

TAKING BIOSIMILARS TO THE NEXT LEVEL: WHY FEDERALIZING THE SUBSTITUTION OF BIOSIMILARS PROMOTES INNOVATION, COMPETITION, AND PATIENT SAFETY

I. INTRODUCTION

At 71 years old, Philip DeLuca knows it's no easy task keeping up with ten grandchildren.¹ While that would intimidate any grandparent, Mr. DeLuca finds it especially difficult to summon the energy to play catch or tag—his bone marrow produces insufficient red blood cell amounts, making his blood less able to successfully transport oxygen throughout his body.²

Although weekly injections that boost his red blood cell levels have given him hope, the cost of a single shot is something to turn pale over—\$1,500.³ His medication, Procrit, is part of a class of drugs called “biologics,”⁴ which are defined under the Public Health Service Act as any “virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings.”⁵ In other words, biologics are derived from other living organisms⁶ and are used

1. *What's Keeping Less Expensive Biologic Drugs From the U.S. Market?*, PBS NEWSHOUR (Apr. 19, 2014, 5:00 PM), <http://www.pbs.org/newshour/bb/whats-keeping-generic-version-biologic-drugs-u-s-market>.

2. *Id.*

3. *Id.*

4. *Id.*

5. 42 U.S.C. § 262(i) (2012).

6. Shawn P. Gorman et al., *The Biosimilars Act: The United States' Entry Into Regulating Biosimilars and Its Implications*, 12 J. MARSHALL REV. INTELL. PROP. L. 322, 327 (2012-2013); FOOD & DRUG ADMIN., FREQUENTLY ASKED QUESTIONS ABOUT THERAPEUTIC BIOLOGICAL PRODUCTS, (Dec. 24, 2009), <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/>

to treat various diseases or conditions in humans⁷ such as rheumatoid arthritis, macular degeneration, and possibly even Alzheimer's and cancer.⁸

Biologics tend to be so expensive, in part, because they are often composed of large molecules⁹ that can only be produced through relatively complex¹⁰ biological processes.¹¹ Accordingly, slight changes in the manufacturing process can significantly affect the product's protein structure, thereby affecting its safety, efficacy, and potency.¹²

Until recently,¹³ the United States did not have an abbreviated drug approval pathway for biologics like it has for chemical drugs.¹⁴ Those drugs are generally less structurally complex, making them easier and cheaper to produce than biologics.¹⁵ Under the current regulatory framework for chemical drugs,¹⁶ the Food and Drug Administration (FDA)¹⁷ may approve a

HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/ucm113522.htm [hereinafter FDA FAQ].

7. FDA FAQ, *supra* note 6.

8. *What's Keeping Less Expensive Biologic Drugs From the U.S. Market?*, *supra* note 1; see John Carroll, *Amgen Clears PhIII Hurdle in Crowded Biosimilar Race to Topple Humira*, FIERCE BIOTECH (Feb. 4, 2015), <http://www.fiercebiotech.com/story/amgen-clears-phiii-hurdle-crowded-biosimilar-race-topple-humira/2015-02-04> (detailing how Amgen's biosimilar to treat rheumatoid arthritis passed phase III of developmental testing).

9. Henry Grabowski et al., *Implementation of the Biosimilar Pathway: Economic and Policy Issues*, 41 SETON HALL L. REV. 511, 512-13 (2011).

10. Paul J. Declerck, *Biosimilar Monoclonal Antibodies: A Science-Based Regulatory Challenge*, 13 EXPERT OP. BIOLOGICAL THERAPY 153, 154 (2013).

11. Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 515. Further adding to the expense, biologics are typically administered as injections by physicians. Kevin E. Noonan, *FDA Approves Sandoz Filgrastim Biosimilar*, PATENT DOCS (Mar. 8, 2015, 11:41 PM), <http://www.patentdocs.org/2015/03/fda-approves-sandoz-filgrastim-biosimilar.html>.

12. Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 515; BIOTECHNOLOGY INDUSTRY ORG., HOW DO DRUGS AND BIOLOGICS DIFFER?, (Nov. 10, 2010), <http://www.bio.org/articles/how-do-drugs-and-biologics-differ>.

13. *Infra* note 25.

14. *What's Keeping Less Expensive Biologic Drugs From the U.S. Market?*, *supra* note 1; see *infra* note 16.

15. BIOTECHNOLOGY INDUSTRY ORG., HOW DO DRUGS AND BIOLOGICS DIFFER?, *supra* note 12.

16. 21 U.S.C. § 355(j) (2012). The Drug Price Competition and Patent Term Restoration Act, commonly known as the Hatch-Waxman Act, is the legislation codified in this section. It contains data and market exclusivity and patent litigation provisions, addressed *infra* note 101, which are similar to those contained in the Biosimilars Act.

17. The FDA is the federal agency responsible for ensuring that products, including pharmaceuticals and biological drugs, are safe and effective. Ryan Abbott, *Big Data and Pharmacovigilance: Using Health Information Exchanges to Revolutionize Drug Safety*, 99 IOWA L. REV. 225, 231 (2013).

generic drug manufacturer's abbreviated new drug application (ANDA) if the applicant can demonstrate the drug is bioequivalent (identical) to an already-approved innovator drug¹⁸ (the reference product) whose patent has expired.¹⁹ This pathway has significantly reduced both the time²⁰ and money²¹ it takes for a generic drug to safely reach the market, with savings passed onto consumers.²²

Unbeknownst to a majority of the American public,²³ the 2010 Patient Protection and Affordable Care Act ("Affordable Care Act") has set the stage for patients like Mr. DeLuca to access essential biological medications at more feasible prices.²⁴

The Affordable Care Act included a section called the Biologics Price Competition and Innovation Act ("the Biosimilars Act"), which established an abbreviated biologic approval pathway regulated by the FDA.²⁵ Supplementing the traditional approval pathway for biologics created under section 351 of the Public Health Service Act,²⁶ the new pathway²⁷ allows the FDA to approve "biosimilars," also known as "follow-on biologics," that meet certain requirements.²⁸ This paper will only use the term "biosimilar" when referring to drugs brought through this abbreviated biologic pathway, but will use the terms "innovator drug" or "reference product"

18. Typically referred to as the brand-name drug.

19. 21 U.S.C. § 355(j).

20. Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 *FOOD & DRUG L.J.* 187, 193 (1999).

21. See Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 *J. HEALTH ECON.* 151, 162 (2003).

22. OFFICE OF THE ASSISTANT SEC'Y FOR PLANNING & EVALUATION, U.S. DEP'T OF HEALTH & HUMAN SERVS., *EXPANDING THE USE OF GENERIC DRUGS* (2010); Grabowski et al., *Implementation of the Biosimilar Pathway*, supra note 9, at 545 (noting that the government will also realize savings by reducing federal budget deficits to the tune of \$7 billion from 2010-2019).

23. Bobby Rush, *Biosimilars: Another Untold Story of the Affordable Care Act*, HUFFINGTON POST, (Nov. 6, 2014, 11:56 AM), http://www.huffingtonpost.com/rep-bobby-rush/biosimilars-another-untol_b_6115332.html. In his article for the Huffington Post, Representative Bobby Rush of the First Congressional District of Illinois lamented that the public is unfortunately unaware of the Affordable Care Act's biosimilar approval pathway and its potential impact on healthcare. *Id.*

24. *Id.*; see *What's Keeping Less Expensive Biologic Drugs From the U.S. Market?*, supra note 1.

25. Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 7001-7003, 124 Stat. 119 (2010) [hereinafter "the Biosimilars Act"]. The "Biosimilars Act" is the relevant section of the ACA.

26. 42 U.S.C. § 262(a) (2012).

27. 42 U.S.C. § 262(k) (2012).

28. *Id.*; see also *infra* text accompanying notes 61-74.

interchangeably when referring to the drug on which a generic chemical drug or biosimilar is based. “Generic drug” will refer to any chemical-based drug approved under the ANDA system.

Although the biosimilar approval pathway mirrors the well-established generic chemical drug pathway created under the 1984 Drug Price Competition and Patent Term Restoration Act, commonly referred to as the Hatch-Waxman Act,²⁹ biosimilars call for different regulations³⁰ than chemical drugs due to their unique compositions³¹ and manufacturing processes.³² For reasons that will be addressed later in this paper, a biosimilar may never be *completely* identical to the innovator drug.³³

Accordingly, the Biosimilars Act provides two designations a successful applicant may obtain:³⁴ “biosimilarity,” which means that a drug is highly similar, but not identical to, the innovator drug,³⁵ and a more stringent classification of “interchangeability,” meaning the drug is therapeutically interchangeable with the innovator and does not adversely affect safety or efficacy.³⁶

While the Biosimilars Act outlined the standards for when a biosimilar may be considered “interchangeable,”³⁷ it left each state independently responsible for enacting laws that regulate when and how pharmacists may *actually* substitute interchangeable biosimilars for the innovator drugs.³⁸ Because of the difficulty, if not impossibility, of creating a biosimilar that is

29. Drug Price Competition and Patent Term Restoration Act of 1981, Pub. L. No. 417, 98 Stat. 1585; Gorman et al., *supra* note 6, at 327. This paper will refer to that act as “the Hatch-Waxman Act.” See *supra* text accompanying note 16.

30. Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 513-15; Bruce S. Manheim, Jr. et al., “Follow-On Biologics”: *Ensuring Continued Innovation in the Biotechnology Industry*, 25 HEALTH AFFAIRS 394, 397 (2006).

31. FDA FAQ, *supra* note 6.

32. *Id.*

33. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: SCIENTIFIC CONSIDERATIONS IN DEMONSTRATING BIOSIMILARITY TO A REFERENCE PRODUCT 4, 6 (Feb. 2012) [hereinafter SCIENTIFIC GUIDANCE FOR INDUSTRY].

34. BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON FOLLOW-ON BIOLOGICS (Jan. 19, 2008), <http://www.bio.org/articles/bio-principles-follow-biologics>.

35. *Id.*; 42 U.S.C. § 262(k)(2)(A) (2012).

36. BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON FOLLOW-ON BIOLOGICS, *supra* note 34; 42 U.S.C. § 262(k)(2)(B) (2012).

37. 42 U.S.C. § 262(k)(4) (2012). Currently, the FDA has approved only one biosimilar product, but has not approved any interchangeable products.

38. RICHARD CAUCHI, NAT’L CONFERENCE OF STATE LEGISLATURES, STATE LAWS AND LEGISLATION RELATED TO BIOLOGIC MEDICATIONS AND SUBSTITUTION OF BIOSIMILARS (2015).

completely identical to the innovator drug,³⁹ there is a growing concern that states may inappropriately apply laws designed to govern generic *chemical* drugs to biosimilars, sacrificing patient wellbeing in the process.⁴⁰

This paper is divided into four sections. Section II will elaborate on the Biosimilars Act, its impact, and why biosimilars raise different issues than chemical drugs. Section III details the undesirable effects of leaving biosimilar substitution to the states and presents my thesis that a uniform, federal biosimilar substitution standard would promote innovation and competition while maintaining consumer safety. Finally, Section IV will dispel of concerns regarding misappropriation and unconstitutional takings of innovator drug makers' trade secrets and explain how their intellectual property remains protected.

II. THE U.S. DRUG SYSTEM AND THE BIOSIMILARS ACT

A. *The Biologic Development Pipeline and Biotech Industry*

As mentioned,⁴¹ the Public Health Service Act regulates traditional biologic drugs in the United States.⁴² After the passage of the Biosimilars Act, the Public Health Service Act's reach expanded to cover biosimilars under a regulatory framework resembling Hatch-Waxman's generic drug system.⁴³ In balancing the interests of innovation and competition,⁴⁴ as well as manufacturers and consumers,⁴⁵ the new framework seeks to expedite the time it takes for a biosimilar to reach the market by avoiding the lengthy process an innovator drug must go through.⁴⁶

A new biologic takes 97.7 months, on average, to go through the traditional drug development process, compared to only 90.3 months for a

39. *Id.*

40. *Id.*

41. See Public Health Service Act definition of biologics, *supra* note 5 and accompanying text.

42. Henry Grabowski, *Follow-on Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, NATURE REVS. DRUG DISCOVERY 1, 1 (2008).

43. Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 512.

44. Kyle Barrett, Note, *Implementing the Biologics Price Competition and Innovation Act: Why Legal Principles Justify A Broad Definition of Biosimilarity*, 85 S. CAL. L. REV. 1597, 1598 (2012).

45. Grabowski, *Follow-on Biologics*, *supra* note 42, at 1.

46. *Id.*

chemical drug.⁴⁷ This process, also known as “the pipeline,” consists of several phases.⁴⁸

Once scientists thoroughly understand a disease or condition and have conducted preclinical animal testing, they may commence clinical, or human, testing of a drug.⁴⁹

Phase I consists of testing on a small number of typically healthy volunteers to determine if the drug is safe in humans.⁵⁰ This phase of testing includes analyses of how the drug affects the body (pharmacodynamics), how the body processes the drug (pharmacokinetics),⁵¹ and how the drug affects the immune system (immunogenicity).⁵²

If successful, the drug moves on to Phase II, where it is tested on a small group of about 100 to 500 patients who currently have the disease or condition in order to assess potential side effects.⁵³

Next in Phase III, the drug is tested on a larger group of about 1,000 to 5,000 patients to attain statistically significant data regarding safety, efficacy, and potency.⁵⁴

If successful up to this point, the manufacturer will typically submit the drug for FDA approval.⁵⁵ The manufacturer may conduct ongoing Phase IV studies that measure long-term safety and effects of the drug,⁵⁶ as well as post-marketing surveillance and monitoring of the drugs to ensure patient safety.⁵⁷

Biologics have an average success rate of 30% through clinical testing.⁵⁸ Though this is comparatively higher than the rate for chemical

47. *Id.* at 3.

48. PHARM. RES. & MFRS. OF AM., DRUG DISCOVERY AND DEVELOPMENT: UNDERSTANDING THE R&D PROCESS (2007).

49. *Id.* For a discussion of the premarket and postmarket approval process, see generally Ryan Abbott & Ian Ayres, *Evidence and Extrapolation: Mechanisms for Regulating Off-Label Uses of Drugs and Devices*, 64 DUKE L.J. 377 (2014).

50. PHARM. RES. & MFRS. OF AM., DRUG DISCOVERY AND DEVELOPMENT: UNDERSTANDING THE R&D PROCESS, *supra* note 48.

51. *Id.*

52. Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 513.

53. PHARM. RES. & MFRS. OF AM., DRUG DISCOVERY AND DEVELOPMENT: UNDERSTANDING THE R&D PROCESS, *supra* note 48.

54. *Id.*

55. *Id.*

56. *Id.*

57. BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON FOLLOW-ON BIOLOGICS, *supra* note 34.

58. Grabowski, *Follow-on Biologics*, *supra* note 42, at 3.

drugs, biologics are more susceptible to failure at Phase III, which is the most expensive phase.⁵⁹ This is particularly worrisome because of the time, money, and resources already invested in the drug, only to have it fail at such a late stage.⁶⁰

Although the FDA has not specified *exactly* what tests or data it requires in approving a biosimilar, the agency has broadly indicated that applicants must provide animal-based, clinical (human-based), and comparative (between drugs) data to show “no clinically meaningful differences” between the biosimilar and reference product exist.⁶¹

On March 6, 2015, the FDA approved the first biosimilar in the U.S., Sandoz’s Zarxio, based on head-to-head comparisons of structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamic data, immunogenicity, and other clinical safety and effectiveness data.⁶² The drug, however, was not designated as interchangeable.⁶³

The FDA takes a “step-wise approach” in reviewing biosimilar applications, assessing each application one step at a time based on the totality of the evidence.⁶⁴ This analysis begins with “extensive structural and functional” comparisons between the reference and biosimilar products, which informs the agency of what other data is required to find biosimilarity.⁶⁵ Accordingly, it may waive the need for certain studies or data in particular cases as the application review progresses.⁶⁶ The FDA also has the discretion to deem a drug class ineligible from receiving a biosimilar license altogether.⁶⁷

59. *Id.*

60. *See id.*

61. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: CLINICAL PHARMACOLOGY DATA TO SUPPORT A DEMONSTRATION OF BIOSIMILARITY TO A REFERENCE PRODUCT 2 (May 2014) [hereinafter DATA GUIDANCE FOR INDUSTRY].

62. FOOD & DRUG ADMIN., NEWS RELEASE, FDA APPROVES FIRST BIOSIMILAR PRODUCT ZARXIO (Mar. 6, 2015), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm436648.htm>; Noonan, *FDA Approves Sandoz Filgrastim Biosimilar*, *supra* note 11.

63. Noonan, *FDA Approves Sandoz Filgrastim Biosimilar*, *supra* note 11.

64. Gorman et al., *supra* note 6, at 329-31.

65. FOOD & DRUG ADMIN., BRIEFING DOCUMENT FOR ONCOLOGIC DRUGS ADVISORY COMMITTEE MEETING 7 (Jan. 7, 2015).

66. Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 513.

67. Gorman et al., *supra* note 6, at 330. Based on “science and experience with a particular product class,” the FDA may determine a drug is not eligible for a biosimilar license. However, the FDA may later modify or reverse such a designation.

The FDA's conservative "risk-based approach"⁶⁸ rates an applicant's similarity to the reference drug along a continuum with designations of "not similar," "similar," "highly similar," and "highly similar with fingerprint-like similarity."⁶⁹ Despite the purportedly conservative approach,⁷⁰ innovator drug manufacturers have been strongly urging the FDA to require that biosimilar applicants conduct their *own* clinical testing, and not rely solely on comparative data that uses the innovator manufacturer's information.⁷¹ While the FDA has only provided nonbinding guidance and recommendations on these matters,⁷² the approved Zarxio application included data attained through its own testing.⁷³ Thus, the FDA may favor biosimilar applicants who have conducted independent testing and have not primarily relied on the innovator's data.⁷⁴

Given the significant amount of time and resources devoted to getting a drug through the development pipeline,⁷⁵ it is no surprise that the costs can be staggering – total out of pocket costs for preclinical and clinical phases of a new biologic have been estimated to exceed \$500 million.⁷⁶ Biopharmaceutical companies also spend an average of 30% of their revenues on research and development.⁷⁷ As mentioned previously,⁷⁸ the cost of creating a biologic is higher than that of a chemical drug due to the more volatile nature of biologics and the necessity for maintaining precise manufacturing conditions.⁷⁹ A chemical drug may be created through as little

68. DATA GUIDANCE FOR INDUSTRY, *supra* note 61, at 4.

69. *Id.* at 5. The FDA considered Zarxio "highly similar" to the innovator drug. See Jonathan D. Rockoff & Peter Loftus, *U.S. Clears First Copycat Biotech Drug, Jolting Sector*, WALL ST. J. (Mar. 6, 2015), <http://www.wsj.com/articles/fda-approves-first-biosimilar-drug-1425651840>.

70. See MARGARET HAMBURG, FOOD & DRUG ADMIN., STATEMENT FROM FDA COMMISSIONER MARGARET HAMBURG TO GPHA (Feb. 22, 2013) (transcript available at <http://www.fda.gov/NewsEvents/Speeches/ucm340870.htm>).

71. Brian J. Malkin, *Challenges to the Development of a Biosimilars Industry in the United States*, in RECENT DEVELOPMENTS IN FOOD & DRUG LAW, 83, 87 (2013).

72. See DATA GUIDANCE FOR INDUSTRY, *supra* note 61.

73. Noonan, *FDA Approves Sandoz Filgrastim Biosimilar*, *supra* note 11.

74. See *id.*

75. See *supra* text accompanying notes 47-60.

76. Grabowski, *Follow-on Biologics*, *supra* note 42, at 4.

77. Erwin A. Blackstone & Joseph P. Fuhr, Jr., *The Future of Competition in the Biologics Market*, 31 TEMP. J. SCI. TECH. & ENVTL. L. 1, 3 (2012).

78. See *supra* text accompanying notes 9-12.

79. See *supra* text accompanying notes 9-12.

as five to ten chemical reactions, while a biologic may take as many as 5,000 to 10,000, resulting in a more expensive development process.⁸⁰

This expense, however, is tempered by the high economic returns a successfully developed and marketed biologic brings.⁸¹ A new chemical drug takes an average of sixteen years to break even.⁸² In contrast, a biologic has been estimated to break even in only 12.9 years.⁸³ This is partly attributable to the greater potential (compared to a chemical drug) for discovering “multiple therapeutic interventions . . . in the biological cascade of proteins . . . [acting on] the same ultimate target,” and “new indications associated with the same or related pathways.”⁸⁴ These new uses would provide sufficient economic prospects that outweigh the costly and risky development process.⁸⁵

In 2010, the top twelve biologic products in the United States generated combined sales of roughly \$30 billion.⁸⁶ Further, the average peak sales of a biologic drug is \$712.5 million,⁸⁷ and “biotechnology drugs are the fastest growing segment of new therapeutics,” jumping from 4% in the period between 1982 and 1992 to 16% in the period between 1993 and 2003.⁸⁸ The biologic market (and biotech industry broadly) is “rapidly expanding by any number of measures, including the quantity of approved products, the size of the market, and the importance of these drugs to the health of U.S. citizens.”⁸⁹ The big prescription-benefit manager Express Scripts, Inc. estimated that the United States alone could save \$250 billion in drug costs over the next ten years if eleven biosimilars that are currently in development get approved.⁹⁰

80. Malkin, *Challenges to the Development of a Biosimilars Industry in the United States*, *supra* note 71, at 3.

81. Grabowski, *Follow-on Biologics*, *supra* note 42, at 6.

82. *Id.*

83. *Id.* at 8. Though this estimate would likely be affected by the actual entry of biosimilars into the pharmaceutical market.

84. *Id.* at 6.

85. *Id.* at 5-6. While the new uses would have to be cleared clinically, the greater potential remains significant.

86. ANDREW F. BOURGOIN, *WHAT YOU NEED TO KNOW ABOUT THE FOLLOW-ON BIOLOGIC MARKET IN THE U.S.: IMPLICATIONS, STRATEGIES, AND IMPACT 1* (2011).

87. Grabowski, *Follow-on Biologics*, *supra* note 42, at 7.

88. *Id.* at 5.

89. JOHN R. THOMAS, CONG. RESEARCH SERV. REPORT, *FOLLOW-ON BIOLOGICS: THE LAW AND INTELLECTUAL PROPERTY ISSUES 1* (2014).

90. Sabrina Tavernise & Andrew Pollack, *F.D.A. Approves Zarxio, Its First Biosimilar Drug*, N.Y. TIMES (Mar. 6, 2015), <http://www.nytimes.com/2015/03/07/health/fda-approves-zarxio-first-biosimilar-drug.html>.

A testament to the industry's predicted expansion, the CEO of Swiss drug manufacturer Novartis AG expressed his belief that biosimilars will not cause "a big impact" until at least 2017,⁹¹ despite the fact that in 2014 the company's biosimilar production unit, Sandoz, enjoyed around \$514 million in sales, up 23% from 2013.⁹²

This tantalizing expected growth in the biosimilar realm has led to increased competition, even disagreement, between innovator and biosimilar manufacturers,⁹³ which Congress attempted to mitigate through the following Biosimilars Act provisions.

B. *Exclusivity Period Provisions*

Anticipating friction between both sides of the biosimilars debate, Congress sought to incentivize innovator drug manufacturers with four years of data exclusivity followed by eight years of market exclusivity against biosimilar applicants.⁹⁴

During the innovator's four-year *data exclusivity* period, the FDA does not accept any biosimilar applications alleging similarity or interchangeability to that innovator drug.⁹⁵ The FDA also prevents biosimilar manufacturers from utilizing data the innovator provided in securing approval for its original biologic application.⁹⁶

In the ensuing eight-year *market exclusivity* period, the FDA may review and approve biosimilar applications, but will not let them go to market until twelve years after the innovator drug's approval.⁹⁷ These exclusivity periods apply only *against biosimilar applicants*, and will not be renewed if a "new

91. 2017 is when many lucrative biologics lose their patents, thus opening the door for biosimilar competition. Nine of the top-selling biologics may even lose patent protection by 2016. Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 546.

92. Caroline Copley, *No Biotech Copycat Drug Lift Off Before 2017: Novartis CEO*, REUTERS.COM (Aug. 25, 2014), <http://www.reuters.com/assets/print?aid=USKBN0GP1KK20140825>; Rockoff & Loftus, *supra* note 69.

93. Grabowski, *Follow-on Biologics*, *supra* note 42, at 4.

94. 42 U.S.C. § 262(k)(7)(A) (2012).

95. 42 U.S.C. § 262(k)(7)(B) (2012). Data exclusivity is also referred to as Hatch-Waxman exclusivity. Ryan Abbott, *Treating the Health Care Crisis: Complementary and Alternative Medicine for PPACA*, 14 DEPAUL J. HEALTH CARE L. 35, 67 (2012) ("Data-based exclusivity prevents generic drug manufacturers from making use of data submitted in an initial application by an originator pharmaceutical manufacturer for a fixed period of time.").

96. 42 U.S.C. § 262(k)(7)(B).

97. 42 U.S.C. § 262(k)(7)(A).

indication, route, dosing schedule, form, delivery system, device, strength, or change in structure” is discovered even without a change in safety, purity, or potency.⁹⁸ This prevents “evergreening,” where the exclusivity period would be renewed if one of the above novel uses were discovered.⁹⁹

An approved non-interchangeable biosimilar does not receive data or market exclusivity, but the *first interchangeable biosimilar* of a reference product receives between twelve and forty-two months of market exclusivity,¹⁰⁰ resembling the Hatch-Waxman exclusivities.¹⁰¹

Arguably, these exclusivity periods provide stronger and more predictable protection than formulation or process patents,¹⁰² which may be “narrow, uncertain, or near expiry.”¹⁰³ While a biosimilar manufacturer may theoretically be able to design around an innovator’s specific or narrow patents, the exclusivity periods “act as an insurance policy” that guarantees protection for the innovator until the term’s end date.¹⁰⁴

C. *Patent Litigation Provisions*

Considering the “production process [of a biologic] is 90 percent of the intellectual property related to the product,”¹⁰⁵ it is no surprise that innovator manufacturers have sought strong patent protection for their drugs,¹⁰⁶ development processes, and devices.¹⁰⁷ Though Federal patent protection exists independently of the Biosimilars Act, Congress anticipated the inevitable patent disputes between innovator and biosimilar producers.¹⁰⁸ The Biosimilars Act states that a biosimilar applicant who submits an

98. Gorman et al., *supra* note 6, at 337-38.

99. *Id.*

100. 42 U.S.C. § 262(k)(6) (2012); Gorman et al., *supra* note 6, at 338.

101. Under the Hatch-Waxman Act, the FDA will not approve a chemical drug manufacturer’s abbreviated new drug application (ANDA) for five years after the innovator’s new drug has been approved. 21 U.S.C. § 355(c)(3)(e)(ii) (2012). This exclusivity period only lasts three years for innovator drug *supplements* that have successfully undergone new clinical testing. 21 U.S.C. § 355(c)(3)(e)(iii) (2012).

102. Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 551.

103. *Id.*

104. *Id.*

105. WENDY H. SCHACHT & JOHN R. THOMAS, CONG. RESEARCH SERV. REPORT FOR CONG., FOLLOW-ON BIOLOGICS: INTELLECTUAL PROPERTY AND INNOVATION ISSUES I, 8 (2009).

106. Manheim Jr. et al., *supra* note 30, at 398.

107. Blackstone & Fuhr, Jr., *supra* note 77, at 21.

108. Gorman et al., *supra* note 6, at 345.

application to the FDA “shall provide to the reference product sponsor a copy of the [biosimilar] application . . . and such other information that describes the process or processes used to manufacture [it].”¹⁰⁹ Such a disclosure, if the biosimilar applicant decides to make it, is to occur within twenty days.¹¹⁰

Innovator and biosimilar producers have been at odds over how to interpret this statutory language, with innovators arguing it is mandatory and biosimilar producers contending it is optional.¹¹¹

On this issue, the Federal Circuit recently held that a biosimilar applicant is *not required* to disclose its application information to the innovator manufacturer¹¹² because the statute explicitly allows the innovator to seek patent infringement remedies under 42 U.S.C. § 262(1)(9)(C)¹¹³ and 35 U.S.C. § 271(e).¹¹⁴ Moreover, the Federal Circuit stated that an innovator who brings infringement actions under these sections “can access the required information through discovery”¹¹⁵ once litigation commences.

While ostensibly no longer required to disclose,¹¹⁶ if the biosimilar applicant nonetheless decides to, the innovator then has a sixty-day period to

109. 42 U.S.C § 262(1)(2)(A) (2012) (emphasis added).

110. 42 U.S.C § 262(1)(2) (2012); see *infra* note 266 and accompanying text.

111. Andrew Williams, Amgen v. Sandoz – *Federal Circuit Oral Argument*, PATENT DOCS (June 7, 2015, 11:59 PM), <http://www.patentdocs.org/2015/06/amgen-v-sandoz-federal-circuit-oral-argument.html>.

112. Amgen, Inc. v. Sandoz, Inc., 794 F.3d 1347, 1354-57 (Fed. Cir. 2015) (holding that 42 U.S.C. § 262(1)(9)(c) and 35 U.S.C. § 271(e) expressly provide patent infringement remedies when a biosimilar applicant does not disclose to the innovator); see Kevin E. Noonan, *Federal Circuit Decides Amgen v. Sandoz (In An Opinion That Will Make Neither Party Happy)*, PATENT DOCS (July 21, 2015, 2:51 PM), <http://www.patentdocs.org/2015/07/federal-circuit-decides-amgen-v-sandoz-in-an-opinion-that-will-make-neither-party-happy.html>. The Federal Circuit did, however, enjoin Sandoz from marketing its biosimilar Zarxio. See *infra* text accompanying notes 268-74.

113. This section states that, “[i]f a [biosimilar] applicant fails to provide the application and information required under paragraph (2)(A), the reference product sponsor, but not the [biosimilar] applicant, may bring an action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product.”

114. The Court found that failure of a biosimilar applicant to provide its application and information to the reference product producer is “an artificial act of infringement” that falls within 35 U.S.C. § 271(e)(2)(C)(ii) and allows the innovator to seek declaratory judgments on the patents at issue. *Sandoz*, 794 F. 3d at 1356.

115. *Id.*

116. As of the writing of this article, both Sandoz and Amgen have filed petitions for *en banc* rehearings concerning the Federal Circuit’s July 21, 2015 rulings in *Amgen v. Sandoz*. Andrew Williams, Amgen v. Sandoz *Update – En Banc Rehearing Petitions Filed*, PATENT DOCS (Sept. 10, 2015, 10:20 PM), <http://www.patentdocs.org/2015/09/amgen-v-sandoz-update-en-banc-rehearing-petitions-filed.html>.

compile a list of patents it could assert against the biosimilar or offer up for license.¹¹⁷ Upon receiving this list from the innovator, the biosimilar applicant then has sixty days to make a list of patents *it* believes the innovator may assert.¹¹⁸ The applicant also must provide claims, supported by facts and law, alleging how each of the innovator's patents is invalid, unenforceable, or would not be infringed by the applicant.¹¹⁹ Alternatively, the applicant may claim that it does not plan to market the biosimilar until after the innovator's patent has expired,¹²⁰ or it may seek to acquire a license.¹²¹

The innovator accordingly has sixty days to respond to any of the applicant's invalidity, unenforceability, or non-infringement claims.¹²²

Once both sides have received a list from each other, the parties have fifteen days to come to an agreement on the patents they will litigate.¹²³ If they agree, the innovator has thirty days to bring the infringement claim.¹²⁴ If no agreement is reached, the biosimilar applicant provides a final number of patents that will be the subject of the innovator's infringement action.¹²⁵ The innovator has thirty days to take action for the listed patents¹²⁶ and provide notice to the FDA.¹²⁷

To facilitate the patent litigation process, the FDA recently published "the Purple Book," which lists all approved biologic products and interchangeable biosimilars.¹²⁸ The list includes each product's date of licensure, reference product exclusivity date, whether there is a biosimilar or interchangeable drug based on it, and whether the product has been withdrawn.¹²⁹ While this format mirrors "the Orange Book," which serves

117. 42 U.S.C. § 262(l)(3)(A)(ii) (2012).

118. 42 U.S.C. § 262(l)(3)(B)(i) (2012).

119. 42 U.S.C. § 262(l)(3)(B)(ii)(I) (2012).

120. 42 U.S.C. § 262(l)(3)(B)(ii)(II) (2012).

121. 42 U.S.C. § 262(l)(3)(B)(i).

122. 42 U.S.C. § 262(l)(3)(C) (2012).

123. 42 U.S.C. § 262(l)(4)(B) (2012).

124. 42 U.S.C. § 262(l)(6)(A) (2012).

125. 42 U.S.C. § 262(l)(5)(A) (2012).

126. 42 U.S.C. § 262(l)(6)(B) (2012). There are special provisions for preliminary injunctions and limited declaratory judgment allowances, but a full discussion is unnecessary here.

127. 42 U.S.C. § 262(l)(6)(C)(i) (2012).

128. CTR. FOR BIOLOGIC EVALUATION & RESEARCH, LIST OF BIOLOGICAL PRODUCTS WITH REFERENCE PRODUCT EXCLUSIVITY AND BIOSIMILARITY OR INTERCHANGEABILITY EVALUATIONS (1st ed. 2014) [hereinafter LIST OF BIOLOGICAL PRODUCTS].

129. *Id.*

the same purpose for chemical drugs,¹³⁰ the Purple Book notably distinguishes between biosimilarity and interchangeability.¹³¹ However, both the Purple and Orange Books aim to clearly list therapeutic equivalence and patent exclusivities.¹³²

The detailed, if complex, patent litigation procedures help protect an innovator's product,¹³³ but also promote free competition, ultimately benefitting both consumers through reduced drug prices and manufacturers through increased sales.¹³⁴

While patent disputes are sure to arise,¹³⁵ trade secret issues, addressed later, may be more significant¹³⁶ as the Biosimilars Act does not explicitly deal with them like it does with patents.¹³⁷

D. Issues With Interchangeability

As even the FDA has admitted,¹³⁸ a biosimilar's complexity may prevent it from being identical to its reference product in the way a generic chemical drug is considered identical to its reference product.¹³⁹ This greater variability is undoubtedly why the FDA has differentiated between "biosimilarity" and "interchangeability,"¹⁴⁰ and established such high standards for biosimilar approval.¹⁴¹ Congress may have noted that, although several biosimilars have

130. U.S. DEP'T OF HEALTH & HUMAN SERVS., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (34th ed. 2014) (the compilation's preface even acknowledges that it is commonly referred to as "the Orange Book").

131. LIST OF BIOLOGICAL PRODUCTS, *supra* note 128.

132. Alexander Gaffney, *In Major Move on Biosimilar Interchangeability, FDA Establishes New 'Purple Book,'* REGULATORY AFFAIRS PROF'L SOC'Y (Sep. 9, 2014), <http://www.raps.org/Regulatory-Focus/News/2014/09/09/20246/In-Major-Move-on-Biosimilar-Interchangeability-FDA-Establishes-New-Purple-Book/>.

133. Gorman et al., *supra* note 6, at 346.

134. EXPANDING THE USE OF GENERIC DRUGS, *supra* note 22.

135. Manheim Jr. et al., *supra* note 30, at 398.

136. Richard A. Epstein, *The Constitutional Protection of Trade Secrets and Patents under the Biologics Price Competition and Innovation Act of 2009*, 66 FOOD & DRUG L.J. 285, 287 (2011); *see infra* text accompanying notes 233-48.

137. *See* 42 U.S.C. § 262(l) (2012).

138. SCIENTIFIC GUIDANCE FOR INDUSTRY, *supra* note 33, at 4.

139. *Id.*

140. *See supra* text accompanying notes 34-36.

141. *See* MARGARET HAMBURG, FOOD & DRUG ADMIN., *supra* note 70.

been approved in the European Union, the lack of interchangeability provisions abroad has hampered biosimilar market share growth there.¹⁴²

Aware of the significant research and development costs that may deter manufacturers from pursuing a biologic or biosimilar,¹⁴³ the FDA has incentivized manufacturers by awarding the first interchangeable biosimilar an exclusivity period¹⁴⁴ and providing a patent dispute system.¹⁴⁵ These incentives are likely substantial enough for biopharmaceutical firms to invest in developing interchangeable biosimilars.¹⁴⁶

However, the Biosimilars Act's distinction between biosimilar and interchangeable drugs creates ambiguity not present in the chemical drug scheme.¹⁴⁷ Chemical drugs that meet the FDA's generic drug application requirements are typically considered "interchangeable."¹⁴⁸ Thus, a pharmacist may freely substitute a generic for a brand name, subject to any specific state laws.¹⁴⁹

In contrast, a pharmacist may only substitute an innovator drug with a biosimilar if it has been deemed interchangeable.¹⁵⁰ And even if a drug meets the difficult standard of interchangeability, the Biosimilars Act left each state to enact its own laws for when and how a pharmacist may actually substitute.¹⁵¹ This may lead to inconsistent interchangeability procedures,¹⁵²

142. Blackstone & Fuhr, Jr., *supra* note 77, at 12; see Barbara Mounho et al., *Global Regulatory Standards for the Approval of Biosimilars*, 65 FOOD & DRUG L.J. 819, 832-34 (2010). The reluctance of the E.U. and other countries to include a potential interchangeability designation arises from a fundamentally erroneous assumption that the same provisions and laws governing chemical drugs can successfully govern biologic drugs. The biosimilar landscape must be approached in light of the reality that biosimilars fall short of true bioequivalence. Accordingly, concepts such as automatic substitution applicable to chemical drugs should be amended, if not eliminated, in the biosimilar context in favor of policies accounting for biologic and biosimilar drugs' inherent natures.

143. Blackstone & Fuhr, Jr., *supra* note 77, at 5-7.

144. 42 U.S.C. § 262(k)(6) (2012); Malkin, *supra* note 71, at 5.

145. 42 U.S.C. § 262(l) (2012); see *supra* text accompanying notes 109-134.

146. Blackstone & Fuhr, Jr., *supra* note 77, at 29; see MARGARET HAMBURG, FOOD & DRUG ADMIN., *supra* note 70.

147. Christine Ju, *Assessing Biosimilarity and Interchangeability of Biosimilar Products Under the Biologics Price Competition and Innovation Act*, GENERICS & BIOSIMILARS INITIATIVE J. 7 (2013).

148. Blackstone & Fuhr, Jr., *supra* note 77, at 7; Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 524.

149. Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 524.

150. See 42 U.S.C. § 262(k)(3)(A) (2012).

151. CAUCHI, *supra* note 38.

152. See ALISON MASSON & ROBERT L. STEINER, STAFF REPORT OF THE BUREAU OF ECON. OF THE FED. TRADE COMM'N, GENERIC SUBSTITUTION AND PRESCRIPTION DRUG PRICES:

medication access,¹⁵³ healthcare costs,¹⁵⁴ and regulation across the states.¹⁵⁵ In more human terms, unaffordable prices may prevent Mr. DeLuca from receiving his essential red blood cell-boosting medication, even though a similar patient would not face such a barrier across state lines.¹⁵⁶

III. PROPOSAL FOR FEDERAL INTERCHANGEABILITY STANDARD

A. *Problems With State Law Regulation*

Regarding *generic chemical drugs*, state law determines whether or not substitution is mandatory, whether patient consent is required before substitution, and whether the prescriber must indicate if substitution is or is not acceptable.¹⁵⁷

Though states have already implemented *generic* substitution laws,¹⁵⁸ the innate discrepancy between *biosimilarity* (between biosimilar and biologic) and *bioequivalency* (between generic and brand name chemical drug) renders this legal framework undesirable for biosimilars and calls for more stringent and consistent regulation.¹⁵⁹

Inconsistent substitution practices between states, coupled with the necessarily high standards for biosimilarity and interchangeability, would likely affect consumers' access to biosimilars across state lines.¹⁶⁰

For example, Indiana recently approved a biosimilar interchangeability bill allowing a pharmacist to substitute if 1) the FDA has deemed the biosimilar to be interchangeable; 2) the prescriber includes a "may substitute" instruction in the prescription; 3) the pharmacist informs the customer of the

ECONOMIC EFFECTS OF STATE DRUG PRODUCT SELECTION LAWS 73-110 (1985) [hereinafter MASSON & STEINER] (finding that differing state chemical drug substitution laws affected rates of consumption and drug prices).

153. Jason Kanter & Robin Feldman, *Understanding and Incentivizing Biosimilars*, 64 HASTINGS L.J. 57, 60 (2012).

154. MASSON & STEINER, *supra* note 152; EXPANDING THE USE OF GENERIC DRUGS, *supra* note 22, at 7.

155. Kanter & Feldman, *supra* note 153, at 74; CAUCHI, *supra* note 38.

156. See *What's Keeping Less Expensive Biologic Drugs From the U.S. Market?*, *supra* note 1.

157. EXPANDING THE USE OF GENERIC DRUGS, *supra* note 22, at 7.

158. *Id.*

159. See Gorman et al., *supra* note 6, at 328; see CAUCHI, *supra* note 38; see Kanter & Feldman, *supra* note 153, at 74.

160. See Kanter & Feldman, *supra* note 153, at 74.

substitution; 4) the pharmacist notifies the prescriber within five days of substitution; 5) a record is kept of the substitution for at least five years.¹⁶¹

The Biotechnology Industry Organization (BIO) commended Indiana's Governor and Legislature, stating that the "bill is a model for [biosimilar] legislation."¹⁶² The bill comports with BIO's biosimilar substitution principles as it "puts patients first" by ensuring transparency and communication, but also "maintains incentives for innovation and promotes [a] competitive market for biologic[s]."¹⁶³

On the other hand, California Governor Jerry Brown vetoed a similar bill that would have allowed pharmacist substitution as long as the prescriber did not write "do not substitute" on the prescription, the patient received notice, and the pharmacy notified the prescriber within five days.¹⁶⁴

These examples are important for two reasons. First, the fact that one was approved while the other was vetoed portends the inevitability of states enacting substitution laws at different speeds.¹⁶⁵ Currently, sixteen states have successfully implemented biosimilar substitution laws, with ten states having passed such laws in 2015.¹⁶⁶ The remaining thirty-four states have either failed to file biosimilar substitution bills, or such bills have failed in the Legislature or by governor veto.¹⁶⁷ Any statutory void in one state would inequitably limit consumer access to important and potentially life-saving biosimilar drugs, even if that drug would be available to the patient in another state.¹⁶⁸

161. S.B. 262, 118th Gen. Assemb., 2d Reg. Sess. (Ind. 2014); Donald Zuhn, *Indiana Governor Signs Biosimilar Substitution Bill*, PATENT DOCS (Apr. 10, 2014, 11:59 PM), <http://www.patentdocs.org/2014/04/indiana-governor-signs-biosimilar-substitution-bill.html>.

162. GEORGE GOODNO, BIOTECHNOLOGY INDUSTRY ORGANIZATION, GOVERNOR PENCE SIGNS BILL GRANTING PATIENT ACCESS TO INTERCHANGEABLE BIOLOGIC MEDICATIONS (Mar. 26, 2014), <https://www.bio.org/media/press-release/governor-pence-signs-bill-granting-patient-access-interchangeable-biologic-medic>.

163. *Id.*; see BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON FOLLOW-ON BIOLOGICS, *supra* note 34; BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON PATIENT SAFETY IN THE SUBSTITUTION OF BIOLOGIC PRODUCTS (Jan. 24, 2013), <https://www.bio.org/advocacy/letters/bio-principles-patient-safety-substitution-biologic-products>.

164. S.B. 598, 2013-14 Leg., Reg. Sess. (Cal. 2013); Donald Zuhn, *Governor Brown Vetoes California Biosimilar Bill*, PATENT DOCS (Oct. 16, 2013, 11:59 PM), <http://www.patentdocs.org/2013/10/governor-brown-vetoes-california-biosimilar-bill.html>.

165. See Zuhn, *Indiana Governor Signs Biosimilar Substitution Bill*, *supra* note 161; see Zuhn, *Governor Brown Vetoes California Biosimilar Bill*, *supra* note 164.

166. CAUCHI, *supra* note 38.

167. See *id.*

168. See Zuhn, *Indiana Governor Signs Biosimilar Substitution Bill*, *supra* note 161; see Zuhn, *Governor Brown Vetoes California Biosimilar Bill*, *supra* note 164.

The other important takeaway is the differing language used in each bill.¹⁶⁹ While this variance may seem inconsequential at first, even minor differences in phrasing such as the affirmative “may substitute” or negative “do not substitute” can affect prescribing tendencies.¹⁷⁰ Formats that make it easier for a doctor to prohibit substitution (i.e. requiring “do not substitute”) lead to fewer substitutions,¹⁷¹ affecting what drugs consumers receive and the prices paid for them.¹⁷²

Pharmacists and prescribers in states less allowing of substitution would likely give consumers the more expensive innovator drug, driving up healthcare costs¹⁷³ and leading to inequitable drug accessibility.¹⁷⁴

A uniform federal standard governing when and how pharmacists may substitute an interchangeable biosimilar would avoid the undesirable discrepancies noted above¹⁷⁵ by creating consistent substitution patterns between states.¹⁷⁶ Moreover, elucidating the protocols affecting substitution practices and frequency¹⁷⁷ would incentivize pharmaceutical companies¹⁷⁸ to channel resources towards developing interchangeable biosimilars. This also ensures consumers receive only the safest products that meet the FDA’s strict interchangeability criteria.¹⁷⁹

169. See *supra* text accompanying notes 161 and 164. Indiana’s bill allows doctors to write “may substitute” for substitution to be permissible, whereas California’s bill would have required stating “do not substitute” to prevent it from occurring.

170. See MASSON & STEINER, *supra* note 152, at 89.

171. See *id.*

172. EXPANDING THE USE OF GENERIC DRUGS, *supra* note 22, at 7. The study found that state generic substitution laws can “have a significant effect on drug spending.” The same rationale applies to biosimilar substitution, although specific savings numbers would vary by industry.

173. EXPANDING THE USE OF GENERIC DRUGS, *supra* note 22, at 7-8.

174. See *supra* text accompanying notes 157-64.

175. See *supra* text accompanying notes 147-56, 157-64.

176. See CAUCHI, *supra* note 38.

177. See Kanter & Feldman, *supra* note 153, at 74; see Sara Margolis, Note, *Destined For Failure? An Analysis of the Biological Price Competition and Innovation Act of 2009*, 2013 COLUM. BUS. L. REV. 209, 227 (2013); see *supra* text accompanying notes 75-92. A clearer picture of when biosimilars will be substituted will provide greater incentives for producers to undertake the research and development expenditures.

178. Adriana Lee Benedict, *State-Level Substitution on Follow-On Biologic Substitution*, 1 HARV. J.L. & BIOSCIENCES 190, 200 (2014).

179. See BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON FOLLOW-ON BIOLOGICS, *supra* note 34; see MARGARET HAMBURG, FOOD & DRUG ADMIN., *supra* note 70. The interchangeable designation is more stringent than one of mere biosimilarity.

The following proposed federal standard would harmonize substitution policies between states, thereby equalizing patient access to safe, affordable drugs¹⁸⁰ while also promoting innovation and competition in the industry.¹⁸¹

B. Proposed Federal Standard

1. Federalization

Although state law governs substitution practices for generic chemical drugs,¹⁸² the differences inherent in biologic drugs mandate novel treatment under the law.¹⁸³ The FDA would not be the first agency adapting to changing times and technology, as the United States Copyright Office has proposed the full federalization of pre-1972 sound recordings, an area historically reserved to the states.¹⁸⁴

The Copyright Office recognized that traditional laws covering pre-1972 sound recordings are maladapted to the modern landscape of digital music and technology.¹⁸⁵ It thus recommended bringing these works under uniform federal law, thereby eliminating the disparate, inconsistent, and outdated state laws.¹⁸⁶

Similarly, the FDA must recognize that the substitution of biologic and biosimilar drugs may be better overseen by a uniform federal standard.¹⁸⁷ The *chemical drug system's* success with state-governed substitution should not be a roadblock to the *biologic drug system's* development of unique standards, procedures, and policies.¹⁸⁸

To borrow language from current Register of Copyrights Maria A. Pallante, ignoring the modern realities of biologic drugs would force the biotech industry to “do[] business in legal quicksand.”¹⁸⁹

180. *See supra* text accompanying notes 157-60.

181. *See* BIOTECHNOLOGY INDUSTRY ORG., *supra* note 34.

182. CAUCHI, *supra* note 38; *see supra* text accompanying notes 157-58.

183. *See supra* text accompanying notes 9-12, 39-40, 78-80.

184. MARIA A. PALLANTE, U.S. COPYRIGHT OFFICE, COPYRIGHT AND THE MUSIC MARKETPLACE 85 (2015).

185. *Id.*

186. *Id.*

187. *See supra* text accompanying notes 175-81.

188. *See* Gorman et al., *supra* note 6, at 327.

189. MARIA A. PALLANTE, U.S. COPYRIGHT OFFICE, COPYRIGHT AND THE MUSIC MARKETPLACE, *supra* note 184, at preface.

2. “May Substitute” Requirement

The uniform federal standard should *presume that a biologic prescription does not allow substitution* unless the prescriber actively writes that a biosimilar may be substituted. This is similar to Indiana’s recently passed “may substitute” bill.¹⁹⁰ This preemptive opt-in protocol would ensure that the doctor already cleared the patient for biosimilar substitution based on his or her familiarity with the patient’s body and drug reactions.¹⁹¹

Unlike state generic drug laws, which frequently allow substitution unless the prescriber included preventative language in the prescription such as “dispense as written” or “medically necessary,”¹⁹² the uniform biosimilar substitution law should presume non-substitution unless the prescriber actually wrote out the affirmative “may substitute.” This change accounts for the greater potential variance inherent in biologic drugs¹⁹³ by ensuring that the prescriber consciously approved biosimilar use by that specific patient.¹⁹⁴

Concern of inhibiting biosimilar substitution is mitigated by the fact that generic market share actually increases when prescribers are required to write out substitution instructions on prescriptions (as opposed to merely checking a box).¹⁹⁵ Further, the presumption against substitution acts as a filter against unsafe substitutions; prescribers will only allow substitutions for those whom they believe will not experience an adverse effect from a biosimilar.¹⁹⁶

Given that physician perceptions about generic drugs also affect prescribing tendencies,¹⁹⁷ the proposed system’s affirmative language

190. *See supra* text accompanying notes 161-63.

191. *See* EXPANDING THE USE OF GENERIC DRUGS, *supra* note 21, at 11-12; *see* BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON PATIENT SAFETY IN THE SUBSTITUTION OF BIOLOGIC PRODUCTS, *supra* note 163.

192. *See* James J. Wheaton, *Generic Competition and Pharmaceutical Innovation: The Drug Price Competition and Patent Term Restoration Act of 1984*, 35 CATH. U. L. REV. 433, 445 (1986).

193. *See supra* text accompanying notes 9-12, 78-80.

194. *See supra* text accompanying notes 190-92; *see* BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON PATIENT SAFETY IN THE SUBSTITUTION OF BIOLOGIC PRODUCTS, *supra* note 163.

195. *See* Wheaton, *supra* note 192.

196. *See id.*; BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON PATIENT SAFETY IN THE SUBSTITUTION OF BIOLOGIC PRODUCTS, *supra* note 163.

197. William H. Shrank et al., *Physician Perceptions About Generic Drugs*, 45 ANNALS OF PHARMACOTHERAPY 31, 35-36 (2011).

reinforces the positive view that biosimilars are safe and effective when dispensed properly.¹⁹⁸

Requiring the preventative language (i.e. “dispense as written” or “do not substitute”) frequently used with chemical drugs¹⁹⁹ may not only give the impression that biosimilars are not to be trusted, but would also likely make it easier for physicians to prohibit biosimilar substitution.²⁰⁰ Such ease of prohibiting substitution is associated with significantly reduced generic drug use.²⁰¹ On the other hand, the affirmative “may substitute” promotes biosimilar use,²⁰² but prevents over-substitution through the reversed presumption and opt-in protocol.²⁰³

Moreover, this provision does not conflict with the Biosimilars Act’s language that an interchangeable biosimilar may be substituted “without the intervention of the healthcare provider.”²⁰⁴ The prescribing doctor preemptively opts in, authorizing the pharmacist to substitute the prescription without any further permission or “intervention” needed from the prescriber.²⁰⁵ Once a prescriber signs off on substitution when writing the prescription, the pharmacist need only provide *notice* to the prescriber and patient if a substitution *actually occurs*, not permission when actually performing the substitution.²⁰⁶

3. Notice, Not Consent, Is Mandatory

Notice to both patients and physicians should be mandatory, but not patient consent, because it significantly reduces substitution rates when

198. See BIOTECHNOLOGY INDUSTRY ORG., *BIO PRINCIPLES ON PATIENT SAFETY IN THE SUBSTITUTION OF BIOLOGIC PRODUCTS*, *supra* note 163.

199. See Wheaton, *supra* note 192.

200. See *id.*; see MASSON & STEINER, *supra* note 152, at 89.

201. MASSON & STEINER, *supra* note 152, at 89.

202. See BIOTECHNOLOGY INDUSTRY ORG., *BIO PRINCIPLES ON PATIENT SAFETY IN THE SUBSTITUTION OF BIOLOGIC PRODUCTS*, *supra* note 163. One of the organization’s top substitution principles is allowing the prescribing physician to permit or prevent substitution.

203. See *supra* text accompanying notes 190-200.

204. 42 U.S.C. § 262(i)(3) (2012).

205. See Carly Helfand, *To Substitute or Not to Substitute? Biotechs and Biosim Makers Compromise on Legislation*, FIERCE PHARMA (Dec. 11, 2014), http://www.fiercepharma.com/story/substitute-or-not-substitute-biotechs-and-biosim-makers-compromise-legislat/2014-12-11?utm_medium=nl&utm_source=internal.

206. See *supra* text accompanying notes 204-05.

required.²⁰⁷ This in turn drives up costs for both consumers and healthcare systems.²⁰⁸ States that require patient consent for generic drug substitution have experienced substitution rates 25% lower than those without such requirements.²⁰⁹ Further, eliminating consent requirements could save more than \$100 million in Medicaid coverage expenses.²¹⁰ Laws requiring consent may increase undue patient anxiety towards biosimilars (and generics) and deter their use.²¹¹ This ultimately forces individuals, employers, and taxpayers to shoulder higher healthcare costs.²¹²

The lack of mandatory patient consent does not preclude the normal dialogue between prescribing physician and patient, as well as patient and pharmacist, in which the patient may still choose the innovator drug over the biosimilar.²¹³ This proposed protocol would still require that the patient and prescriber receive notice of a substitution,²¹⁴ and that all parties involved make a well-informed decision with patient health as the priority. In fact, eighteen pharmaceutical companies, including Hospira, Actavis, Amgen, Genentech, and Sandoz, all support such a notice requirement.²¹⁵

In 2010, the Congressional Budget Office estimated that a well-implemented biosimilar system could save the federal government between \$9 billion and \$12 billion over ten years.²¹⁶ More recently, Express Scripts estimated that the first two biosimilars expected to enter the U.S. market would save *patients and insurers* around \$22.7 billion in healthcare costs over the first ten years.²¹⁷ Thus, requiring consent would undercut the system's efficiency and savings.²¹⁸

207. EXPANDING THE USE OF GENERIC DRUGS, *supra* note 22, at 7-8; see LEIGH PURVIS, AM. ASS'N OF RETIRED PERS. PUB. POLICY INST., A SENSE OF DÉJÀ VU: THE DEBATE SURROUNDING STATE BIOSIMILAR SUBSTITUTION LAWS 2 (2014).

208. See William H. Shrank et al., *State Generic Substitution Laws Can Lower Drug Outlays Under Medicaid*, 29 HEALTH AFFAIRS 1383-90 (2010); see PURVIS, *supra* note 207.

209. Shrank et al., *State Generic Substitution Laws Can Lower Drug Outlays Under Medicaid*, *supra* note 208.

210. *Id.*

211. See PURVIS, A SENSE OF DÉJÀ VU: THE DEBATE SURROUNDING STATE BIOSIMILAR SUBSTITUTION LAWS, *supra* note 207.

212. *Id.*

213. See *infra* text accompanying notes 214-15.

214. See *supra* text accompanying note 207.

215. Jordan Paradise, *The Legal and Regulatory Status of Biosimilars: How Product Naming and State Substitution Laws May Impact the U.S. Healthcare System*, 41 AM. J.L. & MED. (2015).

216. EXPANDING THE USE OF GENERIC DRUGS, *supra* note 22, at 10.

217. Rockoff & Loftus, *supra* note 69.

218. EXPANDING THE USE OF GENERIC DRUGS, *supra* note 22, at 7-8.

This proposed system comports with BIO's principles on biosimilarity²¹⁹ and would add clarity in an area currently mired in uncertainty and inconsistency.²²⁰ It incentivizes pharmaceutical companies to develop safe interchangeable drugs that would enjoy an increasingly large biosimilar market share²²¹ and provide a strong return on their investment.²²² Due to the desirability of the interchangeable label,²²³ these companies would be more willing to take on the substantial research and development costs knowing when and how their products will be substituted and used by prescribers, pharmacists, and patients.²²⁴ This is especially true given the pending expiration of numerous biologic drug patents²²⁵ and coincident expansion of the biotechnology industry.²²⁶

Between the incentives for pharmaceutical companies to develop interchangeable biosimilars²²⁷ and the proposal's facilitation of substitution,²²⁸ more biosimilars would enter the pharmaceutical market. Patients like Mr. DeLuca would enjoy increased access to affordable FDA-approved biologics, while drug manufacturers enter a competitive market without worrying about losing intellectual property protection.²²⁹

219. Donald Zuhn, *California Biosimilar Bill Aligns with BIO Principles on Biologic Substitution*, PATENT DOCS (Oct. 3, 2013, 11:49 PM), <http://www.patentdocs.org/2013/10/california-biosimilar-bill-aligns-with-bio-principles-on-biologic-substitution.html>.

220. See Dr. James V. DeGuilio, *FDA Guidance Uncertainty May Deter Use of Abbreviated Biosimilar Approval Pathway*, 6 LIFE SCI. L. & INDUS. REP. 467 (2012); Kanter & Feldman, *supra* note 153, at 74; Margolis, *supra* note 177, at 227.

221. Margolis, *supra* note 177, at 227-28; see Benedict, *supra* note 178, at 199.

222. Grabowski, *Follow-on Biologics*, *supra* note 42, at 7-8 (noting, however, that estimates vary on market penetration rates and when the return may be fully realized).

223. See DeGuilio, *supra* note 220, at 470; see Kanter & Feldman, *supra* note 153, at 73.

224. Kanter & Feldman, *supra* note 153, at 73-74; Benedict, *supra* note 178.

225. Henry G. Grabowski et al., *Entry and Competition in Generic Biologics*, 28 MANAGERIAL & DECISION ECON. 439 (2007); Grabowski et al., *Implementation of the Biosimilar Pathway*, *supra* note 9, at 546.

226. See *supra* text accompanying notes 86-92.

227. See *supra* text accompanying notes 81-104.

228. See *supra* text accompanying notes 190-98.

229. Gorman et al., *supra* note 6, at 324-25. Some scholars have estimated fewer biosimilar competitors with more difficult market penetration compared to the chemical drug market, but these differences are not prohibitive of a successful biosimilar market developing in the United States. While biosimilar development costs are certainly higher, the economic payoffs and room for growth in the field likely will incentivize manufacturers to invest.

IV. PROTECTION OF INNOVATORS' INTELLECTUAL PROPERTY

A few critics have raised concerns that the Biosimilars Act harms the intellectual property interests of innovator drug manufacturers whose products serve as the basis for biosimilar applications.²³⁰ These critics have framed the FDA's use of the innovator's data in approving a biosimilar as either trade secret misappropriation²³¹ or an unconstitutional taking under the 5th Amendment.²³²

A. *Trade Secrets*

The FDA defines a trade secret as:

[A]ny commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort. There must be a direct relationship between the trade secret and the productive process.²³³

The proprietary information that innovator drug manufacturers submit to the FDA in their drug applications, such as manufacturing processes, analytical, preclinical, and clinical data, falls within this definition's purview.²³⁴

Some have alleged that the Biosimilars Act misappropriates innovator drug companies' trade secrets by using their manufacturing process information and data when approving a biosimilar application.²³⁵ However there are numerous federal safeguards that protect these trade secrets even when the FDA utilizes them in this way.²³⁶

For example, the FDA's purely internal use of the information to compare and approve a biosimilar application would likely be a "socially compelling interest[]" that justifies marginally limiting the rights of a trade

230. See Epstein, *supra* note 136, at 285; see Andrew Wasson, Note, *Taking Biologics for Granted? Takings, Trade Secrets, and Off-Patent Biological Products*, 4 DUKE L. & TECH. REV. 1, 9 (2005).

231. Epstein, *supra* note 136, at 288; see Dan L. Burk, *Misappropriation of Trade Secrets in Biotechnology Licensing*, 4 ALB. L.J. SCI. & TECH. 121 (1994).

232. Epstein, *supra* note 136, at 297.

233. 21 C.F.R. § 20.61(a) (2002).

234. See Epstein, *supra* note 136, at 287-88.

235. See *id.* at 288; Carly Miller et al., *Pathway for Biosimilars Survives the Supreme Court*, 28 WESTLAW J. PHARM. 1, 4 (2012).

236. See *infra* text accompanying notes 237-48.

secret owner to ensure only the safest drugs are approved and dispensed to the public.²³⁷

Further, disclosing confidential data, such as a trade secret, to a regulatory agency pursuant to its requirements does not divest the trade secret owner of his or her rights.²³⁸ Thus, innovator drug manufacturers who provide confidential biologic drug information to the FDA will retain their trade secret protection even if the FDA uses it in approving a biosimilar application.²³⁹

The Federal Trade Secrets Act (FTSA) also prohibits federal employees, in this case FDA employees reviewing biosimilar applications, from disclosing trade secrets or related information obtained during the course of employment.²⁴⁰ The FTSA criminalizes any FDA employee who misappropriates information contained in an innovator biologic or biosimilar application submitted for approval.²⁴¹

In addition to the federal trade secret protection for disclosures to the FDA, courts have frequently opposed mandatory *public disclosures* of trade secrets for fear that doing so unconstitutionally destroys their value and confidentiality.²⁴² Even laws mandating the public disclosure of cigarettes and tobacco products have not withstood judicial scrutiny, demonstrating the high regard courts have for trade secret protection.²⁴³

The Biosimilars Act does not require public disclosure of trade secrets, and in fact states that “the disclosure of *any confidential information* . . . shall be deemed to cause the . . . applicant to suffer irreparable harm for which there is no adequate legal remedy and the court shall consider immediate injunctive relief to be an appropriate and necessary remedy for any violation or threatened violation.”²⁴⁴

FDA employees’ use of proprietary information in reviewing a biosimilar application is somewhat analogous to USPTO patent examiners

237. See 3 ROGER M. MILGRIM & ERIC E. BENSON, MILGRIM ON TRADE SECRETS § 12.02, at 12-20.2 to 12-20.3; 12-23 (2014).

238. *Id.* at 12-21 to 12-22.

239. See *id.*

240. 18 U.S.C. § 1905 (2012); see Epstein, *supra* note 136, at 288.

241. See 18 U.S.C. § 1905. An individual in violation of the FTSA is subject to a fine, imprisonment not exceeding a year, or both, and shall be removed from their office or employment.

242. Philip Morris, Inc. v. Reilly, 312 F.3d 24, 45-46 (1st Cir. 2002) (affirming district court’s holding that Massachusetts Disclosure Act unconstitutionally required tobacco companies to disclose trade secret ingredient lists, thereby destroying their value).

243. *Id.*

244. 42 U.S.C. § 262(l)(1)(H) (2012) (*italics added*).

within an Art Group who “routinely examine patent applications from competitors regarding highly similar subject matter,” which has not been found to misappropriate trade secret protection or infringe patent rights.²⁴⁵

Lastly, while the Freedom of Information Act allows any member of the public to obtain access to federal agency records,²⁴⁶ the information submitted to the FDA by both biologic and biosimilar applicants is protected by “Exemption 4,” which precludes disclosure of trade secrets.²⁴⁷

The Biosimilars Act’s prohibition against public disclosure, the FDA’s strictly internal use in promoting the public good, state trade secret laws, and judicial respect for trade secrets all should allay drug manufacturers’ concerns about providing their information to the FDA and avoid trade secret misappropriation issues.²⁴⁸

B. 5th Amendment Takings

In April 2012, pharmaceutical company Abbott Laboratories filed a citizen petition requesting that the FDA not accept for filing, file, approve, or take any action indicating the agency would consider, a biosimilar application based on one of the company’s biologics, Humira.²⁴⁹ Abbott based its request on the 5th Amendment’s takings clause, which states that no “private property [shall] be taken for public use, without just compensation.”²⁵⁰

Although the takings clause does extend to intellectual property,²⁵¹ including trade secrets,²⁵² one may only assert a 5th Amendment violation if

245. Gorman et al., *supra* note 6, at 332; see Annemarie L. M. Field et al., *Patent Examiner Recruitment: An Interactive Qualifying Project for the USPTO* 81 (2007), <https://www.wpi.edu/Pubs/E-project/Available/E-project-121207-102952/unrestricted/USPTOFINALREPORT.pdf>.

246. 5 U.S.C. § 552(a)(3)(B) (2012).

247. 5 U.S.C. § 552(b)(4) (2012); 21 C.F.R. § 20.61(c) (2002).

248. See *supra* text accompanying notes 237–47.

249. COVINGTON & BURLING LLP CITIZEN PETITION FOR ABBOTT LABORATORIES, (Apr. 2, 2012) [hereinafter CITIZEN PETITION] (requesting FDA not approve biosimilar applications using information company submitted in its pre-BPCIA biologic applications).

250. U.S. CONST. amend. V.

251. Paul F. Kilmer, *Taken by the Fifth: The Fifth Amendment “Taking Clause” and Intellectual Property*, 22 A.B.A. INTELL. PROP. L. NEWSL. 8, 9 (Fall 2003).

252. *Id.*; see *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986 (1984) (finding that trade secrets constitute intellectual property that may be subject to 5th Amendment taking). *But see* *Coll. Sav. Bank of Fla. v. Fla. Prepaid Postsecondary Educ. Expense Bd.*, 527 U.S. 666 (1999) (court *inter*

he or she had reasonable “investment-backed expectation[s]”²⁵³ of privacy from the government.²⁵⁴

Biologic manufacturers who submitted applications after the March 23, 2010 effective date of the Biosimilars Act had no reasonable investment-backed expectation of privacy from the government as they had notice their proprietary information may be used *internally* for the FDA to approve biosimilar applications.²⁵⁵ The FDA did not pledge that it would not use the information for comparison purposes, and in fact the entire biosimilar system is premised on comparative data that takes innovator drug information into account.²⁵⁶ Moreover, no chemical drug manufacturer has filed a suit alleging that the analogous Hatch-Waxman Act violates the takings clause regarding generic and brand name chemical drugs.²⁵⁷

Although the FDA could likely use information submitted *after* the enactment of the Biosimilars Act without invoking a takings clause claim, the FDA should not, however, use information submitted by innovator drug manufacturers *prior* to the Biosimilars Act’s effective date as these manufacturers lacked notice that their information could be used to approve a biosimilar.²⁵⁸ This information will likely be safe.²⁵⁹

Alternatively, if courts find there is a taking of post-Biosimilars Act proprietary information, the Act convincingly provides just compensation via the data and market exclusivity periods,²⁶⁰ and likely avoids a constitutional violation.²⁶¹

alia noting that not every right recognized under unfair competition claim constitutes property for 5th Amendment taking purposes).

253. Penn Cent. Transp. Corp. v. N.Y.C., 438 U.S. 104 (1978); see Daniel R. Mandelker, *Investment-Backed Expectations: Is There a Taking?*, 31 WASH U. J. URB. & CONTEMP. L. 3 (1987).

254. See Epstein, *supra* note 136, at 302.

255. See *Ruckelshaus*, 467 U.S. at 1006. In that case the FDA “took” the company’s trade secrets when it *subsequently* enacted regulations that would make them *public*. Here, pharmaceutical companies who submitted information *after* the Biosimilars Act was enacted were on notice that the FDA could use them for *purely internal purposes*, as prescribed by statute.

256. See *id.* at 1007 (finding no taking because the company was “aware of the conditions under which the data are submitted, and the conditions [were] rationally related to a legitimate Government interest”); Wasson, *supra* note 230, at 9.

257. Wasson, *supra* note 230, at 12.

258. *Id.*; see Epstein, *supra* note 136; see CITIZEN PETITION, *supra* note 249.

259. See *Ruckelshaus*, 467 U.S. at 1007.

260. See text accompanying notes 94-104.

261. See U.S. CONST. amend. V.

Public policy²⁶² also demands the use of the proprietary information to ensure applicants meet the necessarily high standards²⁶³ of biosimilarity and interchangeability. The public policy consideration of maintaining medication quality, safety, potency, and efficacy is paramount.²⁶⁴ Any minor trade secret limitation (again, only for internal FDA use) is justified, particularly in light of the economic benefits provided through the exclusivity periods.²⁶⁵

V. CONCLUSION

On March 6, 2015, the FDA approved Sandoz's Zarxio, a biosimilar of Amgen's filgrastim biologic that boosts the weakened immune systems of cancer patients undergoing chemotherapy.²⁶⁶ Express Scripts has estimated that over the next ten years, Zarxio's introduction in the United States may save \$5.7 billion in drug costs.²⁶⁷

Further, in September 2015, the Federal Circuit denied Amgen's attempt to extend its July 2015 injunction against Zarxio,²⁶⁸ essentially lifting the injunction²⁶⁹ and paving the way for Sandoz to market the first biosimilar in the United States.²⁷⁰ While Zarxio isn't expected to fully penetrate the market

262. See 3 MILGRIM & BENSON, *supra* note 237, at 12-20.2 to 12-20.3.

263. Kanter & Feldman, *supra* note 153, at 74; see MARGARET HAMBURG, FOOD & DRUG ADMIN., *supra* note 70.

264. BIOTECHNOLOGY INDUSTRY ORG., BIO PRINCIPLES ON FOLLOW-ON BIOLOGICS, *supra* note 34.

265. See 3 MILGRIM & BENSON, *supra* note 237, at 12-20.2 to 12-20.3 and accompanying text.

266. Rockoff & Loftus, *supra* note 69; Noonan, *FDA Approves Sandoz Filgrastim Biosimilar*, *supra* note 11 (noting, however, that Amgen's injunction was eventually granted because Sandoz failed to provide its biosimilar application and information).

267. Tavernise & Pollack, *supra* note 90.

268. *Federal Circuit Denies Amgen's Emergency Motion for a Temporary Injunction in Amgen v. Sandoz*, BIG MOLECULE WATCH (Sept. 2, 2015), <http://www.bigmoleculerwatch.com/2015/09/02/breaking-news-federal-circuit-denies-amgens-emergency-motion-for-a-temporary-injunction-in-amgen-v-sandoz/>.

269. Kevin E. Noonan, *Federal Circuit Lifts Injunction Against Sandoz*, PATENT DOCS (Sept. 2, 2015, 11:11 PM), <http://www.patentdocs.org/2015/09/federal-circuit-lifts-injunction-against-sandoz.html>.

270. Kevin E. Noonan, *Sandoz' NEUPOGEN® Biosimilar Now on the Market*, PATENT DOCS (Sept. 7, 2015, 11:22 PM), <http://www.patentdocs.org/2015/09/sandoz-neupogen-biosimilar-now-on-the-market.html>. Zarxio will reportedly be priced at a 15% discount compared to Amgen's innovator drug, Neupogen. *Id.*

for one to five years,²⁷¹ these moves by the FDA,²⁷² the Federal Circuit,²⁷³ and biopharmaceutical manufacturers²⁷⁴ nonetheless are promising indications that the biosimilar market may be ready to take flight domestically.

Despite the biotech industry's position at the forefront of advances in science, health, and business, the legal sector appears to be struggling most to keep pace with these developments. The idea that a biosimilar system cannot exist in the United States is based on the mistaken belief that laws governing chemical drugs should apply to biologic drugs. Eschewing the substitution practices traditionally used for generic chemical drugs would avoid the inertia threatening to inhibit the industry's growth and prevent the benefits of affordable breakthrough medications from reaching patients.

Federalized substitution standards such as those set forth in this article would incentivize drug manufacturers to create interchangeable biosimilars that pharmacists would more readily substitute in place of a pricier biologic. Failure to account for the differences between biologic and chemical drugs, as well as the greater variance between an innovator biologic drug and biosimilar, would likely lead to inconsistent biosimilar substitution laws between states, disparate substitution practices by doctors and pharmacists, unequal medication access for patients, and increases in healthcare spending.

Yet, one cannot forget the human impact, because at its most fundamental level, the implementation of a successful biosimilar system means patients across the country, like Mr. DeLuca, can worry less about how they will survive paying exorbitant medical bills, and more about how they will survive keeping up with ten grandchildren.²⁷⁵

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271. *Id.*

272. *See* Rockoff & Loftus, *supra* note 69.

273. *See Federal Circuit Denies Amgen's Emergency Motion for a Temporary Injunction in Amgen v. Sandoz, supra* note 268.

274. Noonan, *Sandoz' NEUPOGEN® Biosimilar Now on the Market, supra* note 270.

275. *What's Keeping Less Expensive Biologic Drugs From the U.S. Market?, supra* note 1.

* Notes and Comments Editor, J.D. Candidate 2016, Southwestern Law School; B.A. Neuroscience 2013, University of Southern California. Thank you to Professor Ryan Abbott for pointing me in the right direction, to the members of the Southwestern Law Review for guidance in the process, and to everyone else who provided inspiration and insight along the way. To Ana and David Kadin, a sincere thank you for everything you have done and continue to do for me – none of this would be possible with you.