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Essays

Maintaining Incentives for Healthcare Innovation: A Response to the FTC's Report on Follow-On Biologics

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ADDENDUM—CHRISTOPHER M. HOLMAN, MAY 2010

This article was written and accepted for publication prior to the recent passage of health care reform legislation. At that time, Congress was debating creation of an abbreviated marketing approval pathway for follow-on biologics (FOBs). Although there was broad support for the creation of some form of abbreviated FOB approval pathway, the specific contours of the proposed legislation proved to be quite contentious, resulting in the introduction of multiple competing FOB bills in both houses of Congress. The specific provisions of these bills varied dramatically. One of the bills in particular, House Bill 1427, was strongly opposed by the biotechnology industry, which instead supported the relatively pro-innovator House Bill 1548. By the time this article was written, elements taken from these bills had been merged into amendments to health-care reform legislation then pending in the House and the Senate.

Two of the most controversial aspects of the proposed FOB pathways were the data exclusivity period (DEP) and the pre-approval patent dispute resolution process (PPRP). In June

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2009, the Federal Trade Commission (FTC) published a report recommending that Congress enact FOB legislation including a relatively short DEP (e.g., five years as provided in House Bill 1427) and no PPRP (at that time all of the bills included a PPRP, although the specific provisions of the processes varied substantially between the bills). The FTC's conclusion that a longer DEP (e.g., twelve years as provided in House Bill 1548) is unnecessary to adequately incentivize innovation in biologics was based in part on a misapplication of the results of a study I published in 2007 on the patent law's written description requirement. I wrote the present article in late 2009 in response to the FTC Report, explaining why I believe that the FTC over-interpreted the results of my study, and arguing in favor of a longer DEP and inclusion of a fair and nondiscriminatory PPRP in any FOB legislation enacted by Congress.

After the article was written and accepted for publication, Congress enacted health care reform legislation, including the FOB amendment pending in the Senate at the time this article was written.¹ For the moment at least, Congress has chosen not to follow the FTC's recommendations, and the FOB pathway passed into law includes a twelve-year DEP and a PPRP. However, this in no way renders moot the issues relating to DEP and PPRP addressed by the FTC Report and in this article. The PPRP for conventional drugs, provided under the Hatch-Waxman Act, has been amended substantially since it was first enacted, and history suggests that the same will likely hold true for the recently enacted FOB PPRP.² Expert panelists at a recent meeting of biotechnology patent attorneys identified numerous ambiguities and problems with the FOB PPRP that will likely necessitate congressional intervention.³ There is already an active campaign to amend the statute to substantially shorten the DEP for biologic innovators. Such an amendment is supported not only by the FTC, but also the generic drug industry and others who believe a shorter DEP would bring down the cost of biologics, including influential members of Congress

1. Patient Protection and Affordable Care Act, Pub. L. No. 111-148, §§ 7001–7003, 124 Stat. 119, 804–22 (2010).

2. See Natalie M. Derzko, *The Impact of Recent Reforms of the Hatch-Waxman Scheme on Orange Book Strategic Behavior and Pharmaceutical Innovation*, 45 IDEA 165, 228–29 (2005).

3. Biotechnology Industry Organization IP Counsels Committee Conference, New Orleans, Louisiana (Apr. 19–21, 2010).

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(such as the sponsors of House Bill 1427).⁴ Thus, the analysis and recommendations provided in this article remain highly relevant even after the passage of FOB legislation, as the focus shifts from passage of the bill to proposals for amending the legislation in a manner that lowers the cost of biologics without unduly dampening the incentives for innovation.

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4. Victoria Colliver, *New Rules on Generics Seen As Mixed Blessing*, SAN FRANCISCO CHRON., Mar. 28, 2010, at D4.

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I. INTRODUCTION

Congress is considering legislation that would create an abbreviated Food and Drug Administration (FDA) approval process for follow-on biologics (FOBs), which proponents anticipate will promote competition and lower prices in the market for biologic drugs.⁵ A key feature of such legislation would be provisions allowing an FOB applicant to rely on data generated by an innovator company to secure FDA approval to market an FOB (also referred to as a “biosimilar”) in competition with the innovator’s product. If the legislation works as planned, it will appreciably lower the cost and risk associated with bringing an FOB to market. Increased competition as a result of FOB approvals is predicted to bring about lower prices but, will also result in loss of market share and price erosion for the innovator, and potentially, loss of consumer goodwill. This could effectively reduce the expected return on investment and thus the incentive for investment in the development of this increasingly important category of drugs.

There appears to be broad support for the creation of some

5. Biologics are essentially drugs produced in living cells, as exemplified by recombinant therapeutic proteins. FOBs are often conceptualized as analogous to generic versions of biologic drugs, but due to the greater structural complexity of biologics compared to conventional drugs, true generic versions of biologic drugs are not anticipated any time soon. For a review of FOBs (also referred to as biosimilars), and the economic considerations motivating the push for legislation creating an abbreviated approval pathway for FOBs, see FED. TRADE COMM’N, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION 3–24 (2009), *available at* <http://www.ftc.gov/os/2009/06/P083901biologicsreport.pdf> [hereinafter FTC REPORT].

form of abbreviated pathway for FOBs, but much debate as to the precise contours of the legislation. It is important that changes in the law to promote FOB market entry also provide adequate opportunity for biologic innovators to capture an appropriate level of return on investment, so that lower cost biologics do not come at the expense of future innovation and the biologic drug pipeline.

In June 2009 the Federal Trade Commission (FTC) published a report on FOBs (“the FTC Report”), which attempts to forecast the nature of competition between innovator biologics and FOBs and offers a number of substantive recommendations regarding specific provisions of the various FOB bills.⁶ In particular, the FTC Report concludes that there is essentially no justification for the inclusion of a substantial data exclusivity period (DEP) for innovators in pending FOB legislation, and that Congress should not include a pre-approval patent dispute resolution process (PPRP).⁷ The FTC Report bases its conclusion that a substantial DEP is unnecessary to adequately incentivize innovation in biologics in part on a misapplication of the results of a study I conducted on the written description doctrine of patent law.⁸

In this article I offer a response to some of the conclusions and recommendations set forth in the FTC Report. In particular, I think it is important to clarify the scope and implications of my study on the written description doctrine, and explain why I believe that the FTC over-interpreted the results of the study to arrive at a conclusion that is unsupported by the data. As explained below, in my view an extended DEP for innovators is justified and should be included in FOB legislation enacted by Congress. I also disagree with the FTC’s conclusion that a PPRP is unnecessary and unwarranted for biologic drugs; in my view, such a process is appropriate and would be important for maintaining adequate incentives for innovation.

A fair and balanced PPRP would be especially important should Congress follow the FTC’s suggestion to provide only a relatively short DEP for biologic innovators. Some of the proposed FOB legislation would discriminate against the develop-

6. *Id.*

7. *Id.* at v–x.

8. Christopher M. Holman, *Is Lilly Written Description a Paper Tiger?: A Comprehensive Assessment of the Impact of Eli Lilly and Its Progeny in the Courts and PTO*, 17 ALB. L.J. SCI. & TECH. 1 (2007) [hereinafter Holman, *Lilly*].

ers of innovative biologic drugs, not only with respect to FOB producers, but also in comparison to the treatment currently afforded conventional drug innovators. These discriminatory provisions should be removed or rectified to provide a more balanced approach to promoting competition, while still maintaining adequate incentives for investment in biotechnology.

As I write this I am aware of and have reviewed multiple FOB bills currently pending in Congress. House Bill 1548 provides a pathway that is relatively pro-innovator,⁹ and has been generally supported by the biotechnology industry.¹⁰ House Bill 1427¹¹ and Senate Bill 726¹² are essentially identical bills that would attempt to speed FOB market entry by severely curtailing the intellectual property rights of biologic drug innovators;¹³ not surprisingly, these bills have been strongly opposed by the biotechnology industry.¹⁴ More recently, FOB draft legislation has been reported in the form of amendments to currently-pending health care reform bills by the Committee on Energy and Commerce in the House, and the Committee on Health, Education, Labor and Pensions (HELP) in the Senate (referred to hereafter as the “House Amendment”¹⁵ and “Senate Amendment”¹⁶). The House and the Senate Amendments are based in large part on elements taken from House Bill 1427, House Bill 1548, and, importantly, also on Senate Bill 1695¹⁷ (an FOBs bill which was reported by the Senate HELP Committee during the

9. H.R. 1548, 111th Cong. (2009).

10. *Biologics and Biosimilars: Balancing Incentives for Innovation: Hearing Before the Subcomm. on Courts and Competition Policy of the H. Comm. on the Judiciary*, 111th Cong. 68 (2009) (statement of Jeffrey P. Kushan on behalf of the Biotechnology Industry Organization).

11. H.R. 1427, 111th Cong. (2009).

12. S. 726, 111th Cong. (2009).

13. Since the House and Senate bills are essentially identical, I will simply refer to the House bill, H.R. 1427.

14. *Biologics and Biosimilars: Balancing Incentives for Innovation: Hearing Before the Subcomm. on Courts and Competition Policy of the H. Comm. on the Judiciary*, 111th Cong. 65 (2009) (statement of Jeffrey P. Kushan on behalf of the Biotechnology Industry Organization).

15. Eshoo-Inslee-Barton Amendment of 2009, H.R. 3200, 111th Cong. (2009) [hereinafter “House Amendment”] (as passed by the House Energy and Commerce Committee on July 31, 2009 by a vote of 47-11).

16. Hagan-Enzi-Hatch Amendment of 2009, H.R. 3200, 111th Cong. (2009) [hereinafter “Senate Amendment”] (as passed by the Senate Health, Education, Labor and Pensions Committee on July 13, 2009 by a vote of 16-7).

17. S. 1695, 110th Cong. (2008).

110th Congress) — but each amendment also incorporates substantial differences, both in comparison with the originally filed bills and with respect to each other.

II. FOB LEGISLATION SHOULD PROVIDE AN EXTENDED PERIOD OF DATA EXCLUSIVITY FOR INNOVATORS

All of the FOB legislative proposals provide a DEP for innovators. During the DEP, FDA will not be permitted to approve any FOB through an abbreviated process relying on innovator-generated data submitted to FDA by the innovator in order to gain marketing approval for the innovator's approved biologic drug.¹⁸ If FOB legislation works as planned, the ability of an FOB applicant to rely on innovator-generated data will substantially reduce the cost of bringing an FOB to market. It is important to remember, however, that an FOB applicant could choose to generate its own data and forgo the abbreviated FOB pathway. The DEP would not prevent FDA approval in this case because the FOB applicant would not be relying on the data of the innovator.¹⁹ Furthermore, an FOB applicant relying on innovator data would not be required to wait until the DEP has expired before applying for FDA approval. Under the current proposals, an FOB applicant would be able to submit an application relying on an innovator's data, and the FDA would be permitted to review and tentatively approve the application prior to the expiration of the DEP. Upon expiration of the DEP, the FDA would make the approval effective.

House Bill 1427 would provide innovators a short five-year DEP,²⁰ while House Bill 1548 would provide a minimum of twelve years of DEP, extendable up to 14.5 years for innovators that conduct pediatric studies of the drug and gain approval for a significant new use of the drug.²¹ The House and Senate amendments both provide a twelve-year DEP extendable up to twelve and a half years if pediatric studies are conducted.

The FTC Report argues in favor of a relatively short DEP, less than twelve years, based on its conclusion that a twelve-year DEP will not be needed to incentivize adequate innovation

18. H.R. 1427, at § 3(a)(2).

19. Of course, there could be patent and other non-regulatory barriers that would delay FOB market entry.

20. H.R. 1427, at § 3(a)(2).

21. H.R. 1548, 111th Cong. § 101(a)(2) (2009).

in biologic drugs.²² A primary basis upon which FTC bases this recommendation is its conclusion that strong and effective patent protection will be available for biologics, comparable to that currently enjoyed by conventional small molecule drug innovators, thus obviating the role of data exclusivity in providing innovators with de facto market exclusivity.²³

In this section, I point out that if the FTC is correct in its assumption that patents will provide strong and effective protection for biologics, a 12-year DEP running concurrently with a patent term will have little impact on the timing of FOB market entry. However, it is far from clear that effective patent protection will be available for all, or even most, biologic drugs, in which case an extended DEP could prove critical in ensuring that biologic innovators are able to maintain a sufficient period of market exclusivity in order to adequately incentivize future innovation.

A. AN APPROPRIATE PERIOD OF MARKET EXCLUSIVITY FOR INNOVATORS IS REQUIRED TO INCENTIVIZE FUTURE INNOVATION

Bringing a new drug to market is a notoriously expensive and risky endeavor, and the requisite investment of time and capital will only occur in an environment that provides adequate incentives. Although grant funding plays some role at early stages of discovery and development, the primary incentive driving drug innovation is the innovator's expectation of some period of market exclusivity in which to secure an adequate return on its investment. Market entry by generic versions of the drug dramatically drives down the price of the drug, and inevitably the innovator's profits as well. Competition by "me too" drugs in the same class can also reduce innovator profits, albeit usually to a lesser extent than true generic competition.²⁴ The optimal legal regime will balance the consumer's interest in timely generic competition with the recognition that innovators must be allowed to benefit from an adequate period of marketing exclusivity during which they compete only against other innovator products, if any, in order to incentivize adequate investment to support the desired pipeline of future drug innovation.

22. See FTC REPORT, *supra* note 5, at 44–46.

23. See *id.*

24. See *id.* at 12.

As with any innovative technology, patents play an important role in providing market exclusivity for drug innovators. However, drug innovators also face FDA regulatory barriers that operate to delay market entry for first-in-class innovators and subsequent competitors alike, placing drug originators on a more or less equal footing.²⁵ In the absence of an abbreviated approval process, a competitor is required to generate all the necessary clinical and nonclinical data to establish the safety and efficacy of its product, which is very expensive.²⁶ This expense is a potent barrier to market entry—one that the innovator invested heavily in overcoming. An abbreviated approval pathway allows competitors to come onto the market without incurring the full impact of this expense. Thus FOB manufacturers have the advantage of substantially lower market entry costs. The significant role of regulatory barriers distinguishes drugs from most other innovative products, and is one of the reasons why competition and barriers to entry in the pharmaceutical market have been the subject of so much attention by Congress and the FTC.

It is generally acknowledged that some substantial period of market exclusivity for innovators is necessary to incentivize an adequate level of investment in the development of new drugs. This is particularly the case for biologics. However, the actual duration of optimal market exclusivity has been hotly debated. For example, in a 2008 study, Duke University economist Henry Grabowski calculated that it takes between 12.9 and 16.2 years on the market for a biologic innovator to “break even.”²⁷ In response, Alex Brill published a critique challenging some of Professor Grabowski’s assumptions and estimating that seven years of data exclusivity would be sufficient to maintain adequate incentives for biologics innovation.²⁸ Likewise, the FTC Report has criticized the numbers proposed by Grabowski, arguing that the model used to generate the numbers “contains numerous methodological and conceptual weaknesses

25. Christopher M. Holman, *Do Reverse Payment Settlements Violate The Antitrust Laws?*, 23 SANTA CLARA COMPUTER & HIGH TECH. L.J. 489, 509 (2007) [hereinafter Holman, *Reverse Payments*].

26. *Id.*

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

28. ALEX BRILL, PROPER DURATION OF DATA EXCLUSIVITY FOR GENERIC BIOLOGICS: A CRITIQUE 10 (2008), available at http://www.tevad.com/Brill_Exclusivity_in_Biogenics.pdf.

that render its results too imprecise and non-robust to inform discussions about the length of an exclusivity period.”²⁹ On the other hand, Vernon, Bennett and Golec, using contemporary models of risk and return from finance literature, determined that seventeen years of data exclusivity for new biologics are required.³⁰

One logical benchmark for setting the optimal period of market exclusivity for biologic innovators is the actual period of de facto market exclusivity currently afforded small molecule drug innovators. A recent study showed that small molecule drugs average eleven to thirteen years of de facto exclusivity prior to generic competition, primarily as a result of patent protection that typically extends well beyond the short DEP provided under Hatch-Waxman.³¹ The general similarities between the research and development, regulatory approval process, and market economics relating to the conventional small molecule and biologic drugs would seem to warrant comparable protection. Although the FTC may be correct in its prediction that FOB competition will be less vigorous than generic drug competition (at least initially), biologic drugs are also more expensive and risky to develop and manufacture, and the two factors to some extent offset each other. There has also been a noted drop off in the approval of innovative conventional drugs in recent years, suggesting that perhaps the current period of market exclusivity afforded small molecules might be sub-optimal for incentivizing innovation. The FTC Report specifically acknowledges that conventional small molecule drugs generally enjoy eleven to thirteen years of de facto exclusivity, and never suggests that biologic innovators deserve less protection.³² Instead, the Report simply assumes that patent protection will be sufficient to provide biologics with a substantial period of de facto market exclusivity, thus rendering the DEP superfluous, an assumption I challenge later in this article.³³

In a related context, Congress has decided that conven-

29. FTC REPORT, *supra* note 5, at 45–46.

30. John A. Vernon et al., *Exploration of Potential Economics of Follow-On Biologics and Implications for Data Exclusivity Periods for Biologics*, 16 B.U. J. SCI. & TECH. L. 55, 56–57, 71, 74 (2010).

31. See Henry G. Grabowski & Margaret Kyle, 28 MANAGERIAL & DECISION ECON. 491, 493 (2007).

32. FTC REPORT, *supra* note 5, at 43–45.

33. *Id.*

tional and biologic drug innovators should generally benefit from the same period of de facto market exclusivity. Under Hatch-Waxman, 35 U.S.C. § 156 (2006), drug innovators are permitted to extend patent protection for a drug in order to restore a portion of the patent life that is lost due to the time spent obtaining FDA regulatory approval, up to a maximum of fourteen years after the original FDA approval date of the innovator drug.³⁴ This patent term restoration is available both for conventional and biologic drugs, and the same fourteen-year maximum period applies to both conventional and biologic drugs.³⁵

Similarly, the safe harbor from infringement liability provided by Hatch-Waxman for activities relating to the production and submission of data to FDA applies to both conventional and biologic drugs.³⁶ This consistent treatment of biologic and conventional drugs makes sense, in view of the similarities in the development, regulation and economics involved, and suggests that twelve to fourteen years of data exclusivity would be appropriate since it would guarantee a de facto period of market exclusivity for biologic innovators comparable to that already enjoyed by conventional drug innovators. The FTC Report does not provide any compelling support for the creation of a system that effectively discriminates against biologic innovators relative to conventional drug innovators.

B. AN EXTENDED PERIOD OF DATA EXCLUSIVITY WILL NOT SIGNIFICANTLY DELAY FOB MARKET ENTRY IF THE FTC IS CORRECT IN ITS ASSUMPTION THAT PATENTS WILL PROVIDE EXTENDED DE FACTO MARKET EXCLUSIVITY

The FTC Report predicts that strong and effective patent protection will be available for biologics, comparable to that currently enjoyed by small molecule drug innovators, and that it “is likely that few, if any, biologic products will experience FOB entry immediately upon expiration of a limited period of exclusivity.”³⁷ The FTC Report even goes so far as to predict that patents will likely provide a *longer* period of de facto ex-

34. 35 U.S.C. § 156 (2006).

35. *Id.*

36. See 35 U.S.C. § 271(e) (2006). For judicial decisions applying the safe harbor provision, see *Amgen, Inc. v. Int'l Trade Comm'n*, 565 F.3d 846, 851 (Fed. Cir. 2009); *Genentech, Inc. v. Insmmed, Inc.*, 436 F. Supp. 2d 1080, 1095 (N.D. Cal. 2006).

37. FTC REPORT, *supra* note 5, at 43.

clusivity for biologics than currently enjoyed by small molecules.³⁸ This prediction is based on the fact that the current FOB legislation proposals do not include incentives for challenging innovator patents, a key feature of Hatch-Waxman.³⁹

As explained below, for a variety of reasons it is by no means clear that patents will be able to provide the extended period of exclusivity predicted by the FTC. But let us assume, for the sake of discussion, that the FTC is correct in its prediction that patents will provide effective protection for biologics comparable to that currently enjoyed by conventional drug innovators. If that is the case, then an extended DEP will not substantially extend the de facto period of market exclusivity for innovative biologics. The DEP usually plays no role in extending the market exclusivity of small molecule drugs because it has run out long before the relevant patents have expired. If the FTC is correct and patents provide de facto exclusivity to biologics for eleven to thirteen years, then a twelve- to fourteen-year DEP will provide little if any extension to the effective period of actual exclusivity. At times, the FTC Report apparently fails to recognize that the DEP would run concurrently with the patent term, and that the DEP only becomes relevant if and to the extent it extends beyond the period in which patents preclude the entry of competition.

On the other hand, an extended DEP could prove crucial if patents do not provide the effective protection for biologics predicted by the FTC. Even the FTC Report acknowledges that in some cases, effective patent protection might not be available for biologics, and that some biologic products may experience FOB entry immediately upon expiration of a limited DEP.⁴⁰ As explained below, this might be the case even when a biologic is expensive and risky to develop, and the product provides substantial clinical benefit to patients. Even if this scenario plays out only rarely, a twelve-year DEP could provide important insurance for cases where effective patent protection is not available. There would be little downside to this because in cases in which patents are effective, the DEP will have largely, if not entirely, burned up by the time patents expire. The FTC Report explicitly acknowledges that to the extent innovative biologics

38. *Id.*

39. *Id.*

40. *Id.* at 43, 45.

are not amenable to effective patent protection, an extended exclusivity period may be warranted.”⁴¹ Because an extended DEP would only substantially increase de facto market exclusivity in cases where patents prove insufficient, the prudent course would be to provide an extended DEP running concurrent with the patent term as insurance against those cases where patents prove insufficient.

Furthermore, there are compelling advantages to relying more heavily on data exclusivity instead of patent protection to provide the optimal period of market exclusivity for biologic innovators. For example, by preventing market entry of FOB products for twelve years, much wasteful patent litigation could be avoided, since many of the key patents will no longer be an issue by the time the DEP expires. An increased reliance on DEPs could also provide critical incentives for the development of potentially life-saving biologics that, for whatever reason, are not amenable to effective patent protection.

One of the unfortunate consequences of the current heavy emphasis on patent protection for incentivizing small molecule drug innovation is that many potentially meritorious drug candidates are never developed if an innovator is unable to secure effective patent protection for the molecule.⁴² In the past, biologic innovators have invested in the development of important new drugs even in the absence of strong patent protection, relying on the regulatory barrier to market entry by competitors to justify the investment. In a post-FOB regime, biologic innovators will likely be less inclined to invest in the development of products for which they are unable to secure strong, effective, and predictable patent protection. An extended period of data exclusivity, however, could provide the needed assurance of a reasonable likelihood of recouping and profiting from their investment. The requirements of patentability are such that it is very possible that effective patent protection will not be available for a pharmaceutically-useful biological molecule, but the molecule nevertheless would make a substantial contribution to public health if developed and brought to market as a drug.⁴³ An extended period of data exclusivity would provide an appropriate incentive to compensate for this limitation of

41. *Id.* at 45.

42. *See, e.g.*, Benjamin N. Roin, *Unpatentable Drugs and the Standard of Patentability*, 87 TEX. L. REV. 503, 545 (2009).

43. *Id.*

patent law.

C. THE FTC'S CONCLUSION THAT PATENTS WILL NECESSARILY PROVIDE A SUFFICIENT PERIOD OF MARKET EXCLUSIVITY FOR BIOLOGIC INNOVATORS IS BASED ON ILL-FOUNDED ASSUMPTIONS

Not all drug patents are created equal, and some have proven much more effective than others in blocking market entry by a competing product. Composition-of-matter patents claiming a drug active ingredient per se ("true COM patents") are by far the most effective, and are the gold standard for the protection of conventional small molecule drugs. A true COM patent is generally impervious to being designed around, because it effectively precludes others from producing or marketing any product comprising the patented active ingredient. In addition, Hatch-Waxman requires a generic copy of a conventional drug to employ the same active ingredient as the referenced branded product.⁴⁴ Even if a generic company develops a new formulation of the drug, a new process for producing or delivering the drug, or if it seeks approval for a noninfringing therapeutic use of the drug, it will normally be precluded from market entry until the true COM patent has expired. Most drug companies will only risk substantial investment in the development of a drug candidate if true COM patent protection is available for the active ingredient. Small molecule active ingredients are usually novel chemical compositions eligible for true COM patents that will generally withstand challenges to validity. For example, a recent market research report of generic drug patent litigation prepared by Bernstein Global Wealth Management ("the Bernstein Report") reported that out of fourteen total patent challenges involving a true COM patent, nine were won by the branded drug, three settled, and the generic challenger only won twice.⁴⁵

Other drug patents generally provide more attenuated protection for drug products, and experience has shown that small molecule drug innovators are far less successful in asserting

44. 21 U.S.C. § 355(j)(2)(A)(iv) (2006).

45. AARON GAL ET AL., BERNSTEIN GLOBAL WEALTH MGMT., PARAGRAPH IV LITIGATION: A GUIDE FOR THE PERPLEXED 6 (2007) [hereinafter BERNSTEIN REPORT].

these patents against competitors than true COM patents. Examples of non-COM patents include patents directed towards specific formulations of a drug active ingredient, specific combinations of active ingredients, methods of using the drug to treat particular diseases, and processes and technologies used in the production of the drug. The Bernstein Report, for example, found that of the twenty-three generic drug litigations identified in the study that involved patents claiming active ingredient combinations, oral modified release formulations, and first oral formulations, the branded company never prevailed in court, while the generic challenger won thirteen of the cases, and the other ten cases resulted in settlement agreements.⁴⁶

In particular, patents covering the technology and processes used to manufacture a drug tend to play an ancillary role in the protection of conventional drugs relative to true COM patents and even compared to other patents relating to drug formulations or methods of using the drug. In fact, patents on processes and technologies used in drug protection are not even listed in the Orange Book.⁴⁷ The Bernstein Report takes the position that although patents on the processes or technologies relevant to a drug synthesis can be relevant on a case-by-case basis, they are uncommon, and thus not even covered in the report.⁴⁸

The FTC's prediction that effective patent protection will obviate the need for an extended DEP appears to be based largely on an assumption that true COM patents claiming the biologic drug's active ingredient (i.e., the therapeutic recombinant protein) will prove just as effective for biologic innovators as they have been for conventional drug innovators.⁴⁹ However, a review of the history of biologic patent enforcement reveals that true COM patents have been much less effective in protecting biologic molecules.

The FTC Report acknowledges past instances in which

46. *Id.*

47. See OFFICE OF GENERIC DRUGS, U.S. DEPT OF HEALTH & HUMAN SERVS., APPROVED DRUGS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (2010), available at <http://www.accessdata.fda.gov/scripts/cder/ob/eclink.cfm>. This publication, commonly known as the Orange Book, identifies drug products FDA has deemed both safe and effective.

48. BERNSTEIN REPORT, *supra* note 45, at 18.

49. For example, the FTC Report finds that “[t]here is no evidence that the patents claiming the compound or molecule of pioneer biologic drugs have been designed around more frequently than those claiming small-molecule drug products.” FTC REPORT, *supra* note 5, at 36.

competitors have effectively designed around a biologic COM patent, and provides two specific examples: ⁵⁰ *Genentech v. Wellcome*⁵¹ and *Hormone Research Foundation, Inc. v. Genentech*.⁵² Although these decisions are relatively old, dealing with two of the earliest biologic drugs to enter the market (recombinant tissue plasminogen activator⁵³ and human growth hormone,⁵⁴ respectively), they are nevertheless instructive as to the types of obstacles a biologic innovator could face in attempting to enforce a true COM patent against an FOB competitor. In both cases, the alleged infringer produced a competing version of the same human protein, but with structural modifications, which effectively designed around the innovator's patent.⁵⁵

All of the proposed FOB legislation would permit an FOB product to incorporate structural changes that distinguish it from the innovator's reference biologic product while still taking advantage of the abbreviated approval process and reference to innovator-generated data. Thus, in principle, an FOB will be able to circumvent a patent covering the innovator's product while still benefiting from use of the innovator's data. The extent of the problem for biologic innovators will depend upon a variety of factors, including the scope of patent protection available for biologics, the amenability of the innovator molecule to structural changes that would avoid the patent claim while retaining similar functionality, and the level of stringency with which FDA applies its test for biosimilarity.⁵⁶ In any event, it is wrong to assume that biologic innovators will be able to successfully use COM patents to the same extent and as effectively as conventional drug innovators have in the past.

After acknowledging instances where biologic COM patents have been effectively designed around, the FTC Report asserts

50. *Id.* at 37 & n.152.

51. *Genentech, Inc. v. Wellcome Found. Ltd.*, 29 F.3d 1555 (Fed. Cir. 1994).

52. *Hormone Research Found., Inc. v. Genentech, Inc.*, 904 F.2d 1558 (Fed. Cir. 1990).

53. *Wellcome*, 29 F.3d at 1558–59.

54. *Hormone Research*, 904 F.2d at 1560.

55. *See Wellcome*, 29 F.3d at 1555; *Hormone Research*, 904 F.2d at 1560.

56. Under the proposed FOB legislation, the opportunity to rely on innovator data will only be available to an FOB that is "biosimilar" to the innovator biologic, *see, e.g.*, H.R. 1427, 111th Cong. § 3(a)(2) (2009), but it is uncertain how stringent FDA will be in determining biosimilarity.

that in other cases COM patents have been successfully enforced against biologic competitors, and identifies six specific cases purportedly supporting this proposition.⁵⁷ In fact, however, four of the six cases are off-point and do not support the FTC's assertion.⁵⁸ The two cases which support the FTC's assertion are *Amgen, Inc. v. F. Hoffman-La Roche, Ltd.*⁵⁹ and *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*⁶⁰ Both are recent district court decisions involving a family of related patents claiming recombinant and/or therapeutic versions of erythropoietin.⁶¹ At the time this is being written, *Amgen v. Hoechst Marion Roussel* has not been affirmed at the appellate level, and the district court's decision in *Amgen v. F. Hoffman-La Roche* regarding the validity of the asserted COM claims was recently vacated and remanded to the district court to consider whether the COM claims are invalid for obviousness-type double patenting.⁶² Notably, the FTC Report does not identify a single appellate-level decision finding a true COM patent valid and infringed by a biologic product. I have searched and been unable to find such a decision. In any event, there is scant empirical evidence to support any inference that true COM patents are as effective in protecting biologic drugs as they are for small molecule drugs.

Amgen's recent success in enforcing its erythropoietin patents, at least at the district court level,⁶³ is not typical. In many cases, biologic innovators have been unable to achieve ef-

57. FTC Report, *supra* note 5, at 37 & n.153.

58. See *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495 (Fed. Cir. 1997) (regarding an interference contest between two companies involving no assertion of patent infringement); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1991) (claiming a gene used in the production of the biologic, not the biologic drug); *Chiron Corp. v. Genentech, Inc.*, 268 F. Supp. 2d 1126 (E.D. Cal. 2008) (involving patent validity and not addressing the issue of patent infringement); *Genentech, Inc. v. Insmid Inc.*, 436 F. Supp. 2d 1080 (N.D. Cal. 2006) (claiming the process for producing a biologic, not the biologic drug).

59. *Amgen, Inc. v. F. Hoffman-La Roche Ltd.*, 581 F. Supp. 2d 160 (D. Mass. 2008), *aff'd in part, vacated in part, remanded by* 580 F.3d 1340 (Fed. Cir. 2009).

60. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 579 F. Supp. 2d 199 (D. Mass. 2008).

61. *F. Hoffman La-Roche*, 581 F. Supp. 2d at 166–67; *Hoechst Marion Roussel*, 579 F. Supp. 2d at 200.

62. *Amgen, Inc. v. F. Hoffmann-La Roche, Ltd.*, 580 F.3d 1340, 1386 (Fed. Cir. 2009) (affirming the district court's judgment that the COM claims were infringed).

63. *F. Hoffman-La Roche*, 581 F. Supp. 2d at 204, 229; *Hoechst Marion Roussel*, 579 F. Supp. 2d at 210.

fective true COM patent protection, often because the biologic product is essentially a recombinant version of a naturally occurring human protein, and earlier isolation and characterization of the human protein has created prior art precluding broad COM patent protection. This is normally not a problem for small molecule innovators, who generally will not invest in developing a molecule into a drug if there is prior art precluding true COM patent protection. For example, Amgen faced this obstacle with respect to recombinant erythropoietin, but was nonetheless able to obtain three COM patents limited to certain specific therapeutic and recombinant versions of erythropoietin.⁶⁴ It is also instructive to consider the difficulty Amgen has experienced in attempting to enforce its limited COM patents. In *Amgen v. HMR*, the asserted claims of two out of the three COM patents were found to be invalid or not infringed.⁶⁵ Only after multiple appeals has Amgen apparently succeeded in convincing the court that one of its COM claims is valid and has been infringed.⁶⁶

Most innovators that have brought groundbreaking biologic drugs to market have not succeeded in using true COM patents to protect their products. In some cases, they have only been able to secure patents claiming the processes and technologies used in the production of biologics, a more attenuated but nonetheless sometimes successful approach to protecting their product. In other cases, biologic innovators appear to have brought products to market in the absence of any effective patent protection, as suggested by the fact that competing products sometimes enter the market without provoking any lawsuit by the innovator who first achieved regulatory approval for the biologic product. In the absence of patent protection, these

64. U.S. Patent No. 5,547,933 (filed June 7, 1995); U.S. Patent No. 5,621,080 (filed June 6, 1995); U.S. Patent No. 5,955,422 (filed Aug. 2, 1993). Erythropoietin is a naturally occurring human protein that was isolated prior to Amgen's work, so patent protection on the purified protein per se was unavailable. See U.S. Patent No. 4,703,008 (filed Nov. 30, 1984) (summarizing various methods of purifying erythropoietin developed prior to Amgen's cloning of the gene encoding the protein).

65. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.* 457 F.3d 1293, 1296–97 (Fed. Cir. 2006).

66. *Hoechst Marion Roussel*, 579 F. Supp. 2d at 210; Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of the Human Gene Patent Litigation*, 76 UMKC L. REV. 295, 329–30 (2007) [hereinafter Holman, *Impact*].

products would likely not be developed in a post-FOB world unless Congress provides a DEP of sufficient duration.

One of the most common means by which biologic innovators have attempted to secure patent positions on their products is by patenting the genes, genetic constructs, and recombinant cells used in the production of the biologic, as well as the processes themselves. In some cases, these patents have been deployed successfully (for simplicity, I will refer generally to these patents as “gene patents,” since they are based on the gene encoding the biologic rather than the biologic itself). Amgen has been particularly successful in using gene patents to block market entry by competitors in the market for recombinant erythropoietin.⁶⁷ However, there are also numerous examples where competitors have successfully designed around an innovator’s gene patents and brought a competing biologic to market while avoiding infringement liability.⁶⁸ The FTC acknowledges that the ability of drug competitors to design around non-COM patents is “prevalent,”⁶⁹ a crucial concession when one recognizes that effective true COM patent protection has in the past often not been available for biologic innovators and that it is unclear whether things will change to render such protection more available in the future. Notably, the FTC Report fails to identify any basis for which to predict that true COM patent protection will be more available in the future than it has been to date.

Another serious limitation facing biologic innovators relying on patents directed solely toward technologies used in the

67. *Id.*

68. Christopher M. Holman, *Learning from Litigation: What Can Lawsuits Teach Us About the Role of Human Gene Patents in Research and Innovation?*, 18 KAN. J.L. & PUB. POL’Y 215, 223–29 (2009) [hereinafter Holman, *Learning*]. Examples include: *Genzyme, Corp. v. Transkaryotic Therapies, Inc.*, 346 F.3d 1094 (Fed. Cir. 2003) (holding that claims broadly reciting methods for recombinant production of human α -galactosidase A were not infringed by a method employing gene activation technology); *Biogen, Inc. v. Berlex Lab., Inc.*, 318 F.3d 1132 (Fed. Cir. 2003) (holding that claims to cells that have been genetically engineered to express the human interferon gene were not literally infringed by cells produced using alternate transformation method); *Schering Corp. v. Amgen, Inc.*, 222 F.3d 1347 (Fed. Cir. 2000) (holding that a patent claiming a naturally occurring interferon gene was not infringed by consensus interferon product); *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) (holding that a patent on an insulin gene was circumvented by expressing protein as a fusion); *Novo Nordisk of N. Am., Inc. v. Genentech, Inc.*, 77 F.3d 1364 (Fed. Cir. 1996) (holding an apparently broad gene patent circumvented by the use of protein fusion technology).

69. FTC REPORT, *supra* note 5, at 45.

production of the product is that these patents are potentially susceptible to circumvention by a competitor who produces the product outside the United States in a jurisdiction where the innovator has not patented the technology, or where enforcement is more difficult.⁷⁰ This could be an especially important issue if FOB production shifts to countries such as China and India, as some have predicted.

D. MY STUDY OF THE *LILLY* WRITTEN DESCRIPTION REQUIREMENT DOES NOT SUPPORT THE CONCLUSION THAT EFFECTIVE PATENT PROTECTION IS AVAILABLE FOR BIOLOGICS

In concluding that effective patent protection is currently available for biologics, the FTC Report relies in part on the results of an empirical study on the *Lilly* written description requirement (LWD) that I published in 2007.⁷¹ However, the FTC over-interpreted the results of my study to arrive at a conclusion that I never stated, and which does not find support in the data.

In considering the implications of my study, it is important to bear in mind the context from which my article arose. LWD is a distinct form of the written description doctrine which traces its origin to the Federal Circuit's 1997 *Regents of the University of California v. Eli Lilly* decision.⁷² Prior to 2007 there was a widespread perception, particularly among academics, that LWD functioned as a "super-enablement" requirement that effectively limited inventors of novel biomolecules (particularly DNA and proteins) to a single sequence, or a limited number of specifically recited sequences, resulting in an extremely narrow scope of patent protection for biotechnology inventions.⁷³ I conducted a search to identify all decisions in the federal courts and in the U.S. Patent and Trademark Office's Board of Patent Appeals and Interferences (BPAI) which had applied LWD. My central conclusions were that: (1) LWD was generally not functioning as a super-enablement require-

70. Holman, *Learning*, *supra* note 68, at 229–31.

71. FTC REPORT, *supra* note 5, at 36–37 n.151 (citing Holman, *Lilly*, *supra* note 8, at 47).

72. *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566–67 (Fed. Cir.1997).

73. See Holman, *Lilly*, *supra* note 8, at 17.

ment, but rather was applied in a manner that effectively rendered LWD redundant with the enablement requirement; (2) neither the courts nor the Patent and Trademark Office (PTO) had formulated a coherent interpretation of LWD that provided any meaningful limitation on claim scope that could not better be achieved by means of the enablement requirement; and (3) LWD was not restricting inventors to claims encompassing only a small number of sequences; rather, inventors were successfully obtaining and enforcing patent claims encompassing large numbers of variants of a disclosed invention, including newly discovered DNA sequences and proteins.⁷⁴

Based on the findings of my study, the FTC Report concludes that since genus claims encompassing large numbers of variations on a disclosed DNA or protein sequence have survived challenges based on LWD, it must be the case that biologics are adequately protected by patents.⁷⁵ However, this conclusion is not supported by my article. The FTC Report fails to appreciate that the potential for a patent to effectively block market entry by a competing biologic is not merely a function of claim scope per se, but depends critically on the extent to which the structure of the claimed molecule can be altered while retaining substantial functionality. Even a patent that in absolute terms covers a large number of variants will be ineffective in blocking FOB competition if it does not encompass all biosimilar variations of the reference product that could take advantage of the abbreviated FOB pathway to market. I never addressed this issue in my article, and never suggested that my findings supported a conclusion that the scope of patent protection available for biologics would be sufficient to encompass any biosimilar variation of an innovator's molecule.

Although my article identified numerous judicial decisions involving LWD, only two of these decisions involved an infringement lawsuit brought against the manufacture of a biologic. One of these was *Regents of the University of California v. Eli Lilly* (namesake of *Lilly* written description), in which the Federal Circuit applied LWD to invalidate the university's patent claiming the human insulin gene.⁷⁶ The other was *Amgen v. HMR*,⁷⁷ in which the court sided with the patent owner and

74. *Id.* at 78–82.

75. See FTC REPORT, *supra* note 5, at 37–38.

76. *Eli Lilly*, 119 F.3d at 1568–69.

77. See *supra* note 65–67 and accompanying text.

rejected the LWD-based validity challenge raised by the alleged infringer.⁷⁸ However, in that case the LWD challenge was directed specifically at claims reciting recombinant cells, not biomolecules (i.e., the actual biologic or the DNA encoding it), so the decision is not directly relevant to the question of whether patent claims broadly encompassing variations of a biologic or the DNA sequence encoding it, would survive a LWD-based challenge.⁷⁹ The FTC Report specifically focuses on the availability of protein “percent identity claims” to protect biologics,⁸⁰ but my research has been unable to identify a single example of such a patent claim that has been successfully enforced against a biologic competitor.

Perhaps more importantly, there have been significant legal developments affecting LWD since the publication of my 2007 article that could dramatically impact the ability of biologic innovators to obtain effective scope of patent coverage. Prior to 2007, my study showed that for the most part the PTO had applied LWD in a manner effectively redundant with the enablement requirement.⁸¹ When patent examiners attempted to use LWD as a super-enablement requirement to limit the scope of biologic claims, they were generally reversed on appeal by the BPAI.⁸² However, in 2008 the PTO issued revised written description guidelines that in some respects contradict official PTO policy reflected in the original written description guidelines that had been in effect since 1999.⁸³ The revised guidelines apply LWD to biotechnology inventions in a manner that imposes substantial limitations on claim scope in a manner that is distinct, and in some respects more restrictive, than the limitations imposed by the enablement requirement.⁸⁴ This

78. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330–34 (Fed. Cir. 2003).

79. *Id.*

80. FTC REPORT, *supra* note 5, at 36–37.

81. Holman, *Lilly*, *supra* note 8, at 71.

82. *Id.* at 78–79.

83. See U.S. PATENT & TRADEMARK OFFICE, WRITTEN DESCRIPTION TRAINING MATERIALS 13–14 (2008), available at <http://www.uspto.gov/web/menu/written.pdf>; U.S. PATENT & TRADEMARK OFFICE, REVISED INTERIM DESCRIPTION GUIDELINES TRAINING MATERIALS 27–29 (1999), available at <http://www.uspto.gov/web/offices/pac/writtendesc.pdf>.

84. Christopher Holman, *PTO Issues Revised Written Description Guidelines, Further Muddying the Waters*, HOLMAN’S BIOTECH IP BLOG (Apr. 24, 2008, 4:01 PM), <http://holmansbiotechipblog.blogspot.com/2008/04/pto-issues->

applies particularly to protein percent identity claims of the type the FTC Report identifies as amenable to broad claim coverage. Anecdotaly, it also appears that the PTO has started to apply LWD more aggressively as a super-enablement requirement to claims on biomolecules. As a result, the broad seventy percent identity claims identified in the FTC Report are probably no longer available to most patent applicants, who will be forced to settle for a significantly narrower range of protection, ninety-five percent or greater in most cases.⁸⁵

A good example of this is the recent trend towards more stringent application of LWD to limit biomolecule claim scope can be seen in *Ex parte Kubin*, a recent BPAI decision that affirmed an examiner's rejection of claims reciting DNA molecules encoding proteins sharing eighty percent identity with a segment of a disclosed protein, and retaining the function of the disclosed reference protein.⁸⁶ According to the PTO, even though the applicant had enabled the genus of molecules encompassed by the claim, the claim failed to comply with LWD for failing to adequately identify which molecules sharing eighty percent or greater sequence identity retained the function of the reference molecule.⁸⁷ This is a sharp departure from earlier BPAI decisions upon which I based the findings of my article.⁸⁸ *Kubin* signals that in the future, inventions relating to biologic drugs may be afforded substantially narrower patent protection than they have in the past, undercutting the FTC's assumption that broad patent protection will be available for biologics.

Quite recently, the Federal Circuit agreed to reconsider the doctrine of LWD en banc,⁸⁹ and it is possible the court will curtail, or perhaps even jettison LWD. But for the time being LWD appears to be playing an increasing role in restricting the scope of issued patent claims relating to biomolecules, and it could also implicate the validity and scope of issued patents relating to biologics. It is also important to remember that my article was focused entirely on LWD, and there are a variety of other patent doctrines that could also substantially limit the ability of biologic innovators to secure broad patent protection capable of

revised-written-description.html.

85. Based on conversations with patent attorneys working in this area.

86. *Ex Parte Kubin*, 83 U.S.P.Q.2d 1410, 1412, 1417 (B.P.A.I. 2007).

87. *Id.* at 1414.

88. Holman, *Lilly*, *supra* note 8, at 42–57.

89. *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 332 Fed. App'x 636, 637 (Fed. Cir. 2009).

encompassing potential FOB products. In particular, even if the Federal Circuit decides to eliminate LWD, the enablement requirement will still serve to limit the scope of protection available to biologic innovators. In recent years, there has been a renewed emphasis in the courts on the use of the enablement requirement to limit claim scope.⁹⁰

E. ONGOING DEVELOPMENTS IN TECHNOLOGY AND LAW
PERTAINING TO BIOLOGICS COULD CHALLENGE THE ABILITY OF
BIOLOGIC INNOVATORS TO SECURE ADEQUATE PATENT
PROTECTION

Although the past experiences of small molecule and biologic innovators in using patents to maintain market exclusivity is informative, there are significant caveats that should not be forgotten. These include the changing nature of biologic drugs, uncertainty as to how far an FOB will be permitted to deviate in structure from a reference biologic while still maintaining sufficient biosimilarity to benefit from an abbreviated FOB approval process, and ongoing (and at times dramatic) developments in patent law. Historically, most biologic drugs were essentially just recombinant versions of naturally existing human proteins (first-generation human proteins). However, the trend in biologics is towards extensively engineered variants of naturally occurring proteins (second-generation human proteins) and therapeutic monoclonal antibodies. Past experience with the use of patents to protect first-generation human proteins will be of only limited use in predicting the ability of patents to adequately protect more recent and yet-to-be-developed biologic drugs.

For example, the nonobviousness requirement⁹¹ could substantially limit the ability of biologic innovators to effectively patent engineered variants of previously known human proteins. Prior art disclosing the naturally occurring protein and the gene encoding the protein, combined with known methodologies for structurally engineering proteins to improve or modify function, could render a second-generation human protein obvious under the patent laws, even if the product would be ex-

90. See, e.g., *Halliburton Energy Servs., Inc. v. M-I LLC*, 514 F.3d 1244 (Fed. Cir. 2008); *Sitrick v. Dreamworks, LLC*, 516 F.3d 993 (Fed. Cir. 2008); *Auto. Techs. Int'l, Inc. v. BMW of N. Am., Inc.*, 501 F.3d 1274 (Fed. Cir. 2007); *Liebel-Flarsheim Co. v. Medrad, Inc.*, 481 F.3d 1371 (Fed. Cir. 2007).

91. 35 U.S.C. § 103 (2006).

tremely expensive to bring to market and would provide patients with substantial benefit. Historically, it has been generally thought that the nonobviousness doctrine imposes a relatively low barrier to the patenting of newly isolated genetic sequences and other biotechnology-related inventions. However, the Supreme Court's recent decision in *KSR v. Teleflex*⁹² has apparently raised the nonobviousness bar to patentability, and in its wake, pharmaceutical patent claims have been invalidated that would likely have survived and obviousness challenge pre-*KSR*.⁹³

The Federal Circuit recently affirmed a PTO obviousness-based rejection of claims directed to a novel genetic sequence of therapeutic relevance, signaling that in the future patents relating to biologics will face a more stringent interpretation of the nonobviousness doctrine than in the past.⁹⁴ Rapid developments in molecular biology are constantly creating new prior art that could be combined by a patent examiner or court to establish the obviousness of an invention. In tandem, the accumulation of prior art as technology advances and more stringent application of the nonobviousness requirement could substantially restrict the availability of adequate patent protection for the innovative biologic drugs of the future.

To date, monoclonal antibodies have generally been afforded relatively broad patent protection, and recently a jury found a COM patent claiming a monoclonal antibody infringed by Abbott's biologic product adalimumab (HUMIRA).⁹⁵ However, again, there is a concern that the rapidly expanding prior art in this area, combined with a more stringent application of the nonobviousness doctrine, could preclude innovators from securing adequate patent protection on monoclonal antibodies, such as a monoclonal antibody directed against an antigen known in the prior art. Furthermore, although the PTO and courts have up until this point applied LWD and enablement requirements less stringently to monoclonal antibodies than

92. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398 (2007).

93. See *Bayer Schering Pharma AG v. Barr Lab., Inc.*, 575 F.3d 1341 (Fed. Cir. 2009) (affirming based on the obviousness standard articulated in *KSR*); *Perricone v. Medicis Pharm. Corp.*, 539 F. Supp. 2d 571, 584–87 (D. Conn. 2008) (invalidating claims based on the obviousness standard from *KSR*).

94. *In re Kubin*, 561 F.3d 1351, 1360–61 (Fed. Cir. 2009) (declining to adopt a narrow interpretation of *KSR*).

95. *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 669 F. Supp. 2d 756, 759–60, 773 (E.D. Tex. 2009).

other biomolecules, both doctrines are in flux, particularly LWD, and it is by no means certain that broad patent protection will be available to FOB variants of this increasingly important class of biologics.

Some of the early biologic drugs were able to benefit from an extended term of patent protection because the patent applications were filed at a time when patents enjoyed a seventeen-year term beginning on the date the patent issued. The law was changed in 1995, and subsequently filed patent applications result in patents which expire twenty years after the date the initial priority application was filed. Patents that were in force, or pending, when the law was changed were afforded a term that is measured as the longer of twenty years from the priority date or seventeen years from the date of issue. Amgen, for example, holds several patents relating to its erythropoietin products which fall into this in-between category.⁹⁶ This is yet another reason to question whether future biologic innovators will be able to employ patents as effectively as has been the case for the pioneering biologic products.

Some biologic innovators not only benefited from a patent term of seventeen years from time of issuance, but also from continuation or divisional patent applications which were pending on June 6, 1995 (the date the change in law became effective). Patents issuing from these applications are entitled to a term significantly longer than twenty years from their priority date. Today, there are probably very few instances of patents issuing from applications that were filed before the effective date more than fourteen years ago, and it is safe to assume that new biologics coming to market will not enjoy patent protection beyond twenty years from the patent application's initial filing date. Nevertheless, biologics companies today continue to rely heavily on continuation applications in attempts to obtain more robust (albeit not longer) patent coverage for their developmental products.

In order to manage its workload, the PTO recently sought to institute changes that would substantially limit the ability of biologics companies to use continuation applications in this manner.⁹⁷ Those changes have been challenged in the courts

96. Holman, *Impact*, *supra* note 66, at 327.

97. See *Tafas v. Doll*, 559 F.3d 1345, 1350 (Fed. Cir. 2009).

and are currently on hold,⁹⁸ but it is too early to know whether some limitation on continuation practice might be instituted at some point, which could further limit the ability of drug companies to obtain effective patent protection.

The FTC Report argues that an extended DEP is not warranted because it predicts innovators will use citizen's petitions and other non-patent tactics to block market entry by the FOB.⁹⁹ But under the FOB legislative proposals currently being considered, the FOB applicant is allowed to apply for regulatory approval years before the expiration of the data exclusivity period, and during this time FDA should be able to address legitimate citizen's petitions and the like, while denying those that are mere pretense used as a delaying tactic. If a problem exists with abuse of the citizen's petition process, that issue should be addressed by Congress and/or FDA, and not used as an excuse to deny biologic innovators a reasonable period of market exclusivity.

III. FOB LEGISLATION SHOULD INCLUDE A FAIR AND BALANCED PRE-APPROVAL PATENT LITIGATION PROCESS

Despite the FTC's June 2009 recommendations, all of the pending FOB legislative proposals (House Bill 1548, House Bill 1427, Senate Bill 726, and the House and Senate Amendments) include some variation of a pre-approval patent resolution process (PPRP),¹⁰⁰ each more or less distantly related to the PPRP provided under Hatch-Waxman for small molecule drugs (often referred to as "Paragraph IV" litigations).¹⁰¹ However, the FTC Report recommends against the creation of a PPRP for biologics, based in large part on its conclusion that: (1) the primary justification for the inclusion of a PPRP for small molecule drugs in the Hatch-Waxman Act was a concern that generic companies would be underfunded and effectively judgment-proof, but that this rationale will not apply to the more established biotechnology companies that the FTC predicts will be the primary developers of FOBs;¹⁰² and (2) provisions for pro-

98. *Id.* at 1359–62.

99. FTC REPORT, *supra* note 5, at 43.

100. *See supra* notes 9–16 and accompanying text.

101. The Hatch-Waxman PPRP is governed by 35 U.S.C. § 271(e)(2) (2006) and 21 U.S.C.A. § 355(j)(5)(B)(iv) (West 1999 & Supp. 2009).

102. FTC REPORT, *supra* note 5, at 47–48, 57–59.

protecting the confidentiality of information exchanged between the innovator and FOB applicant are insufficient, and the exchange of information could facilitate anticompetitive collusion between competitors.¹⁰³ In this section, I address both of these issues, and explain why a PPRP is important and justified for biologic innovators.

As an initial matter, it should be noted that the importance of a PPRP is directly correlated with the length of a DEP provided to biologic innovators. A twelve- to fourteen-year DEP, for example, would deemphasize the role of patents in protecting biologics and consequently render the availability of a PPRP less critical. However, if Congress provides only a short DEP, such as proposed under House Bill 1427,¹⁰⁴ a PPRP could prove crucial in order to ensure biologic innovators an adequate opportunity to effectively enforce their patents. It should also be stressed that any PPRP should not discriminate against biologic innovators, either with respect to FOB applicants, or in comparison with the rights afforded small molecule drug innovators.

According to the FTC, the PPRP for small molecule drugs was originally included in the Hatch-Waxman Act primarily for the purpose of protecting innovators from the possibility of judgment-proof generic infringers.¹⁰⁵ The FTC forecasts that this will not be a problem in the context of FOBs, based on an assumption that the damages resulting from infringement will be less than in the case of small molecule drugs, and because FOB manufacturers will be better funded and able to satisfy a substantial judgment.¹⁰⁶ However, it is not entirely clear that infringement by an FOB will result in substantially less lost profits to biologic innovators than infringement by generic drugs cause for conventional drugs. Biologics are generally much more expensive to develop and produce than conventional drugs, and at this point it is hard to say to what extent damages would accrue based on market entry by an FOB later found to be infringing, particularly if the judgment of infringement does not occur until years after the FOB has entered the market. It is also unclear that FOB manufacturers will be in a sub-

103. *Id.* at 57–59.

104. H.R. 1427, 111th Cong. § 3(a)(2) (2009).

105. FTC REPORT, *supra* note 5, at 47–48.

106. *See id.* at 53.

stantially better position to pay a larger award of damages than conventional generic drug companies. For example, economist Robert Shapiro recently published a report predicting that an FOB pathway for biologic drugs will result in huge savings for U.S. consumers, based in large part on his assumption that the production of biologic drugs will shift to low-cost countries such as China and India.¹⁰⁷ Leaving aside the potential safety concerns associated with offshoring the production of biologic drugs to foreign companies competing on the basis of cost, these companies might also lack the financial resources to satisfy a large judgment if found liable for infringement subsequent to an extended at-risk product launch.

But more importantly, there are other compelling justifications for a PPRP for drugs that the FTC Report ignores, including the potential for irreversible price erosion and loss of consumer goodwill if a competing drug enters the market prior to a determination of patent infringement. Prescription drugs, and particularly biologic drugs, are to a large extent paid for by third-party payers, according to complex formularies and negotiated rates of reimbursement. In this environment, an innovator unable to block initial market entry by an FOB competitor will suffer not only lost sales, but also faces substantial and potentially irreversible price erosion and loss of goodwill. Absent some mechanism for initiating an infringement lawsuit prior to FOB market entry, the innovator would have no opportunity to convince a court to grant a preliminary injunction to avert this harm, no matter how strong the merits of the patent case might be.

A. FOB LEGISLATION SHOULD INCLUDE A FAIR AND BALANCED PRE-APPROVAL PATENT LITIGATION PROCESS

The issue of irreversible price erosion based on premature market entry by a drug competitor was addressed recently by the Federal Circuit in *Sanofi-Synthelabo v. Apotex*.¹⁰⁸ The issue on appeal was whether the district court was justified in entering a preliminary injunction barring a company from marketing a generic version of the drug Plavix®.¹⁰⁹ The district court

107. ROBERT J. SHAPIRO ET AL., THE POTENTIAL AMERICAN MARKET FOR GENERIC BIOLOGICAL TREATMENTS AND THE ASSOCIATED COST SAVINGS 7 (2008), available at http://www.insmed.com/pdf/Biogeneric_Savings.pdf.

108. *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1381 (Fed. Cir. 2006).

109. *Id.* at 1372–74.

had determined that the market presence of the generic product would likely result in an irreversible erosion in the price that the innovator would be able to charge for its branded product, and that this erosion in price could not be reversed by an injunction ordering the generic product off the market at a later date.¹¹⁰ Even if the branded company were able to drive the generic product off the market, the district court found that third-party payers would resist going back to paying the higher price charged prior to the entry of the generic product.¹¹¹ The court also found that the innovator would be irreversibly harmed by loss of consumer goodwill by customers who will grow accustomed to lower prices while the generic product is on the market.¹¹² On appeal, the Federal Circuit affirmed the district court's judgment.¹¹³

Although *Sanofi-Synthelabo v. Apotex* involved a small molecule drug, the rationale behind the court's conclusion that irreversible price reduction is likely upon market entry by a competitor applies with equal force in the market for biologics, where reimbursement is likewise dictated by the complex negotiated relationships between drug companies and third-party payers eager to cut costs. Indeed, the whole point of the FOB legislation is to create competition that will force innovators either to lower prices or to lose sales of their product to an FOB competitor. Thus, as in the case of conventional drugs, market entry by an FOB will often threaten irreversible damages to the innovator owing to price erosion.

Not surprisingly, in a recent case involving a biologic drug, the court came to a similar conclusion when faced with the question of whether to enjoin market entry by a competing product. In *Amgen v. F. Hoffman-La Roche*, the district court

110. *Sanofi-Synthelabo v. Apotex, Inc.*, 488 F. Supp. 2d 317, 342–43 (S.D.N.Y. 2006).

111. *Id.*

112. *Id.* at 343.

113. *Sanofi-Synthelabo*, 470 F.3d at 1385; see also *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1362 (Fed. Cir. 2008) (citing *Sanofi-Synthelabo*, 470 F.3d at 1383) (affirming the district court's grant of a preliminary injunction and stating that "erosion of markets, customers, and prices is rarely reversible"); *Purdue Pharma L.P. v. Boehringer Ingelheim GMBH*, 237 F.3d 1359, 1368 (Fed. Cir. 2001) (affirming the district court's determination that testimony about the likelihood of price erosion and loss of market position upon market entry by a competing generic drug supported a finding of irreparable harm and entry of a preliminary injunction).

judge initially considered denying Amgen an injunction while the case was on appeal, in the belief that the availability of a competing biosimilar could benefit patients.¹¹⁴ However, upon further reflection the judge decided to enter the injunction, concluding that even a short period of market entry by the infringing product would result in irreversible harm to the patent owner Amgen.¹¹⁵ The judge also opined that the injunction benefited the “public’s interest in a robust patent system that maintains incentives for pharmaceutical innovation.”¹¹⁶ The Federal Circuit affirmed the injunction on appeal.¹¹⁷

Market entry by an infringing FOB could also result in loss of goodwill for the innovator, for a variety of reasons. For example, consider a scenario where an FOB has entered the market for some period of time prior to a finding of infringement, but is then enjoined by the court from further marketing the product for the remainder of the patent term. It is highly foreseeable that some patients who have been using the FOB will strongly resist being compelled to switch over to the innovator’s product, either because of a perception that the FOB is somehow superior to the innovator product, or simply based on an unwillingness to accept the risk that some subtle difference between the products could render the two products not entirely interchangeable. Even if there is no scientific basis to think that the FOB is in any way superior to the innovator product, the innovator will be in a very difficult position if patients plead for continued access to the FOB on humanitarian grounds.

The recent case of *Genentech v. Insmmed* appears to provide an example of this phenomenon.¹¹⁸ The patent owner prevailed in a patent infringement lawsuit against a competing biologic manufacturer and obtained a consent judgment that included an injunction requiring the infringer to exit the market.¹¹⁹

114. *Amgen, Inc. v. F. Hoffmann-La Roche Ltd.*, 581 F. Supp. 2d 160, 209–10 (D. Mass. 2008).

115. *Id.* at 210, 212 (finding that market entry by a competing biologic “would cause immense, immeasurable, irreparable harm, with the balance of the hardships falling on [the innovator],” and would result in “lost profits, market share, and goodwill”).

116. *Id.* at 210.

117. *Amgen, Inc. v. F. Hoffman-La Roche, Ltd.*, 296 Fed. App’x 69, 70 (Fed. Cir. 2008).

118. *Genentech, Inc. v. Insmmed, Inc.*, 436 F. Supp. 2d 1080 (N.D. Cal. 2006).

119. *Consent Judgment & Permanent Injunction, Genentech, Inc. v. Insmmed, Inc.*, 436 F. Supp. 2d 1080 (N.D. Cal. 2006) (No. 4:04CV05429), 2007 WL

However, a number of patients who had been taking the infringing product complained vociferously that the infringing product was somehow more effective in the treatment of their condition than the innovator's product, and launched a petition drive demanding availability of the infringing product in the United States.¹²⁰ Note that there appears to be no compelling scientific basis for concluding that the infringing product is in fact superior, but faced with patient concerns an innovator company will often feel compelled to give in to public sentiment, regardless of the scientific merits of the case, both for humanitarian reasons and to maintain the goodwill of patients and doctors. In fact, faced with public pressure the patent owner, Genentech, agreed to a modified settlement permitting limited distribution of the infringing product in the United States.¹²¹

Of course, if a competing biologic truly does have superior properties relative to the first product to enter the market, it is important to facilitate early patient access to the best therapeutic available. But if in fact an FOB has significant clinical benefits compared to the original innovator product, the company producing the FOB should use the conventional FDA regulatory process to gain approval of its drug, including an FDA-validated determination of the distinct safety and efficacy properties of its new biologic. The purpose behind FOB legislation is to provide improved access to biosimilar molecules that can be substituted for innovator molecules, not to provide an abbreviated pathway for the approval of different and allegedly superior biologics.

Economic injury to an innovator resulting from market entry by a competitor due to price erosion and loss of goodwill might not only be irreversible, but also inadequately compensable by a post-judgment award of money damages owing to difficulties in quantifying the extent of injury. Although courts will sometimes award a prevailing patent owner lost profit damages, in practice, it will often prove difficult, if not impossible, for the patent owner to satisfy the high degree of proof required by courts to substantiate an award of lost profit damages. The patent owner bears the burden of establishing the

775609; Holman, *Learning, supra* note 68, at 233.

120. Holman, *Learning, supra* note 68, at 233 & n.117.

121. *Id.* at 233.

amount of damages,¹²² and courts often require patent owners seeking lost profit damages to provide a detailed and quantitative economic analysis to establish the amount of profits that would have been earned in a hypothetical “but for” world in which the infringement never occurred.¹²³ Judge Easterbrook has described in great detail the sorts of complex economic analysis required to support an award of lost profit damages.¹²⁴ Even if a court is convinced that the patent owner has suffered lost profits, it will often balk at awarding lost profit damages if unconvinced that the patent owner has marshaled “[sufficient] evidence from which a fair determination could be made as to the *amount* of profit plaintiff would have made.”¹²⁵

This could prove particularly problematic for a biologic innovator that has prevailed in a patent infringement suit, but it is unable to establish the actual amount of loss with a sufficient degree of economic rigor to satisfy a court. As noted by the court in *Sanofi-Synthelabo v. Apotex*, market entry by a competing drug is likely to result in large losses to the patent owner due to price erosion, but the specific amount can be extremely difficult to calculate with the required degree of certainty.¹²⁶ There are many examples where courts have denied a prevailing patent owner lost profit damages because the court found the amount of lost damages requested by a patent owner was too “speculative.”¹²⁷ This strict requirement of proof to establish lost profit damages could preclude a biologic innovator from obtaining adequate compensation for lost profits.

Courts are particularly inclined to deny an award of dam-

122. See, e.g., *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1578–79 (Fed. Cir. 1992) (stating that a plaintiff’s burden to establish lost profits is a preponderance of the evidence).

123. See, e.g., cases cited *infra* note 127.

124. *In re Mahurkar Double Lumen Hemodialysis Catheter Patent Litigation*, 831 F. Supp. 1354, 1383–85 (N.D. Ill. 1993).

125. *Panduit Corp. v. Stahlin Bros. Fibre Works, Inc.*, 575 F.2d 1152, 1156 (6th Cir. 1978) (emphasis added).

126. *Sanofi-Synthelabo v. Apotex, Inc.*, 488 F. Supp. 2d 317, 342–43 (S.D.N.Y. 2006).

127. *Hebert v. Lisle Corp.*, 99 F.3d 1109, 1119 (Fed. Cir. 1996) (“Damage awards can not be based upon speculation or optimism, but must be established by evidence.”); see also *King Instruments Corp. v. Perego*, 65 F.3d 941, 952 (Fed. Cir. 1995) (reviewing application of the “but for” standard); *State Indus. v. Mor-Flo Indus.*, 883 F.2d 1573, 1577 (Fed. Cir. 1989) (explaining requirements for awarding lost profit damages); *Del Mar Avionics, Inc. v. Quinton Instrument Co.*, 836 F.2d 1320, 1327 (Fed. Cir. 1987) (acknowledging that determination of actual damages may be difficult).

ages based on future lost profits, which could preclude adequate compensation for a biologic innovator that has suffered irreversible losses due to the ongoing effects of price erosion and loss of goodwill.¹²⁸ This would leave the innovator with nothing more than reasonable royalty damages, which will generally be far lower than the actual harm caused by FOB market entry. Clearly, it is important to provide innovators with an opportunity to gain access to the courts to attempt to obtain a preliminary injunction blocking market entry. This might be the only way for a biologic innovator to ward off the irreversible and uncompensable injury resulting from market entry by an FOB later found to be infringing.

It bears noting that none of the proposed FOB PPRPs would include a mandatory stay of the approval of the FOB. This is a key feature of the Hatch-Waxman PPRP, pursuant to which FDA will impose a mandatory thirty-month stay in the approval of a generic drug after a Paragraph IV infringement suit is filed. In contrast, the proposed FOB PPRPs would merely provide standing for the innovator to initiate an infringement suit. To block market entry by the FOB, an innovator would need to convince a court to enter a preliminary injunction, which would require a showing of reasonable likelihood of success on the merits of the patent case, as well as equitable considerations weighing in favor of injunction.¹²⁹ An innovator with a weak patent case would not be allowed to block market entry by means of a preliminary injunction, and an FOB applicant facing an infringement suit of dubious merit would likely not be dissuaded from entering the market once the FOB application has been approved.

B. FOB LEGISLATION LACKING A PPRP WOULD DISCRIMINATE AGAINST COMPANIES DEVELOPING INNOVATIVE BIOLOGIC MEDICINES

FOB legislation that fails to provide a PPRP would unjustifiably discriminate against biologic innovators in comparison

128. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1581 (Fed. Cir. 1992) (affirming the district court's holding that determination of future estimated damages was speculative and reasoning that "[t]he burden of proving future injury is commensurately greater than that for damages already incurred, for the future always harbors unknowns.")

129. *See, e.g., Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1374 (Fed. Cir. 2006).

with small molecule innovators. In other contexts, the two types of drug innovators have generally been afforded equivalent treatment. For example, Hatch-Waxman includes a regulatory approval exemption, 35 U.S.C. § 271(e)(1), which exempts a generic company from patent infringement liability arising out of activities relating to generation of data for submission to FDA.¹³⁰ This exemption allows a generic company to conduct the study necessary to secure FDA approval prior to the expiration of the innovator's patents, and thus be poised to enter the market immediately upon patent expiration. While this exemption limits the patent rights of the innovator, the PPRP provided under Hatch-Waxman provides balance by permitting the innovator to bring suit prior to market entry in order to resolve issues of infringement prior to market entry by the generic. In conjunction, the two provisions work to ensure that generic drugs can enter the market promptly upon patent expiration, but that innovators have the opportunity to block generic market entry that would infringe their patents.

Subsequent court decisions have established that the regulatory approval exemption is not limited to conventional drugs, but also shields activities relating to regulatory submissions made in connection with the approval of a biologic product.¹³¹ Thus, FOB applicants already benefit from the regulatory approval exemption from patent infringement liability, so creation of a PPRP for FOBs would provide balance comparable to the balance that already exists for small molecule innovators and generic competitors.

The FTC Report seems to assume that under the current system biologic innovators are only able to sue for patent infringement after a competing product has entered the market. However, it is actually quite common for a biologic innovator to bring a declaratory judgment action seeking a declaration of patent infringement and an injunction blocking market entry by a potential competitor. The courts have allowed these declaratory judgment actions to proceed based on the imminent threat of infringement established by the potential competitor's application for marketing approval of its product.¹³² But under

130. 35 U.S.C. § 271(e) (2006).

131. *See* Amgen, Inc. v. Int'l Trade Comm'n, 565 F.3d 846, 851 (Fed. Cir. 2009); Genentech, Inc. v. Insmmed, Inc., 436 F. Supp. 2d 1080, 1095 (N.D. Cal. 2006).

132. *See, e.g.,* Amgen, Inc. v. Hoechst Marion Roussel, Inc., 457 F.3d 1293, 1295–96 (Fed. Cir. 2006); Amgen, Inc. v. F. Hoffmann-La Roche Ltd., 581 F.

the current system, there is no guarantee that a court will find the innovator has standing to bring a declaratory judgment action, and there have been cases where such actions have been dismissed for lack of sufficient controversy to satisfy the standing requirement.¹³³ Once an FOB applicant has applied for approval to market a competing version of an innovator's drug, the innovator should be able to begin proceedings to resolve patent issues, and a PPRP would provide clarity as to when an innovator will have standing to bring such a suit.

Generic companies routinely challenge small molecule drug patents with the expectation of having to litigate the matter prior to market entry; this is simply part of the cost of doing business in the industry. The FTC Report predicts that FOB competitors will generally be well established and well-funded biotechnology companies, the type of company that should be able to manage the cost of commencing litigation of patents prior to market entry.¹³⁴ If they are not, they could be the type of judgment-proof company which the FTC Report would find to justify the availability of a PPRP. A PPRP that does not automatically stay approval of the allegedly infringing product would not block FOB market entry unless a court determines that there is a substantial likelihood that the patent owner will ultimately prevail, thus ensuring that biologic innovators will not be able to game the PPRP by filing a non-meritorious infringement lawsuit merely as a tactic to delay market entry.

IV. AN EXCHANGE OF CONFIDENTIAL INFORMATION WILL BE NECESSARY TO ASSESS INFRINGEMENT AND SHOULD NOT CREATE AN UNDUE OR UNIQUE RISK OF COLLUSION

Because of the complex nature of biologics and biologic production, and the heavy reliance of biologic innovators on patents relating to the processes and technologies used to produce the product, it will be necessary for the innovator to have some access to information about the specific nature of the proposed FOB product and production process in order to assess whether infringement would occur. Proposed FOB legislation would in-

Supp. 2d 160, 166, 229 (D. Mass. 2008).

133. See, e.g., *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F.Supp.2d 104, 111-13 (D. Mass. 1998).

134. FTC REPORT, *supra* note 5, at 53.

clude various provisions governing the exchange of confidential information, as well as provisions designed to limit access to the confidential information. In spite of these provisions to maintain confidentiality of proprietary information, the FTC Report voices concern that these safeguards will be insufficient to prevent an unreasonable likelihood that the data exchange could lead to collusion between the innovator and FOB companies.¹³⁵ However, without this information it will be difficult in many cases for an innovator to assess whether an FOB product would infringe its patent. This is particularly true since, unlike a generic version of a drug, an FOB product could differ substantially from the innovator product and be produced using a very different process.

The FTC's concerns regarding the potential for collusion are probably overstated. Litigation, particularly litigation involving technology and intellectual property, often requires some exchange of information between representatives of competing companies, and methods have been created for minimizing the anticompetitive potential of these exchanges. For example, some generic drug patent litigation involves patents claiming specific formulations or processes used in drug production, and resolution of these cases necessarily requires some exchange of information between the competing companies' attorneys.

Even if there is no PPRP for biologics, biologic innovators will often be able to bring declaratory judgment actions to establish that marketing of the FOB would be infringing, and even if denied standing in a declaratory judgment action, they still will be able to bring an infringement lawsuit once the FOB enters the market. This type of litigation will likewise necessitate some exchange of information, but there are safeguards that can be used to minimize the danger that this exchange of data will result in collusion. In recent years, the FTC has closely scrutinized the activities of both generic and branded drug companies, and particularly their interactions with each other, and should be able to continue to do so, thus minimizing the potential for anticompetitive collusion. In any event, the FTC has failed to articulate any rational basis for thinking that the exchange of information that would occur as part of a PPRP for biologics raises a unique potential for collusion that does not already exist with respect to the PPRP for conventional drugs,

135. *Id.* at 58.

and with non-PPRP patent litigation in the pharmaceutical industry and beyond.

V. PPRP PROVISIONS THAT WOULD COMPEL INNOVATORS TO IDENTIFY AND ASSERT PATENTS PRIOR TO FOB APPROVAL ARE UNNECESSARY, DISCRIMINATORY, AND WOULD WEAKEN INCENTIVES FOR INNOVATION

Some of the proposals, particularly House Bill 1427, include provisions that would seek to compel a biologic innovator to identify all patents that might be infringed by an FOB, and to assert those patents in a lawsuit against an FOB applicant prior to FOB marketing approval.¹³⁶ Failure to identify a patent or to assert it in a timely manner would result in draconian penalties for the innovator. These heavy-handed attempts to compel an innovator to bring a lawsuit prior to FOB marketing approval are unjustified, and would hurt innovation by severely degrading the value of patents held by innovators.

The provision requiring innovators to identify patents that could be infringed by an FOB are unfair and unnecessary. As noted in the FTC Report, patent information is freely available in the public domain, and an FOB applicant will have ample opportunity to identify and address relevant issued patents.¹³⁷ It is important to remember that by entering the market an FOB producer will be subject to lawsuits not only by the innovator, but by third parties owning patents allegedly covering the FOB, or processes and technologies used in manufacturing it. These sorts of third-party patent infringement lawsuits, which do not involve direct market competitors, are quite common in the context of biologic drugs. This is not surprising in view of the large number of complex technologies used in the development and manufacturing of biologics, and the large number of patents covering these technologies and owned by dispersed parties.

The threat of being sued for patent infringement after market entry is a simple reality that any biologic producer faces, and that also applies to FOB producers. For a variety of reasons, some of which were addressed in the FTC Report,¹³⁸ it

136. H.R. 1427, 111th Cong. (2009).

137. See FTC REPORT, *supra* note 5, at 30–31.

138. See *id.* at 59–60.

would be entirely impractical and unwise to attempt to force all third-party patent owners to identify patents that might be infringed by an FOB, and to bring a lawsuit prior to the marketing approval of FOB. At the same time, it makes no sense to discriminate against biologic innovators by requiring them to bring suit early but not requiring the same of other third-party patent owners. Thus, any PPRP provisions enacted for biologics should not include any provisions that would seek to compel biologic innovators to identify potentially infringing patents, or to bring suit prior to FOB marketing approval or risk loss of patent rights. This would be consistent with the PPRP process currently available for conventional drug innovators, which contains no provision that would force an innovator to choose between bringing suit immediately or forfeiting the ability to obtain sufficient remedies for patent infringement later.¹³⁹

Not only are provisions compelling innovators to identify and assert patents prior to FOB marketing approval unnecessary, they also discriminate against biologic innovators compared to conventional drug innovators. These provisions would dramatically weaken the patent rights of biologic innovators, which would result in reduced investment and innovation in biologics.

A. HATCH-WAXMAN STRIVES TO BALANCE THE INTERESTS OF INNOVATORS AND GENERIC COMPANIES

To better appreciate the harshness of some aspects of the PPRP provisions currently being considered by Congress, it is instructive to first consider the relatively balanced approach embodied in the Hatch-Waxman PPRP. Under Hatch-Waxman, an innovator marketing an approved conventional drug is required to list all of its patents that claim the drug, or a method of using the drug, in an FDA publication known as the Orange Book.¹⁴⁰ The Orange Book listing requirement only applies to drugs regulated under the Food Drug and Cosmetic Act (FDCA),¹⁴¹ and thus does not apply to most biologic drugs, which are regulated under the Public Health Services Act (PHSA).¹⁴² Listing a patent in the Orange Book not only pro-

139. *See id.* at 49-50; *see also* Holman, *Reverse Payments*, *supra* note 25, at 509-16 (2007) (explaining PPRP for conventional drugs under Hatch-Waxman).

140. *See id.* at 49.

141. 21 U.S.C. §§ 301-399a (2006).

142. 42 U.S.C. §§ 201-300jj-38 (2006).

vides notice to potential generic competitors of the most relevant patents, but also effectively puts a bounty on each of the listed patents, in the form of a 180-day period of generic exclusivity that is granted to any generic company that challenges an Orange Book-listed patent by applying for approval to commence marketing of the generic version prior to patent expiration.¹⁴³ The generic company must specifically allege that the challenged patent is invalid or would not be infringed by the company's proposed generic product. During these 180 days, FDA will not authorize the marketing of any other generic version of the drug, a boon for the generic company and a substantial financial incentive for patent challenges.

Orange Book listing also provides substantial benefit to the patent owner. FDA will not approve a generic version of a drug until all of the Orange Book-listed patents relating to the drug have expired, unless the generic applicant explicitly challenges a patent as described above. If a generic company does challenge an Orange Book-listed patent, Hatch-Waxman authorizes the patent owner to immediately file an infringement lawsuit before the proposed generic product has been approved for marketing. If suit is filed within forty-five days, the statute specifies that FDA will not approve the generic application for at least thirty months.¹⁴⁴ In effect, Orange Book listing allows the patent owner to obtain an automatic preliminary injunction of at least thirty months, blocking generic market entry without having to establish the reasonable expectation of success and other equitable factors normally necessary to convince a court to grant a preliminary injunction.¹⁴⁵ Ideally, the thirty months provides the parties an opportunity to resolve patent issues prior to generic market entry.

The benefits of Orange Book listing for innovators tend to balance other provisions of Hatch-Waxman that worked as a disadvantage, such as the regulatory approval exemption from patent infringement that permits generic companies to conduct the tests necessary to achieve FDA approval prior to the expiration of the innovator's patents. Another substantial benefit to generic companies is the abbreviated approval process which allows them to gain marketing approval based on data generat-

143. Holman, *Reverse Payments*, *supra* note 25, at 509–16 (2007).

144. *Id.*

145. *Id.*

ed and submitted by the innovator, and also permits FDA to authorize pharmacists to substitute the generic drug for a branded drug prescribed by a physician.

B. SOME OF THE PROPOSED PPRP PROVISIONS DEVIATE DRAMATICALLY FROM THE BALANCED APPROACH EMBODIED IN HATCH-WAXMAN

In stark contrast with the balanced approach of Hatch-Waxman, House Bill 1427 would create a PPRP weighted heavily against the patent owner. Under House Bill 1427, any applicant or prospective applicant for approval of an FOB would be authorized to demand from any innovator marketing an approved biologic a list of all patents owned, licensed or controlled by the innovator, that could potentially be infringed by a follow-on product.¹⁴⁶ This request could be made at any time, long before an FOB application is submitted, and even if an application is never submitted.¹⁴⁷ Not only would the innovator be required to identify patents claiming the biologic drug and methods of using it, but also components of the drug and processes that could be used to produce the product, regardless of whether or not the patented process is actually used in the production of the innovator's product. In other words, the innovator would not only be required to identify product-specific patents, but any patent covering a process or reagent which could conceivably be adapted for use in the production of a biosimilar product. To ensure innovator compliance, House Bill 1427 would punish the failure to list any patent by rendering that patent unenforceable, not only against the FOB applicant but against the whole world.¹⁴⁸

Facing the draconian threat of patent unenforceability, and uncertainty as to the range of potential variation that would be permitted under the nebulous concept of "biosimilarity," innovators will likely feel compelled to err on the side of overinclusion and list any patent that could conceivably be related to the production of a biosimilar product. Unfortunately for the innovator, however, listing a patent will subject that patent to a number of provisions of House Bill 1427 that dramatically limit the rights of the patent owner. For example, once a patent has been identified in such a list, House Bill 1427 would bar the pa-

146. H.R. 1427, 111th Cong. § 3(a)(2) (2009).

147. *See id.*

148. *Id.* at § 3(b)(2).

tent owner from bringing a pre-marketing declaratory judgment lawsuit against the FOB applicant, forcing the innovator to wait until the FOB has entered the market at risk before commencing a lawsuit for infringement.¹⁴⁹ In the past, innovators have used declaratory judgment actions to bring suit prior to market entry by the competitor. Such declaratory judgment actions provide patent owners an opportunity to plead their case before a court, and to obtain a preliminary injunction that prevents the competing product from being launched until the litigation is resolved. Importantly, a court will not issue a preliminary injunction unless it is convinced that the patent owner is likely to prevail in its lawsuit, and that the public interest is not adversely affected by the injunction.¹⁵⁰ By barring the innovator from bringing suit until after the FOB has entered the market at risk, House Bill 1427 substantially weakens the patent rights of the innovator.

While innovators would be blocked from bringing a declaratory judgment action with respect to any listed patent, House Bill 1427 explicitly authorizes an FOB applicant to bring a declaratory judgment lawsuit alleging invalidity or noninfringement of any of the listed patents at any time.¹⁵¹ The bill would allow an FOB applicant to challenge any patent any time prior to approval and marketing, or to decide not to challenge any patent and enter the market at risk, while denying the patent owner any corresponding right to bring an action prior to market entry.

Not only does House Bill 1427 provide a unilateral right to an FOB applicant to bring a declaratory judgment action prior to marketing approval, it also provides an alternate mechanism for challenging a patent without bringing suit. Under the bill, an FOB applicant can, at any time, provide notice to the innovator alleging that one or more of the innovators' patents is either invalid or would not be infringed by the FOB product.¹⁵²

149. *Id.* at § 3(a)(2).

150. *Am. Signature, Inc. v. United States*, 598 F.3d 816, 823 (Fed. Cir. 2010) (quoting *Winter v. Natural Res. Def. Council, Inc.*, 129 S. Ct. 365, 374 (2008)) ("A plaintiff seeking a preliminary injunction must establish (1) that he is likely to succeed on the merits, (2) that he is likely to suffer irreparable harm in the absence of preliminary relief, (3) that the balance of equities tips in his favor, and (4) that an injunction is in the public interest.")

151. *Id.* at § 3(a)(2).

152. *Id.*

The innovator would then have to bring in infringement suit within forty-five days.¹⁵³ If a lawsuit is not filed in time, the innovator will be barred from asserting the patent in court until the FOB product is on the market. And as punishment for not bringing suit within the forty-five day window, House Bill 1427 would forever limit the innovator's remedy for patent infringement to reasonable royalty damages, even if the innovator ultimately prevails in court and proves that the FOB product infringes a valid patent.¹⁵⁴ The more potent remedies that are available to any other patent holder—a permanent injunction to prevent ongoing or impending infringement, lost profit damages to adequately compensate the innovator, and enhanced damages for willful infringement—would be unavailable for biologic innovators. In effect, failure to file suit within forty-five days would result in a compulsory license of the patent in favor of the FOB applicant.

As alluded to in the FTC Report, in many cases forty-five days will be insufficient time for the patent owner to thoroughly assess the merits of a patent infringement suit.¹⁵⁵ Compounding the problem, there is nothing to prevent an FOB applicant from changing its production process, and consequently the nature of the product, after the forty-five days have expired.¹⁵⁶ Thus, an innovator might decide not to bring suit within forty-five days because of its understanding of the proposed product and process, but subsequent changes to the production process could change the nature not only of the process but of the product itself, thereby rendering it infringing. Even so, the innovator's remedies will be limited to reasonable royalties as determined by a court, which will likely fall short of adequate compensation for the innovator. The FTC Report notes that FOB applicants would be incentivized to engage in this sort of gamesmanship.¹⁵⁷

House Bill 1427 also includes a change of venue provision that authorizes an FOB applicant that has been sued for patent infringement to request that the court transfer the action to another judicial district.¹⁵⁸ This provision would only operate in one direction, since no complementary right is provided to in-

153. *Id.*

154. *Id.* at § 3(b)(2).

155. FTC REPORT, *supra* note 5, at 52 n.219.

156. *Id.* at 55.

157. FTC REPORT, *supra* note 5, at 54 n.225.

158. H.R. 1427, at § 3(b)(1).

novators to seek a change of venue in a declaratory judgment action filed by an FOB applicant. When considering a request for change of venue under the bill, the greatest weight would be placed on moving the case to a district court which will adjudicate the matter promptly so that the FOB product can be launched as quickly as possible.¹⁵⁹ Any other considerations would be secondary. By depriving innovators of any meaningful control over the venue in which to enforce their patent rights, the bill further weakens the patent rights of innovators relative to any other participants in the patent system.

Unlike its predecessor, House Bill 1548,¹⁶⁰ the PPRP provisions of the House Amendment do not include such discriminatory measures. To be sure, the House and Senate Amendments are largely similar and follow the same general structure. In both, the acceptance of a biologics license application for abbreviated approval triggers an obligation to provide reference product sponsors and certain patent owners with confidential access to the FOB application and information about the FOB manufacturing process.¹⁶¹ The burden of identifying relevant patents then falls largely on the reference product sponsor or the patent owner. Relevant patents include product and method-of-use patents with respect to which a claim of infringement could reasonably be asserted, as well as manufacturing and process patents and patents to biological starting materials and intermediates. Because the PPRP is tied to the submission of an FOB application, the earliest date under which litigation could commence under both Amendments is during year four after first licensure of the reference product.¹⁶² Before pre-approval patent litigation can commence, the parties exchange detailed statements concerning the infringement, validity and enforceability of the identified patents. A statement by the FOB

159. *Id.*

160. H.R. 1548, 111th Cong. (2009).

161. Note that House Bill 1427 follows a different pattern, which was discussed in more detail in previous sections of this paper. *See* H.R. 1427. This section focuses on what appears to be a developing consensus view, as embodied in House Bill 1548 and the recent House and Senate Amendments. *See* H.R. 1548.

162. The House and Senate Amendments, as well as House Bill 1548 and Senate Bill 1695, each provide that the earliest date on which an FOB application may be submitted is on the fourth anniversary of the date the reference product was first licensed by FDA. *See* H.R. 1548, at § 101(a); S. 1695, 110th Cong. § 2(a) (as introduced in the Senate, June 26, 2007).

applicant that an identified patent would not be infringed, is invalid, or unenforceable, triggers a limited window within which the plaintiff can bring a patent infringement suit.¹⁶³ Patent litigation that is concluded before data exclusivity expires, and that results in a finding of infringement, will operate to delay the effective date of the FOB approval until the expiration of the infringed patent. Thus, on the simplest level, the House and Senate Amendments both contemplate that the submission of an FOB application would open a time window for patent litigation long before the FOB application would be approved by the FDA, without the need for special stays of FDA approval pending litigation. Patents would be litigated to a final decision within this window, thus providing patent certainty for both parties and a date certain at which the FOB product could be launched.

Despite these many similarities, the PPRP provisions of the Senate Amendment are also related to those provided in House Bill 1427, albeit not quite as draconian. Unlike the House Amendment, the Senate Amendment would limit an innovator to reasonable royalties for not promptly filing a lawsuit once an FOB applicant challenged the patent. It would also punish an innovator for failing to identify a relevant patent by rendering the patent unenforceable with respect to the biological product at issue, which is at least an improvement over House Bill 1427, which would render the patent totally unenforceable against the world. Still, the threat is so severe that an innovator will be effectively compelled to list any patent that could conceivably be infringed by an FOB.

These provisions clearly discriminate against biologic innovators. In no other area of technology is a patent owner required to identify patents that it thinks might be infringed, particularly with respect to a product that might still be changed prior to market entry. Patent owners are not ordinarily compelled to choose between immediately bringing a lawsuit against a competitor, to say nothing of a potential competitor perhaps years from market entry, or being limited to reasonable royalty damages (which, in effect, amount to a compulsory

163. The Senate Amendment provides that this statement would constitute an “act of infringement” - the formal basis for bringing an infringement lawsuit. The House Amendment currently does not contain this necessary provision, possibly due to a technical omission. Note that this provision was properly included in House Bill 1548, the predecessor to the House Amendment. See H.R. 1548, at § 101(a).

license of the technology). Conventional drug innovators do not face this burden, nor do third-party patent owners who do not make the reference product but nonetheless have patents relating to the production of the FOB. In this sense, these provisions favor the non-practicing entity over the innovator who invests in bringing an actual product to market. This is inconsistent with the more general trend in patent law that favors parties who actually commercialize their patented technology over non-practicing entities.¹⁶⁴

VI. CONCLUSION

Any abbreviated approval pathway for FOBs should include a substantial data exclusivity period and a fair mechanism for the early resolution of patent disputes. The pending proposals vary widely in many regards, including the patent provisions. Several of the proposals would impose unduly complex procedures and exceedingly unfair burden and risk on biotech innovators. This stands in contrast to the patent laws governing all other technologies. Such an approach is also inconsistent with the relatively balanced mechanism adopted for the generic drug regime established by the Hatch-Waxman Act and is unwarranted in the biotechnology context where the challenges of getting a new medicine to patients are even greater.

164. See *EBay, Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 396–97 (2006) (Kennedy, J., concurring).