

Note

Biologics Price Competition and Innovation Act: Striking a Delicate Balance Between Innovation and Accessibility

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The Biologics Price Competition and Innovation Act of 2009 (BPCIA, also known as the Biosimilar Act) was signed into law in 2010 by President Barack Obama as part of the healthcare reform bill.¹ The central mission of the BPCIA is two-fold: (1) providing sufficient incentives for continuous innovations in biologic therapies (i.e., promoting innovation); and (2) lowering the price of biologic therapies (i.e., promoting accessibility).² To promote innovation, the BPCIA provides twelve-year Food and Drug Administration (FDA) exclusivity to innovator biologics.³ This twelve-year FDA exclusivity prevents generic biologics, also known as follow-on biologics (FOBs),

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1. Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, § 7001, 124 Stat. 119, 804 (2010). The Biologics Price Competition and Innovation Act (BPCIA) was enacted as part of the Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119, 804 (2010).

2. Biologics Price Competition and Innovation Act § 7001(b), 124 Stat. at 804 (“It is the sense of the Senate that a biosimilars pathway balancing innovations and consumer interests [i.e., accessibility] should be established.”).

3. *Id.* § 7002(k)(2)(A), 124 Stat. at 805.

from being approved.⁴ To promote accessibility, the BPCIA provides an abbreviated pathway for FOBs—the abbreviated biologic license application (ABLA).⁵ The ABLA allows FOB manufacturers to cut short the time and the expensive cost of clinical testing by referring to innovator biologics' clinical data to establish safety and efficacy.⁶

The goal of this Note is to discuss the advantages and drawbacks of the mechanisms established in the BPCIA and to suggest modifications to strike a better balance between innovation and accessibility. Part I of this Note introduces the legal and scientific background of the BPCIA and Hatch-Waxman Act in order to engage in further analyses. Part II of this Note analyzes the competing interests of innovation and accessibility and suggests a novel six-year data exclusivity and a six-to-twelve-year market exclusivity regulatory scheme. This Note concludes that the current design of the BPCIA tips too favorably toward innovation and compromises accessibility. The suggested six-year data exclusivity and six-to-twelve-year market exclusivity regulatory scheme potentially strike a better balance between innovation and accessibility.

I. BACKGROUND: INTRODUCING THE LEGAL AND SCIENTIFIC BACKGROUND OF THE BPCIA AND THE HATCH-WAXMAN ACT

The BPCIA is highly analogous to the Drug Price Competition and Patent Term Restoration Act introduced in 1984, also known as the Hatch-Waxman Act, which established

4. *Id.* (stating that the Commissioner of the FDA may not make effective an approval of a generic biologic until a twelve-year period after the referenced biologic was approved). Follow-on biologic (FOB) essentially means the generic version of a biologic pharmaceutical. Agencies, such as the Federal Trade Commission (FTC), and commentators have adopted the term “follow-on biologic” to distinguish it from “generic drug” (i.e., a small-molecule drug that is *bioequivalent* to a reference small-molecule drug). This is because it is agreed among scientific communities that it is impossible to make a “generic biologic” that is *bioequivalent* to a reference biologic, as one can with small-molecule drugs. Thus, the term FOB is adopted to emphasize *biosimilar* and distinguish from *bioequivalent*.

5. *Id.* § 7002, 124 Stat. at 805. Section 7002 was subsequently codified in 42 U.S.C. § 262(k) (defining Licensure of Biological Products (LBP)). LBP is an abbreviated pathway to get FDA approval on generic versions of biologic pharmaceuticals. Commentators usually refer to a LBP as an abbreviated biologic license application (ABLA) in recognition of the highly similar structure with abbreviated new drug applications (ANDA) established in the Hatch-Waxman Act.

6. 42 U.S.C. § 262(k) (Supp. V 2011).

the abbreviated approval process for small molecule drugs.⁷ Similar to the goals of the BPCIA, the Hatch-Waxman Act tries to balance two competing interests: innovation and accessibility.⁸ To incentivize innovation, the Hatch-Waxman Act provides patent term extension (PTE) that prolongs the patent exclusivity period so that innovator companies have an extended period of market monopoly.⁹ On the other side of the scale, to increase public access to drugs, the Hatch-Waxman Act established an abbreviated new drug application (ANDA) to introduce competing generic drugs through a fast approval process.¹⁰ The Hatch-Waxman Act establishes the modern generic drug industry and was incredibly successful in increasing the accessibility of small molecule drugs.¹¹ In 1984, when the Hatch-Waxman Act was introduced, generic drug use

7. Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 15, 21, 28, and 35 U.S.C.). The provisions of abbreviated new drug applications (ANDAs) were subsequently codified in 21 U.S.C. § 355(j). ANDAs are similar to 42 U.S.C. § 262(k) ABLAs. Both ANDAs and ABLAs allow generic drug companies to reference the clinical data originally submitted by the innovator drug companies to establish the safety and efficacy of the generic drugs/biologics. This saves generic drug companies a tremendous amount of time and money by avoiding full-scale clinical trials so that generic drugs/FOBs can enter the market quickly after the patent terms of the innovator drugs expire. One major difference between ANDAs and ABLAs is that ANDAs regulate small-molecule drugs and ABLAs regulate biologics.

8. Hatch-Waxman Act, 98 Stat. at 1585 (“To amend the Federal Food, Drug, and Cosmetic Act to *revise the procedures* for new drug applications, to amend title 35, United States Code, to authorize the *extensions of the patents* for certain regulated products, and for other purposes.” (emphasis added)). The “revised procedure” for new drug applications refers to ANDAs. ANDAs increase drug accessibility by introducing generic drug competition quickly after the patents covering the reference drug expire. The “extension of patent” term refers to patent term extension (PTE), which extends the patent term by 50% of the FDA approval time. PTE is to incentivize innovation. See Colleen Kelly, *The Balance Between Innovation and Competition: The Hatch-Waxman Act, the 2003 Amendments, and Beyond*, 66 *FOOD & DRUG L.J.* 417, 418 (2011).

9. See Hatch-Waxman Act § 201.

10. See Hatch-Waxman Act § 101.

11. *Examining the Senate and House Versions of the “Greater Access to Affordable Pharmaceuticals Act”*: Hearing Before the S. Comm. on the Judiciary, 108th Cong. 7–13 (2003) (statement of Daniel E. Troy, Chief Counsel, U.S. Food & Drug Administration). The FDA stated that the Hatch-Waxman Act was working well. Since the Hatch-Waxman Act’s passage in 1984, 10,000 generic drugs have entered the market. By 2003, 50% of the prescriptions were filled by generic drugs. *Id.*

was less than 20% of all prescription drug use.¹² By 2010, the percentage increased to 78%.¹³ The popularity of generic drugs drove down small molecule drug prices by an average of almost 75%.¹⁴ However, the Hatch-Waxman Act regulates only small molecule drugs, not biologics.¹⁵ This is probably because, as of 1984, biologic pharmaceuticals were still in their infancy.¹⁶ In other words, there was no abbreviated approval process for biologics before the BPCIA was signed into law in 2010.¹⁷

A. SMALL MOLECULE DRUGS V. BIOLOGICS

Biologics are very different from small molecule drugs. Small molecule drugs are chemically synthesized.¹⁸ Biologics

12. Richard G. Frank, *The Ongoing Regulation of Generic Drugs*, 357 NEW ENG. J. MED. 1993, 1993 (2007).

13. IMS INST. FOR HEALTHCARE INFORMATICS, THE USE OF MEDICINES IN THE UNITED STATES: REVIEW OF 2010, at 3 (2011), available at http://www.imshealth.com/imshealth/Global/Content/IMS%20Institute/Documents/IHII_UseOfMed_report%20.pdf.

14. CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 32–33 (1998).

15. *Corporate Chronology*, GENENTECH, <http://www.gene.com/media/company-information/chronology> (last visited Nov. 12, 2013). In modern biotechnology, recombinant DNA is the major technology used to create biologics. The first recombinant DNA biologic, human insulin made by Genentech, was approved by the FDA in 1982, only two years before the Hatch-Waxman Act was enacted in 1984. Thus, at the time the Hatch-Waxman Act was enacted, there was no need for an abbreviated pathway for FOBs, because at that time the innovator biologics are all protected by patents. See Trader Thoughts, *Biogenerics: Not Yet a Reality in the U.S.*, SEEKING ALPHA (Dec. 24, 2007), <http://seekingalpha.com/article/58230-biogenerics-not-yet-a-reality-in-the-u-s>.

16. *Corporate Chronology*, *supra* note 15.

17. WENDY H. SCHACHT & JOHN R. THOMAS, FOLLOW-ON BIOLOGICS: THE LAW AND INTELLECTUAL PROPERTY ISSUES 5 (2012), available at <http://www.fas.org/sgp/crs/misc/R41483.pdf> (stating that prior to the enactment of the BPCIA, there was no generally-applicable abbreviated statutory pathway for follow-on biologics).

18. 42 U.S.C. § 262(i) (2006 & Supp. V 2011) (“[T]he term ‘biological product’ means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, [protein (except any chemically synthesized polypeptide),] or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.”); see also SCHACHT & THOMAS, *supra* note 17, at 5 (stating that chemical drugs are based on small molecules that typically contain dozens of atoms, while biologics are based on macro-molecules that may consist of millions of atoms).

are the products of living cells.¹⁹ Biologics include: “therapeutic serums, toxins, antitoxins, vaccines, blood, blood components or derivatives, allergenic products, proteins, and viruses.”²⁰ Compared to small molecule drugs, biologics have much larger molecular weights and much more complicated three dimensional structures.²¹ Biologics are usually proteins and antibodies which possess high binding affinity with specific substrates.²² Unlike small molecule drugs, which usually have larger tolerance to heat or contamination in the production process, biologics are extremely heat-sensitive and susceptible to microbial contamination.²³ A minor change in the manufacturing process, such as a minor change in temperature of cell culture, can change the overall characteristic of a final biologic product.²⁴ Thus, quality control for biologics is much more costly and complex than for small molecule drugs.²⁵

Traditionally, biologics were extracted from animals or humans bodies.²⁶ This production method is limited in quantity, and obviously undesirable.²⁷ In 1973, the development of recombinant DNA technology made mass production of biologics possible.²⁸ Since then, the medical

19. SCHACHT & THOMAS, *supra* note 17, at 5.

20. 42 U.S.C. § 262(j).

21. See SCHACHT & THOMAS, *supra* note 17, at 2–3.

22. Simon D. Roger, *Biosimilars: How Similar or Dissimilar Are They?*, 11 NEPHROLOGY 341, 343 (2006) (stating that in assessing efficacy of biosimilars, receptor-binding affinity is an important index).

23. *What Are “Biologics” Questions and Answers*, FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133077.htm> (last visited Sept. 14, 3013) (“In contrast to most drugs that are chemically synthesized and their structure is known, most biologics are complex mixtures that are not easily identified or characterized. Biological products, including those manufactured by biotechnology, tend to be heat sensitive and susceptible to microbial contamination. Therefore, it is necessary to use aseptic principles from initial manufacturing steps, which is also in contrast to most conventional drugs.”).

24. Michal Nowicki, *Basic Facts About Biosimilars*, 30 KIDNEY BLOOD PRESSURE RES. 267, 268 (2007).

25. *Id.*

26. *What Is a Biological Product?*, FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm194516.htm> (last visited Sept. 14, 2013).

27. *Id.*

28. See *Biotechnology at 25: The Founders*, U. CAL. BERKELEY LIBR., <http://bancroft.berkeley.edu/Exhibits/Biotech/25.html> (last updated May 23, 2000); see also Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 15, 21, 28, and 35 U.S.C.).

importance of biologics has grown exponentially.²⁹ The FDA states: “biological products often represent the cutting-edge of biomedical research and, in time, may offer the most effective means to treat a variety of medical illnesses and conditions that presently have no other treatments available.”³⁰ Conditions currently treated by biologics include diseases such as cancer, arthritis, chronic plaque psoriasis, anemia, and chronic renal failure.³¹ Commentators called biologics “the wonder drug” of the 21st Century.³² In 2007 there were 400 biologics treating more than 200 conditions.³³ By 2011, there were more than 900 biologics in various clinical trial phases targeting more than 100 diseases.³⁴ There is little doubt that biologics will make up the majority of pharmaceutical therapies to treat the most difficult diseases in the future.³⁵

The economic importance of biologics also grew exponentially in the pharmaceutical industry.³⁶ In 2000, biologics sales accounted for 11% of all drug sales in the United States. By 2005, that figure rose to 18%, and by 2010, it grew to 26% of total consumer spending on pharmaceuticals.³⁷

29. Vincent J. Roth, Will FDA Data Exclusivity Make Biologic Patents Passé? 6 (unpublished manuscript), available at http://works.bepress.com/context/vincent_roth/article/1000/type/native/viewcontent (“In 2002, biologics sales accounted for 11% of all U.S. drug sales. By 2006, spending on biologics totaled \$54 billion in the U.S.-approximately 20% of total spending on pharmaceuticals. By 2010, biologics were estimated at 26% of the total cost of pharmaceuticals . . . with sales of biologics expected at over \$60 billion.”).

30. *What Are “Biologics” Questions and Answers*, *supra* note 23.

31. *Biologic Medical Product*, WIKIPEDIA, http://en.wikipedia.org/wiki/Biologic_medical_product (last visited Sept. 14, 2013).

32. Zach Patton, *Complex Rx: Biologic Meds Are the Wonder Drugs of Our Time. Can We Afford Them?*, GOVERNING, <http://www.governing.com/topics/politics/Complex-Rx.html> (last visited Oct. 20, 2013).

33. *Id.*

34. Grady Forrer, *900 New Medicines in Development Show the Biotechnology Medical Revolution Is Going Strong*, CATALYST (Sept. 14, 2011, 11:18 AM), <http://www.phrma.org/catalyst/900-new-medicines-development-show-biotechnology-medical-revolution-going-strong/>.

35. See *What Are “Biologics” Questions and Answers*, *supra* note 23 (stating that biologics represent the forefront of biomedical research and may be used to treat a variety of medical conditions for which no other treatments are available).

36. *Id.*

37. Nowicki, *supra* note 24, at 267.

B. THE URGE FOR BIOSIMILARS BEFORE 2010

During 2003 and 2004, patents protecting several multi-billion dollar sale biologics expired.³⁸ Yet innovator companies faced no market competition because, at that time, there was no abbreviated pathway to approve FOBs.³⁹ Since then, there has been increasing pressure on Congress to provide for an abbreviated approval pathway (i.e., biosimilar pathway, similar to ANDA in the Hatch-Waxman Act to approve FOBs).⁴⁰ The pressure on Congress intensified after both the European Union (EU) and Canada implemented their versions of biosimilar pathways in 2004 and 2006 respectively.⁴¹ In 2004, Dr. Carole Ben-Maimon, President of Barr Research, Inc., testified in front of the Senate Judiciary Committee: “[G]eneric competition for biotech pharmaceuticals has the potential to offer consumers dramatic and substantial savings, while also lowering America’s healthcare bill.”⁴² Kathleen Jaeger, the

38. Trader Thoughts, *supra* note 15 (“Patent for Biogen’s Avonex (2006 sales: \$1Bn) expired in 2003, Eli Lilly’s Humatrope (\$390M) expired in 2003, Genentech’s Humulin (\$1Bn) expired in 2004, while the blockbuster anemia drug—Amgen’s Epogen (\$2.5 Bn) is set to expire in 2012.”).

39. See SCHACHT & THOMAS, *supra* note 17, at 5 (stating that prior to the enactment of the BPCIA in 2010, there was no generally applicable abbreviated statutory pathway for FOBs); see also *What We Do*, DRAGONFLY SCIENCES, <http://www.dragonflysciences.com/whatWeDo/index.html> (last visited Mar. 30, 2013) (stating that monoclonal antibody (mAB) manufacturers (mAB is a kind of biologic) have enjoyed market monopoly due to both patent protection and the lack of regulatory mechanisms to approve generic versions of biologics).

40. ROBERT J. SHAPIRO ET AL., THE POTENTIAL AMERICAN MARKET FOR GENERIC BIOLOGICAL TREATMENTS AND ASSOCIATED COST SAVINGS 1, 2 (2008) available at http://www.sonecon.com/docs/studies/0208_GenericBiologicsStudy.pdf. (“Congress created an accelerated regulatory process for FDA approval of generic pharmaceuticals in 1984, under the Hatch-Waxman Act, but the law covers only traditional, small-molecule pharmaceuticals and not biologics.”); see also Gregory N. Mandel, *The Generic Biologics Debate: Industry’s Unintended Admission that Biotech Patents Fail Enablement*, 11 VA. J.L. & TECH., Fall 2006, at 1 (“[Generic] manufacturers currently are significantly limited in their ability to sell generic copies of biologics even after the pioneer biologic patents expire. As early biologics are starting to go off-patent, this regulatory mix-up is having a notable impact on the availability of biologics and raising the cost of health care.”).

41. Noel Courage & Ainslie Parsons, *The Comparability Conundrum: Biosimilars in the United States, Europe and Canada*, 66 FOOD & DRUG L.J. 203, 209–12 (2011).

42. *Law of Biologic Medicine: Hearing Before the S. Comm. of the Judiciary*, 108th Cong. 24–25 (2004) (statement of Carole Ben-Maimon, M.D., President and Chief Operating Officer, Barr Research, Inc., Bala Cynwyd, Pennsylvania).

president of the Generic Pharmaceutical Association stated in 2005: "Sound science already has enabled citizens in the European Union, Australia, India and South America to have access to these medicines. And, the EU estimates that it will save \$2.8 billion from the market entry of just a few products Clearly, the U.S. must stop dragging its feet."⁴³ In 2009, President Obama also urged Congress to act on a biosimilar pathway: "[W]e need to introduce generic biologic drugs into the marketplace But right now, there is no pathway at the FDA for approving generic versions of these drugs."⁴⁴

C. DATA EXCLUSIVITY V. MARKET EXCLUSIVITY

The BPCIA's mission is to promote both innovation and accessibility of biologics.⁴⁵ In striking the balance, the key point is how long of a period of exclusivity the FDA should provide for innovator biologics.⁴⁶ Currently, the BPCIA provides a twelve-year FDA exclusivity for a new biologic entity (NBE).⁴⁷ A further question is whether this twelve-year exclusivity is *data* exclusivity or *market* exclusivity. The statute is currently unclear on this.⁴⁸

43. Kathleen Jaeger, President & CEO, GPhA, Speech at the Windhover FDA/CMS Summit (Dec. 5, 2006), *available at* <http://gpha.hfwebdev.com/resources/2006/12/04/gpha-speech-windhover-fdacms-summit>.

44. President Barack Obama, Address to the American Medical Association in Chicago (June 15, 2009), *available at* http://www.huffingtonpost.com/2009/06/15/obama-ama-speech-full-text_n_215699.html.

45. See Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, § 7001(b), 124 Stat. 119, 804 (2010).

46. Lewis Krauskopf, *Teva Executive Upbeat on Biogenerics in 2009*, REUTERS (Dec. 23, 2008), <http://uk.reuters.com/article/2008/12/23/businesspro-us-teva-idUKTRE4BM40A20081223> (noting the key point in the legislation of the FOB pathway is the amount of exclusivity that would be afforded to brand-name biotech drugs; generic drug makers like Teva want to limit it to seven years, while the brand name companies want fourteen years). Teva is the biggest generic drug company in the world, headquartered in Israel, having 46,000 employees, running annual revenue more than \$20 billion in 2012. *About Us*, TEVAPHARM.COM, <http://www.tevapharm.com/About/Pages/AboutUs.aspx> (last visited Oct. 10, 2013).

47. 42 U.S.C. § 262(k)(7)(A) (Supp. V 2011).

48. Margo Bagley, *Patent Term Restoration and Non-Patent Exclusivity in the United States* 22 (Univ. of Va. Sch. of Law, Public Law and Legal Theory Research Paper Series, No. 2011-25, 2011), *available at* <http://ssrn.com/abstract=1899533>.

The contrast between *data* and *market* exclusivity has significant implications for the general public.⁴⁹ Data exclusivity prohibits FOB manufacturers from relying on the clinical trial data submitted by the innovator companies.⁵⁰ Notice that, by definition, ABLA is a regulatory pathway allowing FOB manufacturers to rely on innovators' clinical data to establish safety and efficacy.⁵¹ Thus, if the twelve-year exclusivity is a data exclusivity, it essentially means ABLA is not available to FOB manufacturers during the first twelve years after a reference biologic is approved.⁵² Market exclusivity, as opposed to data exclusivity, does not prohibit the FDA from accepting and reviewing an ABLA.⁵³ Market exclusivity merely prohibits the FDA from approving an FOB to sell on the market.⁵⁴ In other words, the FDA can accept and review an ABLA but will not approve it until the applicable market exclusivity expires.⁵⁵

Years of delay in introducing drug price competition equal to the FDA review period of FOBs is the difference between a *data* or *market* exclusivity.⁵⁶ This delay of drug price

49. See Kurt R. Karst, *Tussle Over BPCIA "Market" Versus "Data" Exclusivity Continues; This Time the Generic Supporters Chime in*, FDA L. BLOG (Jan. 21, 2011, 6:38 AM), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2011/01/tussle-over-bpcia-market-versus-data-exclusivity-continues-this-time-the-generics-side-chimes-in.html (asserting that generic supporters argue that interpreting the twelve-year FDA exclusivity as a data exclusivity, which prevents biosimilar (i.e., ABLA) submission has serious consequences and that consumers will have to endure an unknown period of delay of FDA review and approval that could stretch far beyond the twelve-year total that was set in the legislation).

50. See Bagley, *supra* note 48, at 14 (noting that the five-year data exclusivity period for a new chemical entity (NCE) prevents generic drug companies from even filing an ANDA).

51. 42 U.S.C. § 262(k)(2)(A) (stating that the biological product can establish biosimilarity to a reference product based upon data derived from analytical studies, animal studies, and clinical studies).

52. See Bagley, *supra* note 48, at 22.

53. See *id.* at 15–18 (explaining market exclusivity within the context of pediatric testing exclusivity and orphan drug exclusivity). Market exclusivity does not prevent generic companies from *filing* an ANDA, as in data exclusivity. During the market exclusivity period, the FDA can receive and review an ANDA but will not *approve* it until the reference drug's market exclusivity expires.

54. *Id.*

55. *Id.*

56. See Karst, *supra* note 49 (stating that data exclusivity which prevents ABLA submission stretches the market monopoly far beyond the twelve-year period); see also *infra* note 242 (establishing that a reasonable expectation for the FDA to approve an ABLA is about *three to four* years).

competition in biologics translates to tens of billions of medical expenses to the general public.⁵⁷

D. BIOSIMILAR V. INTERCHANGEABLE

The BPCIA provides two categories of FOBs: (1) biosimilar, defined in 42 U.S.C. § 262 (k)(2); and (2) interchangeable, defined in 42 U.S.C. § 262 (k)(4).⁵⁸ An FOB is biosimilar to a referenced biologic if the FOB (1) shows sufficient similarity through analytical, animal, and clinical studies; (2) utilizes the same therapeutic mechanism; (3) is used for the same indications; (4) uses the same drug administration and dosages; and (5) the quality control of the manufacture facility of the FOB assures safety, purity, and potency.⁵⁹ An FOB is interchangeable with a referenced biologic, if it is (1) biosimilar; (2) expected to produce the same clinical result as reference drug in any given patient; and (3) the risk of switching between the FOB and reference drugs is not greater than the risk of continuous use of the reference drug.⁶⁰ If an FOB is biosimilar, it has to be prescribed by the medical doctor; on the other hand, if an FOB is interchangeable, it can be switched by a pharmacist without informing the patient or the prescribing doctor.⁶¹

57. Saurabh Aggarwal, *What's Fueling the Biotech Engine—2011 to 2012*, 30 NATURE BIOTECHNOLOGY 1191, 1192 (2012) (showing that the annual sales of biologics was (in billions USD) \$44.5 in 2007, \$46.5 in 2008, \$48.2 in 2009, \$51.3 in 2010, and \$53.8 in 2011). From the experience of small-molecule drugs, the price of a brand-name drug drops 50% instantly in the first year of the introduction of generic drug competition. Applying this dropping rate to biologics means the general public can save around \$20 billion to \$25 billion each year through drug-price competition, assuming each innovator biologic has an FOB competitor.

58. 42 U.S.C. § 262(k) (Supp. V 2011).

59. § 262(k)(2).

60. § 262(k)(4).

61. § 262(i)(3) (“The term ‘interchangeable’ or ‘interchangeability’, in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.”).

II. ANALYSIS: PROMOTING INNOVATION AND ACCESSIBILITY

A. PROMOTING INNOVATION

The general public benefits from the innovation of new biologics because they provide life-quality improving treatments that did not exist before.⁶² It is important for the government to offer proper incentives to insure innovator drug companies in recouping the heavy investments and ensure their ability to fund new research to continue innovation.⁶³ Commentators view the twelve-year FDA exclusivity provided in 42 U.S.C. § 262(k)(7)(A) to be the most important and effective measure in the BPCIA to promote innovation.⁶⁴

This twelve-year FDA exclusivity is complementary to, independent from, and even stronger than patent exclusivity.⁶⁵ There are four reasons to support these assertions. First, this NBE exclusivity de facto covers more than one patent.⁶⁶ The FDA grants this exclusivity on each new biological entity, which covers 2.7 patents on average.⁶⁷ Second, this twelve-year exclusivity is likely to last longer than the active patent life

62. See Patton, *supra* note 32 (stating that biologics are the wonder drugs of this age, promising to treat AIDS, cancer, Alzheimer's, and multiple sclerosis).

63. Henry Grabowski, *Follow-On Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, 7 NATURE REVIEWS DRUG DISCOVERY 479, 486 (2008) (stating that developing a new biologic entity costs around \$1.24–\$1.33 billion, and the cost has to be recouped from the sales of approved product).

64. Don Ware & Nick Littlefield, FOLLOW-ON BIOLOGICS AND PATENT REFORM: WILL THEY DISCOURAGE VENTURE CAPITAL INVESTMENT IN THE BIOTECHNOLOGY INDUSTRY? 5 (2009), available at <http://www.foleyhoag.com/publications/ebooks-and-white-papers/2008/june/follow-on-biologics-and-patent-reform> ("One of the issues of greatest importance involves the number of years of data exclusivity provided for a licensed biological product. 'Data exclusivity' refers to a period of time during which an FOB applicant is precluded from relying on clinical data from the innovator product as evidence of safety and effectiveness. Too short an exclusivity period could serve as a serious deterrent for VC investors if they believe the risk of early market entry of a biosimilar product will reduce the profitability of the branded compound. The loss of VC funding would seriously hinder, if not destroy, biotechnology innovation.").

65. Grabowski, *supra* note 63, at 480 (stating that data exclusivity provides an important back-up to the patent system).

66. C. Scott Hemphill & Bhaven N. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 31 J. HEALTH ECON. 327, 330 (2012).

67. *Id.*

during which innovator companies recoup their investments.⁶⁸ Third, FDA exclusivity is independent from patent exclusivity.⁶⁹ Even if the patents covering the biologic are invalidated, the FDA exclusivity still stands.⁷⁰ Fourth, FDA exclusivity practically eliminates the design-around issues.⁷¹ Innovator companies often rely on method patents to protect the manufacturing process of the final products.⁷² These method patents are relatively easy to design around.⁷³ FDA exclusivity prevents design-around because FDA exclusivity protects the final product, regardless of how it is manufactured.⁷⁴ Even if a generic company develops a different manufacturing process to make the same biologic that does not infringe the innovator companies' patents, the final product is still precluded from FDA approval.⁷⁵

The importance of using FDA exclusivity in promoting innovation can be further analyzed in three different perspectives: cost of capital and time in research and development, patent uncertainty, and drops in new drug applications.

68. Linfong Tzeng, *Follow-on Biologics, Data Exclusivity, and the FDA*, 25 BERKELEY TECH. L.J. 135, 156 (2010) (stating that the twelve-year exclusivity runs potentially longer than patent protection). A detailed calculation is provided later in this Note showing that this twelve-year exclusivity lasts longer than an average, remaining active patent term of a biologic.

69. *Id.* (explaining that FDA exclusivity is independent from patent exclusivity and stating that “[t]his is potentially troubling as data exclusivity is *unchallengeable* in court” (emphasis added)). Whether the FDA decision in granting data exclusivity is challengeable is a complex legal issue in administrative law, which is out of the scope of this Note. My research shows that there is indeed no judicial challenge to an FDA decision granting data exclusivity.

70. *Id.*

71. *See id.* at 154–55.

72. *See* Hemphill & Sampat, *supra* note 66, at 330.

73. BIOTECH. INDUSTRY ORG., FTC BIOSIMILARS REPORT REBUTTAL (2009), available at http://www.bio.org/sites/default/files/FTC_biosimilars_report_rebuttal.pdf (stating that patents covering biologics are often narrower and easier to “design around” than those of small-molecule drugs, and innovator companies need additional data exclusivity to secure their market monopolies).

74. *See* Tzeng, *supra* note 68, at 154–55.

75. *Id.*

1. Cost of Capital and Time in Research and Development

The cost to bring a biologic drug to the market is higher than that for a small-molecule drug.⁷⁶ This higher cost is partly due to the high manufacture quality required in making a biologic.⁷⁷

Any minor change in the manufacture or drug-delivery process can change the overall characteristic of a final biologic product.⁷⁸ For example, with exactly the same manufacturing process, a manufacturer of interferon beta-1a produced two batches of products with drastically different immunogenicity.⁷⁹ One batch was safe and effective, yet another batch caused serious immune responses.⁸⁰ The only difference between the two batches was the manufacture site.⁸¹ The manufacturing conditions that affect the properties of biologics generally include: the cell lines used to produce the biologics, culture/fermentation conditions, purification procedures, and container closure/packaging systems.⁸² Thus, a much higher quality control standard is required for biologics than for small molecule drugs.⁸³ This high quality standard translates to higher capital investment in research and

76. Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 *MGMT. & DECISION ECON.* 469, 477 (2007) (showing that, on average, it costs \$1.24 billion to bring a biologic to the market compared to \$899 million for a small-molecule drug).

77. FDA, *SCIENTIFIC CONSIDERATIONS IN DEMONSTRATING BIOSIMILARITY TO A REFERENCE PRODUCT 5–6* (2012) [hereinafter *SCIENTIFIC CONSIDERATIONS*], available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291128.pdf> (stating that different cell lines, raw materials, equipment, processes, process controls, and acceptance criteria are all likely to affect the quality of produced biologics).

78. See Nowicki, *supra* note 24, at 268.

79. Sungae S. Park et al., *Biochemical Assessment of Erythropoietin Products From Asia Versus US Epoetin Alfa Manufactured by Amgen*, 98 *J. PHARMACEUTICAL SCI.* 1688, 1689 (2009). Biologics are proteins. The folding process of a protein is highly sensitive to environmental conditions (e.g., temperature, ion concentration, virus/bacteria contamination, etc.). A protein that is properly folded (i.e., having a proper three-dimensional structure) can be an effective drug. In contrast, the same protein that is not properly folded can cause serious immune response and death.

80. *Id.*

81. *Id.*

82. *Id.*

83. *SCIENTIFIC CONSIDERATIONS*, *supra* note 77, at 4 (stating that even minor structural differences, including certain changes in glycosylation patterns, can significantly affect a protein's safety, purity, and potency). It will be important to evaluate these differences.

development.⁸⁴ In addition, the sensitive nature of biologics results in a longer period of clinical trial and regulatory review.⁸⁵ The average period of clinical trial and regulatory review for a biologic is 97.7 months, which is 7 months longer than for a small-molecule drug.⁸⁶

Higher manufacturing cost translates to higher drug price, which consequently reduces the market demand.⁸⁷ This reduction of market demand negatively impacts the profitability of innovator companies.⁸⁸ Longer clinical trials and regulatory review periods mean a shorter active patent life to recoup the investment.⁸⁹ This also negatively impacts the innovator companies' profitability. The twelve-year FDA exclusivity provided in the BPCIA might be justified as increasing the profitability of innovator companies (i.e., providing a long enough monopoly period so that innovator companies can recoup their investments and continue to innovate).⁹⁰

2. Patent Uncertainty

Patent uncertainty seriously affects the profitability of innovator drug companies.⁹¹ Generic drug companies are in an advantageous position in patent-invalidity challenges and have

84. Compare Grabowski, *supra* note 63, at 480 (showing that in oncology, the area with the greatest concentration of biological entities, the mean cost is “US\$1.016 billion compared with \$868 million” in small-molecule drugs), with DiMasi & Grabowski, *supra* note 76, at 477.

85. DiMasi & Grabowski, *supra* note 76, at 473; Grabowski, *supra* note 63, at 481.

86. Grabowski, *supra* note 63, at 481.

87. *Id.* at 482 (“This [higher development cost of biologics] reflects the need to resolve novel manufacturing challenges at the R&D stage. By contrast, manufacturing process issues in R&D are typically more straightforward for drugs based on chemical synthesis [i.e., small-molecule drugs].”).

88. *Id.*

89. *Id.* at 481–82. Because patent protection is a fixed term (i.e., twenty years from filing), the longer it takes for a drug to hit the market, the less patent term left to recoup the investment.

90. See 42 U.S.C. § 262(k)(7)(A) (Supp. V 2011).

91. Matthew J. Higgins & Stuart J. H. Graham, *Balancing Innovation and Access: Patent Challenges Tip the Scales*, 326 SCI. 370, 370 (2009) (“The Congressional Budget Office estimated that increased competition from generic drugs resulted in a 12% loss in revenues on sales of brand-name drugs [The patent invalidity] challenges diminish [brand-name company] revenues and profits, contributing to the current crisis in industry R&D pipelines.”).

strong incentives to file such challenges.⁹² In addition, current developments in patent law make the invalidation of biotechnology-related patents especially easy.⁹³ The twelve-year FDA exclusivity provides a complementary protection to this patent vulnerability, because FDA exclusivity is a monopoly power independent of patent protection.⁹⁴ In other words, even if the patents covering the innovator drugs or biologics were invalidated, the granted FDA exclusivity is unaffected.

Recent Federal Circuit decisions further weaken the already vulnerable patents owned by innovator companies by imposing particularly stringent patent disclosure requirements.⁹⁵ The Federal Circuit decisions imply that if a field of art is more predictive, such as mechanical engineering and software programming, less disclosure is required to fulfill the written description and enablement requirements.⁹⁶ On the contrary, if the field of art is less predictive, such as chemistry or biotechnology, more disclosure is required.⁹⁷ Recently, many

92. See FTC, *GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY*, at viii (2002), available at <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf> (“[G]eneric applicants prevailed in nearly 75% of the patent litigation ultimately resolved by a court decision.”); see also Higgins & Graham, *supra* note 91, at 370 (suggesting that generic companies have incentives to bring patent invalidity challenges, because the costs of challenging a patent are relatively small, i.e., “\$5 million compared with the large average potential payoff of \$60 million in the first 180 days alone”).

93. See Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?*, 17 *BERKELEY TECH. L.J.* 1155, 1173–82 (2002) (noting that the Federal Circuit has adopted a particularly stringent disclosure standard for patenting macromolecules (i.e., biologics)). This heightened 35 U.S.C. § 112 “written description” requirement ends up becoming the legal ground for invalidating many biotechnology and chemical patents. *Id.*

94. See Grabowski, *supra* note 63, at 480 (stating data exclusivity provides an important back-up to the patent system in cases where the patents could be invalidated).

95. See Burk & Lemley, *supra* note 93, at 1173 (“In contrast to the Federal Circuit decisions regarding software, recent decisions involving genetic material have imposed a stringent disclosure standard for patenting macromolecules.”).

96. *Id.* at 1157; e.g., *N. Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 942 (Fed. Cir. 1990) (“The computer language is not a conjuration of some black art, it is simply a highly structured language . . . [T]he conversion of a complete thought (as expressed in English and mathematics, i.e. the known input, the desired output, the mathematical expressions needed and the methods of using those expressions) into a language a machine understands is necessarily a mere clerical function to a skilled programmer.” (quoting *In re Sherwood*, 613 F.2d 809, 817 n.6 (C.C.P.A. 1980))).

97. Burk & Lemley, *supra* note 93, at 1157.

biotechnology patents have been invalidated because of these stringent requirements.⁹⁸ In addition, the safe harbor created by the Hatch-Waxman Act in patent law, 35 U.S.C. § 271, significantly strengthens generic companies' legal positions in patent-invalidity challenges by creating an exemption for generic drug companies that conduct research on patent-protected reference drugs with the intention to gain FDA approval.⁹⁹ This allows generic companies to gain thorough, hands-on knowledge regarding the targeted reference drugs and strengthens generic companies' legal theories in patent-invalidity challenges.¹⁰⁰

98. *E.g.*, *Fiers v. Revel*, 984 F.2d 1164, 1170–71 (Fed. Cir. 1993). The Federal Circuit invalidated a biologic patent, which disclosed methods for isolating a fragment of the DNA sequence coding for β -IF, a biologic, and for isolating messenger RNA coding for β -IF. *Id.* at 1167, 1170. The invalidation was largely based on the fact that Revel did not describe the actual sequence of the DNA at issue, *id.* at 1170–71, even if transferring an RNA sequence to DNA sequence is considered merely a mechanical routine that involves no technical challenge. *See Reverse Transcriptase Enzymes*, LIFE TECHNOLOGIES, <http://www.lifetechnologies.com/us/en/home/life-science/pcr/reverse-transcription/reverse-transcriptase-enzymes.html> (last visited Sept. 15, 2013) (listing an enzyme cost per reaction as low as \$1.15); *see also Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1575 (Fed. Cir. 1997). The Federal Circuit invalidated a patent which claimed human insulin DNA but only disclosed rat insulin DNA, *id.* at 1567–68, disregarding that the research methods used in sequencing rat and human are exactly the same and that rat and human DNA sequences are 95% identical. *See Nonconfidential Brief for Defendant-Appellee Eli Lilly & Co.* at 43, *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) (No. 96-1175), 1996 WL 33419502 (“The trial evidence established that a change in only four nucleotides of the rat DNA sequence would have yielded a sequence capable of producing human insulin.”).

99. 35 U.S.C. § 271(e)(1) (2006 & Supp. V 2011). The safe harbor excuses generic drug companies from patent infringement in conducting otherwise infringing acts in relation to FDA submissions. Section 271(e)(1) states:

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of *drugs* or veterinary *biological products*.

Id. (emphasis added). It should be noted that this safe harbor provision language is general and covers both small-molecule drugs and biologics.

100. *See generally Paragraph Four Explained*, PARAGRAPHFOUR.COM, http://www.paragraphfour.com/explained/why_challenge.html (last visited Sept. 15, 2013) (describing the incentives that the Hatch-Waxman Act provides to generic companies).

Generic drug companies have strong incentives to challenge innovator companies' patents.¹⁰¹ The Hatch-Waxman Act provides five-year *data* exclusivity to new chemical entities, during which generic drug companies cannot submit an ANDA referring to the patented drug's clinical data.¹⁰² However, there is an exception that can shorten data exclusivity by one year.¹⁰³ An ANDA can be submitted at the end of the fourth year if the ANDA is submitted under 21 U.S.C. § 355(j)(5)(B)(iv), which commences a patent-invalidation challenge.¹⁰⁴ The first approved generic drug submitted under Paragraph IV is entitled to 180-day market exclusivity.¹⁰⁵ During this market exclusivity period, the FDA will not approve another ANDA application (i.e., during this 180 days, the successful challenger's generic drug will be the only generic drug on the market).¹⁰⁶ This 180-day market exclusivity provides generic drug companies with strong incentives to challenge innovator drug patents.¹⁰⁷ Indeed, patent-invalidation challenges commenced under Paragraph IV ANDA submissions generally increased in the past decade.¹⁰⁸ The BPCIA provides similar mechanisms for FOB companies to raise patent-invalidation

101. See Higgins & Graham, *supra* note 91, at 370 (suggesting generic companies have an incentive to bring patent-invalidation challenges).

102. 21 U.S.C. § 355(c)(3)(E)(ii) (2012). The statute provides:

[N]o application [i.e., ANDA] . . . may be submitted . . . before the expiration of *five* years from the date of the approval of the application under subsection (b) of this section [i.e., the approved reference drug], except that such an application [i.e., ANDA] may be submitted under subsection (b) of this section after the expiration of *four* years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A) of this section [i.e., paragraph IV challenge].

Id. (emphasis added). In sum, that statute specifically prevents a generic company from submitting an ANDA during the five-year data exclusivity period.

103. § 355(b)(2)(A)(iv). An ANDA submitted under § 355(b)(2)(A)(iv), also known as a Paragraph IV submission, includes a patent-invalidation challenge. Higgins & Graham, *supra* note 93, at 370. This provision states: "such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted." § 355(b)(2)(A)(iv).

104. § 355(j)(5)(B)(iv).

105. § 355(j)(5)(B)(iv)(I). This provision incentivizes generic companies to challenge weak patents. See FTC, *supra* note 92.

106. § 355(j)(5)(B)(iv)(I).

107. See FTC, *supra* note 92.

108. Higgins & Graham, *supra* note 91, at 370 (displaying the number of Paragraph IV challenges (counts): 35 in 2001, 33 in 2002, 96 in 2003, 90 in 2004, 81 in 2005, 87 in 2006, 162 in 2007, and 165 in 2008).

challenges.¹⁰⁹ This ever-increasing number of patent-invalidation challenges denotes that innovator drug companies suffer a high level of patent uncertainty, which drastically decreases the profitability of innovator drugs.¹¹⁰ Fosamax, a popular osteoporosis drug made by Merck that generates \$3 billion in annual sales, illustrates clearly the serious economic damages caused by patent uncertainty.¹¹¹ Teva, the largest generic drug company in the world,¹¹² brought an invalidation challenge under Paragraph IV and successfully invalidated Fosamax patents about four years before they were due to expire.¹¹³ Fosamax's sales drastically decreased in the subsequent year of 2008 from \$3 billion to \$1.5 billion.¹¹⁴ In addition, Teva alone had 160 pending ANDAs in 2007, including 92 Paragraph IV challenges, which put at risk over \$100 billion in sales.¹¹⁵

The Federal Trade Commission (FTC) reported that generic companies prevailed in 75% of patent-invalidation challenges,¹¹⁶ while the challenge success rate across all technical fields was at 52%.¹¹⁷ This patent uncertainty seriously affects innovator drug companies' ability to fund the

109. 42 U.S.C. § 262(l)(3)(B)(ii)(I) (Supp. V 2011). The statute states:
[An ABLA] applicant [e.g., an FOB company] shall provide to the reference product sponsor [i.e., innovator company] . . . a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the opinion of the subsection (k) applicant [i.e., the FOB company] that such patent is invalid, unenforceable, or will not be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application.

Id.

110. Higgins & Graham, *supra* note 91, at 370.

111. *Id.* at 370–71.

112. Kathlyn Stone, *Top Generic Drug Companies*, ABOUT.COM PHARMA, <http://pharma.about.com/od/Generics/a/Top-Generic-Drug-Companies.htm> (last visited Sept. 15, 2013).

113. Higgins & Graham, *supra* note 91, at 371.

114. *Id.*

115. *Id.*

116. See FTC, *supra* note 92.

117. PRICEWATERHOUSECOOPERS, A CLOSER LOOK: 2008 PATENT LITIGATION STUDY: DAMAGES AWARDS, SUCCESS RATES AND TIME-TO-TRIAL 10 (2008), available at http://www.pwc.com/en_us/us/forensic-services/assets/2008_patent_litigation_study.pdf. The PricewaterhouseCoopers report shows that, across all technical fields, 52% of the patent invalidations in which the alleged infringer is the plaintiff are successful. In contrast, the FTC reported that 75% of litigated biotechnology patents are declared invalid. This suggests that biotech patents are particularly vulnerable to patent-invalidity challenges.

research for new drugs.¹¹⁸ Many commentators argue that extended FDA exclusivity is necessary to promote innovation because it is independent from patent exclusivity and stays effective regardless of the validity of the covering patents.¹¹⁹

3. Decrease in New Drug Applications

The annual number of new drug applications generally decreased in the past fifteen years,¹²⁰ despite significant development in biological science and technology.¹²¹

Science and technology in the biomedical field has hugely advanced in the past sixty years.¹²² For example, during the 1980s to 1990s, the number of drug candidates that could be synthesized by an individual chemist in a year increased 800-fold.¹²³ The speed of DNA sequencing increased a billion times since 1970.¹²⁴ The time required to deduce a protein structure via X-ray diffraction decreased more than a thousand times.¹²⁵

Despite the advancement of technology, the number of new drugs approved per \$1 billion spent on research and development has decreased by half every nine years since 1950.¹²⁶ This rate of decrease falls short roughly eighty-fold in inflation-adjusted terms.¹²⁷ The average number of new drugs approved each year between 1995 and 1999 was 37.6. The number decreased to 30.0 during 2000–2004, and the number dropped to 20.2 during 2005–2009.¹²⁸

118. See Higgins & Graham, *supra* note 91, at 371 (“Economic research shows that there is a [pharmaceutical] market failure . . .”).

119. *Id.* at 371; see also Grabowski, *supra* note 63, at 479. Contrary to the uncertainty inherent in the patent system, FDA exclusivity provides a defined period of monopoly with absolute certainty.

120. Cf. *Is It True FDA Is Approving Fewer New Drugs Lately?*, FOOD & DRUG ADMIN., <http://www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM247465.pdf> (last visited Sept. 16, 2013) (displaying charts outlining the steady decrease of new molecular entity applications from 1996–2010).

121. Jack W. Scannell et al., *Diagnosing the Decline in Pharmaceutical R&D Efficiency*, 11 NATURE REVIEWS DRUG DISCOVERY 191, 191 (2012).

122. *Id.*

123. *Id.*

124. *Id.*

125. *Id.*

126. *Id.*

127. *Id.*

128. K.I. Kaitin & J.A. DiMasi, *Pharmaceutical Innovation in the 21st Century: New Drug Approvals in the First Decade, 2000–2009*, 89 CLINICAL PHARMACEUTICS & THERAPEUTICS 183, 185 (2011).

Commentators have suggested many possible reasons that explain the constant decrease of innovation in the pharmaceutical industry.¹²⁹ One explanation is that in vitro experiments conducted in the laboratory are not necessarily repeatable in humans, meaning the basic research is performed without benefiting the medical industry.¹³⁰ Another explanation is the “low-hanging fruit” theory: fruit that hangs lower will get picked first. This is saying the relatively easier medical problems have been solved earlier, and what remains today are issues that are more difficult.¹³¹ Another explanation is it is harder to develop a better new drug.¹³² If a new drug is not better than existing therapies, the drug will likely be abandoned because the marginal profit does not justify the investments.¹³³

The explanations provided by commentators are speculative in nature and hard to verify.¹³⁴ However, it is a fact that the number of approved new drugs has decreased steadily in the past two decades.¹³⁵ This steady decrease in innovation may justify twelve-year FDA exclusivity¹³⁶ that provides a longer period of market monopoly and a higher profit margin for innovator drug companies.¹³⁷

129. *E.g.*, Scannell et al., *supra* note 121, at 193–97. Scannell et al. introduced several different theories to explain the drop in innovation, including: the “better than the Beatles” problem, the “cautious regulator” problem, the “throw money at it” tendency, and the “basic research brute-force” bias. *Id.* at 193. Yet Scannell et al. admit that none of the theories are conclusive.

130. David F. Horrobin, *Modern Biomedical Research: An Internally Self-Consistent Universe with Little Contact with Medical Reality?*, 2 NATURE REVIEWS DRUG DISCOVERY 151, 152 (2003).

131. *Id.* at 151.

132. *See* Scannell et al., *supra* note 121, at 193 (“An ever-improving back catalogue of approved medicines increases the complexity of the development process for new drugs, and raises the evidential hurdles for approval, adoption and reimbursement.”).

133. *Id.* (“[T]he fruit [the authors’ metaphor for pharmaceutical drugs] that has been picked reduces the [average] value of the fruit that is left in the tree.”).

134. *See id.* at 198. By suggesting possible reasons to explain the steady decrease in new drug applications, Scannell et al. wanted to “provoke further analysis.”

135. Kaitin & DiMasi, *supra* note 128, at 185.

136. 42 U.S.C. § 262(k)(7)(A) (Supp. V 2011).

137. *Cf.* Higgins & Graham, *supra* note 91, at 371 (“A robust system of market innovation is built on financial incentives.”).

B. PROMOTING ACCESSIBILITY

New biologics promise cutting edge therapies for the toughest diseases faced in our time.¹³⁸ However, there will be no meaningful benefit to society if these therapies are prohibitively expensive and not accessible to the general public.¹³⁹

Unfortunately, many biologic therapies are prohibitively expensive.¹⁴⁰ Biologics on average cost twenty times more than small-molecule drugs.¹⁴¹ For example, Enbrel, an anti-arthritis biologic, costs \$20,000 per year, compared to \$300 per year for the most expensive small-molecule drug treatment for arthritis.¹⁴² Treating breast cancer with a year's worth of the biologic Herceptin can cost \$48,000.¹⁴³ Remicade, a biologic treatment for rheumatoid arthritis costs \$20,000 a year.¹⁴⁴ Cerezyme, a treatment for a rare genetic disorder, Gaucher disease, which causes fatty deposits to build up in certain organs and bones, costs \$200,000 to \$300,000 per year.¹⁴⁵ From 1998 to 2006, the overall costs for biologics went up 505%, according to Kaiser Permanente.¹⁴⁶ The overall sales of biologics reached around \$100 billion in 2010, representing 26% of the total cost of pharmaceuticals.¹⁴⁷

The ABLA aims to replicate the successful experience of ANDA to lower the drug price by introducing market

138. See Patton, *supra* note 32 (stating that biologics are the “wonder drugs” of our age because they promise to treat AIDS, cancer, Alzheimer’s, and multiple sclerosis).

139. Victoria Colliver, *Priced Out of Pain Relief: Insurers Balk at High Costs of Promising New Treatments*, S.F. CHRON., May 8, 2007, at C1 (stating that insurance companies balk at covering the full price of biologic therapies because they are too expensive).

140. Patton, *supra* note 32 (“From 1998 to 2006, the costs of [biologic drugs] shot up 505 percent . . .”).

141. Karen Tumulty & Michael Scherer, *You Don’t Know Him (He’s a Lobbyist) but He May Be the Biggest Winner in Health-Care Reform. So Who Loses?*, TIME, Nov. 2, 2009, at 38, available at <http://www.time.com/time/magazine/article/0,9171,1931729,00.html>.

142. Patton, *supra* note 32.

143. Tumulty & Scherer, *supra* note 141, at 38.

144. *Id.*

145. Alfred B. Engelberg et al., *Balancing Innovation, Access, and Profits—Market Exclusivity for Biologics*, 361 NEW ENG. J. MED. 1917, 1917 (2009); Andrew Pollack, *Cutting Dosage of Costly Drug Spurs a Debate*, N.Y. TIMES, Mar. 16, 2008, at 1, available at http://www.nytimes.com/2008/03/16/business/16gaucher.html?pagewanted=all&_r.

146. Patton, *supra* note 32.

147. Roth, *supra* note 29, at 6.

competition.¹⁴⁸ However, the ABLA faces distinct challenges that may hinder the purpose to promote accessibility. Part II.B explores four aspects of these challenges: complexity and delicacy of biologics, statutory and administrative ambiguity, excessively long FDA exclusivity, and evergreening.

1. The Complexity and Delicacy of Biologics

Many commentators opine that it is scientifically impossible to produce a bioequivalent generic biologic, as in generic small-molecule drugs, due to the natural complexity and delicacy of biologics.¹⁴⁹ Biologic products are extremely sensitive to environmental conditions.¹⁵⁰ Any minor change in the manufacturing process, such as temperature, water quality, or even external packaging, can change the overall safety and efficacy of biologics.¹⁵¹

The story of Eprex highlights the extreme delicacy of biologics and the difficulties in making FOBs.¹⁵² Eprex, made by Janssen-Cilag,¹⁵³ is an FOB of Epogen, made by Amgen.¹⁵⁴ Eprex, like Epogen, treats chronic kidney disease patients for aplasia.¹⁵⁵ In 1998, incidence of pure red-cell aplasia, a rare disorder that manifests as a severe, sudden-onset anemia with complete absence of red blood cell precursors in the bone marrow, were noticed among the patients receiving Eprex.¹⁵⁶ The uncommon scenario was that the incidents happened in patients receiving Eprex in Europe, but not in the United

148. Tzeng, *supra* note 68, at 135.

149. *E.g.*, Park et al., *supra* note 79, at 1688–89. Many scientists believe that it is impossible to produce a generic biologic that is bioequivalent and bioavailable as the referenced biologic. This is the reason why the scientific communities use the term “follow-on biologics” instead of “generic biologics.” See Huub Schellekens, *Biosimilar Epoetins: How Similar Are They?*, 3 EUR. J. HOSP. PHARMACISTS 43, 43–44 (2004).

150. Park et al., *supra* note 79, at 1689.

151. *Id.*; see also JUDITH A. JOHNSON, CONG. RESEARCH SERV., FDA REGULATION OF FOLLOW-ON BIOLOGICS, at i (2010) (“Biologics often require special handling (such as refrigeration) and are usually administered to patients via injection or infused directly into the bloodstream.”).

152. Katia Boven et al., *The Increased Incidence of Pure Red Cell Aplasia with an Eprex Formulation in Uncoated Rubber Stopper Syringes*, 67 KIDNEY INT’L 2346, 2346 (2005).

153. *Id.*

154. See EPOGEN, <http://www.epogen.com> (last visited Sept. 16, 2013) (directing the homepage to Amgen).

155. Boven et al., *supra* note 152, at 2346.

156. *Id.*

States.¹⁵⁷ The reason turned out to be that the medical facilities in Europe administered Eprex using syringes with *uncoated* rubber stoppers instead of coated ones.¹⁵⁸ The uncoated rubber stopper releases certain organic compounds that cause coagulation of the active proteins that induce increased immunogenicity.¹⁵⁹ The whole incident highlights the natural delicacy of biologics, showing that even a minor change in the delivery equipment (e.g., rubber stopper), could be lethal.¹⁶⁰ Commentators argue that this natural delicacy of biologics potentially renders the interchangeability of the FOB—the idea that the FOB can be substituted by a pharmacist without consulting medical doctors—impracticable.¹⁶¹

2. Statutory and Administrative Ambiguity

The BPCIA has been enacted, but the statutory interpretation and administrative implementation are far from definite.¹⁶² Particularly, whether the twelve-year FDA exclusivity is a *data* or *market* exclusivity is still under debate.¹⁶³ The provision of “exclusivity for reference product” of the BPCIA states:

(A) Effective date of biosimilar application approval

Approval of an application [i.e., ABLA] under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a).

(B) Filing period

157. *Id.*

158. *Id.* at 2346–47.

159. *See id.* at 2352 (“[T]he evidence of [syringes with uncoated rubber stoppers] capacity to increase the immunogenicity in experimental animals [] suggest[s] that [the organic compounds] were the critical contributory factor in the increased incidence of antibody mediated PRCA attributed to Eprex.”).

160. *Id.* at 2346–47.

161. *E.g.*, Jonathan Stroud, *The Illusion of Interchangeability: The Benefits and Dangers of Guidance-Plus Rulemaking in the FDA’s Biosimilar Approval Process*, 63 ADMIN. L. REV. 599, 618 (2011). As of the time this Note was written, the FDA had not approved any FOB through ABLA.

162. Brian R. Dorn, *Biosimilars Law in Limbo: An Update on Biosimilars and Politics*, <http://www.iptoday.com/issues/2012/02/biosimilars-law-in-limbo-update-biosimilars-and-politics.asp> (last visited Sept. 9, 2013).

163. *Id.*

An application under this subsection may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed under subsection (a).¹⁶⁴

The four-year exclusivity in (B) is generally interpreted to be data exclusivity because the statutory language matches the definition of data exclusivity (i.e., the FDA will not accept any filing of an ABLA until four years after the reference biologic is approved because FOB manufacturers are precluded from relying on innovator data).¹⁶⁵ The debate focuses on whether the twelve-year exclusivity provided in (A) is *market* or *data* exclusivity.¹⁶⁶

The FDA, on October 5, 2010, interpreted the twelve-year exclusivity in (A) as a *market* exclusivity.¹⁶⁷ This is a reasonable interpretation for two reasons. First, the statutory language is: “*Approval* of an application under this subsection may not be made *effective* . . . until the date that is 12 years after the date on which the reference product was first licensed” matches the general understanding of market exclusivity (i.e., the FDA can accept and review an ABLA but will not approve it until the twelve-year market exclusivity expires).¹⁶⁸ Second, reading (A) as data exclusivity renders (B) superfluous.¹⁶⁹ However, Senators Hagan, Hatch, Enzi, and Kerry,¹⁷⁰ and Representatives Eshoo, Inslee, and Barton¹⁷¹

164. Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, sec. 7002, § 262, 124 Stat. 119, 807 (2010).

165. Cf. 21 U.S.C. § 355(c)(3)(E)(ii) (2012).

166. Emily K. Strunk, *Debate Over Exclusivity in Biologics Provision of PPACA Heats Up*, AKIN GUMP HEALTH REFORM RESOURCE CENTER (Feb. 14, 2011), <http://aghealthreform.com/2011/02/14/debate-over-exclusivity-in-biologics-provision-of-ppaca-heats-up>.

167. Notice of Public Hearing, 75 Fed. Reg. 61,498 (Oct. 5, 2010) (“The BPCI Act also includes, among other provisions: A 12-year period of *marketing exclusivity* from the date of first licensure of the reference product . . .”).

168. Karst, *supra* note 49.

169. If (A) were a data exclusivity period then (B) would be superfluous, because a twelve-year period certainly covers a four-year period. In other words, if (A) is a data exclusivity period then (B) has no effect.

170. Letter from Senators Kay R. Hagan, Orrin Hatch, Michael Enzi, and John F. Kerry, U.S. Senate, to Dr. Margaret Hamburg, Comm’r of Food and Drug Admin. (Jan. 7, 2011) [hereinafter Letter from Senators], *available at* <http://www.hpm.com/pdf/1-7-11%20Senate%20Biologics%20letter%20to%20FDA.pdf> (clarifying that the BPCIA does not provide market exclusivity, but provides data exclusivity); *see also* Dorn, *supra* note 162.

171. Letter from Representatives Anna G. Eshoo, Jay Inslee, and Joe Barton, U.S. House of Representatives, to Dr. Margaret Hamburg, Comm’r of Food & Drug Admin. (Dec. 21, 2010), *available at* <http://www.hpm.com/>

responded to the FDA's interpretation, clarifying that § 262(k)(7)(A) is a *data* exclusivity.

The difference between data or market exclusivity is significant; it means three to four years of delay in introducing FOB competition and tens of billions of dollars to the general public.¹⁷² The delay is the time for conducting clinical trials and FDA regulatory reviews.¹⁷³ According to FDA guidance documents, ABLA applicants will generally be required to conduct a certain scale of clinical trials to show biosimilarity or interchangeability.¹⁷⁴ After the clinical trials are completed, the regulatory review phase for the FDA to approve a biologic takes about sixteen months.¹⁷⁵ In the case that the twelve-year exclusivity is data exclusivity, an FOB manufacturer will have

pdf/EIB%20Ltr%20FDA%20DEC%202010.pdf (clarifying the twelve-year exclusivity is a data exclusivity); see Dorn, *supra* note 162.

172. For reasons why ABLA is expected to take, on average, three to four years (including clinical trial phase and regulatory review phase) to be approved, see *Trends in NDA and BLA Submissions and Approval Times*, FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/PDUFA/ucm209349.htm> (last updated May 4, 2010).

173. Clinical trial and regulatory review are two different time periods. An innovator drug company submits an investigational new drug (IND) application to conduct the clinical trials. After the clinical trials are completed, the innovator company then submits a new drug application (NDA) to start the formal regulatory review process. See *Running Clinical Trials*, FOOD & DRUG ADMIN., <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm155713.htm> (last updated Mar. 20, 2013) (listing the regulations governing clinical trials and regulatory reviews).

174. FDA, BIOSIMILARS: QUESTIONS AND ANSWERS REGARDING IMPLEMENTATION OF THE BIOLOGICS PRICE COMPETITION AND INNOVATION ACT OF 2009, at 8–12 (2012) [hereinafter BIOSIMILARS: QUESTIONS AND ANSWERS], available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM273001.pdf> (noting that to demonstrate biosimilarity, an ABLA applicant has to conduct rigorous structural and functional comparisons showing minimal or no difference between the FOB and the referenced biologic (e.g., bench/lab tests); then, the ABLA applicant should produce comparative human clinical trial data showing human pharmaceutical kinetic (PK), pharmaceutical dynamic (PD), and immunogenicity studies in an “appropriate population”). This shows that the FDA will certainly require a level of clinical trials appropriate to the biologic. See also Makiko Kitamura & David Wainer, *Biosimilars Lure Major Drugmakers into the Generics Biz*, BLOOMBERG BUSINESSWEEK (Mar. 21, 2013), <http://www.businessweek.com/articles/2013-03-21/biosimilars-lure-major-drugmakers-into-the-generics-biz> (noting FOB companies might have to do even more clinical trials than those required by the FDA to convince skeptical medical practitioners to use their FOBs—“life-and-death drugs”).

175. Grabowski, *supra* note 63, at 481 (showing in Figure 1 that the regulatory review period for biologics takes an average of sixteen months).

to submit an ABLA after twelve years and take another three to four years to go through the clinical trials and regulatory review process.¹⁷⁶ This de facto extends the monopoly period enjoyed by the innovator biologic manufacturers beyond twelve years. Whereas, if (A) were market exclusivity and (B) were data exclusivity, an ABLA could be submitted four years after the reference biologic was approved, and it could likely go through clinical trials and regulatory reviews before the twelve-year data exclusivity expired.¹⁷⁷ Consequently, the FOB could be on the market the very day the twelve-year market exclusivity expires.

Besides statutory ambiguity, the FDA regulations to implement the ABLA are also not clear. The FDA has ten years from the enactment of the BPCIA to finalize the regulatory structure of abbreviated biological license application, meaning the implementation standards are unlikely to be finalized until 2020.¹⁷⁸ On February 9, 2012, the FDA released three draft guidance documents that shed some light on the implementation of ABLA: (1) Scientific Considerations in Demonstrating Biosimilarity to a Reference Product;¹⁷⁹ (2) Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product: Biosimilars;¹⁸⁰ and (3) Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009.¹⁸¹ The documents highlight that, in approving an FOB, the FDA will make a case-by-case determination, examining the totality of the evidence.¹⁸² In view of the natural delicacy and complexity

176. See Karst, *supra* note 49 (stating that generic supporters argue that interpreting the twelve-year FDA exclusivity as a data exclusivity, which prevents biosimilar (i.e., ABLA) submissions, has serious consequences and that consumers will have to endure an indeterminate delay of FDA review and approval that could extend “far beyond the 12-year total that was set in the legislation”).

177. Cf. Bagley, *supra* note 48, at 15–18 (explaining market exclusivity within the context of pediatric testing exclusivity and orphan drug exclusivity).

178. Stroud, *supra* note 161, at 620.

179. SCIENTIFIC CONSIDERATIONS, *supra* note 77.

180. FDA, QUALITY CONSIDERATIONS IN DEMONSTRATING BIOSIMILARITY TO A REFERENCE PROTEIN PRODUCT: BIOSIMILARS (2012) [hereinafter QUALITY CONSIDERATIONS], available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291134.pdf>.

181. BIOSIMILARS: QUESTIONS AND ANSWERS, *supra* note 174.

182. SCIENTIFIC CONSIDERATIONS, *supra* note 77, at 2; see also Steven Kozlowski et al., *Developing the Nation’s Biosimilars Program*, 365 NEW ENG. J. MED. 385, 386 (2011).

of biologics, additional animal and clinical studies will generally be required.¹⁸³ However, the scope and extent of such studies can be reduced if more extensive, fingerprint-like analyses are provided.¹⁸⁴ Immunogenicity is considered a critical risk factor in assessing biosimilarity.¹⁸⁵ The FDA is aware that pharmaceutical companies often make changes to the manufacturing process.¹⁸⁶ The FDA will continuously monitor the quality of FOBs in regard to those changes.¹⁸⁷ A biologic will be considered interchangeable with a reference product if the developer demonstrates similar clinical results in all types of patients, and the risk associated with switching between the two biologics is not greater than continuously using the reference biologic.¹⁸⁸

3. Excessively Long FDA Exclusivity

The history of the Hatch-Waxman Act shows that the patent-invalidation challenge is an important mechanism to increase drug price competition.¹⁸⁹ However, the twelve-year FDA exclusivity in the BPCIA, regardless of whether it is a data or market exclusivity, arguably vacates the incentives to challenge biological patents.¹⁹⁰ This is because FDA exclusivity

183. SCIENTIFIC CONSIDERATIONS, *supra* note 77, at 10–19.

184. *Id.* at 7.

185. *Id.* at 7–10.

186. See QUALITY CONSIDERATIONS, *supra* note 180, at 3 (“Since 1996, FDA has approved many manufacturing process changes for licensed biological products, based on a demonstration of product comparability before and after the process change, as supported by quality criteria and analytical testing and without the need for additional nonclinical data and clinical safety and/or efficacy studies.”).

187. *Id.* at 4 (stating that if the reference product and the proposed protein product cannot be adequately characterized, the FDA recommends that the sponsor consult the FDA for guidance).

188. *Id.* at 4.

189. See Higgins & Graham, *supra* note 91, at 370 (noting patent invalidity challenges brought by generic companies cut down brand-name companies’ profit significantly).

190. See Engelberg et al., *supra* note 145, at 1917 (noting that the Biosimilar Act guarantees innovator drug companies twelve years of market exclusivity for a new biologic agent before any biosimilar product could be approved, even in the absence of a valid patent); see also Tzeng, *supra* note 68, at 156 (stating that the twelve-year data exclusivity runs potentially longer than patent protection and demonstrating that this twelve-year exclusivity destroys the incentives for generic drug companies to bring patent-invalidation challenges because even if the underlying patents are invalidated, the FOB still has to wait for the twelve-year FDA exclusivity to expire to hit the market). In addition, because this twelve-year period is likely to last longer

remains effective even if the patents covering the reference biologics are invalidated and a twelve-year period after FDA approval is likely to run longer than the underlying patents.¹⁹¹

This twelve-year FDA exclusivity is likely to live longer than the remaining active patent term.¹⁹² Active patent term refers to the overall patent life minus the overall administration time spent in the United States Patent and Trademark Office (USPTO) and the FDA.¹⁹³ The overall patent life is the summation of twenty years from filing, the patent term adjustment (PTA) granted by the USPTO, and the patent term extension (PTE) granted by the FDA.¹⁹⁴ Put simply, PTA is granted if USPTO examination took more than three years from filing to issuance.¹⁹⁵ The examination time in excess of three years will be granted as PTA.¹⁹⁶ On average, the USPTO takes 33.7 months to review a patent application, slightly short of three years.¹⁹⁷ Thus, PTA is likely to be zero. The period of PTE granted by the FDA is calculated by adding one-half of the time during which the drug is evaluated as an “investigational new drug” to the time the drug is pending approval at the FDA.¹⁹⁸ However, the extension cannot exceed a maximum

than the remaining patent life, there is no point for generic drug companies to spend the litigation resources to invalidate the underlying patents.

191. Engelberg et al., *supra* note 145, at 1917.

192. See Tzeng, *supra* note 68, at 156 (stating that the twelve-year data exclusivity runs potentially longer than patent protection). I use the term “active patent term” to mean the patent period that the drug is actually on the market and generating revenue for the patentee. This active patent term is the overall patent life minus overall administration time. Overall patent life means the regular twenty years from filing, plus patent term adjustment, plus patent term extension. Overall administration time is the time spent in the U.S. Patent and Trademark Office to secure the patent and the FDA to get the drug approved.

193. *Id.*

194. *Id.*

195. 35 U.S.C. § 154(b) (2006 & Supp. V 2011) (guaranteeing prompt patent and trademark office responses and specifying the conditions of granting patent term adjustments); see also Bagley, *supra* note 48, at 11 (“[T]he USPTO is expected to take no more than three years to examine and issue a patent on an application. If the USPTO fails to issue a patent within three years from the actual U.S. filing date, it must extend the term of the resulting patent one day for each day beyond the three-year period until the patent issues.”).

196. See Bagley, *supra* note 48, at 11.

197. Jim Singer, *How Long Does Patent and Trademark Prosecution Take?*, IP SPOTLIGHT (Dec. 14, 2011), <http://ipspotlight.com/2011/12/14/1780/>.

198. 35 U.S.C. § 156(c)(2) (2006 & Supp. V 2011).

period of five years,¹⁹⁹ nor can it extend patent expiration to a date more than fourteen years after being approved by the FDA.²⁰⁰ The average PTE awarded by the FDA in approving a new drug is 43.2 months.²⁰¹ The FDA takes an average of 110 months to approve an innovator biologic, counting both the clinical phase and the regulatory review phase.²⁰²

Thus, the average active patent term for a new biologic is (in months): 240 (20 years from filing) + 0 (patent term adjustment) + 43.2 (PTE) – 33.7 (PTO examination time) – 110 (FDA approval time) = 139.5 months (11.65 years). Therefore, it is more likely than not that the patents covering innovator biologics will expire before the twelve-year FDA exclusivity expires.²⁰³

In light of all the characteristics of this twelve-year FDA exclusivity (independent from and likely to last longer than the underlying patents), there is little to no incentive for FOB companies to challenge the patents.²⁰⁴ President Obama expressed his concern that the twelve-year FDA exclusivity tips the balance toward innovator drug companies and proposed to reduce it to seven years.²⁰⁵ Commentators even speculate that,

199. § 156(g)(6)(A).

200. § 156(c)(3).

201. Charles Clift, *The Value of Patent Term Extensions to the Pharmaceutical Industry in the USA*, 5 J. GENERIC MED. 201, 205 (2008) (showing that the average PTE awarded to the forty best selling drugs in 2006 was 43.2 months).

202. See Grabowski, *supra* note 63, at 481–82 (showing that, on average, standard NCE/BLA applications take 110 months to be approved). An innovator biologic (i.e., BLA) takes on average 110 months to be approved, including both the time of clinical trial and regulatory review.

203. See Tzeng, *supra* note 68, at 156.

204. See Engelberg et al., *supra* note 145, at 1919 (noting that a rigid twelve-year exclusivity period essentially eliminates the need for innovator companies to defend any patents).

205. See Mike Palmedo, *Obama's Deficit Plan Would Reduce Data Exclusivity for Biologics and Ban Pay-for-Delay Patent Settlements*, INFOJUSTICE.ORG (Sept. 20, 2011), <http://infojustice.org/archives/5585> (“[The Obama administration’s] proposal would reduce data exclusivity for biologic medicines to 7 years . . . and would ‘prohibit additional periods of exclusivity for brand biologics due [to] minor changes in product formulations, a practice often referred to as ‘evergreening.’” The administration predicts that the shorter periods of data exclusivity will ‘encourage faster development of generic biologics while retaining appropriate incentives for research and development for the innovation of breakthrough products.’”); see also Dorn, *supra* note 162; Andrew Pollack, *Obama Pushes More Competition on Biologic Drugs*, N.Y. TIMES, Sept. 19, 2011, available at

in view of this excessively long twelve-year exclusivity, the ABLA pathway will not be used much because FOB companies will likely ignore ABLAs and file regular Biologics License Applications (BLAs), thus avoiding the delay of the twelve-year period.²⁰⁶ This creates a lose-lose-lose situation for the FOB companies, the innovator companies, and the general public, because FOB companies will not be able to save cost by relying on innovators' clinical data, nor will the innovator drug company get to enjoy the full twelve-year exclusivity, nor will the general public enjoy the drug price competition.²⁰⁷

4. Evergreening

Evergreening strategy refers to patenting activities by innovator drug companies on ancillary aspects of the drugs.²⁰⁸ The natural complexity of biologics provides convenient mechanisms for innovator drug companies to engage in evergreening, such as reformulation of drugs, new manufacturing processes, or quality-control methodologies.²⁰⁹

<http://prescriptions.blogs.nytimes.com/2011/09/19/obama-pushes-more-competition-on-biologic-drugs>.

206. See Engelberg et al., *supra* note 145, at 1918 (“[M]anufacturers of potential follow-on products would probably prefer to ignore the new pathway and opt to file a standard BLA, which would not be subject to the 12-year delay. Any higher cost would be offset by the greater profit opportunity available to early market entrants. Therefore, as currently fashioned, the biosimilar legislation would have no value, because it would create a pathway that would scarcely be used. Innovators would not get the benefit of the exclusivity provision, and the public would not get the benefit of the enhanced price competition that would result from increasing the number of competitors.”).

207. *Id.* Engelberg speculates that the twelve-year FDA exclusivity creates a lose-lose-lose situation among the innovator company, FOB company, and the general public. Innovator companies will not enjoy the twelve-year exclusivity because FOB companies will design around and go through regular BLA to avoid the delay of the twelve-year period. FOB companies will not be able to enjoy the cost-saving, fast track ABLA because regular BLA is preferred. The general public will not be able to enjoy low price biologics because FOB companies will have to price higher in order to recoup the investment for going through regular BLA.

208. See Hemphill & Sampat, *supra* note 66, at 327–28 (describing evergreening as securing or acquiring patents on ancillary aspects with doubtful validity in order to delay generic competition).

209. See Christopher Weaver et al., *Biotech Drugs Still Won't Copy*, WALL ST. J., Feb. 27, 2013, at B1 (noting that innovator biologic companies can gain patents on manufacturing procedures and formulations to extend the market monopoly period). The CEO of AbbVie Inc., a spin-off of Abbott Laboratories, said that AbbVie has more than 200 such patents on Humira, an innovator biologic treating arthritis. *Id.*

For example, an innovator biologic company can secure a patent on a reformulation of a biologic, improving certain peripheral effects.²¹⁰ Then, right before the expiration of the twelve-year exclusivity, the innovator drug company can obtain a quick approval of the reformulated biologic by referring to its own clinical data and enjoy a renewed twelve-year monopoly.²¹¹

The evergreening issue was debated in Congress.²¹² Senator Orrin Hatch and Senator Kay Hagan sent a letter on January 7, 2011 calling on the FDA to interpret the BPCIA such that innovator drug companies should get a renewed twelve years of exclusivity if manufacturers alter an existing product to improve safety or potency.²¹³ Senator Sherrod Brown and proponents of generic companies disagreed with this interpretation and showed great concerns that this tweak-to-renew tactic would increase costs for consumers, businesses, and taxpayers.²¹⁴ President Obama also expressed his intention to prohibit evergreening.²¹⁵ Siding with the President, Pamela Jones Harbour, the then Commissioner of the FTC, expressed her opinion in June of 2009: “no additional period of branded exclusivity is needed to spur the development of new drug products” because pioneer biologics are already covered by varied patents and market-based exclusivities, providing strong incentives to innovate.²¹⁶

210. See Alicia Mundy, *Biotech Firms Fight Generics*, WALL ST. J., Jan. 12, 2011, <http://online.wsj.com/article/SB10001424052748703889204576078252260327210.html> (noting that Senators Hatch and Hagan stated in a letter to the FDA that companies should get an additional twelve years of exclusivity if an existing product is altered to improve safety or potency).

211. *Id.* Note that the twelve-year exclusivity excludes follow-on competitors but *not* the original data owner.

212. *Id.*

213. Letter from Senators, *supra* note 170 (“If a manufacturer modifies an approved product to produce a change in safety, purity or potency, the modified product is rightly considered a new product. It will be protected by the *data* exclusivity provisions afforded new products. Exclusivity on the first generation product will expire as scheduled.”).

214. See Mundy, *supra* note 210.

215. See Palmedo, *supra* note 205 (noting that the Obama administration proposes to prohibit additional periods of exclusivity for brand biologics due to minor changes in product formulations, a practice often referred to as “evergreening”).

216. See Pamela Jones Harbour, Comm’r, FTC, Oral Statement Before the Subcommittee on Health, Committee on Energy and Commerce, United States House of Representatives, Emerging Health Care Issues: Follow-on Biologic Drug Competition (June 11, 2009), *available at* http://democrats.energycommerce.house.gov/Press_111/20090611/testimony_harbour.pdf.

A recent case in 2012, *Momenta Pharmaceuticals, Inc. v. Amphastar Pharmaceuticals, Inc.*, provides an example of evergreening in therapies that require a high level of quality control, such as biologics.²¹⁷ Momenta Pharmaceuticals (Momenta) and Amphastar Pharmaceuticals (Amphastar) are both generic drug companies making generic versions of Lovenox (enoxaparin), produced by Aventis Pharmaceuticals.²¹⁸ Enoxaparin requires a high level of continuous quality control.²¹⁹ In order to ensure quality, the FDA required both Momenta and Amphastar to profile their products via mass spectroscopy, nuclear magnetic resonance spectroscopy, modifying reagents, or modifying enzymes, to show their enoxaparin is equivalent to Lovenox.²²⁰ Amphastar was the first to be approved by the FDA.²²¹ However, Momenta owns a method patent (Patent No. 7,575,886, “the ‘866 patent”) in quality control (i.e., an evergreening patent) to show its product is equivalent to Lovenox.²²² Before Amphastar’s enoxaparin could reach the market, Momenta asserted infringement actions alleging that Amphastar inevitably infringed its ‘866 patent.²²³ Amphastar’s enoxaparin eventually reached the market after Momenta.²²⁴ This scenario highlights an evergreening strategy: a quality-control patent can conveniently be used to extend a market monopoly in therapies

217. *Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1349–52 (Fed. Cir. 2012).

218. *Id.*

219. *Id.* at 1349–50.

220. *Id.* at 1350–51.

221. *Id.* at 1351.

222. *Id.*

223. *Id.*

224. *Id.* at 1351–62. The majority ruled against Momenta in *Momenta v. Amphastar*. Judges Moore and Dyk reasoned that even if Amphastar infringed Momenta’s profiling method, patent ‘866, it was exempted under the safe harbor (35 U.S.C. § 271(e)(1)) because the quality control and profiling of the product falls within the statutory language: “reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use or sale of drugs . . .” *Id.* at 1357–59. The majority ruling partially answers the concern of using quality-control and product-profiling patents to extend market monopoly. However, Judge Rader dissented, arguing that the safe harbor should be limited to *pre-approval* activities. *Id.* at 1361–76 (Rader, J., dissenting). If Judge Rader’s point of view subsequently prevails, the activities of continuous quality-controlling and profiling after an FOB is approved will constitute patent infringement. In other words, brand-name companies can assert quality control method patents to deter FOBs.

that require continuous, high-quality monitoring, such as biologics.²²⁵

C. BIOSIMILAR—A GAME OF BRAND-NAME COMPANIES

Maybe the wrestling between the proponents for innovators and FOB companies will eventually be moot because the biosimilar game is likely among brand-name companies.²²⁶ In 2009, the FTC stated the following in one report:

FOB products are likely to take eight to ten years to develop, and their development will likely cost between \$100 and \$200 million. These amounts differ substantially from the product development costs for small-molecule generic drugs, which typically take three to five years to develop and cost between \$1 and \$5 million.²²⁷

In light of the high cost to enter the market, the dynamics of biosimilar competition will likely be “brand-name to brand-name,” rather than “brand-name to generic” competition.²²⁸ Indeed, Merck and Pfizer, both recognized as brand-name companies, have started to develop FOBs referencing Amgen and Roche’s biologic products.²²⁹

225. See Weaver et al., *supra* note 209 (stating that Merck retreated from a plan to develop an FOB of Enbrel, an innovator biologic made by Amgen, because Amgen recently gained a new patent on Enbrel).

226. See Kitamura & Wainer, *supra* note 174 (noting it would take about \$100 to \$200 million to develop an FOB, much higher than the \$50 million needed to make a generic small-molecule drug). The higher threshold makes biosimilar development likely to be a game among big pharmaceutical companies. *Id.*

227. FTC, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION 6 (2009) [hereinafter EMERGING HEALTH CARE ISSUES], available at <http://www.ftc.gov/os/2009/06/P083901biologicsreport.pdf>. The report highlights that biosimilars are a game for deep pockets. The medium or small generic firms are not likely to have sufficient capital and equipment to participate in the competition. Therefore, biosimilar development is likely to be a war among brand-name companies.

228. See Linda A. Johnson, *Merck, Samsung JV Team Up on Biosimilar Medicines*, BLOOMBERG BUSINESSWEEK (Feb. 20, 2013), <http://www.businessweek.com/ap/2013-02-20/merck-samsung-jv-team-up-on-biosimilar-medicines> (noting that Merck, a brand-name drug company, collaborated with Samsung in a joint venture to develop biosimilars).

229. See Peter Loftus, *Merck Teams Up with Parexel on Biosimilars*, WALL ST. J., Jan. 12, 2011, <http://online.wsj.com/article/SB10001424052748704803604576078160079036994.html> (noting that Merck, Pfizer, and some other big brand-name drug makers view biosimilars as a big market opportunity and aim to participate as FOB companies); see also *Pfizer Carrying out Biosimilar Trastuzumab Trial in US*, GENERICS & BIOSIMILARS INITIATIVE (Oct 19, 2012), <http://www.gabionline.net/Biosimilars/Research/Pfizer-carrying-out-biosimilar-trastuzumab-trial-in-US>. Pfizer is carrying out

D. STRIKING A BETTER BALANCE: A SIX-YEAR DATA EXCLUSIVITY AND A DYNAMIC SIX-TO-TWELVE-YEAR MARKET EXCLUSIVITY

A rigid, twelve-year FDA exclusivity, regardless of whether it is data or market exclusivity, is too long and tips the scale in favor of innovator companies. As articulated previously, a twelve-year exclusivity period is likely to out-live the underlying patents in the majority of the cases and eliminates the incentives to challenge these patents.²³⁰ This works against the public interest of promoting drug accessibility, especially in view of the high market entrance barrier and evergreening tactics in biologic therapies.²³¹ However, reducing the FDA exclusivity straight to a rigid seven-year time frame, as President Obama suggested, might tip the scale too favorably toward the FOB companies' side.²³² In striking a better balance, this Note suggests a regulatory scheme of a *six-year data exclusivity* and a *six-to-twelve-year dynamic market exclusivity*. The dynamic market exclusivity would be adjudicated by a panel of experts from both the FTC and the FDA at the end of the six-year period.

Under this scheme, innovator companies have six years of absolute market monopoly covered by patent exclusivity, data exclusivity, and market exclusivities.²³³ During this period,

an FOB referencing Trastuzumab, a biologic made by Roche to treat breast cancer; Trastuzumab is Roche's third-best-selling drug. *Id.*

230. See *supra* Part II.B. In a nutshell, Part II.B. argues that (1) in view of the natural delicacy of biologics, it is difficult to produce biosimilars; to enter the biologics market requires large capital and advanced technologies compared to entering the market of small-molecule drugs; (2) a twelve-year exclusivity period is likely to out-live the underlying patents in the majority of the cases and eliminates the incentives to challenge the patents; and (3) a twelve-year period is likely to aggregate the negative impacts of evergreening tactics on drug-price competition, especially if the FDA adopted the tweak-to-renew policy.

231. See *supra* Part II.B.

232. See Palmedo, *supra* note 205. President Obama and proponents of generic drug companies supported a seven-year exclusivity. This Note's Author believes a rigid seven-year period is too short and is not sufficient for innovator companies to recoup their investments. The reasons that justify innovator companies having FDA exclusivity longer than seven years are articulated in Part II.A of this Note: (1) it costs a lot more to develop a biologic therapy than a small-molecule drug; (2) biotechnology patents are particularly vulnerable to being challenged; and (3) innovation decreases steadily under the Hatch-Waxman incentive system.

233. See *generally* Bagley, *supra* note 48. During the first six years, an innovator company would have all three kinds of market exclusivities: patent exclusivity, data exclusivity, and market exclusivity. Patent exclusivity prevents FOB companies from using, selling, or importing the protected

innovator companies will face no competition, even if the underlying patents are invalidated.²³⁴ At the end of the six-year period, the FTC and the FDA will assemble an expert panel to adjudicate how many more years of market exclusivity will be granted.²³⁵ In the adjudication process, there should be trial-type procedures allowing the innovator companies to submit briefs, present experts, answer questions, and orally advocate their positions.²³⁶ The benefit of having this adjudication at the end of the six-year period is that it allows the FTC and the FDA to evaluate the sales profile of the biologic during that first five to six years.²³⁷ This sales information is extremely helpful in evaluating how many more years of market exclusivity should be granted to allow innovator companies to recoup their investments.²³⁸

Some commentators might argue that this individualized adjudication is inefficient and will consume heavy administrative resources. This Note disagrees. According to the FDA, the number of approved BLAs was four in 2008, seven in 2009, six in 2010, and six in 2011.²³⁹ Since the annual number

biologic. Data exclusivity prevents FOB companies from submitting an ABLA. Market exclusivity prevents the FDA from approving an ABLA. The overlapping protection of all three exclusivity powers provides innovator companies with absolute market monopoly power.

234. See Tzeng, *supra* note 68, at 156 (explaining that FDA exclusivity is independent from patent exclusivity).

235. See generally EMERGING HEALTH CARE ISSUES, *supra* note 227. The FTC has the expertise in balancing customer protection and market monopoly (e.g., antitrust enforcement). The FDA has the expertise in assessing the technology and clinical effects of the biologic. Thus, an expert panel from both the FTC and the FDA will be ideal in adjudicating the market exclusivity.

236. See 5 U.S.C. §§ 554–557 (2012). Administrative formal/informal adjudication processes specified in this code might shed some light on this market exclusivity adjudication process.

237. See Grabowski, *supra* note 63, at 485 (demonstrating that mean sales of a biologic therapy grow almost linearly from the first year, at \$128 million per year, to the ninth year, peaking at \$713 million per year; the sales slightly decrease after the ninth year but remain above \$600 million through the fourteenth year). Thus, having the first five to six years of sales data helps the expert panels from the FTC and the FDA to accurately predict how many more years an innovator company will need to recoup its investment.

238. *Id.*

239. See FDA, CDER DRUG AND BIOLOGIC APPROVALS FOR CALENDAR YEAR 2008, available at <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/UCM200924.pdf>; FDA, CDER DRUG AND BIOLOGIC APPROVALS FOR CALENDAR YEAR 2009, available at <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/PriorityNDAandBLAApprovals/UC>

of approved BLAs constantly remains single digit, adjudication for each BLA will not impose undue burden on the administrative system.

In promoting innovation, this suggested scheme recognizes the heavy up-front investment in developing a new biologic therapy and provides mechanisms to adjudicate individualized market exclusivity for innovator companies to recoup their investments.²⁴⁰ The innovator companies may present evidence showing how much money they have spent on bringing the biologic to the market and argue for how many more years they need to recoup the investments. In promoting accessibility, this suggested scheme avoids the potential extension of market monopoly due to FOB companies' inability to complete the ABLA approval process before the expiration of innovators' market exclusivity.²⁴¹ This is because FOB companies can submit ABLAs at the end of the six-year period (i.e., the expiration of the data exclusivity, under this scheme) and use the expected three to four years of ABLA approval process to finish the required clinical trials and regulatory review.²⁴² The

M090995.pdf; FDA, CDER DRUG AND BIOLOGIC APPROVALS FOR CALENDAR YEAR 2010, *available at* <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/UCM260585.pdf>; FDA, CDER DRUG AND BIOLOGIC APPROVALS FOR CALENDAR YEAR 2011, *available at* <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/UCM276984.pdf>.

240. See Grabowski, *supra* note 63, at 489.

241. See *supra* Part II.B.2. If the twelve-year FDA exclusivity is explained as a data exclusivity, ABLA applicants can submit applications only after the expiration of the twelve-year data exclusivity and take another three to four years to finish the FDA approval process. This de facto extends innovators' market monopoly period.

242. *Trends in NDA and BLA Submissions and Approval Times*, *supra* note 172. Since no ABLA has been approved by the FDA yet, no one knows how long it would take for an FOB to be approved by the FDA. But we can do some guess-work from the empirical data of innovator biologics and generic small-molecule drugs. The average approval time for innovator biologics (i.e., BLAs) should be the upper limit for an ABLA because the ABLA refers to a BLA's clinical data. This means a much smaller scale of clinical trials and that it should take a shorter time to be approved than a BLA. On the other hand, the average approval time for generic small-molecule drugs (i.e., ANDA) should establish the lower limit for ABLA, because biologics normally take longer to be approved than small-molecule drugs. See Grabowski, *supra* note 63, at 482. An innovator biologic (i.e., BLA) takes on average 110 months to be approved, including both the time for clinical trials and regulatory review. See Kurt R. Karst, *OGD's ANDA Backlog and Median ANDA Approval Times Are Up—WAY UP! "The Solution Lies in Resources," Says FDA Commissioner Hamburg*, FDA L. BLOG (Feb. 25, 2010), <http://www.fdalawblog.net/>

ABLA approval process will likely conclude before, or at least not long after, the expiration of the referenced biologic's market exclusivity.²⁴³

This suggested scheme strikes a good balance for the incentives to bring patent invalidity challenges. The overall number of patent challenges will decrease compared to the current situation in small-molecule drugs. However, it does *not* eliminate the incentive to initiate patent-invalidation challenges, contrary to the current rigid twelve-year FDA exclusivity. Invalidation challenges will be commenced by FOB companies in the case that the remaining patent term of the referenced biologic is *longer* than the adjudicated market exclusivity.²⁴⁴ The time difference between the remaining patent term and the adjudicated market exclusivity provides the additional profit margin that FOB companies gain by invalidating the patents.²⁴⁵ If the market exclusivity is *equal* to or *longer* than the remaining patent terms, there is no incentive for FOB companies to invalidate innovators' patents because there is no extra profit margin.²⁴⁶

fda_law_blog_hyman_phelps/2010/02/ogds-anda-backlog-and-median-anda-approval-times-are-up-way-up-the-solution-lies-in-resources-says-f.html (showing that ANDA median approval time is 26.7 months; approximately two years). Thus, a reasonable expectation is for an ABLA to be approved within *three to four* years.

243. See Karst, *supra* note 49 (referencing a problem which this suggested scheme solves). A rigid twelve-year data exclusivity will cause unknown delay, perhaps stretching far after the expiration of the twelve-year data exclusivity period. This is because under the suggested scheme, FOB companies can submit ABLAs at the time the six-year data exclusivity expires and go through the clinical trial and regulatory review processes while the reference product market exclusivity is still ongoing. The ABLA approval process of, on average, three to four years is likely to be finished before, or at least not long after, the reference product market exclusivity expires.

244. See *generally* Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 15, 21, 28, and 35 U.S.C.). If the patents covering the reference biologic are invalidated, FOB companies can sell the competing product at the expiration of the reference biologic's market exclusivity. See *generally* Ware & Littlefield, *supra*, note 64. If the reference biologic's market exclusivity is equal to or longer than the underlying patents, FOB companies gain nothing by invalidating the patents because the biosimilar products will not be approved by the FDA until the market exclusivity expires anyway.

245. See Hemphill & Sampat, *supra* note 66, at 328 (discussing the process and incentives for generic drug-makers to challenge patents).

246. *Id.*

Finally, innovator companies will have a harder time engaging in evergreening tactics under this scheme.²⁴⁷ During the trial-type adjudication, the experts from the FTC and the FDA and advocates from innovator companies will review factual information and engage in rigorous deliberation. This deliberation process makes it difficult for innovator companies to justify evergreening.²⁴⁸

CONCLUSION

Biologics promise cutting-edge therapies treating the toughest diseases faced in our time.²⁴⁹ In October 2010, the BPCIA was enacted, establishing an abbreviated approval pathway for follow-on biologics, known as the biosimilar pathway.²⁵⁰ Analogous to the Hatch-Waxman Act, the central mission of the BPCIA is to balance two competing interests: innovation and accessibility.²⁵¹ One of the most important provisions in the BPCIA is 42 U.S.C. § 262(k)(7)(A), which provides twelve-year FDA exclusivity.²⁵² At the time of this writing, it remains unclear whether this twelve-year FDA exclusivity is data or market exclusivity.²⁵³ This Note concludes that this rigid twelve-year FDA exclusivity tips the balance toward innovation and compromises accessibility.²⁵⁴ To strike a better balance, this Note proposes a six-year data exclusivity period and a six-to-twelve-year dynamic market exclusivity

247. See generally *id.* (presenting responses to evergreening). In the adjudication process, the innovator companies will submit briefs, present experts, and orally advocate their positions for a longer period of market exclusivity. But if the biologic product at issue is a modified version of a previous product with minor or insignificant safety and efficacy improvements, the company will have a harder time convincing the expert panel to grant extra market exclusivity.

248. *Id.*

249. See Patton, *supra* note 32.

250. See Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, § 7001, 124 Stat. 119, 804 (2010).

251. See *id.* § 7001(b), 124 Stat. at 804; see also Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 15, 21, 28, and 35 U.S.C.).

252. See Krauskopf, *supra* note 46.

253. See Karst, *supra* note 49 (noting that the Commissioner of the FDA interpreted the twelve-year FDA exclusivity as a market exclusivity). On the other hand, some Senators and Representatives interpreted the twelve-year FDA exclusivity as data exclusivity. *Id.*

254. See *supra* Part II.B.3 of this Note for detailed articulations.

scheme.²⁵⁵ In this scheme, experts from the FTC and the FDA will individually adjudicate a six-to-twelve-year market exclusivity period for each innovator biologic to ensure that innovator companies have a sufficient exclusive period to recoup their investment.²⁵⁶ This scheme allows ABLAs to be submitted at the expiration of the six-year data exclusivity period and allows FOBs to enter the market at or near the expiration of the market exclusivity period.²⁵⁷ The scheme reduces, yet does not eliminate, the incentives to challenge innovators' patents.²⁵⁸ Finally, the scheme has the potential to halt evergreening.²⁵⁹ Thus, this regulatory scheme with *six-year data exclusivity* and *six-to-twelve-year dynamic market exclusivity* strikes a better balance between innovation and accessibility.

255. See *supra* Part II.D of this Note for detailed articulations.

256. See *supra* Part II.D.

257. See Karst, *supra* note 49.

258. See Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 15, 21, 28, and 35 U.S.C.).

259. See *generally* Hemphill & Sampat, *supra* note 66.
