents at issue, which prevents design-around attempts. Further, the Paragraph 3 lists are not published, and only the Paragraph 5 patents appear in the complaint.[199] Thus, follow-on biologics manufacturers only have partial notice as to which patents may be at issue for biologics in development.[200] Greater public disclosure in the patent dispute process would allow manufacturers to better design around the pioneer manufacturer's product.

The lack of public disclosure during the patent dispute process is also troubling given the potential for collusion. Because of the inherent secrecy in the BPCIA patent dispute process, there is no public disclosure until a complaint is filed unless one of the participants publicizes an application filing.[201] Although such insulation from public scrutiny may support frank and honest negotiations between the parties, it can also promote collusion.[202] For example, a pioneer manufacturer could convince a follow-on biologic manufacturer not to include weaker Paragraph 3 patents in its Paragraph 5 list in exchange for a promise not to bring suit against a future product.[203] If the pioneer

195 Glidden, *supra* note 47, at 172–73. Different biologics can be produced using the exact same manufacturing method but with different amino acids substituted in a protein. *Id.*

196 42 U.S.C. § 262(*l*)(3)(C).

197 *Id.* § 262(*l*)(6)(C).

198 *See supra* Part I.C.2.a.

199 *See supra* Part I.C.2.c.

200 *See supra* Part I.C.2.b–c.

201 *See supra* Part I.C.2.a–b.

202 For example, many of the sources of abuse under the Hatch-Waxman Act involved collusive actions between pioneer and generic manufacturers. *See supra* Part I.B.2.c.

203 This sort of agreement is very similar to those seen under authorized generics agreements. *See* Avery, *supra* note 110, at 182–83.

and follow-on manufacturers collude to litigate only a portion of the patents that could be litigated, the pioneer could "hide" patents to prevent future design-around attempts by other follow-on manufacturers or prevent the follow-on manufacturer from invalidating weak patents.[204] Because follow-on biologics will cause a decrease in the cost of a pioneer drug only after multiple products arrive on the market,[205] the pioneer drug manufacturer benefits by allowing one follow-on biologic to be approved while preventing other products from entering the market by asserting patent infringement claims against them.[206] Further, the strict forfeiture provisions for failure to list a patent in a Paragraph 3 list[207] require the pioneer manufacturer to broadly identify relevant patents. Nevertheless, because Paragraph 5 lists could be developed through collusive actions and because Paragraph 3 lists are not published, the forfeiture provisions are limited and do not achieve the full public notice benefits they could provide. If the Paragraph 3 listings were made public or if the FDA published notice of a biologics application in the *Federal Register*, secret collusive conduct would be significantly more difficult to accomplish.

2. *Lack of Control over Pay-to-Delay Settlements*

The most likely source of abuse in the BPCIA follow-on biologics approval process is the lack of limits on pay-to-delay settlements.[208] Whether premarket litigation settlements should be banned or subject to reporting requirements was a major point of contention during the negotiations over the BPCIA.[209] The House of Representatives version of the BPCIA included a reporting requirement that would force any settlement between a pioneer manufacturer and follow-on bio-

---

204 *See id.*

205 *See* Seamon, *supra* note 83, at 656–57.

206 *See* Avery *supra* note 110, at 182–83. The economics of generic drugs, as described *supra* in note 107, make such schemes efficient for the pioneer manufacturer. As long as the specter of patent protection exists, even if the patents are objectively invalid, follow-on biologics manufacturers will likely choose to avoid expensive litigation and refrain from developing a follow-on biologic for that drug. Thus, while allowing one follow-on manufacturer to enter the market might transiently increase competition, it ultimately ends up depressing the market. These competing concerns are a major reason that the FTC and FDA have avoided making a conclusive statement regarding authorized generic drugs. *See supra* note 116.

207 *See* 35 U.S.C. § 271(e)(6)(C) (2006).

208 *See supra* Part I.B.2.c.

209 *See* Carver, Elikan & Lietzan, *supra* note 66, at 803–04.

logics applicant to be filed with the FTC.[210] In the final version of the BPCIA, however, all reporting requirements had been removed.[211]

The lack of limits on pay-to-delay settlements is surprising considering troubled history of these settlements in Hatch-Waxman litigation.[212] As discussed above, pay-to-delay settlements arose as a major source of concern under the Hatch-Waxman Act,[213] and Congress responded by passing the MMA, which subjected such settlements to FTC and DOJ scrutiny.[214] Despite this experience with small-molecule drugs, no such reporting requirement was enacted for biologics under the BPCIA.[215] The circuit courts remain split as to the validity of pay-to-delay agreements,[216] implying that Congress is best equipped to limit these potentially anticompetitive agreements.

In the context of biologics approval, the potential for abuse through pay-to-delay settlements is substantial. The development of biologics is expensive, and the market for a specific biologic is smaller than for most small-molecule drugs.[217] As such, pioneer manufacturers have significant incentives to engage in pay-to-delay settlements because any extra market exclusivity they gain will help to recoup the upfront costs of producing the drug.[218] The heavy emphasis on secrecy during the patent dispute resolution process, with almost no government intervention, creates a situation ripe for collusion or cartelization.[219] Further, the first follow-on biologics applicant to receive interchangeable status receives one year of exclusivity, increasing the incentive for collusion between the pioneer and an applicant that is able to achieve interchangeable status.[220] This period of exclusivity

---

210 *See id.* at 803.

211 *See* 42 U.S.C. § 262(k)–(*l*) (Supp. V 2012).

212 *See supra* Part I.B.2.c.

213 *See supra* Part I.B.2.c.

214 Medicare Prescription Drug, Improvement, and Modernization Act ("MMA") of 2003, Pub. L. No. 108-173, § 1112, 117 Stat. 2066, 2461–63; *see also* Avery, *supra* note 110, at 187.

215 *See* 42 U.S.C. § 262(k)–(*l*). .

216 *See supra* note 124.

217 *See supra* Part I.B.1.

218 *See supra* Part I.B.1.

219 *See supra* Part I.B.1.

220 *See supra* note 137 and accompanying text. The BPCIA is inherently better structured to prevent abuses of pay-to-delay settlements compared to the Hatch-Waxman Act. Under the BPCIA, eighteen months after the end of Paragraph 5 litigation, the FDA can begin to consider subsequent generic applications, regardless of any one-year interchangeable status exclusivity held by other generic applicants or any existing pay-to-delay settlements between a pioneer manufacturer and any applicants. Thus, at most, the generic biologics applicant can receive eighteen months of generic exclusivity and there is little incentive to delay entry into the market for more than six months. Further, it will be more difficult to achieve interchangeability status than

makes pay-to-delay settlements attractive to follow-on biologics manufacturers as well.[221]

Although the lack of public disclosure and ability for third-party intervention are significant concerns under the BPCIA, it is the lack of any limits on pay-to-delay settlements that presents the most likely source of abuse under the BPCIA. Nevertheless, all of these holes in the BPCIA provide significant opportunities for exploitation of the follow-on biologics approval process, ultimately limiting public access to more affordable biologics treatments. Congress should therefore act to curb these potential sources of abuse.

III. SOLUTIONS TO THE POTENTIAL ABUSES OF THE PATENT DISPUTE PROCESS UNDER THE BPCIA

Congress can remedy the above sources of abuse recognized in the BPCIA with targeted action.[222] Further, if the Supreme Court adopts a lower standard for analysis of pay-to-delay settlements in *FTC v. Actavis*, Congress will be the only party that can feasibly limit the impact of these settlements.[223] Earlier versions of the BPCIA included provisions that would have allowed interested third parties to participate in the patent dispute process, but these provisions were removed from the final bill.[224] In 2011, House Republicans proposed legislation (the "House Bill") that contained relevant proposals for remedying the BPCIA's lack of public disclosure and third-party participation in the patent dispute process.[225] Although the House Bill

---

to prove bioequivalence under an ANDA application. However, while the effect of pay-to-delay settlements might be lessened for follow-on biologics approval in comparison to generic small-molecule drug approval, the high costs of biologics ensure that any extra exclusivity is exceptionally valuable for the pioneer manufacturer. *See supra* Parts I.A.2, I.B.2.a, II.A.

221 These same factors also explain why pay-to-delay settlements are so popular for small-molecule drugs. *See supra* Part I.B.2.c.

222 Congress is not the only entity that can help to prevent abuses under the BPCIA. The FTC has previously shown concern about such abuses in the drug approval process. For example, the FTC originally proposed amendments to the Hatch-Waxman Act that would require both pioneer companies and first generic applicants to provide copies of certain pay-to-delay settlements to the FTC and the DOJ. FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY viii (2002).

223 *See supra* note 124.

224 Carver, Elikan & Lietzan, *supra* note 66, at 771.

225 Reform Americans Can Afford Act of 2011, H.R. 397, 112th Cong. § 701(a)(2) (2011). This bill stalled in the House, largely because the bill was directed at amending other politically sensitive provisions of the ACA, such as the individual mandate to purchase health insurance. The proposals presented in this Note are smaller, more targeted, and less politically sensitive than the provisions of the House Bill that largely doomed the legislation. This Note advocates only for adoption of those sections of the Reform Americans Can Afford Act explicitly mentioned.

was politically controversial for other reasons, it does present some useful ideas for improving the BPCIA. The appropriate solution for curing the BPCIA's defects lies in a combination of provisions from the House Bill and new limits on pay-to-delay settlements.

A. Congress Should Adopt Aspects of the 2011 House Bill to Cure Sources of Abuse Within the BPCIA

Congress should adopt portions of the House Bill that relate to the patent dispute provisions of the BPCIA in order to limit sources of abuse in the follow-on biologics approval process. First, the House Bill would amend the PHSA to require that the Secretary of HHS publish notice in the *Federal Register* upon acceptance of any 42 U.S.C. § 262(k) application, including identification of the targeted pioneer biologic product.[226] This would cure the lack of public notice that currently plagues the BPCIA.[227] Second, the House Bill would allow interested third parties[228] to assert their relevant patent rights during the patent dispute process.[229] The interested third party could begin a new patent dispute proceeding against the applicant, expanding the scope of litigation beyond just the pioneer manufacturer and the follow-on biologics applicant.[230] Finally, the House Bill would require that any settlement[231] entered between a follow-on biologics applicant and a reference product sponsor during the patent dispute process be filed with the DOJ and the FTC.[232] The settlement would not, however, have to be disclosed to the public.[233] The FTC and the

---

226 *See* H.R. 397 § 701(a)(2) (adding subsection (*l*)(3) to 42 U.S.C. § 262).

227 *See supra* Part II.B.1.

228 "Interested third parties" are defined in the House Bill as persons other than the pioneer manufacturer that own a relevant patent or have the right to commence an action for infringement of a relevant patent. H.R. 397 § 701(a)(2) (adding subsection (*l*)(1)(D) to 42 U.S.C. § 262).

229 *Id.* (adding subsection (*l*)(4)(B) to 42 U.S.C. § 262).

230 *See id.*

231 Technically, the provision applies to agreements between the follow-on biologics product applicant and the pioneer manufacturer or agreements between different follow-on biologics product applicants. To trigger the provisions, the agreements must be related to the follow-on biologics or the reference product. *Id.* (adding subsection (*l*)(6)(B) to 42 U.S.C. § 262).

232 *See id.* (adding subsection (*l*)(6)(C) to 42 U.S.C. § 262). Failure to meet the filing requirement can lead to a civil penalty of no more than $11,000 per day, a similar fine to the one applied to firms that fail to meet the premerger notification requirements under the Hart-Scott-Rodino Act, 15 U.S.C. § 18a (2006). *Compare* H.R. 397 § 701(a)(2) (adding subsection (*l*)(6)(E) to 42 U.S.C. § 262), *with* 15 U.S.C. § 18a(g)(1).

233 *See* H.R. 397 § 701(a)(2) (adding subsection (*l*)(6)(D) to 42 U.S.C. § 262).

DOJ would retain the power to enforce antitrust laws related to such agreements.[234]

The House Bill provides a strong first step towards fixing the substantial areas of abuse in the BPCIA. The public notice provisions would put the general public and industry members on notice of potential abuses. These disclosure provisions would not be particularly burdensome to the parties, as all initial biologics application documents must already be filed with the Secretary under the current system.[235] Nor would publication in the *Federal Register* create any significant burden for the FDA, as the amount of published information would be minimal.[236] Additionally, the *Federal Register* listing would disclose only the reference product and the name and address of the applicant's agent,[237] minimizing any potential concerns regarding disclosure of trade secrets.

The interested-third-party provisions of the House Bill would allow parties with related patents to declare their interest from the beginning of the approval process, rather than requiring the third parties to wait until the period immediately prior to marketing to litigate their patent rights.[238] One potential downside to such a provision is that multiple third parties, each with very tenuous links to the follow-on applicant, could attempt to aver their interests.[239] This early increase in litigation could bog down the approval process and potentially overwhelm the follow-on biologic applicant, creating a possible barrier for small follow-on biologics manufacturers attempting to enter the market.

Such concerns are misplaced. First, as mentioned, most follow-on biologics manufacturers are large corporations that are able to manage substantial litigation burdens.[240] Second, the interests of third-party intervenors outweigh the barrier that such a provision would create. On one hand, limiting third-party intervention to the period

234 *See id.* (adding subsection (*l*)(6)(E) to 42 U.S.C. § 262).

235 *See* 42 U.S.C. § 262(k) (Supp. V 2012).

236 *See* H.R. 397 § 701(a)(2) (adding subsection (*l*)(3) to 42 U.S.C. § 262).

237 *See id.*

238 *See supra* Part II.B.1.

239 It should, however, be noted that this is only a hypothetical argument. Because manufacturing patents could not be asserted under the Hatch-Waxman Act, the generic drug approval process is a poor comparison to measure likelihood of suits by third parties. The limited types of patents that were eligible for challenges under the Hatch-Waxman Act meant that the pioneer manufacturer would usually own most of the patents of interest. *See supra* note 142 and accompanying text.

240 *See* Carver, Elikan & Lietzan, *supra* note 66, at 788–89.

immediately before marketing hastens the early-approval process.[241] On the other hand, such limits also place considerable pressure on a single district court judge to enter a preliminary injunction immediately prior to marketing.[242] The public pressure on that judge in determining the fate of a much-needed follow-on biologic might inappropriately sway the judge to deny the injunction.[243] By allowing for judicial resolution during the initial patent dispute process, third-party interests will be resolved in a more objective manner. Finally, the House Bill's requirement that pay-to-delay settlements be filed with the Attorney General and the FTC provides another important step towards ameliorating the problems with the current procedures under the BPCIA.[244] The House Bill's approach is similar to the MMA provisions amending the Hatch-Waxman Act,[245] which implies that such measures may pass Congress. Although these three identified provisions of the House Bill represent a feasible starting point for revising the BPCIA, more substantial amendments are necessary to further curb the panoply of possible abuses under the current regime.

B. Congress Should Require Disclosure of Patent Dispute Information and Pay-to-Delay Settlements

To prevent substantial abuses of the BPCIA approval process, Congress must enact even stronger disclosure provisions and greater limits on pay-to-delay settlements than those provided in the House Bill. A combination of required public disclosure of Paragraph 3 lists and further limits on pay-to-delay settlements will accomplish this goal.

1. Congress Should Require Publication of Paragraph 3 Patent Lists

First, Congress should require the Secretary to publish the Paragraph 3 patent lists exchanged between applicants and pioneer manufacturers.[246] Because the BPCIA does not require public listing of

---

241 This balancing of interests mirrors the concerns of the pharmaceutical industry during the debate over the BPCIA. In particular, the concern about providing the follow-on applicant with the power to shape the scope of the patent dispute procedures is very similar to the concern over the scope of early third-party intervention. *See supra* Part II.A.

242 *See supra* Part II.A.

243 *See supra* Part II.A.

244 *See* H.R. 397, 112th Cong. § 701(a)(2) (2011) (adding section (*l*)(6)(E) to 42 U.S.C. § 262).

245 *See supra* note 122 and accompanying text.

246 *See supra* Part I.C.2.a.

relevant patents through an *Orange Book*–style document,[247] publication of the Paragraph 3 lists will put future follow-on biologics manufacturers on notice as to the relevant patents for a given biologic.[248] Future applicants can then design around the Paragraph 3 patents, reducing the potential for future litigation.[249] Further, because the pioneer manufacturer's complaint will list the patents that the two sides chose to litigate in the initial infringement action,[250] the public will also become aware of what patents the two parties decided not to litigate, hindering the manufacturers' ability to hide weak or invalid patents through collusion.

If the two manufacturers reach a settlement after the litigation begins, knowledge of what patents were and were not litigated will be evidence of the fairness of the settlement. The list of relevant patents published by the FDA may show that the pioneer manufacturer used the settlement to hide potentially weak or invalid patents.[251] Further, publication of the Paragraph 3 list, which allows for comparison with the patents named in the complaint, might prevent the follow-on biologics manufacturer from abusing its power in the patent dispute process.[252] For example, if both sides list ten patents in their Paragraph 3 lists, and only one patent is listed in the complaint, public disclosure would reveal that the applicant listed zero as the number of relevant patents during the Paragraph 5 exchange.[253] In listing zero, the applicant is, in essence, delaying litigation on the other nine patents until immediately prior to marketing.[254] Such a delay could have a detrimental effect on the ability of the district judge to determine whether an injunction is appropriate.[255] The applicant might hope that the district court judge will deny the preliminary injunction for public health concerns.[256] This will backload the litigation and keep up-front litiga-

247 *See supra* Part I.C.1.

248 *See supra* Part II.B.1.

249 *See supra* Part II.B.1.

250 *See supra* Part I.C.2.b.

251 *See supra* Part II.B.1.

252 The following hypothetical discussion is based on the ability of the follow-on biologics manufacturer to set the scope of the patent dispute resolution process. *See supra* Part I.C.2.b.

253 *See supra* Part I.C.2.b.

254 *See supra* Part I.C.2.b.

255 This is exactly the concern voiced by the pharmaceutical industry in debates leading up to the enactment of the BPCIA. *See supra* Part II.A.

256 While it may seem unlikely that a judge would be swayed by public interest, the Supreme Court recently affirmed that one factor for considering if an injunction would be appropriate in patent litigation is whether "the public interest would not be disserved by a permanent injunction." eBay Inc. v. MercExchange, LLC, 547 U.S. 388, 391 (2006).

tion costs at a minimum.[257] In the face of this unfavorable litigation position, the pioneer manufacturer might seek settlement instead of appropriately asserting its patent rights.[258] Public listing of the Paragraph 3 patents would at least shed light on such anticompetitive practices and inform the public of abuses of this process.

2. *Congress Should Directly Limit the Ease of Entering Pay-to-Delay Settlements.*

Along with publication of the Paragraph 3 patents, Congress should either (1) require public disclosure of redacted settlements entered during litigation, (2) ban pay-to-delay settlements that extend the pioneer manufacturer's marketing exclusivity, or (3) require initial FTC or DOJ approval of such settlements.[259]

First, Congress could require that heavily redacted pay-to-delay settlements be filed with the FDA for public release. Any trade secrets or detailed financial terms would be redacted, but general information about timing for follow-on entry into the market would be exposed for public scrutiny. This additional publication requirement could, however, burden the already limited resources of the FDA.

Another approach to limiting pay-to-delay settlements is to ban settlements that extend the pioneer manufacturer's exclusivity.[260] Such an approach would not ban benign agreements between the parties, which allow the parties to avoid expensive and unnecessary litigation, but would instead prevent only abusive settlements. For effective implementation, this provision would have to include a filing requirement to allow the FTC or the DOJ to review the settlement for anticompetitive terms.[261] A provision that bans settlements that artificially extend pioneer manufacturer exclusivity, in concert with filing

---

257 *See supra* notes 255–56.

258 Injunctions in patent law are a controversial topic that can lead to confusion among the lower courts, particularly when they involve nonpracticing entities or public health concerns. *See, e.g.*, *eBay*, 547 U.S. at 395–97 (Kennedy, J., concurring) (nonpracticing entities).

259 A complete ban on pay-to-delay settlements might not be feasible. *See supra* note 124. As the law currently stands and until the Supreme Court conclusively speaks on the matter, the American justice system continues to strongly favor settlement. *See supra* note 124.

260 Settlements that extend exclusivity include settlements that delay the follow-on biologic manufacturer's marketing of a competing drug even after the pioneer manufacturer's patent has expired. Certain circuits have focused on extension of exclusivity as one reason pay-to-delay settlements could be considered anticompetitive. *See supra* note 124 and accompanying text.

261 This provision could be similar to that found in section 701(a)(2) of the House Bill. H.R. 397, 112th Cong. § 701(a)(2) (2011) (adding subsection (*l*)(6)(E) to 42 U.S.C. § 262); *see supra* Part III.A.

requirements, would greatly reduce the potential for abuse in pay-to-delay settlements.

A final possibility for reducing the abusive tendencies of settlement during the patent dispute process is to alter the reporting requirements in the House Bill.[262] The House Bill requires the filing of any agreements between the pioneer and follow-on biologic manufacturer with the FTC and the DOJ.[263] Although such a requirement might have some self-policing effects, the House Bill does not require the FTC or DOJ to review the filings.[264] A potential middle ground between a simple filing requirement and an outright ban on pay-to-delay settlements would be to require approval of all such agreements by the DOJ and the FTC prior to consummation of the agreement. Such a requirement would give the DOJ and the FTC the right to challenge a settlement agreement for a set time period—for example, ninety days after filing the settlement.[265] This filing provision would be analogous to premerger filings required under the Hart-Scott-Rodino Act,[266] under which firms finalizing a merger must notify the FTC and the DOJ thirty days prior to consummating a merger to allow for FTC or DOJ review.[267]

During the proposed review period for follow-on biologics, either the DOJ or the FTC could seek an injunction from the district court hearing the infringement complaint and with whom the settlement will ultimately be filed for approval. The judge could then hear arguments from both the parties and the FTC or DOJ to determine if the settlement is anticompetitive. If neither the DOJ nor the FTC challenges the settlement for ninety days, the settlement would be presumptively valid.[268] The DOJ or the FTC would still reserve the right to bring an

---

262 *See* H.R. 397 § 701(a)(2) (adding subsection (*l*)(6)(E) to 42 U.S.C. § 262).

263 *See id.*

264 *See generally id.* (requiring a filing, but not review of the filing).

265 The ninety days proposed here would be similar to the one month provided for in merger review under the Hart-Scott-Rodino Act, but would provide a greater window to accommodate the increased burden of this added requirement on the FTC and DOJ staffs. *See infra* note 266.

266 15 U.S.C. § 18a (2006). The FTC and the DOJ could then develop guidelines similar to the FTC/DOJ Horizontal Merger Guidelines that would provide firms with greater guidance over which settlements would likely be subject to DOJ or FTC challenge. U.S. DEP'T OF JUSTICE & FED. TRADE COMM'N, HORIZONTAL MERGER GUIDELINES (2010), *available at* http://www.ftc.gov/os/2010/08/100819hmg.pdf.

267 15 U.S.C. § 18a.

268 *Id.* § 18a(b)(1)(B). This is similar to how silence from the agency is treated during merger reviews under the Hart-Scott-Rodino Act. *How Mergers Are Reviewed*, FED. TRADE COMM'N, http://www.ftc.gov/opa/reporter/competition/mergers.shtml (last modified Mar. 29, 2013).

antitrust action at a later date, but the initial agency silence would be considered a prima facie showing of validity that the government would then have the burden of rebutting. Further, allowing the DOJ or the FTC to challenge the settlement before the presiding judge, who is already well-versed in the facts of the case, would expedite such challenges without requiring an entirely new trial that would further burden the already limited resources of these government agencies. This approach also avoids concerns about an overly broad ban on pay-to-delay agreements that would negate some valid settlements.[269] These limits would thus allow the public, represented by the FTC or the DOJ, to assert their interests in the settlement without a full public vetting of all terms included in the settlement itself.

All three potential solutions limiting pay-to-delay settlements face some administrative difficulties. Public disclosure of redacted settlement agreements might diminish the incentive to settle and require prolonged negotiations between the parties and the FDA over what information must be redacted. An outright ban on pay-to-delay settlements that extend exclusivity could lead to protracted administrative challenges over the true length of exclusivity. Additionally, mandatory review of settlement filings could overwhelm the FTC or the DOJ due to their limited resources. The failure of the FTC or the DOJ to review settlement agreements due to lack of resources could in turn lead to an erroneous presumption of validity for abusive settlements. Despite these concerns, any combination of the three proposed provisions would limit the negative impact of pay-to-delay settlements. Although agency review of pay-to-delay settlements or an outright ban on such settlements might be more effective at limiting abuse under the BPCIA, Congress will need to choose an approach that balances effectiveness with political expediency.

Adopting the disclosure provisions of the House Bill and augmenting these provisions with additional measures targeting pay-to-delay settlements could prevent many potential sources of abuse under the BPCIA. Through greater public input and the adoption of statutory language targeting anticompetitive agreements, follow-on biologics would be able to reach the market at a much faster rate. An approach that strongly favors efficient approval and dispute resolution provisions for follow-on biologics will help to develop the competition necessary to decrease the costs of a multitude of crucial treatments.

---

269 *See supra* note 259 and accompanying text.

CONCLUSION

The BPCIA is a strong first step by Congress towards developing a comprehensive scheme for approval of follow-on biologics. Many biologics present great promise for curing some of the deadliest modern diseases, but their excessive cost limits access to such medications for many Americans. Although the BPCIA creates a system for follow-on biologics approval, it also allows for substantial abuses and delays that prevent follow-on biologics from reaching the market. Congress should adopt a simple bipartisan approach that provides for greater public disclosure during the patent dispute process and significantly limits the availability of pay-to-delay settlements. Congress can use these measures to provide greater protection to the public and to promote the approval and marketing of less-costly follow-on biologics.