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Note

Changing Course to Navigate the Patent Safe Harbor Post-Momenta

Emily M. Wessels*

It is a familiar scene: a patient receives a prescription from her physician and brings it to her local pharmacy. A pharmacist instinctively substitutes the prescribed brand-name drug with one of the many generic options, each made by a different pharmaceutical manufacturer.¹ The interchange is so seamless and familiar that consumers rarely give it a second thought. In fact, currently about three-quarters of prescriptions are filled with a generic drug.²

Thirty years ago the scene would have been strikingly different. In 1983, generic drugs accounted for less than twenty percent of prescriptions.³ But Congress's enactment of the Drug

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1. See U.S. GOV'T ACCOUNTABILITY OFFICE, GAO-12-371R, DRUG PRICING: RESEARCH ON SAVINGS FROM GENERIC DRUG USE 1 n.2 (2012), available at <http://www.gao.gov/assets/590/588064.pdf> ("A brand-name drug is a drug marketed under a proprietary, trademark-protected name."); *id.* at 1 ("[G]eneric drugs . . . are copies of approved brand-name drugs.")

2. See, e.g., *id.* at 2 (estimating that the generic utilization rate is "about 78 percent for drugs dispensed in retail settings"); Martha M. Rumore, *The Hatch-Waxman Act—25 Years Later: Keeping the Pharmaceutical Scales Balanced*, PHARMACY TIMES, Aug. 15, 2009, <http://www.pharmacytimes.com/publications/supplement/2009/GenericSupplement0809/Generic-HatchWaxman-0809> ("[T]oday more than 70% of prescriptions are for generics . . .").

3. See, e.g., U.S. GOV'T ACCOUNTABILITY OFFICE, *supra* note 1, at 2 (placing the generic utilization rate at 19% in 1984); Rumore, *supra* note 2 ("[P]re-Hatch-Waxman generic prescriptions numbered 15%.")

Price Competition and Patent Term Restoration Act of 1984⁴ marked a shift toward generic proliferation.⁵ The Act—also known as the Hatch-Waxman Act (Hatch-Waxman)—introduced an abbreviated pathway for U.S. Food and Drug Administration (FDA) approval of generic drugs.⁶ Reflecting Congress's desire to balance the interests of brand companies, generic manufacturers, and the public, Hatch-Waxman also contained a “safe harbor” provision shielding generic manufacturers from patent infringement liability for activities “reasonably related” to submitting information to the FDA.⁷ This provision was designed so that a generic can enter the market as soon as—but not before—the patent on the brand medication expires.⁸

Notably, since its enactment the scope of the safe harbor has progressively widened to apply to medical devices, research tools, and even information that is ultimately never included in an FDA submission.⁹ The Federal Circuit's 2011 decision in *Classen Immunotherapies, Inc. v. Biogen IDEC*¹⁰ seemed to slow this momentum toward an unbound interpretation of the safe harbor. The *Classen* court appeared to draw a bright line strictly limiting the application of the safe harbor doctrine to activities occurring before the FDA approves a drug for commercial

4. Pub. L. No. 98-417, 98 Stat. 1585.

5. See, e.g., U.S. GOV'T ACCOUNTABILITY OFFICE, *supra* note 1, at 2 (“Increased use of generic drugs can partly be attributed to the regulatory framework that was established in the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act.”).

6. Hatch-Waxman Act, §§ 101–106, 98 Stat. at 1585–97 (codified as amended in scattered sections of 21 U.S.C.); see also Keysha Bryant, *Biosimilars: The Long and Winding Pathway to Approval*, U.S. PHARMACIST: GENERIC DRUG REV., June 21, 2013, <http://www.uspharmacist.com/content/s/253/c/41438/>.

7. Hatch-Waxman Act, § 202, 98 Stat. at 1603 (codified as amended at 35 U.S.C. § 271 (2006)); see also B. Scott Eidson, Note, *How Safe Is the Harbor? Considering the Economic Implications of Patent Infringement in Section 271(e)(1) Analysis*, 82 WASH. U. L.Q. 1169, 1171–75 (2004) (discussing the enactment of Hatch-Waxman's safe harbor).

8. See, e.g., *Examining the Senate and House Versions of the “Greater Access to Affordable Pharmaceuticals Act”*: Hearing Before the S. Comm. on the Judiciary, 108th Cong. 124–25 (2003) (statement of Daniel E. Troy, Chief Counsel, FDA) (explaining that in enacting Hatch-Waxman, “Congress sought to ensure that, once the statutory patent protection and marketing exclusivity for . . . new drugs has expired, consumers would benefit from the rapid availability of lower priced generic versions of innovator drugs”).

9. See *infra* Part I.D.1.

10. 659 F.3d 1057 (Fed. Cir. 2011), *cert. denied*, 133 S. Ct. 973 (2013).

sale.¹¹ The respite, however, was short lived. In August 2012, the Federal Circuit changed course in *Momenta Pharmaceuticals, Inc. v. Amphastar Pharmaceuticals, Inc.*, an infringement suit between two manufacturers of enoxaparin, the generic version of the complex drug Lovenox.¹² The split *Momenta* panel held that Amphastar's *post*-approval use of Momenta's patented method for analyzing an enoxaparin sample was protected under the safe harbor because the FDA required the analysis as a condition of the generic's continued drug approval.¹³ Judge Rader dissented, noting that the decision essentially rendered the patent worthless by sanctioning unrestricted, indefinite commercial infringement at the patentee's expense.¹⁴

Although the *Momenta* court attempted to reconcile its holding with *Classen*, the two decisions' treatments of the temporal scope of the safe harbor are arguably at odds. Satisfactory resolution of this tension is needed to restore Hatch-Waxman's intended balance between brand and generic drug manufacturers. *Momenta* highlights the importance of timely resolution as the pharmaceutical industry prepares to usher in a new age of biopharmaceutical—or "biologic"—innovation.¹⁵ Similar to the complex drug at issue in *Momenta*, large biologic molecules necessitate strict quality control analyses to demonstrate the "sameness" required to qualify as a "follow-on"¹⁶ product (which

11. For commentary contemporaneous with *Classen* interpreting the decision as a bright-line limit, see, for example, Aaron F. Barkoff, *Federal Circuit Confines 271(e)(1) Safe Harbor to Pre-Approval Activities*, ORANGE BOOK BLOG (Aug. 31, 2011), <http://www.orangebookblog.com/2011/08/federal-circuit-confines-271e1-safe-harbor-to-pre-approval-activities.html>; Gray Buccigross, *Safe-Harbor Provision of Hatch-Waxman Act Does Not Protect Post-Approval Research Activities*, FDA L. UPDATE (Oct. 24, 2011), <http://www.fdalawblog.com/2011/10/articles/legislation/safe-harbor-provision-of-hatch-waxman-act-does-not-protect-post-approval-research-activities/>.

12. 686 F.3d 1348 (Fed. Cir. 2012), *cert. denied*, 133 S. Ct. 2854 (2013).

13. *Id.* at 1357–59.

14. *Id.* at 1369–70 (Rader, J., dissenting).

15. See Ian Evans, *Follow-on Biologics: A New Play for Big Pharma*, 83 YALE J. BIOLOGY & MED. 97, 99 (2010) (discussing the potential of biopharmaceuticals to reshape the face of medicine in light of a slowdown in traditional small-molecule pharmaceutical innovation). For purposes of this Note, the text refers to the terms biopharmaceutical and biologic interchangeably.

16. Compare *Momenta*, 686 F.3d at 1350–51 (explaining the complex requirements for determining "sameness" between enoxaparin and Lovenox due to the drug's molecular diversity), with FDA, DRAFT GUIDANCE: QUALITY CONSIDERATIONS IN DEMONSTRATING BIOSIMILARITY TO A REFERENCE PROTEIN PRODUCT 9–15 (2012), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291134.pdf> (de-

is comparable to the biologic equivalent of a generic¹⁷). If *Momenta* is allowed to stand for the unfettered proposition that post-approval quality control processes are unenforceable against infringers, the result could chill an entire field of intellectual property rights essential for the development of any sort of meaningful follow-on biologic market.

This Note advocates for a statutory scheme that narrows safe harbor protection for activities occurring after FDA approval and provides compensation to all affected patentees. The proposed changes would restore the balance between easing the barrier to competitors' market entry and preserving the intellectual property rights of patent holders responsible for pharmaceutical innovation. It would also lay groundwork for the growth of a successful follow-on biologic regime. To this end, Part I provides a brief overview of the context, enactment, and judicial evolution of the safe harbor doctrine. Part I also presents a summary of the Federal Circuit's decisions in *Classen* and *Momenta*. Part II examines the safe harbor's application as a liability exception and extrapolates the likely consequences of the *Momenta* decision to the field of biopharmaceuticals. Part III concludes that the safe harbor should provide adequate recompense to patent holders, whether they are brand, generic, or follow-on manufacturers. Keeping the interests of both private and public stakeholders in mind, the proposed solution includes enhanced procedures for notifying follow-on manufacturers of potential infringement, as well as a reasonable royalty for all patent owners subjected to the safe harbor and a period of commercial exclusivity for those facing excused post-approval infringement.

scribing the many different analytical factors involved in demonstrating similarity between a follow-on biologic and reference product).

17. See JUDITH A. JOHNSON, CONG. RESEARCH SERV., RL 34045, FDA REGULATION OF FOLLOW-ON BIOLOGICS 1 & n.1 (2010), available at http://primaryimmune.org/advocacy_center/pdfs/health_care_reform/Biosimilars_Congressional_Research_Service_Report.pdf (explaining that “[a] follow-on biologic is similar but not identical to the brand-name . . . product,” and that although sometimes referred to “as biogenerics or generic biologics[, t]he FDA and many others consider the use of the word generic to be inaccurate because the term has been used, in the context of chemical drugs, to mean identical”); see also *id.* at 9–12 (discussing the unique scientific challenges associated with comparing follow-on biologics with the brand-name drugs).

I. EVOLUTION OF THE SAFE HARBOR DOCTRINE

The intersection of innovation, patent protection, and FDA regulation creates challenges unique to the pharmaceutical field. This Part introduces the nuanced development of the law in these areas that resulted in the enactment of the safe harbor doctrine. It continues with an explanation the doctrine's expansion and finishes with a discussion of the Federal Circuit's decisions in *Classen* and *Momenta*.

A. PHARMACEUTICAL INDUSTRY

The U.S. pharmaceutical market is a multi-billion dollar industry with \$330 billion in sales in 2012.¹⁸ The market traditionally has been dominated by small molecule drugs,¹⁹ which are chemicals with a “well-defined structure [that] can be thoroughly characterized.”²⁰ Unfortunately, innovation of truly novel small molecule pharmaceuticals has arguably slowed in recent years.²¹ Instead, companies have concentrated resources on producing imitation “me-too” products.²² These drugs tend to target saturated markets and generally offer few advantages in terms of therapeutic benefits or favorable side effect profiles.²³

18. *Worldwide Pharmaceutical Sales by Region 2010–2012*, STATISTA, <http://www.statista.com/statistics/272181/world-pharmaceutical-sales-by-region/> (last visited Mar. 10, 2014).

19. See *Biotech Products in Big Pharma Clinical Pipelines Have Grown Dramatically*, TUFTS CENTER FOR STUDY DRUG DEV. (Nov. 14, 2013), http://csdd.tufts.edu/news/complete_story/pr_ir_nov_dec_2013 (noting the “historical concentration on small molecule drugs”).

20. *Frequently Asked Questions About Therapeutic Biological Products*, FDA, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/ucm113522.htm> (last updated Dec. 24, 2009).

21. See, e.g., Donald W. Light & Joel R. Lexchin, *Pharmaceutical Research and Development: What Do We Get for All That Money?*, BRIT. MED. J., Aug. 7, 2012, at 22, 23 (“This is the real innovation crisis: pharmaceutical research and development turns out mostly minor variations on existing drugs . . .”).

22. See AIDAN HOLLIS, ME-TOO DRUGS: IS THERE A PROBLEM? 1 (2004), available at http://www.who.int/intellectualproperty/topics/ip/Me-tooDrugs_Hollis1.pdf (noting the increased “criticism on the drug industry for the increasing extent to which investment appears to be focused on developing drugs which have a similar mechanism of action to pre-existing drugs”).

23. *Id.* at 1 (acknowledging the varying definitions of a me-too drug while defining it as “one that is approved after a pioneering drug and which is [comparable or similar] . . . and is not clinically superior”).

Recent developments in biopharmaceuticals, however, represent a possible return to significant innovation.²⁴ Biologics are complex molecules produced from living organisms.²⁵ Biologics are generally on the cutting edge of treatment, offering new therapeutic options for previously untreatable diseases.²⁶ It is projected that by 2015, biologics will account for \$167 billion of U.S. pharmaceutical sales.²⁷

The shift from small molecule drugs to biologics underscores a key public policy consideration: the need to balance innovation of new treatments with affordable access to these life-saving therapies.²⁸ The recent skyrocketing of health care costs highlights the importance of this balancing act.²⁹ On the one hand, experts estimate that bringing a new small-molecule therapy to market may cost as much as \$1.3 billion in research and development (R&D).³⁰ On the other, brand-name drugs can cost consumers hundreds of dollars.³¹

24. ERNST & YOUNG, BEYOND BORDERS: GLOBAL BIOTECHNOLOGY REPORT 1 (2007), available at <http://www.biocity.co.uk/file-manager/Group/reports2007/2007-beyondborders.pdf> ("There is no question that biotechnology is now the engine of innovation for the drug development industry."); Michael Pohlscheidt & Robert Kiss, *Recent Advances and Trends in the Biotechnology Industry—Development and Manufacturing of Recombinant Proteins and Antibodies*, AM. PHARMACEUTICAL REV., Sept./Oct. 2013, <http://www.americanpharmaceuticalreview.com/Featured-Articles/148856-Recent-Advances-and-Trends-in-the-Biotechnology-Industry-Development-and-Manufacturing-of-Recombinant-Proteins-and-Antibodies/> ("A large number of [biologics] have been approved, delivering meaningful contributions to patients' lives, and are anticipated to be the major growth driver for the industry in the upcoming years.").

25. *Frequently Asked Questions About Therapeutic Biological Products*, supra note 20.

26. *What Are "Biologics" Questions and Answers*, FDA, <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133077.htm> (last updated Apr. 14, 2009).

27. Bhupinder Singh Sekhon & Vikrant Saluja, *Biosimilars: An Overview*, BIOSIMILARS, Mar. 14, 2011, at 1, 1.

28. LAURENCE J. KOTLIKOFF, STIMULATING INNOVATION IN THE BIOLOGICS INDUSTRY: A BALANCED APPROACH TO MARKETING EXCLUSIVITY 1 (2008), available at http://people.bu.edu/kotlikoff/New%20Kotlikoff%20Web%20Page/Kotlikoff_Innovation_in_Biologics21.pdf ("The key issue in providing affordable access to biologic wonder drugs is doing so without limiting their development.").

29. *The Skyrocketing Cost of U.S. Health Care: By the Numbers*, THE WEEK, Mar. 30, 2012, <http://theweek.com/article/index/226276/the-skyrocketing-cost-of-us-health-care-by-the-numbers>.

30. Compare Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151, 180 (2003) (calculating the cost of drug development as \$802 million), and Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Differ-*

The R&D costs are just as high, if not higher, for biologics.³² Biologics also take longer to develop and have a lower success rate than small-molecule drugs.³³ These consequences stem from the complexity of biologic molecules.³⁴ Because biologics are derivatives of living organisms, even small manufacturing differences can cause significant variations in the end product.³⁵ The increased development costs are then passed on to consumers.³⁶ To illustrate, the yearly cost of biologic therapy averages \$16,425, compared to \$730 for traditional pharmaceuticals.³⁷

Fortunately, market competition can help control consumers' costs.³⁸ The proliferation of generics demonstrates the bene-

ent?, 28 *MANAGERIAL & DECISION ECON.* 469, 476 (2007) (using a time-adjusted drug development cost of \$1.318 billion), with Donald W. Light & Rebecca Warburton, *Demythologizing the High Costs of Pharmaceutical Research*, 6 *BIOsocieties* 34, 34, 46 (2011) (critiquing DiMasi et al. and placing the cost of drug development at a median of \$43.4 million). *But see Tufts CSDD's Official Response to the Recent Light & Warburton Commentary*, TUFTS CENTER FOR STUDY DRUG DEV. (Mar. 2011), http://csdd.tufts.edu/news/complete_story/internal_news (responding to Light & Warburton's critique in support of DiMasi et al.).

31. See, e.g., Ganesan Marimuthu et al., *Maintaining Patents Protecting Biologics or Small-Molecule Drugs*, 30 *NATURE BIOTECHNOLOGY* 50, 50 (2012); Linda A. Johnson, *Drug Prices to Plummet in Wave of Expiring Patents*, NBCNEWS.COM (July 25, 2011, 1:44:43 PM), http://www.nbcnews.com/id/43882446/ns/health-health_care/t/drug-prices-plummet-wave-expiring-patents/#.Us3j87Q0wqc.

32. See DiMasi & Grabowski, *supra* note 30, at 475–76 (recognizing that overall figures for biologic development may be higher than traditional pharmaceuticals depending on the accuracy of time-adjusted calculations).

33. WENDY H. SCHACHT & JOHN R. THOMAS, CONG. RESEARCH SERV., R 41483, FOLLOW-ON BIOLOGICS: THE LAW AND INTELLECTUAL PROPERTY ISSUES 3–4 (2012), available at <http://www.fas.org/sgp/crs/misc/R41483.pdf> [hereinafter SCHACHT & THOMAS, INTELLECTUAL PROPERTY ISSUES].

34. See ANDREW F. BOURGOIN, WHAT YOU NEED TO KNOW ABOUT THE FOLLOW-ON BIOLOGIC MARKET IN THE U.S.: IMPLICATIONS, STRATEGIES, AND IMPACT 1 (2011), available at <http://thomsonreuters.com/business-unit/science/pdf/ls/newport-biologics.pdf> (“[M]any [biologics] demand substantial investment to manufacture due to the product complexity.”).

35. SCHACHT & THOMAS, INTELLECTUAL PROPERTY ISSUES, *supra* note 33, at 15.

36. BOURGOIN, *supra* note 34, at 1 (“The high development cost of biologic products is often reflected in their price.”).

37. ROBERT J. SHAPIRO WITH KARAN SINGH & MEGHA MUKIM, THE POTENTIAL AMERICAN MARKET FOR GENERIC BIOLOGICAL TREATMENTS AND THE ASSOCIATED COST SAVINGS 4 (2008), available at http://www.sonecon.com/docs/studies/0208_GenericBiologicsStudy.pdf.

38. See U.S. GOV'T ACCOUNTABILITY OFFICE, *supra* note 1, at 1 (“The competition that brand-name drugs face from generic equivalents is associated with lower overall drug prices . . .”).

ficial effects of competition. Since generic small molecule drugs have become widely available, these products have been substituted for brand-name drugs at an average cost savings of seventy-five percent.³⁹ It is further estimated that a successful biosimilars market could produce savings of up to forty percent,⁴⁰ demonstrating the importance of fostering competition as the biopharmaceutical field continues to grow.

B. U.S. PATENT SYSTEM

Faced with such high R&D costs, the patent system offers pharmaceutical companies an opportunity to recover some of those costs. A patent allows its holder to exclude others from making, using, or selling the patented invention for a defined period of time.⁴¹ The U.S. system of exclusivity is grounded in an economic/utilitarian philosophy, providing the economic reward of a limited monopoly as an incentive for conferring the "ultimate benefit to the public" through technological advancement and increased institutional knowledge.⁴² The economic reward of exclusivity not only offers the patentee a chance to recoup its investment by singularly exploiting the technology, but the patentee may ultimately realize profits above and beyond the cost of innovation.⁴³ Alternatively, the patent owner may license the invention for use by others, which generally involves a reasonable royalty or other form of compensation to the patentee.⁴⁴ It is this potential for significant return on investment that is a key driver of pharmaceutical innovation.⁴⁵

39. *Id.*

40. BOURGOIN, *supra* note 34 ("At the individual product level, reports are estimating that biosimilars may cost between 60 and 80 percent of the reference biologic therapy upon market entry.").

41. 35 U.S.C. § 154(a)(1) (2006); *see also id.* §§ 101–03 (specifying that an inventive process, machine, manufacture, or composition of matter that meets three basic requirements—namely utility, novelty, and nonobviousness—may be eligible for patent protection).

42. *See* Ruth E. Freeburg, Comment, *No Safe Harbor and No Experimental Use: Is It Time for Compulsory Licensing of Biotech Tools?*, 53 BUFF. L. REV. 351, 358–59 (2005); *see also* Maureen O'Rourke, 100 COLUM. L. REV. 1177, 1182 (2000) ("In the absence of some mechanism to allow the originator to at least recoup his or her investment, information will be under-produced.").

43. *See* Adi Gillat, *Compulsory Licensing to Regulated Licensing: Effects on the Conflict Between Innovation and Access in the Pharmaceutical Industry*, 58 FOOD & DRUG L.J. 711, 715–16 (2003).

44. *See* 35 U.S.C. § 154(d)(1) (describing the right to a reasonable royalty).

45. *See* Gillat, *supra* note 43.

Unrestrained exclusivity, however, undercuts the utilitarian underpinnings of the patent system.⁴⁶ It leads to overprotection and limits access to information, decreasing the net benefit to society.⁴⁷ U.S. patent law, therefore, does not grant unfettered exclusivity. Rather, certain liability exceptions exist for situations where society has determined that the benefits of access to the invention outweigh the costs to the patent holder.⁴⁸ These liability exceptions limit the patent owner's exclusive right to use or license the patented invention.⁴⁹ In the interest of maintaining the balance between the economic and utilitarian underpinnings of the U.S. patent system, such exceptions are granted sparingly.⁵⁰

C. FDA REGULATION

Simply having a patent, however, does not give a pharmaceutical company an affirmative right to sell its product.⁵¹ A manufacturer must have an FDA-approved application before it can bring a drug to market.⁵² The scope of information required in the initial application makes the approval process expensive and time consuming, adding to the costs of R&D.⁵³ The FDA can also condition continued approval on the collection of post-approval safety and efficacy data.⁵⁴

The approval process itself has evolved over time. In most circumstances, a company wanting to market a new, or "pioneer," drug must file a New Drug Application (NDA) demon-

46. See O'Rourke, *supra* note 42, at 1183.

47. *Id.* at 1183 n.16.

48. Gillat, *supra* note 43, at 713–14.

49. *Id.*

50. *Id.* at 714 (describing the exceptions to patent exclusivity as "narrow and specific").

51. WENDY H. SCHACHT & JOHN R. THOMAS, CONG. RESEARCH SERV., R 41114, THE HATCH-WAXMAN ACT: A QUARTER CENTURY LATER 1 (2012), available at http://www.law.umaryland.edu/marshall/crsreports/crsdocuments/R41114_03132013.pdf.

52. See 21 U.S.C. § 355 (2012) (mandating FDA approval of "new drugs" and describing the application requirements); 42 U.S.C. § 262 (2006) (requiring the licensure of biologics).

53. ALAN MINSK ET AL., FOOD & DRUG LAW INST., THE 505(b)(2) NEW DRUG APPLICATION PROCESS: THE ESSENTIAL PRIMER ii (2010), available at <http://www.fdpi.org/resources/resources-order-box-detail-view/the-505%28b%29%282%29-new-drug-application-process-the-essential-primer> (describing the studies required by the FDA as the "most time-consuming and expensive part of the drug development process").

54. See 21 C.F.R. § 211.165 (2013).

strating the drug is safe and effective.⁵⁵ Historically, another company wanting to sell its generic version of that drug also had to file its own NDA.⁵⁶ Unfortunately, this system produced some unintended consequences. The NDA process could tie up years of patent exclusivity for the pioneer drug before the drug could enter the market.⁵⁷ At the same time, later companies had to invest millions of dollars to produce the same safety and efficacy data provided by the pioneer company.⁵⁸ Furthermore, the Federal Circuit's decision in *Roche Products, Inc. v. Bolar Pharmaceutical Co.* prevented generic manufacturers from conducting tests with the pioneer drug until the patent expired.⁵⁹ This essentially granted the pioneer manufacturer a de facto extension of its monopoly during the time it took the generic company to perform the required studies.⁶⁰ Delayed generic entry decreased market competition, keeping drug prices high.⁶¹

Congress responded to these unintended consequences by enacting Hatch-Waxman. Addressing the first issue, Hatch-Waxman included limited patent term extensions to offset the delays associated with FDA approval.⁶² Regarding the second

55. 21 U.S.C. § 355.

56. WENDY H. SCHACHT & JOHN R. THOMAS, PATENT LAW AND ITS APPLICATION TO THE PHARMACEUTICAL INDUSTRY: AN EXAMINATION OF THE DRUG PRICE COMPETITION AND PATENT TERM RESTORATION ACT OF 1984 ("THE HATCH-WAXMAN ACT") 20 (2005), available at <http://www.law.umaryland.edu/marshall/crsreports/crsdocuments/rl3075601102005.pdf> [hereinafter SCHACHT & THOMAS, EXAMINATION].

57. See *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858, 864 (Fed. Cir. 1984) (noting that it could take up to ten years for a drug to be approved after the NDA was submitted to the FDA), superseded by statute, Hatch-Waxman Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, as recognized in *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348 (Fed. Cir. 2003); Elizabeth Stotland Weiswasser & Scott D. Danzis, *The Hatch-Waxman Act: History, Structure, and Legacy*, 71 ANTITRUST L.J. 585, 588 (2003) ("[T]he 1962 Amendments [to the FDA drug approval process] resulted in a significant erosion of the term of exclusivity provided to pharmaceutical manufacturers under the patent laws.").

58. See *Roche*, 733 F.2d at 860 (describing federally mandated premarket-ing tests); SCHACHT & THOMAS, EXAMINATION, *supra* note 56, at 20 (noting characterization of the requirement that generic manufacturers independently prove safety and effectiveness as "needlessly costly, duplicative and time-consuming"); cf. *supra* note 30 and accompanying text (describing the high costs of drug development).

59. *Roche*, 733 F.2d at 861.

60. See *Freeburg*, *supra* note 42, at 366.

61. See Weiswasser & Danzis, *supra* note 57, at 590.

62. *Id.* at 590-91.

concern, Hatch-Waxman introduced an Abbreviated New Drug Application (ANDA) pathway to eliminate the duplicity associated with requiring an NDA for subsequent versions of approved drugs.⁶³ Rather than requiring independent safety and efficacy data, an ANDA allows a generic manufacturer to designate an already-approved product as a “reference” product and rely on the data included in the reference product’s NDA to meet the FDA’s approval criteria.⁶⁴ The generic manufacturer need only demonstrate that its product is bioequivalent to the reference product.⁶⁵ Finally, Hatch-Waxman created a process for resolving patent disputes before the generic is approved for market entry.⁶⁶ The Act made it “an act of infringement to submit [an ANDA] . . . for a drug claimed in a patent or the use of which is claimed in a patent”⁶⁷ and detailed a procedure for challenging those patents.⁶⁸

The ANDA process itself, however, did not remedy the de facto patent extension ratified by the court in *Roche*. A generic manufacturer still could not commence the required bioequivalence studies until the patents on the reference product expired.⁶⁹ Congress thus included a safe harbor provision in Hatch-Waxman to address this problem, essentially overturning *Roche*.⁷⁰ This provision, codified at 35 U.S.C. § 271(e)(1), provides:

It shall not be an act of infringement to make, use, offer to sell, or sell within 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 drugs⁷¹

The theory behind the safe harbor was that a generic manufacturer could complete the necessary bioequivalence studies

63. *Id.* at 593–94.

64. *Id.* at 594–95.

65. *Id.*; see also *Generic Drugs: Questions and Answers*, FDA, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/QuestionsAnswers/ucm100100.htm> (last updated Sept. 3, 2013) (describing bioequivalence as “identical . . . in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use”).

66. Weiswasser & Danzis, *supra* note 57, at 595.

67. Hatch-Waxman Act, § 202, Pub. L. No. 98-417, 98 Stat. 1585, 1603 (1984) (codified as amended at 35 U.S.C. § 271(e)(2) (2006)).

68. See *id.* §§ 201–202, 98 Stat. at 1598–1603; Weiswasser & Danzis, *supra* note 57, at 595–603.

69. Weiswasser & Danzis, *supra* note 57, at 605.

70. *Id.*; see Hatch-Waxman Act, § 202, 98 Stat. at 1603 (codified as amended at 35 U.S.C. § 271(e)(1)).

71. 35 U.S.C. § 271(e)(1).

and receive approval of its ANDA during the life of the patent.⁷² But the generic manufacturer could not sell its product so long as the product or its use was covered by a patent, preserving the patent owner's right to commercial exclusivity during the patent term by preventing the generic from entering the market until the patent expired.⁷³

Notably, Hatch-Waxman's patent dispute resolution procedures and ANDA provisions were implemented as amendments to the Food, Drug, and Cosmetic Act, the statute that regulates small-molecule drugs.⁷⁴ Most biologics, on the other hand, are regulated under the Public Health Services Act.⁷⁵ As a consequence, neither the patent term extension nor the ANDA process introduced by Hatch-Waxman generally applies to biologics.⁷⁶ Some portions of Hatch-Waxman, however, amended statutes outside the Food, Drug, and Cosmetic Act.⁷⁷ The safe harbor was one of these broader provisions and was incorporated as a general amendment to the Patent Act.⁷⁸ As a result, the safe harbor is considered applicable to biologics.⁷⁹

72. SCHACHT & THOMAS, EXAMINATION, *supra* note 56, at 25.

73. H.R. REP. NO. 98-857, pt. 1, at 45 (1984) [hereinafter Committee Report] (“[Section 271(e)(1)] does not permit the commercial sale of a patented drug”); *id.* at pt. 2, at 30 (“In this case the generic manufacturer is not permitted to market the patented drug during the life of the patent”); see also *Innovation and Patent Law Reform: Hearing on H.R. 3285, H.R. 3286, and H.R. 3605 Before the Subcomm. on Courts, Civil Liberties & the Admin. of Justice of the H. Comm. on the Judiciary*, 98th Cong. 926 (1984) [hereinafter *Hearing*] (memorandum of Alfred B. Engelberg, Patent Counsel, Generic Pharmaceutical Industry Association) (agreeing on behalf of the Generic Pharmaceutical Industry Association that the safe harbor “does not authorize any activity which would deprive the patent owner of the sale of a single tablet during the life of a valid patent”).

74. WENDY H. SCHACHT & JOHN R. THOMAS, CONG. RESEARCH SERV., RL 33901, FOLLOW-ON BIOLOGICS: INTELLECTUAL PROPERTY AND INNOVATION ISSUES 13 (2009), available at <https://openers.com/document/RL33901/> [hereinafter SCHACHT & THOMAS, INNOVATION ISSUES].

75. *Id.* at 3; *Frequently Asked Questions About Therapeutic Biological Products*, *supra* note 20.

76. SCHACHT & THOMAS, INNOVATION ISSUES, *supra* note 74, at 13 (“To the extent that a particular biologic is approved under the auspices of the PHS Act, however, these provisions would be inapplicable.”). *But see id.* at 6 (“Because the definition of ‘drugs’ under the FDC Act is broad, however, the FDA states that ‘[b]iological products subject to the PHS Act also meet the definition of drugs under the Federal Food, Drug, and Cosmetic Act.’” (alteration in original) (quoting *Frequently Asked Questions About Therapeutic Biological Products*, *supra* note 20)).

77. *See id.* at 13.

78. *Id.*

79. *Id.*

Because biologics were excluded from the ANDA provisions of Hatch-Waxman, until recently no procedure existed for expedited approval of follow-on biologics.⁸⁰ Previously, a company wanting to market its version of an approved biologic had to follow the same approval pathway as the pioneer and file its own Biologic License Application (BLA).⁸¹ Needless to say, the system suffered from the same wasted resources problem that plagued the small-molecule approval process prior to Hatch-Waxman.⁸² Expedited approval of follow-on biologics, however, presented its own unique challenges. First, developing a follow-on biologic is generally much more costly than developing a generic small-molecule drug.⁸³ Second, the complexity of biologic molecules can make it extremely difficult to demonstrate the “sameness” required to establish bioequivalence.⁸⁴

Nevertheless, Congress turned its attention to establishing an abbreviated approval mechanism for biosimilars in the Biologics Price Competition and Innovation Act of 2009 (BPCIA).⁸⁵ The BPCIA allows a company to designate an approved biologic as a reference product and file an Abbreviated Biologic License Application for approval of its follow-on product.⁸⁶ The Act divides these follow-on products into two categories: biosimilars and interchangeable biologics.⁸⁷ To be biosimilar, the biologic must be “highly similar” to the reference product with no clini-

80. See Jeanne Yang, Note, *A Pathway to Follow-On Biologics*, 3 HASTINGS SCI. & TECH. L.J. 217, 218 (2011).

81. *Id.*; see also 42 U.S.C. § 262(a) (2006); *Biologics License Applications (BLA) Process (CBER)*, FDA, <http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicsLicenseApplicationsBLAProcess/> (last updated Feb. 13, 2010).

82. See *supra* notes 56–65 and accompanying text.

83. See, e.g., Yang, *supra* note 80, at 219; Andrew Jack, *Pharmaceuticals: Biosimilar Drugs Show the Copycats Keeping Up with Creators*, FINANCIAL TIMES, Oct. 17, 2013, available at Factiva, Doc. No. FTFT000020131017e9ah0000h; Denise Myshko, *What's Ahead for Biosimilars*, PHARMAVOICE (Feb. 2012), <http://www.imshealth.com/ims/Global/Content/Corporate/Press%20Room/IMS%20in%20the%20News/Documents/PharmaVOICE0212-IMS-Biosimilars.pdf>.

84. See, e.g., Sekhon & Saluja, *supra* note 27, at 2–3; Yang, *supra* note 80, at 230.

85. Though introduced separately in 2009, the BPCIA was ultimately incorporated into the Affordable Care Act. See Patient Protection and Affordable Care Act, Pub. L. No. 111-148, §§ 7001–7003, 124 Stat. 119, 804–21 (2010).

86. See *id.* § 7002(a)–(b), 124 Stat. at 804–15 (codified at 42 U.S.C. § 262 (2006)).

87. *Id.*

cally meaningful differences in safety, purity, or potency.⁸⁸ An interchangeable biologic is a biosimilar “expected to produce the same clinical result as the reference product” such that switching between the two products presents no more risk to the patient than repeat administration with the reference product.⁸⁹ An interchangeable can be freely substituted for the reference product.⁹⁰ The first approved interchangeable biologic for each reference product is granted a period of market exclusivity, the length of which varies depending on its commercial and litigation status.⁹¹

The statute also provides a mechanism for identifying and resolving patent disputes.⁹² The BPCIA system differs from the Hatch-Waxman process, accounting for the fact that small differences in manufacturing can significantly impact the end product and recognizing that novel, complex processes may be necessary to establish the high degree of similarity required for classification as a biosimilar.⁹³ Unlike Hatch-Waxman’s focus on patented compounds and their methods of use, the BPCIA framework also facilitates challenges to patents on the “method of making” a drug.⁹⁴ The ability to challenge these types of patents reflects the increased importance of manufacturing and quality control patents in the biologic industry.⁹⁵

88. 42 U.S.C. § 262(i)(2).

89. *Id.* § 262(k)(4).

90. *Id.* § 262(i)(3).

91. *Id.* § 262(k)(6).

92. *Id.* § 262(l).

93. See Trevor Woodage, *Blinded by (A Lack of) Science: Limitations in Determining Therapeutic Equivalence of Follow-On Biologics and Barriers to Their Approval and Commercialization*, 2012 STAN. TECH. L. REV. 9, ¶¶ 5, 30, 42–46.

94. *Id.* ¶ 30 (“Another important difference between the ANDA and [follow-on biologic] approval pathways is that under [Hatch-Waxman], method-of-production (or process) patents cannot be asserted. In contrast, the BPCIA allows infringement actions against an entity ‘making’ the allegedly infringing product, so method-of-production patents can be asserted against [follow-on biologic] sponsors.”). Compare 21 U.S.C. § 355(b)(1) (2012) (“The [NDA] applicant shall [include] . . . any patent which claims the drug . . . or which claims a method of using such drug . . .”), with 42 U.S.C. § 262(l)(2)–(3) (2006) (requiring the follow-on applicant to provide the reference product sponsor with a copy of its application and “such other information that describes the process or processes used to manufacture the biological product” and allowing the product sponsor to list all patents potentially infringed based on that information).

95. See Woodage, *supra* note 93 (discussing the challenges facing follow-on manufacturers caused by the scientific and regulatory differences between bio-

D. EXPANSION OF THE SAFE HARBOR⁹⁶

While its statutory language has remained relatively unchanged since 1984, the reach of the safe harbor has not remained static. Rather, important questions about the proper interpretation of § 271(e)(1) have led to judicial decisions significantly enlarging its protections in the intervening decades since its enactment.⁹⁷ More recently, two Federal Circuit decisions have focused renewed attention on the question of the safe harbor's scope.

1. Previous Judicial Developments

Reflecting a generally liberal approach to the safe harbor, courts have endorsed a broad interpretation of § 271(e)(1)'s text.⁹⁸ In one of the first landmark safe harbor decisions, the Supreme Court extended the safe harbor beyond its statutory "drug" language and declared that § 271(e)(1) applies to medical devices as well.⁹⁹ Courts have also interpreted the word "solely" such that safe harbor protection can exist even if submission requirements under federal law are not the only, or even the primary, motivating factor behind the infringing action.¹⁰⁰ The Supreme Court has further construed the term "solely" to support its conclusion that the safe harbor does not categorically deny protection to activities that ultimately do not result in a submission to the FDA.¹⁰¹

logics and small molecule drugs); *see also infra* notes 200–03 and accompanying text.

96. Rather than attempting to be comprehensive, this section presents a representative selection of cases interpreting the safe harbor in the years since its enactment.

97. *See* Eidson, *supra* note 7, at 1180.

98. *See, e.g.,* Telectronics Pacing Sys., Inc. v. Ventritex, Inc., 982 F.2d 1520, 1525 (Fed. Cir. 1992); Intermedics, Inc. v. Ventritex, Inc., 775 F. Supp. 1269, 1279–80 (N.D. Cal. 1991).

99. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 679 (1990) (reasoning that safe harbor protection applies to medical devices because even though they were not specifically included in the statutory text, they are subject to lengthy FDA regulatory approval processes similar to the drug approval process that motivated the enactment of Hatch-Waxman).

100. *See, e.g., Telectronics*, 982 F.2d 1520 ("Federal Circuit precedents indicate that . . . ulterior motives or alternate purposes do not preclude application of the section 271(e)(1) exemption."); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104, 107–08 (D. Mass. 1998) (citing *AbTox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997)).

101. *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 208 (2005) ("[T]he use of patented compounds in preclinical studies is protected under § 271(e)(1) as long as there is a reasonable basis for believing that the experi-

2. Recent Federal Circuit Interpretations

More recently, the Federal Circuit issued two critical decisions interpreting the scope of the safe harbor. First was *Classen Immunotherapies, Inc. v. Biogen IDEC* in August 2011.¹⁰² The *Classen* plaintiff sued several biotech companies for infringing its various patents on methods for evaluating and improving immunization schedules.¹⁰³ The allegedly infringing activities involved evaluating vaccination schedules of already-approved vaccines.¹⁰⁴ The defendants argued that these activities were protected under the safe harbor doctrine because they were “reasonably related” to regulations that required vaccine manufacturers to review and report adverse reactions to the FDA.¹⁰⁵

A split panel—with Judge Moore dissenting—rejected the defendants’ argument, holding that the safe harbor “does not apply to information that may be routinely reported to the FDA, long after marketing approval has been obtained.”¹⁰⁶ The court continued to conclude that the defendants’ activities were not immune because they were “not related to producing information for a [new drug application], and [were] not a ‘phase of research’ possibly leading to marketing approval.”¹⁰⁷ Legal commentary interpreted this decision as endorsing a strict pre-approval limitation on the safe harbor’s scope.¹⁰⁸

Then, in August 2012, the Federal Circuit issued a seemingly conflicting decision in *Momenta Pharmaceuticals, Inc. v. Amphastar Pharmaceuticals*.¹⁰⁹ *Momenta* involved a suit between two generic manufacturers over a patented method for

ments will produce ‘the types of information that are relevant to a [new drug application].’”)

102. 659 F.3d 1057 (Fed. Cir. 2011), *cert. denied*, 133 S. Ct. 973 (2013).

103. *Id.* at 1060; *see also* *Classen Immunotherapies, Inc. v. Biogen IDEC*, No. WDQ-04-2607, 2006 WL 6161856, at *1 (D. Md. Aug. 16, 2006); *Classen Immunotherapies, Inc. v. Biogen IDEC*, 381 F. Supp. 2d 452, 454 (D. Md. 2005).

104. *Classen*, 659 F.3d at 1070.

105. *Id.*; *Classen*, 381 F. Supp. 2d at 455.

106. *Classen*, 659 F.3d at 1070.

107. *Id.* at 1072.

108. *See, e.g.*, Barkoff, *supra* note 11; Buccigross, *supra* note 11; *see also* *Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1369 (Fed. Cir. 2012) (Rader, J., dissenting) (“[T]he [*Classen*] parties and the amici certainly thought *Classen* turned on a pre-/post-approval distinction.”), *cert. denied*, 133 S. Ct. 2854 (2013).

109. 686 F.3d 1348.

analyzing samples of the complex drug enoxaparin.¹¹⁰ Because of the molecular diversity of enoxaparin, the FDA had prescribed five criteria generic companies would need to satisfy to establish bioequivalence for purposes of an ANDA, including analysis of the molecular identity of the drug.¹¹¹ The FDA further specified that continued analysis of each batch of drug was required to maintain marketing approval.¹¹² The patent-in-suit, directed to satisfying these requirements, was assigned to Momenta,¹¹³ which claimed that Amphastar infringed the patent “by ‘manufacturing generic enoxaparin for commercial sale’ using the claimed methods”¹¹⁴ to test “each commercial batch of enoxaparin [to] be sold after FDA approval.”¹¹⁵

Focusing on the statutory language, Judge Moore’s majority opinion rejected Momenta’s argument that *Classen* had decisively limited safe harbor protection to pre-approval activities.¹¹⁶ The court determined that Amphastar’s post-approval uses of the patented method fell squarely under the safe harbor because “the requirement to maintain records for FDA inspection satisfied[d] the requirement that the uses be reasonably related to the development and submission of information to the FDA.”¹¹⁷ The court distinguished *Classen* on the grounds that the specific studies performed in that case were not mandated by the FDA.¹¹⁸ The court further declined to condition its exten-

110. *Id.* at 1349.

111. *Id.* at 1350.

112. *Id.* at 1352 (“FDA requires a generic manufacture to include in its manufacturing process the analysis of each batch of its enoxaparin drug substance to confirm that . . . [it] includes a 1, 6-anhydro ring structure.” (alteration in original) (quoting Letter from FDA to Aventis Pharmaceuticals, Inc. (July 23, 2010))).

113. *Id.* at 1351.

114. *Id.* at 1352.

115. *Id.* at 1353.

116. *Id.* at 1353, 1358–60.

117. *Id.* at 1357.

118. *Id.* at 1358 (“This case, however, fits well within *Classen* because the information submitted is necessary both to the continued approval of the ANDA and to the ability to market the generic drug. . . . The submissions to the FDA in this case are anything but ‘routine’—they implicate Amphastar’s very ability to continue its FDA approval for its ANDA and to continue manufacturing and marketing enoxaparin under its ANDA. We also note that, unlike in *Classen* where the patented studies performed were not mandated by the FDA, the information here is not generated voluntarily by the manufacturer but is generated by FDA requirements the manufacturer is obligated under penalty of law to follow. Under such circumstances, the information can be said to have been gathered solely for submission to the FDA and not, as in *Classen*, primarily for non-FDA purposes.”).

sion of the safe harbor to post-approval activities on the absence of non-infringing alternatives, allowing competitors “the freedom to use an otherwise patented means to develop the necessary information” even when non-infringing methods exist.¹¹⁹

Judge Rader issued a strongly worded dissent, critiquing the majority’s purported failure to adequately consider the purpose of the statute in light of the “not plainly comprehensible” text.¹²⁰ Citing extensively to the legislative history of Hatch-Waxman, Judge Rader maintained that Congress clearly intended the safe harbor to be limited to pre-approval activities in order to balance competition and innovation.¹²¹ He emphasized that the majority’s contrary interpretation endorsed “*continuous, commercial* infringing sales during any portion of the life of the patent.”¹²² Judge Rader also took issue with the majority’s construction of the word “submission” to mean the required retention of records that may or may not be inspected by the FDA¹²³ and its acceptance that the statutory requirement that infringement be “solely for uses reasonably related” to the development of required data could be satisfied by uses “primarily for production of a commercial product.”¹²⁴ In conclusion, Judge Rader foreshadowed that the majority’s extension of the safe harbor would “essentially render manufacturing method patents worthless.”¹²⁵

II. CONTEMPORARY APPLICATION OF THE SAFE HARBOR

Momenta is a landmark decision as the first extension of safe harbor protection to activities that occur after FDA approval.¹²⁶ Its practical consequences for the patentee—as high-

119. *Id.* at 1359 (“This makes good sense because it . . . avoids the situation here, where a drug has received approval, but is nevertheless kept from the market based on an FDA mandated testing requirement.”).

120. *Id.* at 1362 (Rader, J., dissenting) (quoting *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 669 (1990)).

121. *Id.*

122. *Id.* at 1366.

123. *Id.* at 1367 (“This new interpretation would allow almost all activity by pharmaceutical companies to constitute ‘submission’ and therefore justify a free license to trespass.”).

124. *Id.* at 1374.

125. *Id.* at 1369.

126. *See, e.g.*, Isabelle Blundell, *Safe Harbor Protects Post-Approval Activities*, GENETIC ENGINEERING & BIOTECHNOLOGY NEWS, Oct. 1, 2012, at 11, 11,

lighted by Judge Rader—also demonstrate that the safe harbor presents an outdated model for an evolving pharmaceutical industry that places increased emphasis on manufacturing methods.¹²⁷ This Part explores why biologics and other complex drugs do not fit neatly into the current framework of the safe harbor. It reaches the conclusion that neither limiting the safe harbor to pre-approval experimentation nor expanding protection to all post-approval activities would adequately promote Hatch-Waxman's intended balance between innovation and access in today's pharmaceutical landscape.

A. THE SAFE HARBOR AS A LIABILITY EXCEPTION

Section 271(e)(1)'s safe harbor operates as one of the few liability exceptions granted under U.S. patent law.¹²⁸ It excuses certain, otherwise infringing practices encompassed by the statutory language and terminates the patent owner's right to exclude with respect to those practices.¹²⁹ In order to best evaluate the practical implications of applying the current safe harbor exemption to the field of biologics, one must first examine the underlying policy considerations of imposing a liability exception.

1. Balancing Stakeholder Interests: Patentees' Rights

Liability exceptions arise out of a desire to excuse certain infringing activities.¹³⁰ Several existing exceptions in U.S. patent law, including the safe harbor, reflect a "public benefit" theory—a desire to "allow socially beneficial uses that generate

available at <http://www.genengnews.com/gen-articles/safe-harbor-protects-post-approval-activities/4518/>.

127. See Terry G. Mahn & Dr. Erin L. Baker, *Is the Safe Harbor Too Safe for Certain Biologic Patents?*, PHARMACEUTICAL COMPLIANCE MONITOR (Aug. 16, 2013), <http://www.pharmacompliancemonitor.com/is-the-safe-harbor-too-safe-for-certain-biologic-patents/5396/> ("The implications of Momemta [sic] are particularly significant for biologic manufacturers who are required to maintain and provide to FDA, batch-by-batch data on drugs being offered for commercial sale."); *supra* notes 93–95, 122, 125 and accompanying text.

128. See O'Rourke, *supra* note 42, at 1197–98; see also *supra* notes 46–50 and accompanying text (discussing liability exceptions in U.S. patent law).

129. See, e.g., Patcharin Pisut, *Freedom to Research: Room for Trial and Error in Drug Development After Merck KGaA v. Integra Lifesciences I, Ltd.*, 2005 U. ILL. J.L. TECH. & POL'Y 339, 339.

130. See O'Rourke, *supra* note 42, at 1181; *supra* text accompanying note 48.

large positive externalities."¹³¹ Under this theory, exceptions are justified when the net public benefit outweighs the intrusion on the private rights granted to the patent holder.¹³²

The existence and scope of an exception based in public benefit theory therefore represents a balancing of stakeholder interests between the patentee and the public. Specifically, the greater the benefit and the smaller the intrusion, the more justified the exception—and vice versa.¹³³ Due to the substantial intrusion on the patentee's rights, infringement that furthers direct commercial competition weighs significantly against granting an exception for such activities.¹³⁴

2. Balancing Stakeholder Interests: Impact on Innovation

In addition to the individual costs to the patentee, social costs imposed by a disincentive to innovate can decrease the net public benefit.¹³⁵ Patent exclusivity not only offers an opportunity to recover costs associated with invention, but it also includes the lure of a substantial return on investment if an invention is successful.¹³⁶ These potential revenues are often a strong driver behind innovation.¹³⁷ If these exclusivity incen-

131. *Id.* at 1197–98 (listing examples of “situations in which the public benefit from the infringement may be so great that it outweighs the patentee’s interest in its exclusive rights”).

132. *Id.*

133. *See* O’Rourke, *supra* 42, at 1189 (using copyright law to explain the doctrine of positive externalities for later discussion within the context of patent law). The importance of minimizing intrusion on the patentee’s rights is echoed in the international arena. *See id.* at 1201 (“[Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement] members may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.”).

134. *See id.* at 1204–05 (noting a lack of authority “support[ing] excusing commercial infringement that occurs in the marketing of a directly infringing product”).

135. *See, e.g.*, WILLIAM JACK, PRINCIPLES OF HEALTH ECONOMICS FOR DEVELOPING COUNTRIES 180 (1999); O’Rourke, *supra* note 42, at 1182–83 (describing the underproduction of information associated with the public goods problem).

136. *See* Gillat, *supra* note 43, at 715–16 (“It has been proposed that innovation is stimulated not merely by the potential of recouping the costs of R&D and capturing profits. Rather, it is stimulated also by the skew of the reward distribution; in other words, by the odds—however small—of hitting the ‘jackpot’ and to be one of the small minority of inventions that collect spectacular profits.”).

137. *See id.*

tives are removed—not only limiting the opportunity to recoup costs but increasing the risk of loss—the motive to invent can often disappear with them.¹³⁸ Thus while the public may benefit from a liability exception through increased access to a particular invention, any corresponding slowdown in innovation and advancement caused by the exception detracts from its overall net benefit.¹³⁹

Several factors influence the scope and likelihood of a potential slowing in innovation caused by limiting a patent holder's right to exclusivity.¹⁴⁰ These factors include the market significance of competing activities, the predictability of losing patent exclusivity, and the availability of alternative means for recouping costs and reaping profits.¹⁴¹ Notably, these factors present unique considerations in the context of pharmaceutical innovation, which is particularly sensitive to the financial incentives of the patent system.¹⁴²

a. Market Significance

A first—and arguably most substantial—factor presaging an undesirable effect on innovation is market significance.¹⁴³ In this context, market significance depends on the degree of competition between the patent holder and the entity practicing the unauthorized use.¹⁴⁴ It also correlates with the expected market harm to the patentee.¹⁴⁵ Direct competition between an unauthorized user and an established product or service of the patentee has high market significance.¹⁴⁶ Market significance is lower, however, if the unauthorized use involves an untested product or the parties operate in different markets.¹⁴⁷ The lower

138. *Id.*

139. *Id.*

140. See, e.g., Colleen Chien, *Cheap Drugs at What Price to Innovation: Does the Compulsory Licensing of Pharmaceuticals Hurt Innovation?*, 18 BERKELEY TECH. L.J. 853, 873 (2003) (using a compulsory licensing format to explore factors affecting pharmaceutical companies' incentive to innovate); Gillat, *supra* note 43, at 716 (“[I]nnovation is highly responsive to economic stimuli. Incentives to innovate depend on[, among other things,] . . . the rate and ease at which competitive imitation of the innovation occurs.”).

141. See *infra* Part II.A.2(a)–(c).

142. See Henry G. Grabowski & John M. Vernon, *Effective Patent Life in Pharmaceuticals*, 19 INT'L J. TECH. MGMT. 98, 98–99 (2000).

143. Chien, *supra* note 140, at 873, 879–80.

144. *Id.* at 873.

145. *Id.*

146. *Id.*

147. *Id.*

the market significance, the less likely the unauthorized use will negatively impact the patent holder's potential profits.¹⁴⁸ The smaller the potential impact on the patentee's return on investment, the less likely financial considerations will deter innovation.¹⁴⁹ On the other hand, the higher the market significance and risk of financial injury is, the greater the patentee's disincentive to innovate.¹⁵⁰

In a pharmaceutical context, generic small molecule drugs and interchangeable biosimilars represent products with the greatest market significance. These products are direct competitors because they can be substituted for the respective reference product without prescriber intervention.¹⁵¹ In fact, some states require that pharmacists substitute a generic for the brand drug unless the prescriber specifically requests the latter.¹⁵² Distinct drugs in the same therapeutic class also generally have high market significance as they "compete for essentially the same population of patients" and may be "virtually indistinguishable" with respect to safety and effectiveness.¹⁵³ This category likely includes biosimilars that do not meet the criteria for interchangeability.¹⁵⁴ Still, these products have a lesser effect on profits than direct substitutes.¹⁵⁵ Drugs from different classes used to treat the same condition may also have some market significance, but the level of competition between such products is often minimized by important differences in

148. *Id.*

149. Gillat, *supra* note 43, at 716–17.

150. *See id.*

151. *See* 42 U.S.C. § 262(i)(3) (2006) (defining an interchangeable biologic as a biosimilar that can be substituted "without the intervention of the healthcare provider"); William H. Shrank et al., *State Generic Substitution Laws Can Lower Drug Outlays Under Medicaid*, 29 HEALTH AFF. 1383, 1384 (2010) (explaining generic substitution laws); *see also supra* notes 33–34 and accompanying text.

152. Shrank et al., *supra* note 151.

153. David A. Kessler et al., *Therapeutic-Class Wars—Drug Promotion in a Competitive Market*, 331 NEW ENG. J. MED. 1350, 1350 (1994) (explaining the "highly competitive marketplace" among drugs in discrete therapeutic classes).

154. Alfred B. Engelberg et al., *Balancing Innovation, Access, and Profits—Market Exclusivity for Biologics*, 361 NEW ENG. J. MED. 1917, 1918 (2009) ("If biosimilar products are not similarly interchangeable with the original biologic product, they could not be substituted for the original and would have to be marketed to physicians as therapeutic alternatives. . . . The market for [these] biosimilar products is likely to resemble that for new members of a chemical class that already has established therapeutic value.").

155. *Id.*

effectiveness or side effects.¹⁵⁶ This same logic suggests that absent extenuating circumstances, the market significance of individual drugs used to treat different diseases is minimal.

Notably, because of its relationship with competition, market significance also corresponds with the degree of consumer cost savings realized by the introduction of another product.¹⁵⁷ Direct substitutes, with their highest market significance, also produce the greatest price decreases.¹⁵⁸ The addition of distinct competitors in the same (or another) therapeutic class, however, does not necessarily result in significantly lower prices because usurping sales from the established drug requires prescriber intervention.¹⁵⁹ In fact, companies can sometimes charge more for a new drug, even in an already-crowded class.¹⁶⁰ And “entirely new classes of compounds to treat a disease or condition are often priced at a premium relative to older classes.”¹⁶¹

b. Predictability

A second factor affecting the incentive to innovate is the foreseeability of lost or diminished exclusivity.¹⁶² A key variable of this factor is whether the exception is applied to existing technology or future developments.¹⁶³ When an unpredictable

156. See, e.g., Atholl Johnston et al., *Effectiveness, Safety and Cost of Drug Substitution in Hypertension*, 70 BRIT. J. CLINICAL PHARMACOLOGY 320, 322–23 (2010), available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2949902/pdf/bcp0070-0320.pdf> (explaining that although switching between two different classes of blood pressure medications is common, differences in safety, effectiveness, and drug interactions impact the desirability of the interchange).

157. See, e.g., Engelberg et al., *supra* note 154, at 1918 (contrasting the market for drugs in the same therapeutic class “from that for small-molecule generics, in which interchangeability creates intense price competition that swiftly reduces the market share of the expensive branded product”).

158. *Id.*

159. Kessler et al., *supra* note 153 (“Traditional economics might suggest . . . that a late entry would have to be priced below its competitors to win a market share. Sometimes this is the case. However, companies also rely on the widely held notion—not always true—that what is newer is better and is therefore worth more.”).

160. *Id.* (“Aggressive advertising campaigns and lack of information among prescribing physicians about comparative costs can facilitate the higher pricing of ‘me too’ drugs.”).

161. JOSEPH A. DIMASI, PRICE TRENDS FOR PRESCRIPTION: PHARMACEUTICALS: 1995–1999 (2000), available at <http://aspe.hhs.gov/health/reports/drug-papers/dimassi/dimasi-final.htm>.

162. Chien, *supra* note 140, at 873.

163. See *id.* (“Unpredictable licenses that cover only existing technologies are more limited in scope than those that are predictable and cover future inventions.”).

reduction in exclusivity is granted on existing technology, it may be too late to make any significant strategy alterations, minimizing the impact on innovation.¹⁶⁴ If a company is able to predict that a certain project will be subject to lessened patent protection, however, it can prospectively alter its course of action related to the technology.¹⁶⁵ Adjustments may include reducing investment in the project or abandoning it altogether.¹⁶⁶ Thus, even academics who downplay diminished exclusivity's potential to stifle innovation recognize that such an effect is more likely under a system that applies exceptions liberally.¹⁶⁷

As previously discussed, since its enactment the safe harbor's protections have been applied with growing frequency to an increasing number of settings.¹⁶⁸ This trend toward a broad interpretation increases the chance that a particular pharmaceutical development will be subject to lost exclusivity under the safe harbor. Although each new widening of the safe harbor may come too late to affect existing R&D, pharmaceutical companies have the ability to tailor future developments to avoid circumstances where the courts have interpreted § 271(e)(1) to apply broadly.

c. Availability of Alternative Means for Recouping Costs

Taken together, the first two factors demonstrate that a liability exemption combining high market significance and great predictability can result in a significant disincentive to innovate.¹⁶⁹ Nonetheless, even an adverse impact on innovation caused by high market significance and predictability may be mitigated by alternative means for recouping return on investment.¹⁷⁰ Trade secrecy is the most comparable alternative to patenting for protecting the value of an invention that would

164. *Id.*

165. *Id.* at 873–74.

166. *Id.* at 874.

167. See, e.g., Joseph A. Yosick, Note, *Compulsory Patent Licensing for Efficient Use of Inventions*, 2001 U. ILL. L. REV. 1275, 1292; see also Gillat, *supra* note 43, at 717 (“A compulsory license that is relatively easy to obtain and that involves low royalties set by someone other than the patentee has a potential negative effect on the incentives for innovation.”).

168. See *supra* Part I.D.

169. Chien, *supra* note 140, at 879–80.

170. See Alan M. Fisch, *Compulsory Licensing of Pharmaceutical Patents: An Unreasonable Solution to an Unfortunate Problem*, 34 JURIMETRICS J. 295, 304 (1994) (exploring the various options available to companies faced with lost patent exclusivity).

otherwise have limited or no patent protection.¹⁷¹ Such an approach, however, can decrease overall social welfare by reducing the amount of information publicly available.¹⁷² An entity may alternatively increase revenues by raising prices.¹⁷³ But in a truly competitive market, this is generally not a viable option as sales will simply shift to the cheaper alternative.¹⁷⁴ A third option is to decrease expenditures.¹⁷⁵ Unfortunately, limited expenditures can raise serious questions about resource allocation affecting R&D.¹⁷⁶

On the whole, the pharmaceutical industry is foreclosed from many of the alternative means for recouping investment costs. The extreme disclosure requirements associated with FDA approval make trade secret protection unfeasible.¹⁷⁷ As far as raising revenues, a competitive market with generic entrants forecloses the option of increased prices.¹⁷⁸ A company operating in a truly competitive market also likely would be as ill-advised in cutting advertising expenditures as in raising prices—either option is apt to result in a loss of market share.¹⁷⁹ The bulk of a pharmaceutical manufacturer's remaining expenditures consist of R&D.¹⁸⁰ As a result, a manufacturer needing to compensate for the lost value of patent exclusivity without raising prices would be most inclined to reduce risk.¹⁸¹ This could mean limiting research to more reliable, less-

171. Gillat, *supra* note 43, at 723.

172. *See, e.g.*, *Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1376 (Fed. Cir. 2012) (Rader, J., dissenting) (explaining the information disclosure problems associated with keeping inventions secret), *cert. denied*, 133 S. Ct. 2854 (2013).

173. Fisch, *supra* note 170, at 305.

174. *Id.* at 306–07 (“Price theory teaches that in a competitive marketplace, a seller will not profit from a unilateral price increase because purchasers will select a less expensive substitute.”).

175. *Id.* at 308.

176. *See id.* at 308–13.

177. Gillat, *supra* note 43, at 723 (“The most obvious alternative protection—trade secrecy—is not an option for the pharmaceutical industry because detailed disclosure is required for purposes of approval of the drug, and then for marketing. This is amplified by patent law rules and the industry’s tendency to patent its compounds and processes at an early stage of research . . .”).

178. Fisch, *supra* note 170, at 307 (“[P]harmaceutical companies cannot expect to create a healthy balance sheet by increasing prices on pharmaceuticals in a competitive marketplace.”).

179. *Id.* at 306–11.

180. *Id.* at 308–13.

181. *See id.* at 311–12.

cutting-edge developments¹⁸² or cutting R&D expenditures altogether,¹⁸³ either of which foreshadows a corresponding decrease in innovation.¹⁸⁴

Importantly, an aversion to risk is likely to disproportionately affect the developing field of biologics and biosimilars. Not only are the development costs higher, but much of the technology is still theoretical and success is uncertain.¹⁸⁵ Without the promise of exclusive commercial exploitation and the potential windfall of a successful product, many companies will expectedly shy away from biosimilars altogether in favor of less risky investments.¹⁸⁶ A shift in resources will temper the current momentum toward finding breakthrough biologic treatments for otherwise untreatable diseases, decreasing the public's overall access to effective healthcare.¹⁸⁷ In sum, the lack of practical alternatives for recovering costs means the imposition of a highly significant, highly predictable system denying patent exclusivity in the field of pharmaceuticals would make a reduction in innovation almost inevitable.

B. THE SAFE HARBOR'S IMPACT ON INNOVATION

As just demonstrated, the balance between the benefits and costs of a liability exception is strongly weighted in favor of the benefits when the impact on the patentee's market is minimal. Not only does protecting the market curtail the patentee's specific costs, but it diminishes the risk of a negative impact on

182. *Id.* at 312 ("A pharmaceutical company seeking to reduce risk by diversifying into less risky . . . research and development will likely seek out activities in which it already possesses existing expertise. . . . In such a scenario, pharmaceutical research and development is curtailed to achieve the reduced risk via diversification.").

183. *Id.* ("[A] pharmaceutical company may attempt to achieve a healthy balance sheet by reducing expenditures on research, development, and testing.").

184. *See id.* at 312–13 ("The result of reducing risks by not developing pharmaceuticals that might be [subject to lost exclusivity] is the same as reducing risks through diversification—a decrease in the creation of breakthrough pharmaceuticals. . . . Studies [also] indicate that the level of spending on research, development, and testing directly corresponds with the creation of new pharmaceuticals. . . . Accordingly, reducing research, development, and testing expenditures would most likely result in the reduction, and possibly the elimination, of the creation of breakthrough pharmaceuticals."); *see also* SCHACHT & THOMAS, INTELLECTUAL PROPERTY ISSUES, *supra* note 33, at 3.

185. *See* BOURGOIN, *supra* note 34, at 4–5.

186. *See* SCHACHT & THOMAS, INTELLECTUAL PROPERTY ISSUES, *supra* note 33, at 13.

187. *See supra* note 26 and accompanying text.

innovation, maximizing overall social welfare and information production. *Pre-Momenta*, the combination of two factors kept the safe harbor's market impact in check: (1) the restriction of the safe harbor to pre-approval activities; and (2) the historical dominance of small molecule drugs. *Post-Momenta*, these factors no longer function to adequately curb market harm to the patentee.

1. *Pre-Momenta* Safeguards

The first factor traditionally limiting the safe harbor's market impact was the lack of jurisprudence extending safe harbor protection after FDA approval.¹⁸⁸ Restricting the safe harbor to pre-approval activities shields pharmaceutical patent holders from market harm by excluding essentially all commercially significant activities from protection.¹⁸⁹ Because a drug cannot be sold until approved, pre-approval infringement does not result in significant commercial competition for the patent holder;¹⁹⁰ continued unauthorized use after approval to commercialize a product would expose the unauthorized user to infringement liability.¹⁹¹ Competitors faced with such a pre-approval restriction must therefore refrain from unauthorized sales of an infringing product until the relevant patents expire or risk an infringement suit.¹⁹² Either way, the patent holder's commercial exclusivity expectations are preserved during the life of the patent.

Even absent an explicit restriction limiting the safe harbor's scope to pre-approval activities, the established dominance of small molecule drugs has been a second factor limiting market harm. Specifically, the relatively straightforward na-

188. See *supra* note 126 and accompanying text.

189. See, e.g., Committee Report, *supra* note 73, pt. 1, at 45 ("This section does not permit the commercial sale of a patented drug by the party using the drug to develop such information . . ."); *id.* pt. 2, at 30 (noting that the interference from the limited testing of a drug for approval purposes is "de minimus"). But see *id.* pt. 1, at 45 ("[I]t does permit the commercial sale of research quantities of active ingredients to such party.")

190. See *Hearing*, *supra* note 73, at 926 (memorandum of Alfred B. Engelberg, Patent Counsel, Generic Pharmaceutical Industry Association) ("[T]he limited testing activity required to obtain FDA approval of a generic drug would not normally result in the use of even a single generic tablet for its therapeutic purpose during the life of a valid patent.")

191. Committee Report, *supra* note 73, pt. 2, at 30 ("[T]he generic manufacturer is not permitted to market the patented drug during the life of the patent . . .").

192. See 35 U.S.C. § 271(a) (2006).

ture of small molecule drug development creates a de facto barrier to post-approval commercial competition.¹⁹³ Because “small molecule drugs . . . can [generally] be synthesized relatively easily and characterized readily with laboratory techniques,”¹⁹⁴ protection for small-molecules is focused on patents claiming either the product itself or a method of using the product to treat a particular condition.¹⁹⁵ Prior to approval, unauthorized use of these patented compounds or methods has value related to information production but cannot result in drug sales.¹⁹⁶ After approval, however, the value of the compound or treatment method is generally associated with commercial sales.¹⁹⁷ This commercial consumption lacks a nexus to FDA requirements.¹⁹⁸ Without that nexus, most post-approval unauthorized uses fall outside the safe harbor’s statutory language specifying the use be related to submitting information required by law.

2. Post-Momenta Considerations

Unfortunately, evolution of the safe harbor and the pharmaceutical industry has eroded the effectiveness of these implicit safeguards, leaving the safe harbor in need of reform for the twenty-first century. Still, neither strictly limiting the safe

193. See Woodage, *supra* note 93, ¶ 11 (“Because small-molecule drugs . . . have simple chemical structures, it is relatively easy to establish chemical identity between a generic competitor and its corresponding reference product.”).

194. Therapeutic Research Center, *Approval of Generic Enoxaparin (Lovenox)*, PHARMACIST’S LETTER/PREScriBER’S LETTER, Sept. 2010, at 1, 1, available at <http://pharmacytechniciansletter.therapeuticresearch.com/pldetaildocuments/260902.pdf?cs=&s=PTL>.

195. See 21 U.S.C. § 355(b)(1) (2012) (requiring applicants to only list patents claiming the drug or its method of use, not patents on manufacturing methods); Woodage, *supra* note 93, ¶ 5 (“[C]onsideration of manufacturing methods will play an important role . . . in patent litigation between . . . biologic manufacturers in ways that they have not in the small-molecule drug context.”).

196. See *supra* notes 51–52 and accompanying text.

197. See, e.g., Michael Vella et al., *Behind the Footnote in Merck KGaA v. Integra*, PHARMACEUTICAL L. INSIGHT, Oct. 2005, at 1, 2, available at <http://www.mofo.com/files/Publication/e729ab19-a8f6-42fd-a4b6-2dda18b5ce8c/Presentation/PublicationAttachment/3c993a04-f119-4a58-b276-dede5a9cd846/0510Merck.pdf> (“[P]atented drug products['] . . . value primarily resides in commercial sales to the general public after FDA approval . . .”).

198. See *Teva Pharm. USA, Inc. v. Sandoz Inc.*, Nos. 09 Civ. 10112(KBF), 10 Civ. 7246(KBF), 2013 WL 3732867, at *8 (S.D.N.Y. July 16, 2013) (emphasizing that selling a patented invention to others is not a use protected under the safe harbor and likening such commercialization to “a square peg in a round hole”).

harbor to pre-approval activities (*Classen*) nor unrestrictedly expanding it post-approval (*Momenta*) adequately balances innovation and access in a complex-molecule drug market. The *Momenta* decision itself highlights the significant shortcomings of such a bright-line distinction.

a. *The Reduced Benefits of a Pre-Approval Limitation*

Hatch-Waxman's expedited market entry for generic competitors upon expiration of the brand patents does not always work as intended when it comes to complex small molecule drugs and biosimilars. For traditional small molecules, a chemical compound that comes off patent generally can be copied and its identity verified through basic, publicly available, analytical chemistry techniques.¹⁹⁹ But with more complex molecules, small differences in manufacturing can significantly affect the end product and cause its molecular composition to vary.²⁰⁰ This potential for variation creates challenges for showing bioequivalence of small molecule drugs or establishing that a biosimilar is "highly similar" to its reference product.²⁰¹ Satisfying these standards may often require developing novel analytical techniques to verify the identity of each commercial batch of drug marketed after FDA approval.²⁰² While developing such techniques could create significant barriers to generic entry, those techniques may also be eligible for patent protection

199. See, e.g., SCHACHT & THOMAS, INNOVATION ISSUES, *supra* note 74, at 2–3 ("Typical pharmaceutical products consist of small molecules . . . that may be readily characterized and reproduced through well-understood chemical processes."); see also *supra* notes 193–94 and accompanying text.

200. Huub Schellekens, *Biosimilar Therapeutics—What Do We Need to Consider?*, 2 NEPHROLOGY DIALYSIS TRANSPLANTATION PLUS i27, i28 (2009), available at http://ckj.oxfordjournals.org/content/2/suppl_1/i27.full.pdf+html ("Small changes in, or differences between, manufacturing processes may have a significant impact on the quality, purity, biological characteristics and clinical activity of the final product.").

201. See, e.g., *Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1350 (Fed. Cir. 2012), *cert. denied*, 133 S. Ct. 2854 (2013); Lisa S. Rotenstein et al., *Opportunities and Challenges for Biosimilars: What's on the Horizon in the Global Insulin Market?*, 30 CLINICAL DIABETES 138, 139 (2012), available at <http://clinical.diabetesjournals.org/content/30/4/138.full.pdf+html>.

202. Ewa M. Davison & David K. Tellekson, *Murky Waters: Post-Approval Regulatory Activities and the § 271(e)(1) Safe Harbor*, INTELL. PROP. BULL. (Fenwick & West LLP, Mountain View, Cal.), Winter 2013, at 3, 5, available at <https://www.fenwick.com/FenwickDocuments/Intellectual-Property-Bulletin-Winter-2013.pdf> ("Such manufacturers may . . . seek patent protection for the analytical and quality control methods that they often must develop to satisfy FDA regulations requiring a demonstration that the biosimilar 'is highly similar to the reference product.'"); see also *Momenta*, 686 F.3d at 1348.

and reward those entities investing in their development with a period of exclusivity.²⁰³

The fact that the *Momenta* dispute was between two generic manufacturers punctuates this new reality. *Momenta* sought to exclude other generic competitors on the basis of a patent wholly separate from any patents on the actual drug product, which had already entered the public domain.²⁰⁴ Furthermore, the litigated patent related to a method endorsed, although not specifically required, by the FDA for producing the identity data necessary to maintain approval of any generic version of the drug.²⁰⁵ The additional hurdle created by the extra identity requirements gave *Momenta* an edge over other generic rivals and slowed the proliferation of generic competition.²⁰⁶

But it is exactly this competition created by *multiple* generic entrants that produces meaningful reductions in price.²⁰⁷ A system imposing additional patent-based barriers to market entry after the brand patents expire hinders subsequent entrants and encumbers realization of the social benefits associated with generic competition.²⁰⁸ Thus a public-benefit rationale exists for limiting the right to exclude associated with these added patent barriers, similar to the justifications supporting the safe harbor's original enactment.²⁰⁹ In fact, the significantly higher prices associated with complex pharmaceuticals like biologics mean the positive externalities associated with competition are particularly acute.²¹⁰ At the same time, categorically limiting the safe harbor to pre-approval uses could allow patent protection on required post-approval manufacturing and quality control methods to completely freeze competitors out of the

203. See Davison & Tellekson, *supra* note 202, at 5.

204. *Momenta*, 686 F.3d at 1349–52.

205. See *id.* at 1351–53.

206. *Id.* at 1351.

207. See, e.g., U.S. GOV'T ACCOUNTABILITY OFFICE, *supra* note 1, at 1 n.4 (“[R]esearch has shown that generic drug prices decrease relative to the number of generic manufacturers that enter the market.”).

208. See *supra* notes 60–61 and accompanying text (discussing the patent-based barrier to entry ratified in *Roche*).

209. See Weiswasser & Danzis, *supra* note 57, at 590 (highlighting Congress's concern with escalating drug prices and its desire to remove barriers to competition to control costs).

210. See BOURGOIN, *supra* note 34, at 1 (presenting both the high costs of biologics and the estimated cost savings from biosimilars); see also *supra* notes 35–37, 40 and accompanying text.

market.²¹¹ A pre-approval liability exception alone is therefore insufficient to achieve the safe harbor's intended public benefits of reduced prices and increased access in a world of biologics and complex small molecule drugs.

b. The Increased Costs of a Post-Approval Application

An unqualified extension of safe harbor protection to all post-approval activities, however, also does not adequately balance innovation and access. This approach—the approach essentially endorsed in *Momenta*—would produce individual and social costs arguably outweighing the benefits associated with increased biologic competition. Again, the explanation rests in the importance of manufacturing method patents to complex drugs.²¹² These patents implicate commercial activities that occur after FDA approval in a manner dissimilar to product patents. Unlike a patented product, whose value derives primarily from post-approval commercial consumption that is unequivocally excluded from safe harbor protection,²¹³ a method patent has independent commercial value when used to produce a sellable product.²¹⁴ This commercial production intrinsically implicates post-approval activities. *Momenta* demonstrates that if the method generates FDA-required information—which it arguably often will²¹⁵—extending § 271(e)(1) to cover post-approval uses could shield infringers from liability for the entire useful lifespan of the patent.²¹⁶

Permitting rivals to freely exploit the patented method allows them to capitalize on the method's commercially beneficial uses and produce a competing product without incurring any of the costs associated with developing the method.²¹⁷ This essentially creates a free-rider situation and imposes significant in-

211. *Momenta*, 686 F.3d at 1359 (expressing concern for the situation “where a drug has received approval, but is nevertheless kept from the market based on an FDA mandated testing requirement”).

212. See *supra* notes 200–03 and accompanying text.

213. See *supra* note 198 and accompanying text.

214. See *Momenta*, 686 F.3d at 1351.

215. See *id.* at 1367 (Rader, J., dissenting) (noting that the interpretation of “submission” to include record retention for inspection purposes “would allow almost *all* activity by pharmaceutical companies to constitute ‘submission’ and therefore justify a free license to trespass” (emphasis added)).

216. *Id.* at 1366 (“[T]his court rewrites the law to allow Amphastar to infringe *Momenta*’s patent throughout the *entire life of Momenta*’s patent and for the purpose of obtaining profits on *commercial sales* of a product that *competes with the patentee*.”).

217. See *id.* at 1362.

dividual market harm on the patentee.²¹⁸ Because market harm correlates with the ease of substitution, the greatest risk for market harm with biologics stems from directly substitutable interchangeable biologics and closely competing biosimilars²¹⁹—the exact products the BPCIA was designed to foster.²²⁰ This explains why the developing biosimilar market is particularly affected by post-approval application of the safe harbor.

The potential for market harm is compounded by the safe harbor's design, which forecloses several options a patent owner generally has when its exclusive rights are threatened. First, the statute fails to secure a royalty or alternative remuneration for the patentee to offset a decrease in market share.²²¹ Second, the safe harbor actually creates a disincentive to license the patented technology. Not only does § 271(e)(1) not require any sort of dialogue between the parties,²²² but the lack of remuneration hinders potential licensing agreements.²²³ While a patent owner faced with the safe harbor may be more inclined to negotiate, the competitor's incentive is reduced—the possibility of free, unrestricted use of the patent is apt to outweigh the terms of most potential licensing agreements.²²⁴ Even the threat of litigation loses its luster as a bargaining tool under the safe harbor, as the wide array of information mandated by the FDA and the significant judicial expansion of the safe harbor's scope have greatly increased the likely umbrella of protection for would-be infringers.²²⁵

Absent remuneration or a license, the primary benefit retained by a patent holder faced with competition from an infringer excused under the safe harbor is whatever market position it was able to secure prior to the competitors' entrance.²²⁶

218. *See id.*

219. *See supra* notes 146, 151–54 and accompanying text.

220. *See supra* notes 85–87 and accompanying text.

221. *See* 35 U.S.C. § 271(e) (2006 & Supp. V 2011); *see also Momenta*, 686 F.3d at 1362 (Rader, J., dissenting).

222. *See* 35 U.S.C. § 271(e)(1) (2006).

223. *Cf. Yosick, supra* note 167, at 1303 (explaining that the threat of remuneration for excused infringement “provide[s] a strong incentive for parties to negotiate among themselves to reach an agreement”).

224. *See Momenta*, 686 F.3d at 1362 (Rader, J., dissenting).

225. *See id.* at 1367; *supra* note 215.

226. *See, e.g., Henry G. Grabowski et al., Evolving Brand-Name and Generic Drug Competition May Warrant a Revision of the Hatch-Waxman Act*, 30 HEALTH AFF. 2157, 2158 (2011) (associating early entry and exclusivity with price discrimination that can lead to “substantial revenues and profits,” as

But while the BPCIA grants a pioneer biologic a substantial twelve years of regulatory exclusivity,²²⁷ the first interchangeable approved only receives a median period of exclusivity of eighteen months.²²⁸ There is no exclusivity granted for subsequent interchangeable products or biosimilars.²²⁹ These exclusivity periods remain unchanged even if the follow-on manufacturer invests substantial time and resources developing methods to satisfy the FDA's criteria for demonstrating "sameness."²³⁰ After *Momenta*, the safe harbor permits later entrants to use those same methods to produce interchangeable or easily substitutable products without consideration for the timing of the innovator's market entry or the opportunity for exclusive market occupation.²³¹ Thus the safe harbor makes it likely two manufacturers will be similarly situated in the market despite only one of them having invested the resources to produce the necessary technology. The result is little to no advantage—patent or otherwise—bestowed on these forerunners of follow-on biologic development.

Nowhere is the potential for extreme devaluation of these types of process patents by an unrestrained safe harbor more obvious than in the *Momenta* decision itself. As Judge Rader noted in his dissent, the unchecked application of the safe harbor to post-approval uses of process patents removes the patent owner's right to exclude during any part of the patent life and "essentially render[s] manufacturing method patents worthless."²³² He concluded by emphasizing the inequities of such a

well as the "first mover' advantage, meaning that even when price is matched, the first [entrant] may be likely to capture a higher share of the market").

227. 42 U.S.C. § 262(k)(7)(A) (2006).

228. See *id.* § 262(k)(6) (providing a range of exclusivity from twelve to forty-two months depending on the litigation status of the interchangeable application at the time of the subsequent filing, with eighteen months of exclusivity granted for applications unencumbered by litigation).

229. See *id.*; Ronald A. Rader, *An Analysis of the US Biosimilars Development Pipeline and Likely Market Evolution*, BIOPROCESS INT'L, June 2013, at 16, 20, available at http://www.bioprocessintl.com/multimedia/archive/00219/BPI_A_131106SUPAR02_219312a.pdf ("[B]iosimilars get no reward for being first to market. In fact, the first companies to file will probably bear the brunt of resolving patent disputes, which could cost tens of millions of dollars, allowing products filed/approved later to avoid much of that trouble. The first to file also will probably have to face more regulatory hurdles.").

230. See 42 U.S.C. § 262(k)(6); Rader, *supra* note 229, at 20.

231. See 35 U.S.C. § 271(e)(1) (2006).

232. *Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1369 (Fed. Cir. 2012) (Rader, J., dissenting), *cert. denied*, 133 S. Ct. 2854 (2013).

system that “abrogates [an entity’s] hard-achieved property right and reallocates that entitlement to its competitors.”²³³

Momenta also foreshadows the corresponding decrease in innovation likely to accompany this extreme devaluation of manufacturing method patents. Because Amphastar manufactured an exact substitute for Momenta’s enoxaparin product, the court excused otherwise infringing activities with the highest market significance for the patentee.²³⁴ The court’s liberal interpretation of § 271(e)(1)’s liability exception also makes its applicability to similar analytical methods for demonstrating “sameness” not only predictable, but almost a foregone conclusion.²³⁵ Together those factors create the perfect storm to deter would-be innovators considering investing the significant time and resources needed to bring a biosimilar or generic complex small molecule drug to market.²³⁶ They also discourage later entrants from innovating better methods for meeting the FDA’s similarity requirements.²³⁷ Ultimately, *Momenta* makes clear that unchecked application of the safe harbor to post-approval activities fails to adequately uphold the safe harbor’s objective of preserving innovation.

III. A NEW SAFE HARBOR FRAMEWORK POST- *MOMENTA*

The time has come to take the safe harbor in a new direction. This Part reasons that § 271(e)(1)’s impact on market significance must be readjusted to preserve an equilibrium between the costs and benefits of the safe harbor in today’s changing pharmaceutical landscape. While some desirable im-

233. *Id.* at 1376 (further characterizing the development as “a sad day for property owners and an undeserved victory for those who decline to invest in the expense and difficulty of discovery and invention”).

234. *See id.* at 1351 (majority opinion) (“The approval of Amphastar’s version of enoxaparin, and the resultant ruinous competition of another generic version of the drug, threatened [Momenta’s] unique market position.”); *supra* notes 144–46, 151–52 and accompanying text.

235. *See Momenta*, 686 F.3d at 1370 (Rader, J., dissenting); *supra* note 167 and accompanying text.

236. *See Momenta*, 686 F.3d at 1370 (Rader, J., dissenting) (comparing the court’s outcome to “a teacher who rewards the top student by allowing her peers to copy her exam answers” to explain how the decision “does violence to patent law and future research incentives in this field”).

237. *See, e.g., id.* at 1369 (“Amphastar is free to invent its own method to satisfy these requirements. Instead it chooses to trespass.”); *id.* at 1370 (“[If] this court would permit copiers to infringe[, w]hat incentive remains to invest in inventing a better test?”).

provements to the safe harbor are specific to biologics, other ways to enhance the overall equity of the doctrine apply indiscriminately to all pharmaceuticals. Regardless, change is required to increase the chance that the BPCIA's abbreviated approval pathway will produce a meaningful follow-on biologic market that balances innovation and access.

The complexities of the problem suggest a three-step approach. First, the BPCIA's patent litigation procedures should include enhanced notification provisions that better reflect the types of patent protection associated with biologic development. Second, the FDA should delay market entry for all entities relying on safe harbor protection as a shield from infringement liability for activities related to the commercial manufacture, use, or sale of a product that has obtained federal regulatory approval. This step specifically includes extending the BPCIA's exclusivity provisions for interchangeable products to all follow-on biologics. Finally, patent owners should receive a reasonable royalty for all safe harbor uses of their respective patents. By reducing the market harm to patentees, the combination of these compensation mechanisms should minimize potential barriers to innovation.

A. LITIGATION FRAMEWORK

A key component of the abbreviated approval pathways under both Hatch-Waxman and the BPCIA is that they provide mechanisms for identifying and resolving patent disputes.²³⁸ These dispute resolution procedures work to facilitate equitable competition by resolving patent challenges posed by subsequent competitors before the competing product is approved.²³⁹ This prevents market entry from being delayed by unproductive litigation while identifying valid patent barriers to competition.²⁴⁰ It is during this dispute resolution process that a biologic manufacturer accused of infringement might invoke safe harbor protection in defense of its activities.

The existing BPCIA provisions, however, are inadequate to fully embrace effective patent dispute resolution because they only address conflicts between the sponsors of reference prod-

238. See *supra* notes 66, 92 and accompanying text.

239. See, e.g., Weiswasser & Danzis, *supra* note 57, at 595.

240. See, e.g., Ashlee B. Mehl, Note, *The Hatch-Waxman Act and Market Exclusivity for Generic Drug Manufacturers: An Entitlement or an Incentive?*, 81 CHI.-KENT L. REV. 649, 650 (2006).

uct applications and follow-on manufacturers.²⁴¹ But as explained above, potential patent disputes in the biologic realm are not confined between reference product sponsors and manufacturers of follow-on products.²⁴² Disputes can just as easily arise between two follow-on manufacturers.²⁴³ Although nothing prevents approved follow-on applicants from relying on traditional channels to uncover potential infringement,²⁴⁴ the absence of any notice mechanism increases the chance that potentially infringing activities will not be discovered until well after the competing product is commercialized. Thus, in order to fully embrace the equities of the proposed solution, the biologic dispute resolution procedures should also facilitate the identification and resolution of patent conflicts between these stakeholders. Such provisions would decrease the chance of unknown infringement of patented manufacturing methods, bolstering confidence in the value of the invention.

Helpfully, the BPCIA already incorporates a framework for notifying the reference product sponsor of all patents—including manufacturing and quality control method patents—potentially infringed by a follow-on applicant.²⁴⁵ The BPCIA should be amended to further require that subsequent follow-on applicants give similar notice to all previously approved manufacturers of the particular product for which they are seeking approval. Although a complete assessment of the intricacies of the BPCIA is beyond the scope of this Note, an effective amendment could theoretically be as simple as adding the language “or previously approved subsection (k) applicant(s)” wherever the term “reference product sponsor” appears in 42 U.S.C. § 262(l).²⁴⁶

Of course, increased disclosure raises concerns about confidentiality for manufacturing systems and other proprietary information. As an initial safeguard, the BPCIA protects the dis-

241. See 42 U.S.C. § 262(l) (2006).

242. See *supra* notes 201–06 and accompanying text.

243. Cf. *Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1361 (Fed. Cir. 2012) (deciding a suit between generic manufacturers of a complex small molecule drug), *cert. denied*, 133 S. Ct. 2854 (2013).

244. Cf. *id.* at 1349–52 (resulting in patent infringement litigation despite the absence of notification procedures covering the patent-in-suit).

245. See 42 U.S.C. § 262(l).

246. 42 U.S.C. § 262(l) refers to an applicant for a follow-on product as a “subsection (k) applicant” in reference to § 262(k), the subsection governing the “licensure of biological products as biosimilar or interchangeable.” See *id.* § 262(k); *id.* § 262(l).

semination of confidential data by limiting the permitted recipients of such information.²⁴⁷ The proposed amendment includes a further safeguard by only requiring notice be given to previously approved follow-on applicants. This limitation recognizes the increased risk for improper appropriation of information by entities competing for approval as those entities are actively engaged in modifying their applications. Further, because the FDA could ultimately deny both applications, the potential controversy between two unapproved applicants is not ripe. If one manufacturer's follow-on application is ultimately granted, that manufacturer could activate the disclosure requirements by following procedures similar to those laid out in the BPCIA for newly acquired patents.²⁴⁸

Notably, the proposed amendment does not address the potential for conflict between two biologic reference product applicants. It also does not provide for notification of potential infringement pertaining to "method of making" patents under Hatch-Waxman. But in response to this first potential concern, a biologic approved as a reference product and not as a follow-on product cannot be directly substituted for another product without prescriber intervention, lessening the threat of direct market competition between two reference products.²⁴⁹ As for the second concern, history demonstrates that the importance of manufacturing method patents is the exception and not the norm in the context of Hatch-Waxman's ANDA provisions.²⁵⁰ And as *Momenta* demonstrates, traditional methods for discovering infringement still exist for those infrequent instances involving the few complex small molecule drugs where manufacturing method patents might play a role.²⁵¹

247. *Id.* § 262(l)(1).

248. *See id.* § 262(l)(7) (requiring notice of all potentially infringed patents within thirty days of the newly acquired right).

249. *See supra* notes 153–56 and accompanying text.

250. *See supra* notes 193–98 and accompanying text (explaining how manufacturing method patents have not been important for small molecule drugs under Hatch-Waxman).

251. *See Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1366 (Fed. Cir. 2012) (Rader, J., dissenting), *cert. denied*, 133 S. Ct. 2854 (2013).

B. MARKET EXCLUSIVITY²⁵²

A second way to restore equity to the safe harbor is to counteract a liability exception granted for activities related to the *commercial* manufacture, use, or sale of an FDA-regulated product with a period of market exclusivity for the patent holder. Thus, when the safe harbor protects these commercial activities, the FDA should be required to stay approval of the otherwise-infringing entity's application. If the competing application is already approved, the FDA should suspend it. Similar to the BPCIA's current provisions granting exclusivity to the first interchangeable biologic, the period of exclusivity should depend on the approval and litigation status of the patent holder's application.²⁵³ In this vein, a system mimicking these highly scrutinized exclusivity periods in the BPCIA might be sufficient—providing exclusivity for twelve months after the first commercial marketing of the patentee's product, eighteen months if the product has yet to be commercialized but is unencumbered by litigation, or forty-two months if litigation is ongoing.²⁵⁴

Set exclusivity periods may not be workable in all conflict permutations, however. Because of the potential for cross-litigation in a field with multiple follow-on entrants, a defined period of exclusivity obtained in litigation with one competitor may expire while locked in litigation with another. Accordingly, a period based on independent expert review that accompanies a safe harbor determination may be more desirable. Nonetheless, even with defined exclusivity periods the proposed solution provides benefits over the status quo by preventing a free-rider from usurping market share from the patentee. Although exclusivity periods already exist for brand-name small molecule drugs,²⁵⁵ biologic reference products,²⁵⁶ the first generic ANDA filer,²⁵⁷ and the first interchangeable biologic,²⁵⁸ this proposal

252. Although referred to as market exclusivity for convenience, the proposal embodied in this section envisions scenarios where the recipient of the "exclusivity" term is not in fact the exclusive market player (or even the exclusive generic or biosimilar manufacturer). Nonetheless, delayed approval of competitors creates some form of exclusivity for the recipient as compared to those later market entrants.

253. See 42 U.S.C. § 262(k)(6).

254. *Id.*

255. 21 U.S.C. § 355(j)(5)(B)(iv) (2012).

256. 42 U.S.C. § 262(k)(7) (2006).

257. 21 U.S.C. § 355(j)(5)(B)(iii).

258. 42 U.S.C. § 262(k)(6).

would further promote innovation and market entrance by subsequent interchangeable biologics, biosimilars, and complex small drug manufacturers.²⁵⁹ Moreover, entities wanting to circumvent an imposed period of exclusivity may be incentivized to innovate alternatives to patented methods for satisfying FDA requirements.²⁶⁰

This prong of the solution eases the burden of the safe harbor on the primary benefit conferred upon a patent holder—the right to exclude. As noted above, elimination of this right under the safe harbor can either be temporary or persist for the entire life of the patent.²⁶¹ Delaying market entry of competitors benefiting from a liability exception granted under the safe harbor reintroduces the concept of exclusivity.

Market exclusivity is a common incentive in the world of pharmaceuticals and FDA regulation, and its frequent use highlights its commercially significant benefits.²⁶² For traditional small molecule pharmaceuticals, early market entrance is a strong predictor of success and profits.²⁶³ Market exclusivity is expected to have an even stronger correlation with success or failure in the field of follow-on biologics, and the availability (or lack thereof) of market exclusivity may determine whether or not the abbreviated pathway for follow-on biologics takes hold.²⁶⁴ Since direct competition from less expensive substitutes lowers drug costs, success of the abbreviated pathway for biologics is key to reducing health care costs in this expanding field.²⁶⁵

Importantly, the proposed solution does not limit this remedy to follow-on biologics, much less interchangeable biologics or even BPCIA-regulated products. *Momenta* demonstrates that the safe harbor indiscriminately imposes its inequities and

259. See *supra* notes 212–16 and accompanying text (explaining how these entities are most likely to be affected by commercially significant applications of post-approval safe harbor protection).

260. Cf. *supra* note 237 and accompanying text.

261. See *supra* note 216 and accompanying text.

262. See Aaron S. Kesselheim, *Using Market-Exclusivity Incentives to Promote Pharmaceutical Innovation*, 19 NEW ENG. J. MED. 1855 (2010).

263. David Reiffen & Michael R. Ward, *Generic Drug Industry Dynamics*, 87 REV. ECON. & STAT. 37, 39 (2005) (“If a [generic pharmaceutical] firm obtains early approval, it is likely to earn a positive return on its application-related costs, whereas firms obtaining approval later in the process are likely not to recover their sunk costs.”).

264. See SCHACHT & THOMAS, *INTELLECTUAL PROPERTY ISSUES*, *supra* note 33.

265. See *supra* note 39 and accompanying text.

can have significant commercial implications for certain small molecule drugs.²⁶⁶ In response, indiscriminate market exclusivity for all commercial applications of the safe harbor is desirable. As the class of pharmaceuticals most likely to be impacted by commercial applications of the safe harbor, however, follow-on biologics can be expected to benefit most from this remedy.

C. REASONABLE ROYALTY

Finally, the imposition of a reasonable royalty for all safe harbor uses would reduce the inequities caused by § 271(e)(1)'s invariable creation of "free-riders" that receive the benefits of innovation without incurring any of the costs. To be effective, a royalty must be high enough to ensure the patentee realizes some profits but low enough to allow for price competition by the excused infringer.²⁶⁷ Imposing a royalty in this "sweet spot" should preserve incentives to innovate while still creating meaningful reductions in drug price.²⁶⁸ Importantly, the existence of the royalty alone may actually reduce safe harbor lawsuits by encouraging parties to negotiate a license and forgo litigation.²⁶⁹ And in situations where negotiations are unsuccessful or impractical, courts can readily impose the royalty alongside a judicial determination that the safe harbor applies.²⁷⁰

With the importance of setting an effective royalty rate in mind, opponents of reasonable royalties often lament the difficulty of determining their value.²⁷¹ Specifically, it can be problematic to determine the infringed patent's value to both the patent owner and the infringer.²⁷² This is particularly challenging in a context of a liability exception permitting ongoing behavior because the royalty applies not only to past infringement but also to any future infringement that occurs while the

266. See *Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1376 (Fed. Cir. 2012) (Rader, J., dissenting), *cert. denied*, 133 S. Ct. 2854 (2013).

267. See Yosick, *supra* note 167, at 1303.

268. See *id.*

269. *Id.* at 1298, 1303.

270. See *id.*

271. *Id.* at 1298.

272. *Methodologies for Determining Reasonable Royalty Damages*, FISH & RICHARDSON, <http://www.fr.com/reasonableroyalty/> (last visited Mar. 10, 2014).

exception endures.²⁷³ Because the protection granted by the safe harbor has the potential to last the entire duration of the patent, adequately predicting the future value of the patent is especially important for preserving the incentive to innovate.

This difficulty alone, however, is no justification for embracing an inequitable and detrimental status quo that provides no compensation. Moreover, valuation of reasonable royalties is a common occurrence.²⁷⁴ For example, judicial determinations of non-injunctive relief in antitrust and patent infringement suits provide precedent for setting royalty rates.²⁷⁵ In this context, experts can often assist in valuing the patent.²⁷⁶

Indeed, federal regulation makes the pharmaceutical industry well-suited to expert valuation of royalties.²⁷⁷ Because the date of entry of the generic can be determined in advance, “the size of the potential revenue in each market can be projected with some accuracy.”²⁷⁸ A reasonable royalty based on market potential can then be calculated by extrapolating that data based on the number of entrants at any given time.²⁷⁹

273. See Neal E. Solomon, What Is a Reasonable Royalty? A Comparative Assessment of Patent Damages Methodologies 3 (June 11, 2010) (unpublished manuscript), available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1623982 (arguing that reasonable royalties tend to “undervalue patents by an *ex post facto* view of future and unknowable markets”).

274. Richard F. Cauley, *Defunding the Trolls: Attacking the Damages Claim*, IP LAW 360 (Portfolio Media, Inc., New York, N.Y.), Mar. 14, 2008, at 1, available at <http://www.whglawfirm.com/CM/Articles/Defunding%20the%20Trolls.pdf> (“The most common award for patent infringement . . . is a ‘reasonable royalty’ . . .”).

275. Yosick, *supra* note 167, at 1303; see, e.g., *Maxwell v. J. Baker, Inc.*, 86 F.3d 1098, 1109–10 (Fed. Cir. 1996) (discussing the calculation of reasonable royalties); *TWM Mfg. Co. v. Dura Corp.*, 789 F.2d 895, 900–02 (Fed. Cir. 1986) (same), *cert. denied*, 479 U.S. 852 (1986); see also *Ga.-Pac. Corp. v. U.S. Plywood Corp.*, 318 F. Supp. 1116, 1120 (S.D.N.Y. 1970) (listing fifteen factors courts may consider in determining a reasonable royalty), *modified*, 446 F.2d 295 (2d Cir. 1971), *cert. denied*, 404 U.S. 870 (1971). See generally *Methodologies for Determining Reasonable Royalty Damages*, *supra* note 272 (providing an overview of several methodologies for assessing reasonable royalties).

276. See generally Glenn S. Newman et al., *How Reasonable Is Your Royalty?*, J. ACCT., Sept. 2008, at 56 (detailing considerations for experts assisting in calculating royalties).

277. See Reiffen & Ward, *supra* note 263, at 37 (“[B]ecause a market begins when the patent on an existing drug expires, the date at which the market opens to competitors is known in advance and the potential revenue can be projected with some accuracy . . .”).

278. *Id.*

279. See *id.*

The possibility that some stakeholders will no longer be able to afford to innovate if required to pay for the technology is another primary justification for excluding royalties from the safe harbor.²⁸⁰ The concern is that research and development often implicates several patents held by multiple companies and that a need to pay each company to use the relevant patents may outweigh the value of any potential end-product of the research.²⁸¹ This argument is amplified in contexts where the research is targeted at developing an intermediary product or research tool that has little or no commercial value in and of itself.²⁸² In those situations, an inventor faced with one or more restrictions on the right to exclude may simply choose to abandon the research altogether.²⁸³

This argument, however, is of decreased relevance among pharmaceutical manufacturers as the end research goal is generally a commercial product with the potential for significant market returns.²⁸⁴ Moreover, a case-by-case royalty amount, rather than a fixed rate, mitigates these concerns and allows for adjustment of the remedy in each specific situation to better promote the safe harbor's goals. For one thing, individual royalty awards mean less commercially valuable or less frequently used technology can be priced accordingly.²⁸⁵ And while safe harbor protection does not turn on a lack of non-infringing alternatives, a case-by-case approach permits consideration of available alternatives when setting the rate. Imposing a lower royalty rate when faced with significant technological hurdles and a single means for meeting the FDA's standards could lessen an otherwise high barrier to market entry.²⁸⁶ On the other

280. Cf. Freeburg, *supra* note 42, at 410 ("A common objection to compulsory licensing is that it reduces the incentive to invent . . .").

281. Cf. *id.* at 412 ("Reach-through royalties, where licenses can continue to collect fees on downstream inventions . . . could create a problem of royalty stacking . . .").

282. *Id.* ("[R]oyalty stacking . . . is probably not a good suggestion unless the end product actually *contains* the research tool.").

283. *Id.* (describing how royalty stacking can negatively affect downstream inventions).

284. See *supra* note 45 and accompanying text.

285. *Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1375 (Fed. Cir. 2012) (Rader, J., dissenting) (explaining that patents on research tools have not been proven to impede development because their limited commercial value corresponds with minimal compensation for patent owner), *cert. denied*, 133 S. Ct. 2854 (2013).

286. See *id.* at 1360 (majority opinion) (expressing concern that an FDA requirement for a single testing method will produce a complete barrier to market competition). *But see id.* at 1370 (Rader, J., dissenting) (supporting the

hand, a higher royalty rate could shift activities to non-infringing alternatives if they exist. At the very least, a higher rate rewards subsequent innovators in situations of competing alternatives, which may encourage even more innovation.²⁸⁷ Ultimately, it is this type of flexible system that will best balance the costs of innovation against the costs of increasing access to affordable medication.

CONCLUSION

While the safe harbor once operated to balance innovation and the public interest, market changes and an increasingly broad judicial interpretation of § 271(e)(1) have given rise to the need to revisit its application. In effect, the Federal Circuit's endorsement of the safe harbor's application to post-FDA-approval activities in *Momenta* has the potential to devalue an entire class of key manufacturing method patents related to the quickly developing field of biopharmaceuticals by authorizing unchecked infringement of the patents for commercial purposes. In addition to impacting individual drug markets, the expanded scope of safe harbor protection for significant commercial activity is likely to stifle innovation in an increasingly important field of the pharmaceutical industry, negatively impacting the overall public health and welfare.

The underlying justifications and positive practical effects of the safe harbor can be retained, however, if the statute is adapted to compensate entities whose patent rights are impacted. In addition to enhanced notification provisions for revealing potential infringement among follow-on manufacturers, that compensation scheme should include both a reasonable royalty for all safe harbor applications and a period of exclusivity for patentees faced with excused post-approval commercial infringement of their invention. By allowing patent owners to recoup some of their costs and develop their respective markets, the potentially lucrative return on investment driving current levels of pharmaceutical innovation will be preserved for years to come.

argument that a higher rate could incentivize the development of alternative techniques for meeting requirements).

287. See *id.* at 1370 (discussing the importance of retaining means for incentivizing improvements).

an informed basis, in good faith, and in honest belief the actions they took were in the best interests of the corporation.¹⁸³ The business judgment rule serves as formidable protection for corporate directors and officers. In order for stockholder-plaintiffs to rebut the presumption of enforceability in the context of forum selection clauses, they may introduce evidence of directors' breaches of the duty of care or the duty of loyalty.¹⁸⁴

If stockholder-plaintiffs are successful and rebut the presumption of enforceability, courts should proceed to the third step and review the transaction under an entire fairness standard.¹⁸⁵ This necessarily involves a case-by-case inquiry.¹⁸⁶ In order to flesh out the second and third steps, which are necessarily intertwined, the solution walks through circumstances that may feasibly arise or have arisen in the duty of care and duty of loyalty contexts. Unlike in *Boilermakers*, this exercise does not aim to outline a "parade of horrors" or engage with hypothetical, law school-esque scenarios.¹⁸⁷ Instead, the purpose of ap-

183. *Citron v. Fairchild Camera & Instrument Corp.*, 569 A.2d 53, 64 (Del. 1988) ("As a rule of evidence, [the business judgment rule] creates 'a presumption that in making a business decision, the directors of a corporation acted on an informed basis [i.e., with due care], in good faith and in the honest belief that the action taken was in the best interest of the company.' The presumption initially attaches to a director-approved transaction within a board's conferred or apparent authority in the absence of any evidence of 'fraud, bad faith, or self-dealing in the usual sense of personal profit or betterment.'" (second alteration in original) (citations omitted)).

184. *Smith v. Van Gorkom*, 488 A.2d 858, 872 (Del. 1985) (explaining that the plaintiff has a burden of proof to rebut this presumption by introducing evidence of self-dealing or lack of due care), *overruled on other grounds by Gantler v. Stevens*, 965 A.2d 695 (2009); *see supra* Part I(A).

185. *See Cede & Co. v. Technicolor, Inc.*, 634 A.2d 345, 362-63 (Del. 1993), *modified on reargument*, 636 A.2d 956 (Del. 1994); *Nixon v. Blackwell*, 626 A.2d 1366, 1376 (Del. 1993).

186. *See, e.g., Brown v. Slenker*, 220 F.3d 411, 424 (5th Cir. 2000) ("The existence of a fiduciary duty, and the breach thereof, are both questions of fact."). This approach disavows a bright line rule that advocates for or against the enforceability of forum selection clauses. *Cf. Grundfest & Savelle, supra* note 5, at 402 (rejecting a bright-line rule, but articulating a different fiduciary duties analysis).

187. *Boilermakers Local 154 Retirement Fund v. Chevron Corp.*, 73 A.3d 934, 958 (Del. Ch. 2013). *Compare Grundfest & Savelle, supra* note 5, at 364 ("Courts applying Delaware law to adjudicate the validity of an ICFS provision as adopted therefore need not speculate as to every conceivable circumstance that might later arise in connection with a future effort to enforce that provision under conditions that are unknown and unknowable as of the date of the provision's adoption."), *with Stroud v. Grace*, 606 A.2d 75, 96 (Del. 1992) ("There was no basis to invoke some hypothetical risk of harm rather than an examination of the board's proven, and entirely proper, conduct."). It is appropriate to consider various fact scenarios for the purpose of generating a pre-

plying this framework in possible situations is that they will likely arise in “as-applied” circumstances in future fiduciary duties derivative litigation. Therefore, the duty of care will first be analyzed, followed by the duty of loyalty.

1. The Duty of Care

Plaintiffs may show a violation of the duty of care sufficient to pass step two by demonstrating that directors did not engage in a process of informed decision-making.¹⁸⁸ This analysis requires consideration of more than whether “Delaware courts will fail to hold directors properly responsible for their actions.”¹⁸⁹ Directors must reach their decision to adopt a bylaw with a forum selection clause through “informed, reasonable deliberation.”¹⁹⁰ Fortunately for directors, the travails of multi-jurisdictional litigation and the phenomenon of the lead plaintiff race are well-documented and easily serve as a basis for rational decision.¹⁹¹ In addition, the fiduciaries’ conduct is only actionable if the directors are grossly negligent.¹⁹² Plaintiffs’ assertions that directors fail to consider the effect of forum selection clauses on stockholders likely misses this mark sufficient to rebut the presumption of enforceability à la business judgment rule.¹⁹³ If directors truly were irrational, for example, identifying Delaware as an exclusive forum for a Minnesota corporation, they may come closer to rebutting the presumption of enforceability. Instead, stockholders may be more successful

scriptive decisionmaking framework. In an actual case, the court is bound by the facts, not by hypothetical inquiries. These two situations are distinct, and prescriptive/normative analysis can inform and construct the decisionmaking process.

188. *Van Gorkom*, 488 A.2d at 872. This paragraph assumes that the corporation does not have an exculpation provision described in Delaware law. DEL. CODE ANN. tit. 8, § 102(b)(7) (West 2013).

189. *Contra Grundfest & Savelle*, *supra* note 5, at 402.

190. *Van Gorkom*, 488 A.2d at 872.

191. See *supra* Part I(B). *Contra* Revised Verified Supplement to the Complaint at ¶14, *Boilermakers Local 154 Retirement Fund v. Chevron Corp.*, 73 A.3d 934 (2013) (No. 7220-CS) (“[T]he only duplicative litigation Chevron and its Board have experienced resulted from the *Exclusive Forum Bylaw* whose purported purpose was to avoid duplicative litigation.” (emphasis in original)).

192. See *In re Walt Disney Co. Derivative Litigation*, 907 A.2d 693, 750 (Del. Ch. 2005) (adding that duty of care violations are rarely found).

193. See Verified Complaint at ¶ 95, *Neighbors v. Air Prods. & Chems., Inc.*, No. 7240-CS, 2012 WL 467520 (Del. Ch. Feb. 13, 2012) (arguing *inter alia*, that adoption of a form bylaw evinces directors’ lack of consideration of the specific terms and effects of the bylaw at issue).

in identifying a breach of the duty of loyalty in order to proceed to the third step that triggers the “entire fairness” standard.

2. The Duty of Loyalty

A successful rebuttal of the presumption of enforceability sufficient to proceed to the third step may depend on the timing of the duty of loyalty claim. The timing of duty of loyalty challenges fit into three groups: pre-planning before a suit is filed, after alleged wrongdoing, and in the midst of ongoing litigation. Similarly to the duty of care context, stockholder-plaintiffs face a distinct uphill battle in rebutting the presumption of enforceability sufficient to have a court determine the “entire fairness” of the transaction.

The first scenario is an extension of anti-takeover and poison pill jurisprudence, in which courts allow corporations to keep anti-takeover methods on the shelf for potential, future use.¹⁹⁴ As in that context, it is unlikely that courts would find self-dealing if directors adopted a clause as a form of pre-planning for possible, future derivative litigation.¹⁹⁵

In the second scenario, a board’s adoption of a clause after alleged wrongdoing provides a clearer self-dealing scenario; *Galaviz v. Berg* can be reconciled in this way.¹⁹⁶ In the *Galaviz* scenario, the board can proffer few alternative reasons for their actions other than their self-interest in escaping liability.¹⁹⁷ In so doing, they effectively place their self-interest over the best interests of the corporation and its stockholders. Although confining litigation to Delaware does not assure directors’ success,

194. See Paul H. Edelman & Randall S. Thomas, *Selectica Resets the Trigger on the Poison Pill: Where Should the Delaware Courts Go Next?*, 87 IND. L. J. 1087, 1088–89 (2012) (“Rights plans, or as they are known more pejoratively ‘poison pills,’ enable a target board to ‘poison’ a takeover attempt by making it prohibitively expensive for a bidder to acquire more than a certain percentage of the target company’s stock . . . [Delaware courts generally] have approved traditional rights plans as useful bargaining devices for well-intentioned boards of directors.”).

195. See Grundfest & Savelle, *supra* note 5, at 366 (analogizing forum selection clauses to poison pills as a pre-planning tool for hostile takeovers).

196. See, e.g., *Galaviz v. Berg*, 763 F. Supp. 2d 1170, 11712 (N.D. Cal. 2011). The holding of the *Galaviz* case can be reconciled with this prescriptive framework because, as a matter of corporate law, it implicates a fact scenario that involves self-dealing. *Contra* Grundfest & Savelle, *supra* note 5, at 407 (arguing that the *Galaviz* court ignored controlling precedent when it relied on a vested rights theory to find the forum selection clause unenforceable). A self-dealing supersedes considerations of whether the plaintiffs’ claims have vested.

197. See, e.g., *Galaviz*, 763 F. Supp. 2d at 1171.

it certainly increases their odds.¹⁹⁸ Delaware courts confer benefits on directors, strategic advantages that stockholders do not necessarily share.¹⁹⁹

Finally, directors could also adopt a clause in the midst of pending litigation in a foreign court. Again, stockholders could implicate directors' self-dealing incentives in adopting the clause.²⁰⁰ This scenario provides a direct affront to contract law, although this may be difficult to establish after *Boilermakers* upheld the contractual validity of forum selection in the corporate context.²⁰¹ While the enforceability of forum selection clauses in contract law is well-settled, contract law likely does not allow one party to unilaterally add a forum selection clause after litigation has begun.²⁰² Parties must instead resort to having cases dismissed, transferred, or stayed.²⁰³ Though most cases will likely be stalled at the second step, rebutting the presumption of enforceability of forum selection clauses, the possibility of reaching the "entire fairness" standard provides a roadmap for courts to follow in these cases. Indeed, it provides the best alternative to existing counterarguments.

C. ALTERNATIVES ARE INEFFECTIVE

Yet alternatives exist. Some advocate an outright ban on forum selection bylaws in the corporate context, or a slightly more mediated solution as long as directors engage in good governance.²⁰⁴ Opponents cannot turn a blind eye to the very real inconvenience and waste of resources that is caused by unconstrained multi-jurisdictional litigation.²⁰⁵ In most contexts,

198. See *supra* Part I(B).

199. See *supra* Part I(B).

200. This argument is distinct from whether stockholders have perfected their right to sue in a foreign forum. *But c.f.* Grundfest & Savelle, *supra* note 5, at 377 (discussing how stockholders have typically failed to perfect their right to sue in a foreign jurisdiction).

201. See *Galaviz*, 763 F. Supp. at 1174 ("To whatever degree bylaws may generally be contractual in nature, however, Oracle here seeks to rely on principles of corporate law with respect to how its bylaws could be amended. Oracle has not pointed to any commercial contract case upholding a venue provision that was inserted by a purported unilateral amendment to existing contract terms." (emphasis in original)). *Contra* *Boilermakers Local 154 Retirement Fund v. Chevron Corp.*, 73 A.3d 934, 955 (Del. Ch. 2013).

202. See *supra* Part I(A)(4).

203. See *id.* Whether a court dismisses, transfers, or stays a case depends on the court and/or the state.

204. See *supra* Part II(A)(1).

205. See *supra* Part I(B).

forum selection clauses provide a useful solution to the travails of multi-jurisdictional litigation. A rebuttable presumption of enforceability provides plaintiffs with an avenue in which to bring legitimate fiduciary duties claims, while weeding out strike suits.

Unconditional enforcement of forum selection bylaws faces similar problems, but strikes a different, improper balance. Stockholders with possible fiduciary duties' arguments could be locked out of their preferred venues, in a full concession to multi-jurisdictional problems. Grundfest's "fiduciary out" solution, that allows directors to waive the forum selection bylaw, fits with this Note's proposed solution. Together, they establish a compromise: directors monitor their fiduciary duties and stockholders may rebut the presumption of directors' authority. If directors concede to a venue or stockholders are successful, litigation proceeds; if not, the case continues in Delaware, which is not a bad alternative.

Finally, doing nothing is not an option. This hotly-debated and increasingly-litigated topic demands a solution. This Note provides a fiduciary duties-specific solution for courts outside of Delaware to when they inevitably encounter these cases.

CONCLUSION

In re Revlon, Galaviz, and Boilermakers began the discussion about the enforceability of forum selection bylaws, but significant questions remain. It is unclear how non-Delaware courts will interpret this progression of cases, especially when plaintiffs raise breach of fiduciary duties claims about directors' uses of the forum selection bylaws. This Note proposes and develops a structure for the resolution of these disputes. Forum selection bylaws should be presumptively enforceable because of directors' authority to adopt bylaws. Plaintiffs may challenge this rebuttable presumption by showing that directors breached their duties of care and/or loyalty. If they are successful, directors must demonstrate the "entire fairness" of the forum selection bylaw to stockholders. At all times, directors could waive the forum selection bylaws if their fiduciary duties so require. In this way, courts mediate a compromise between corporate defendants' and stockholder-plaintiffs' competing interests and in effect, organize this section of intracorporate litigation within existing DGCL precedent. For non-Delaware courts, today may not be the day, but when it is, this Note will help them get on their way.
