
THE FRONTIER WITHIN: THOUGHTS ON CARRIER & MINNITI

John R. Thomas*

The history of the Hatch-Waxman Act¹ has been one of unforeseen implications and unintended consequences.² Members of the 98th Congress had little reason to anticipate such practices as reverse-payment settlements,³ bottlenecks,⁴ authorized generics,⁵ fraudulent patent listings,⁶ multiple thirty-month stays,⁷ sample denials,⁸ and product hopping.⁹ Nor could legislators have had much reason to suppose that this seemingly benign legislation linking the Patent Act with the food and drug laws would, over its thirty-year history, require continued antitrust oversight.

Messiers Carrier and Minniti write within this context of extreme unpredictability.¹⁰ This impressive new article reviews the history of antitrust enforcement in the context of Hatch-Waxman. It steps through seven alarming anticompetitive behaviors that remind the reader of the need for persistent vigilance in the field. Realizing that past may not be prologue due to differences in the science and legal regimes governing small- and large-molecule medicines, the authors next predict the behavior of industry actors and recommend antitrust analyses for biologics.

* Professor of Law, Georgetown University.

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

2. See, e.g., Shashank Upadhye, *There's A Hole in My Bucket Dear Liza, Dear Liza: The 30-Year History of the Hatch-Waxman Act: Resolved and Unresolved Gaps and Court-Driven Policy Gap Filling*, 40 WM. MITCHELL L. REV. 1307 (2014).

3. See, e.g., Michael A. Carrier, *Payment After Actavis*, 100 IOWA L. REV. 7 (2014).

4. See, e.g., Glynn S. Lunney, Jr., *FTC v. Actavis: The Patent-Antitrust Intersection Revisited*, 93 N.C. L. REV. 375 (2015).

5. See, e.g., Thomas Chen, *Authorized Generics: A Prescription for Hatch-Waxman Reform*, 93 VA. L. REV. 459 (2007).

6. See, e.g., Esther H. Steinhauser, *Is Noerr-Pennington Immunity Still a Viable Defense Against Antitrust Claims Arising from Hatch-Waxman Litigation?*, 61 FOOD & DRUG L.J. 679 (2006).

7. See, e.g., C. Scott Hemphill & Mark A. Lemley, *Earning Exclusivity: Generic Drug Incentives and the Hatch-Waxman Act*, 77 ANTITRUST L.J. 947, 959-60 (2011).

8. See, e.g., Michael A. Carrier, *Sharing, Samples, and Generics: An Antitrust Framework*, 103 CORNELL L. REV. 1 (2017).

9. See, e.g., Michael A. Carrier & Steve D. Shadowen, *Product Hopping: A New Framework*, 92 NOTRE DAME L. REV. 167 (2016).

10. Michael A. Carrier & Carl J. Minniti III, *Biologics: The New Antitrust Frontier*, 2018 U. ILL. L. REV. 1.

Biologics: The New Antitrust Frontier works a bold stroke in an environment that has inspired unforeseen strategic behaviors and resisted legislative intervention. The piece does an outstanding job of reviewing understood anti-competitive strategies and applying them to a new context. Due to the hazardous nature of predictive writing, it may prove less successful in identifying possible behaviors unique to the biologics market that may deserve the attention of antitrust regulators and the private plaintiffs' bar in the future. Experience will undoubtedly reveal them, for the high stakes involved in patent enforcement in the field of healthcare seem only to be growing greater.

This companion piece offers three principal additions to the work of Carrier and Minnetti on the future role of antitrust in the biologics marketplace. Part I of this Article considers the current state of the patent dispute resolution system applicable to biologics. It downplays the lack of an Orange Book in this context, although it suggests future augmentation of the Purple Book should concerns arise. Part II of this Article considers how, like authorized generics, "authorized interchangeables" may appear in the biologics market and how the antitrust law should react to them.

Finally, Part III of this Article offers a prediction of its own. Over the past decade the Supreme Court has arguably addressed every substantive patenting requirement save those pertaining to the disclosure of the patent instrument. In cases addressing patentable subject matter,¹¹ novelty,¹² nonobviousness,¹³ claim definiteness,¹⁴ and related topics, the Court has tended to raise the standards applicable to patent applicants and proprietors. If the Court follows suit with respect to the doctrines of enablement and written description¹⁵—two doctrines of special import to large-molecule biologics that resist characterization—then patenting may become a less certain proposition in this space. This factor too may alter the balance between innovation and competition that both the antitrust and patent laws try to maintain. Part IV concludes.

I. NOTICE AND THE PURPLE BOOK

In their article, Carrier and Minnetti voice unease over the lack of an Orange Book with respect to biologics.¹⁶ They observe that, thanks to the Orange Book, generic applicants may become aware of potential patents years in advance.¹⁷ Yet, competing biologics manufacturers have no such facility, in their view, due to the distinct dispute resolution proceedings governing biologics. In my opinion, this concern is somewhat oversold but, even if accurate, is amenable to amelioration.

11. 35 U.S.C. § 101.

12. *Id.* § 102.

13. *Id.* § 103.

14. *Id.* § 112(b).

15. *Id.* § 112(a) (housing both of these requirements).

16. Carrier & Minnetti, *supra* note 10, at 40.

17. *Id.*

By way of background, the Orange Book—a publication of the Food and Drug Administration (“FDA”) that is more formally titled *Approved Drug Products with Therapeutic Equivalence Evaluations*—serves as a patent clearinghouse for small-molecule pharmaceuticals. When a brand-name firm obtains FDA approval, it must submit patent information for “any patent which claims the drug for which the applicant submitted the [NDA] or which claims a method of using such drug”¹⁸ This patent submission requirement provides the basis for brand-name firms to protect their intellectual property rights prior to generic entry and, hence, triggers a number of requirements on the part of generic manufacturers that seek to market their products prior to patent expiration. The FDA then “lists” all such patents in the Orange Book, providing notice to all the world over the relevant proprietary interests.¹⁹

In contrast, the FDA maintains a reference guide to licensed biologics products titled *Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*. Informally known as the “Purple Book,” this publication includes information on brand-name biologics, biosimilars, and any relevant regulatory exclusivities. The Biologics Price Competition and Innovation Act of 2009 (“BPCIA”) does not require the FDA to publish the Purple Book, however, unlike the Orange Book, which is mandated by the Hatch-Waxman Act.²⁰ Most notably, the Purple Book does not include patent information to which follow-on applicants must react. As a result, the realm of biologics arguably lacks a repository of patents that inform potential rivals of intellectual property barriers to competition.

With their lament over the lack of patent listings for biologics, Carrier and Minnetti join others who worry about public notice and patents. Concerns about the absence of sufficient notice of the proprietary rights of others have animated numerous features of the current law and continue to provoke passionate critiques. An essential task of the patent system is to ensure that members of the public have ready notice of the intellectual property rights that might be imposed against them.²¹ As a result, patents incorporate detailed, precisely worded claims that inform interested actors of the scope of a proprietor’s exclusive rights.²² They also include a specification²³ and prosecution history²⁴ of the subject matter that further discuss their inventors’ contribution beyond the state of the art.

Going beyond the structure of the patent instrument itself, the Patent Act also encourages patent owners to mark their products with an associated patent number.²⁵ Failure to do so limits damages for infringement to the date

18. 21 U.S.C. § 355(b)(1).

19. See *Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1338 (Fed. Cir. 2003).

20. 21 U.S.C. § 355(b)(1).

21. See Clarisa Long, *Information Costs in Patent and Copyright*, 90 VA. L. REV. 465, 500 (2004).

22. 35 U.S.C. § 112(b).

23. *Id.* § 112(a).

24. See *Pac. Coast Marine Windshields Ltd. v. Malibu Boats*, 739 F.3d 694, 700 (Fed. Cir. 2014) (noting that the doctrine of prosecution history estoppel is “founded on the public notice function of patents”).

25. 35 U.S.C. § 287(a).

the patent proprietor provides the infringer with specific notice of infringement.²⁶ The U.S. Court of Appeals for the Federal Circuit (“Federal Circuit”) has observed that marking aids the public in identifying whether a product is patented and helps avoid innocent infringement.²⁷

In addition to these statutory components, the public notice function has animated numerous judicial flourishes upon the patent law. The Supreme Court of the United States has frequently observed that patents should not only define the proprietary rights possessed by inventors but also provide notice to the public of what activities could lead to infringement liability.²⁸ Pursuant to its desire for clear public notice of patent rights, the Court has recently called for greater clarity in patent drafting and made patents more susceptible to challenge for lack of definiteness.²⁹ It has also limited the scope of the doctrine of equivalents due to its concerns over the lack of public notice associated with nontextual infringement.³⁰ And the Court has, for the most part, required actual knowledge of a patent for liability for induced infringement to accrue.³¹

Despite this emphasis, many commentators have expressed considerable doubt that the patent system serves the notice function well.³² Perhaps the most prominent observers of this perceived breakdown, James Bessen and Michael Meurer, assert that the current innovation environment considerably suffers from a breakdown in patent boundaries.³³ They assert that identification of relevant patents and their owners is too unreliable and that the scope of patent rights is too difficult to decipher.³⁴ According to Bessen and Meurer, the main goal of legal reforms should be to improve patent notice.³⁵ Predictable interpretational protocols, administrative opposition procedures, expanded prior user rights, and an independent creation defense are among the doctrinal mechanisms that observers have advocated in the name of reducing the costs of access to reliable patent information.³⁶

For many of these observers, the patent system’s many deficiencies in providing public notice have one prominent exception: pharmaceutical patents. Here, it is said, the public notice function of patents works reasonably well for several reasons. First, pharmaceutical patents are said to be of higher quality

26. See Eugene Goryunov & Mark Polyakov, *To Mark or Not to Mark: Application of the Patent Marking Statute to Websites and the Internet*, 14 RICH. J.L. & TECH. 2, 2 (2007).

27. *Nike, Inc. v. Wal-Mart Stores, Inc.*, 138 F.3d 1437, 1443 (Fed. Cir. 1998).

28. See *Markman v. Westview Instruments*, 517 U.S. 370, 373 (1996).

29. See *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2129–30 (2014).

30. See *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 28–29 (1997).

31. See *Global-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754, 769–70 (2011).

32. See, e.g., Timothy R. Holbrook, *Patents, Presumptions, and Public Notice*, 86 IND. L.J. 779, 825–26 (2011).

33. JAMES BESSEN & MICHAEL J. MEURER, *PATENT FAILURE: HOW JUDGES, BUREAUCRATS, AND LAWYERS PUT INNOVATORS AT RISK* 21 (2009).

34. Michael J. Meurer, *Current Issues in Patent Law and Policy*, 39 HARV. J.L. & PUB. POL’Y 71, 75 (2016).

35. BESSEN & MEURER, *supra* note 33, at 236.

36. Peter S. Menell & Michael J. Meurer, *Notice Failure and Notice Externalities*, 5 J. LEGAL ANALYSIS 1, 44–45 (2013).

than those in other industries due to a standardized claiming format for chemical inventions.³⁷ Second, brand-name and generic firms operate within a more compact community than those of software and electronics manufacturers and are able conveniently to locate one another.³⁸ Finally, the Orange Book is said to provide the valuable function of listing relevant patents, sparing generic firms the burden of having to search through the patent rolls to discover them.³⁹

This final proposition is quite debatable. Throughout its history, the Orange Book has been subject to persistent controversies over the sorts of patents that may be appropriately identified in that publication, the timing of patent listings, and procedures for resolving disputes over registered patents.⁴⁰ The various administrators of the Hatch-Waxman system have frequently been called to police the Orange Book and have collectively established a complex set of laws, regulations, and rulings to govern that publication.

But even today, the Orange Book does not provide a complete listing of patents that might be pertinent to generic competition. The Federal, Food, Drug, and Cosmetic Act calls for the registration of only a patent “which claims the drug for which the applicant submitted the application or which claims a method of using such drug”⁴¹ The result is that patents claiming such inventions as methods of manufacture, chemical intermediates, and product packaging may not be listed in the Orange Book.⁴² But they may be infringed by generic firms as readily as patents identified to the FDA.

Another lingering issue is whether patents owned by third parties may be listed in the Orange Book. The statutory text requires that brand-name firms identify patents for registration. The statute does not state, however, that they must actually own the patents they identify to the agency. Nor does it stipulate whether third-parties whose patents fulfill the statutory requirements may also list patents in the Orange Book.⁴³

To date, the courts have quashed these possibilities. For example, in *aaiPharma, Inc. v. Thompson*,⁴⁴ the U.S. Court of Appeals for the Fourth Circuit held that third-party patent holders cannot petition the FDA to list their patents, no matter how pertinent they might be. In doing so, the court principally relied upon the judicially endorsed FDA practice of indifference to the Orange Book—with no policing function with respect to the brand-name firm’s listed patents, a hands-off policy with respect to other patents made sense as well. This practice too does not ensure that Orange Book listings canvas the waterfront of patents that may be relevant to particular generic products.

37. *Id.* at 36.

38. Michael J. Meurer, *Bargaining Failure and Failure to Bargain*, 96 B.U. L. Rev. 655, 664 (2016).

39. *Id.* at 659.

40. See JOHN R. THOMAS, PHARMACEUTICAL PATENT LAW 420 (3d ed. 2015).

41. 21 U.S.C. § 355(b)(1).

42. Abbreviated New Drug Applications and 505(b)(2) Applications, 80 Fed. Reg. 6802 (Feb. 6, 2015).

The FDA subsequently corrected some minor typographical errors in that document. 80 Fed. Reg. 13,289 (Mar. 13, 2015).

43. THOMAS, *supra* note 40, at 427–29.

44. 296 F.3d 227, 236–37 (4th Cir. 2002).

From a broader vista, the notoriously thin legislative history of the Hatch-Waxman Act⁴⁵ provides scant guidance as to why Congress decided that one industry should correlate their intellectual property rights with their products. The scholarly literature sought also does not justify the Orange Book or explain how the unique posture of the pharmaceutical industry compels this publication. At first glance it is not obvious why, out of all the various industries and intellectual property rights in existence, pharmaceutical firms are the ones who must identify their patents to the government. The government is, after all, the entity that grants the patents in the first place. Further, patents are typically published both during their pendency⁴⁶ and again when they are finally approved.⁴⁷ These are not concealed intellectual property rights, like trade secrets,⁴⁸ or potentially obscure ones, such as copyrights that are never formally registered⁴⁹ or subject to notice on publicly distributed works.⁵⁰

The usual narrative suggests that the Orange Book provides a convenience to generic firms when making patent certifications. Brand-name firms can presumably provide information on their own patent portfolio in the most efficient manner.⁵¹ The difficulty with this account is that proprietors are always the least cost avoider in identifying their own intellectual property rights, but they are not tasked to do so in other industries. Indeed, outside of the Hatch-Waxman context, individuals and enterprises are presumed to be able to identify and evaluate pertinent patents and negotiate with their owners prior to infringement.⁵²

Further, if one were to pick an industry where a patent clearinghouse would be most appropriate, pharmaceuticals would not seem the most likely choice. As Bill Lee and Doug Melamed explain, the pharmaceutical sector is one “where the potentially relevant patents are both reasonably ascertainable during the product development timeframe and relatively small in number.”⁵³ These circumstances exist due to the relative concentration of the innovative pharmaceutical industry,⁵⁴ high barriers to entry,⁵⁵ and a more standardized

45. See Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 FOOD & DRUG L.J. 187, 187 (1999) (“There is a paucity of legislative history on the Hatch-Waxman Act.”).

46. See generally 35 U.S.C. § 122(b).

47. *Id.* § 153.

48. See, e.g., Mark A. Lemley, *The Surprising Virtues of Treating Trade Secrets as IP Rights*, 61 STAN. L. REV. 311 (2008).

49. 17 U.S.C. § 408.

50. *Id.* § 401. See, e.g., Abigail Bruce, *British Invasion: Importing the United Kingdom’s Orphan Works Solution to United States Copyright Law*, 108 NW. U. L. REV. 243 (2013).

51. See W. Keith Robinson, *A Case Study of Federal Circuit Policy Making*, 66 SMU L. REV. 579, 602 (2013) (discussing policy perspective of patentee as least cost avoider).

52. See William F. Lee & A. Douglas Melamed, *Breaking the Vicious Cycle of Patent Damages*, 101 CORNELL L. REV. 385, 403–04 (2016).

53. *Id.* at 404.

54. See STUART O. SCHWEITZER, PHARMACEUTICAL ECONOMICS AND POLICY 118 (1997) (“Whether in response to rising R&D costs or increased risk associated with developing a successful drug, drug firms throughout the world have consolidated, either through outright mergers or joint marketing agreements.”).

claim formatting technique than may exist in other fields of patentable endeavor.⁵⁶ The need for the Orange Book for small-chain molecules seems far less pronounced than in such fields as smartphones and computer software.⁵⁷

One response would be simply to eliminate the Orange Book. Although this step may seem drastic, Congress essentially did so with respect to biologic drugs when it enacted the BPCIA.⁵⁸ Among the components of the BPCIA was a patent dispute resolution procedure for use by brand-name and follow-on biologic manufacturers.⁵⁹ Notably, the BPCIA does not employ the same framework as the patent dispute resolution proceedings that have been available under the Hatch-Waxman Act for more than three decades. In particular, the BPCIA requires neither brand-name firms to identify relevant patents in advance of competition nor the FDA to publish that information. Rather, in a complex series of steps informally termed the “Patent Dance,”⁶⁰ brand-name firms identify relevant patents to their potential follow-on competitors on a need-to-know, *ad hoc* basis.⁶¹

The adoption of a patent dispute resolution system for the BPCIA, distinct from that of the Hatch-Waxman Act, may suggest a congressional determination that the Orange Book is not an essential patent clearinghouse.⁶² Indeed, biologics typically consist of large, complex molecules that can be difficult to describe in writing.⁶³ Often, claims drafters are left to describe them in terms of their function, their derivation, or on what they bind to, rather than their unique chemical structure.⁶⁴ Given the relative complexity of claiming biologics in comparison with traditional pharmaceuticals, the absence of a wholly symmetrical structure to the Orange Book within the BPCIA seems telling.

The term “patent” itself refers to an open or public letter, as compared to a sealed document.⁶⁵ In view of the inherent accessibility of patent rights, as well as the frailties of the Orange Book in revealing what is already publicly

55. See, e.g., Herbert Hovenkamp, *Sensible Antitrust Rules for Pharmaceutical Competition*, 39 U.S.F. L. REV. 11, 11 (2004).

56. See THOMAS, *supra* note 40, at 296.

57. See Christina Mulligan & Timothy B. Lee, *Scaling the Patent System*, 68 N.Y.U. ANN. SURV. AM. L. 289, 297–304 (2012) (noting that “few, if any, non-chemical patents seem to be indexable” and that searching costs for software patents are particularly problematic).

58. The BPCIA was incorporated as Title VII of the Patient Protection and Affordable Care Act. Pub. L. No. 111-148, 124 Stat. 119 (2010).

59. These provisions were codified at 42 U.S.C. § 262(l).

60. See, e.g., Carl J. Minniti III, *Sandoz v. Amgen: Why Current Interpretation of the Biologic Price Competition and Innovation Act of 2009 is Flawed and Jeopardizes Future Competition*, 97 J. PAT. & TRADEMARK OFF. SOC’Y 172 (2015).

61. See Michael P. Dougherty, *The New Follow-On Biologics Law: A Section by Section Analysis of the Patent Litigation Provisions in the Biologics Price Competition and Innovation Act of 2009*, 65 FOOD & DRUG L.J. 231, 235 (2010).

62. See THOMAS, *supra* note 40, at 856.

63. See Jacob S. Sherkow, *Describing Drugs: A Response to Professors Allison and Ouellette*, 65 DUKE L.J. ONLINE 127, 136 (Mar. 2016).

64. See Jason Kanter & Robin Feldman, *Understanding and Incentivizing Biosimilars*, 64 HASTINGS L.J. 57, 63–64 (2012).

65. John F. Duffy, *Inventing Invention: A Case Study of Legal Innovation*, 86 TEX. L. REV. 1, 23–24 (2007).

known, the absence of patent listings in the Purple Book should not concern us overmuch. Still, if concerns persist, then at least two pathways to improved patent notice present themselves.

First, the FDA and U.S. Patent and Trademark Office (“USPTO”) could undertake such an effort by themselves. The FDA has already gone to the extra-statutory effort of publishing the Purple Book. And, although the FDA has long disavowed patent expertise, doling out these rights constitutes the core mission of the USPTO. Product markings, SEC statements, and brand-name firm announcements should do much of the work for these agencies. As well, the agencies could simply ask biologics manufacturers for the pertinent patent information. Alternatively, the private sector could take up the mantle. Industry associations, patient advocacy groups, and civil society organizations are among those who could perform the research necessary to identify patents associated with particular biologics. Concerns over patent notice may be overstated, but viable options exist for addressing them should they arise in the future.

II. AUTHORIZED INTERCHANGEABLES

Carrier and Minniti do not address a practice that has troubled numerous observers but, to this day, has evaded serious antitrust scrutiny. An “authorized generic” is a pharmaceutical that is marketed by or on behalf of a brand-name drug company, but is marketed under a generic name.⁶⁶ Authorized generics are thus similar to “private label” products, which are manufactured by one firm but sold under the brand of another. Although private-label products are commonplace in food, cosmetic, and other markets, they have only recently attracted attention in the pharmaceutical industry.⁶⁷

Although the availability of an additional competitor in the generic-drug market would appear to be favorable to consumers, authorized generics have nonetheless proven controversial. Some observers believe that authorized generics potentially discourage independent generic firms both from challenging drug patents and from selling their own products.⁶⁸ The same scenario could arise with respect to biologics, likely even more readily.

Authorized generics result from the unique architecture of the Hatch-Waxman Act. That statute provided independent generic firms with a “bounty” for challenging patents held by brand-name firms. That reward consists of a 180-day generic-drug exclusivity period awarded to the first patent challenger.⁶⁹ During the 180-day period, the brand-name company and the first generic applicant are the only firms that receive authorization to sell that pharmaceuti-

66. See, e.g., Erika Lietzan & Julia Post, *The Law of 180-Day Exclusivity*, 71 FOOD & DRUG L.J. 327, 387 (2016).

67. David E. Korn et al., *A New History and Discussion of 180-Day Exclusivity*, 64 FOOD & DRUG L.J. 335, 359 (2009).

68. Chen, *supra* note 5, at 461.

69. 21 U.S.C. § 355(j)(B)(iv).

cal. At the close of this period, other independent generic competitors may obtain marketing approval and enter the market, ordinarily resulting in lower prices for generic medicines.⁷⁰

The possibility of a duopoly market, consisting of the brand-name firm and a single generic, may encourage generic firms to challenge patents held by brand-name firms. Generic firms may sell their products at higher prices for 180 days prior to the onset of full generic competition. On one hand, the possibility that a brand-name firm will sell an authorized generic during the 180-day exclusivity period may decrease the incentives of generic firms to challenge patents in the first instance. On the other hand, authorized generics may benefit consumers by increasing competition in the generic market. And even the FDA touts authorized generics as being “the exact same drug product as the branded product.”⁷¹

The circumstances with respect to biologics present similarities to the 180-day exclusivity for small-molecule drugs. The BPCIA provides for a term of regulatory exclusivity for the applicant that is the first to establish that its product is interchangeable with the brand-name product for any condition of use. Although the statute provides several alternatives for calculating the term of the exclusivity, the most likely duration consists of one year after the FDA approved the first interchangeable biologic.⁷²

If past is prologue, then we can expect to see interchangeable biologics too: a lot of them in fact—the FDA currently lists over 1,100 authorized generic products on its website.⁷³ Because the period of interchangeable biologic exclusivity will most often be more than double the term of generic exclusivity, the potential anticompetitive impact of authorized interchangeables would be more impactful than their generic counterparts. Authorized interchangeables could also be used to compete with biosimilar products. Many physicians and patients would likely have more comfort with a full interchangeable than a similar biologic product.

Another reason suggests that authorized interchangeables will focus renewed attention on the “private label” version of brand-name drugs. With respect to small-molecule pharmaceuticals, Congress has confirmed that all “first

70. See THOMAS, *supra* note 40, at 465–67.

71. FDA, *FDA List of Authorized Generic Drugs*, U.S. FOOD & DRUG ADMIN. (Dec. 29, 2017), <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm126389.htm>.

72. 42 U.S.C. § 262(k)(6)(B). More precisely, the period of regulatory exclusivity is the earlier of (1) one year after the first commercial marketing of the first interchangeable biologic to be approved as interchangeable with that reference product; (2) eighteen months after either a final court judgment in patent infringement litigation under the PHS Act, as amended, or the dismissal of such litigation against the first applicant; (3) forty-two months after the approval of the first interchangeable biologic if patent litigation under the PHS Act, as amended, remains pending; or (4) eighteen months after approval of the first interchangeable biologic if the applicant has not been sued for patent infringement under the PHS Act, as amended. *Id.* This regulatory exclusivity bars the FDA from making a determination of interchangeability with respect to a subsequent product for a period of time. *Id.* The FDA is not prevented from making a determination of biosimilarity during this timeframe.

73. 21 U.S.C. § 355(t); see FDA, *supra* note 71.

applicants” are entitled to the 180-day exclusivity.⁷⁴ Stated differently, if more than one generic applicant challenges a patent on the same day, and no previous challenges have been made, each of these “first” firms may trigger the exclusivity and market during the 180-day period. In practice, numerous generic firms have been seen to enjoy “shared exclusivity” under the Hatch-Waxman Act. Since multiple generic firms may market during the supposed time of “exclusivity,” the addition of the brand-name’s authorized generic may not seem that worrisome.⁷⁵

This scenario would appear to be far less common with respect to the BPCIA. Due to the complexity of this field of drugs and the expense of preparing an application, we do not expect to observe the routine filing of multiple applications for licensure of interchangeable biologics. An authorized interchangeable will likely stand as the only competitor to the interchangeable applicant—and as a more plausible deterrent from filing licensure applications for interchangeable biologics in the first instance.

To date, the reaction of antitrust enforcers to authorized generics has been confoundingly muted. The courts have not yet been concerned about this practice. The leading case reasoned that the wording of the statute authorizing 180-day generic exclusivity makes that proprietary right effective only against other generic applicants.⁷⁶ Under this approach, brand-name firms may market their products as they see fit, including both branded and authorized generic versions. Members of Congress have introduced bills blocking the sale of authorized generics during the 180-day exclusivity period, but this proposed legislation has not gained much traction.⁷⁷ Even the FTC has issued a study on authorized generics, but the agency’s report was understated and seemed to focus more on reverse-payment settlements than the nominal subject of the report.⁷⁸

Through the sale of authorized generics, the 180-day generic exclusivity stands apart as the only intellectual property right that can be deliberately disregarded. The advent of authorized interchangeables will likely bring this troubling aspect of FDA policy into high relief. Time will tell if antitrust law will contribute to a more thorough assessment of the short- and long-term effects of brand-name competition in the market for follow-on drugs.

III. BIOLOGICS PATENTS AND THE SUPREME COURT

Even the most casual observer of the Supreme Court should be aware of that tribunal’s renewed interest in patent law. In earlier years, the grant of certiorari for even a single patent case in a term would arouse great interest. As a

74. 21 U.S.C. § 355(j)(5)(B)(iv)(I).

75. Michael Abramowicz, *Orphan Business Models: Toward a New Form of Intellectual Property*, 124 HARV. L. REV. 1362, 1392–95 (2011).

76. *Teva Pharm., Indus. v. FDA*, 355 F. Supp. 2d 111, 117–19 (D.D.C. 2004).

77. For example, in the 114th Congress, H.R. 6284, the Eliminate Price Increases Act of 2016 would have prevented brand-name firms from selling authorized generics. This legislation was not enacted.

78. FTC, *AUTHORIZED GENERIC DRUGS: SHORT-TERM EFFECTS AND LONG-TERM IMPACT: A REPORT OF THE FEDERAL TRADE COMMISSION* (2011), <http://www.ftc.gov/os/2011/08/2011genericdrugreport.pdf>.

sign of the times, the Court issued six patent decisions during the 2016–2017 term.⁷⁹ Notably, every current Justice except Justice Gorsuch has authored at least one patent-related majority opinion.

This flurry of activity has resulted in a Supreme Court opinion addressing virtually every aspect of modern patent law. The Court has, for example, addressed standards for claim interpretation,⁸⁰ infringement,⁸¹ the doctrine of equivalents, exhaustion,⁸² venue,⁸³ damages,⁸⁴ attorney fees,⁸⁵ and administrative opposition proceedings at the USPTO.⁸⁶ In addition, the Court has addressed most of the substantive standards for obtaining a patent, including patentable subject matter,⁸⁷ novelty,⁸⁸ obviousness,⁸⁹ and claim definiteness.⁹⁰

This body of case law reveals one persistent theme: The Court has made patents more difficult to obtain and, in the case of patents issued under more relaxed standards, less likely to be enforced. The Court invalidated patents on business methods,⁹¹ genetic materials,⁹² personalized medicine,⁹³ and software⁹⁴ because they were deemed to claim abstract ideas or laws of nature, subject matter outside the realm of patentable subject matter. It struck down another patent based on a new, expansive standard for implementing on-sale bar.⁹⁵ The Court also held that the standard of nonobviousness employed by the lower courts was too lenient, raising the presumed capabilities of persons of ordinary skill in the art and indicating that summary judgment was a suitable mechanism for declaring a claimed invention to have been obvious.⁹⁶ And, in contrast to lower courts that held patent claims invalid for indefiniteness only when they were “insolubly ambiguous,” the Court concluded that claims must be written

79. Steven Seidenberg, *US Perspectives: Troubled Federal Circuit Hobbles US Patent System*, INTELLECTUAL PROP. WATCH (July 31, 2017), <https://www.ip-watch.org/2017/07/31/troubled-federal-circuit-hobbles-us-patent-system/>.

80. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831 (2015).

81. *Commil USA, LLC v. Cisco Sys., Inc.*, 135 S. Ct. 1920 (2015); *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S. Ct. 2111 (2014); *Global-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754 (2011).

82. *Impression Prods., Inc. v. Lexmark Int'l, Inc.*, 137 S. Ct. 1523 (2017); *Bowman v. Monsanto Co.*, 569 U.S. 278 (2013).

83. *TC Heartland LLC v. Kraft Foods Grp. Brands LLC*, 137 S. Ct. 1514 (2017).

84. *Halo Elecs., Inc. v. Pulse Elecs., Inc.*, 136 S. Ct. 1923 (2016); *Samsung Elecs. Co., Ltd. v. Apple Inc.*, 137 S. Ct. 429 (2016).

85. *Highmark Inc. v. Allcare Health Mgmt. Sys., Inc.*, 134 S. Ct. 1744 (2014); *Octane Fitness, LLC v. ICON Health & Fitness, Inc.*, 134 S. Ct. 1749 (2014).

86. *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131 (2016).

87. 35 U.S.C. § 101.

88. *Id.* § 102.

89. *Id.* § 103.

90. *Id.* § 112(b).

91. *Bilski v. Kappos*, 561 U.S. 593 (2010).

92. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013).

93. *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66 (2012).

94. *Alice Corp. v. CLS Bank Int'l*, 134 S. Ct. 2347 (2014).

95. *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55 (1998).

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

in a manner that provides “reasonable certainty” about the scope of the claimed invention.⁹⁷

In living memory, at least, the Court has yet to cast its gaze upon two fundamental patentability doctrines—enablement and written description.⁹⁸ The enablement requirement mandates that the patentee disclose sufficient information so that a skilled artisan would be able to practice the claimed invention without undue experimentation.⁹⁹ To satisfy the written description requirement, the patent proprietor must show that he had possessed the claimed subject matter as of the filing date, typically by providing a precise definition of the invention. Specifically, when the patent proprietor claims a genus, the written description requirement typically requires that the patent instrument disclose a representative number of species falling within the genus, or a sufficient number of common traits, so that skilled artisans can recognize the members of the genus.¹⁰⁰

Many large-molecule biologics already face a particularly difficult time satisfying these requirements. Consider, for example, the two best-selling pharmaceuticals in 2017: Humira®, a biologic, and Revlimid®, a small-molecule drug.¹⁰¹ Humira® has a molar mass of approximately 144,190 grams per mole,¹⁰² while Revlimid® has a molar mass of approximately 259 grams per mole.¹⁰³ The fact that biologics have so many more atoms than traditional small-molecule drugs may lead to considerable uncertainty about the connectivity of the atoms and their three-dimensional structure. In addition, because biologics are manufactured using the less predictable machinery of living organisms, scientists may face issues describing their inventions in a manner satisfactory to the patent system.¹⁰⁴

The recent decision of the Court of Appeals for the Federal Circuit in *Amgen Inc. v. Sanofi*¹⁰⁵ suggests the difficulties attendant to describing biologics. In that case, Amgen accused Sanofi of committing patent infringement through sales of its Praluent® product. Praluent®, a monoclonal antibody, is a low-density lipoprotein (“LDL”) cholesterol medication that was the first FDA-approved biologic for the prevention of chronic disease. Antibodies, which are proteins produced by the immune system, are frequently in biologic therapies to bind and alter signaling pathways involved in various diseases such as cancer, infection, and inflammation. Antibodies recognize particular target agents,

97. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120 (2014).

98. 35 U.S.C. § 112(a) (identifying both requirements).

99. *Cephalon, Inc. v. Watson Pharms., Inc.*, 707 F.3d 1330, 1338–40 (Fed. Cir. 2013).

100. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351–54 (Fed. Cir. 2010) (en banc).

101. Keith Speights, *The 5 Best-Selling Drugs of 2017*, MOTLEY FOOL (Dec. 18, 2017, 7:03 AM), <https://www.fool.com/investing/2017/12/18/the-5-best-selling-drugs-of-2017.aspx>.

102. *Humira Review*, MEDICALLOOK, <http://www.medicallook.com/reviews/Humira.html> (last visited Feb. 11, 2018).

103. *Lenalidomide*, PUBCHEM, <https://pubchem.ncbi.nlm.nih.gov/compound/Lenalidomide> (last visited Feb. 11, 2018).

104. See generally Dmitry Karshedt, *Limits on Hard-to-Reproduce Inventions: Process Elements and Biotechnology's Compliance with the Enablement Requirement*, 3 HASTINGS SCI. & TECH. L.J. 109 (2011).

105. 872 F.3d 1367 (Fed. Cir. 2017).

called “antigens,” which are bound via variable domains at the end of the antibody. Praluent® works by inhibiting the protein PCSK9 from binding with the LDL Receptor (“LDL-R”), leading to a reduction of LDL cholesterol in the blood. The claimed antibody binds to specific amino acid residues of the PCSK9 molecule in a manner that blocks the PCSK9 from binding and promoting LDL-R.¹⁰⁶

Amgen’s patent did not actually claim its own product, Repatha®, or any other antibody for that matter, by its amino acid sequence. The first claim of the asserted patent instead recited:

An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following residues: S153, I154, . . . or S381 of SEQ ID NO:3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDL-R.¹⁰⁷

A central issue in *Amgen v. Sanofi* was whether this claim, which reads upon all isolated monoclonal antibodies capable of performing the required binding function, was sufficiently supported by the patent’s specification. The specification disclosed the amino acid sequence of many exemplary antibodies; the screening process that the inventors used to find those examples; and the three-dimensional structure of two antibodies, including Repatha® (which had been obtained via x-ray crystallography).¹⁰⁸ In keeping with the written description requirement, the question was whether that disclosure demonstrated that the inventors possessed the invention of claim one as of the filing date. The patent proprietor argued that because antibodies are defined by their binding affinity to their antigens, describing the claimed antibody by stating that it binds to a disclosed antigen satisfied the written description requirement.

Although the Federal Circuit did not definitely decide the matter, it did rule that the district court had improperly instructed the jury concerning the written description requirement. The jury instructions included the following explanation:

In the case of a claim to antibodies, the correlation between structure and function may also be satisfied by the disclosure of a newly characterized antigen by its structure, formula, chemical name, or physical properties if you find that the level of skill and knowledge in the art of antibodies at the time of filing was such that production of antibodies against such an antigen was conventional or routine.¹⁰⁹

According to the Federal Circuit, this instruction was incorrect because it allowed the patent proprietor to claim an antibody by describing something that is not the antibody—namely, an antigen—and then rely upon fact producing antibodies is a routine matter for skilled artisans. Such a disclosure would not, in the view of the Court of Appeals, demonstrate that the inventor was in pos-

106. *Id.* at 1371.

107. *Id.* at 1372 (quoting U.S. Patent No. 8,829,165 (filed Apr. 10, 2013)).

108. *Id.*

109. *Id.* at 1376.

session of the claimed antibody.¹¹⁰ The matter was therefore remanded for a determination of whether an actual written description within the patent instrument demonstrated that the inventor actually possessed the invention.

Following this decision, the claims of the patent-in-suit seem unlikely to withstand a written description challenge. Many other broadly drafted antibody patents seem similarly to be at risk, particularly if they define the antibody via the antigen rather than by its structure. This reasoning will likely apply to other receptor-binding patent claims, such as intracellular receptors, ligand-gated ion channels, and enzyme-linked receptors.¹¹¹ More generally, the Federal Circuit has made clear its preference for fully developed structural information regarding biologics—information that inventors in the biological arts might struggle to produce.

Suggesting that the Supreme Court might agree to hear a case involving the enablement or written description requirements is highly conjectural. But should the Court do so, and should it follow its usual pattern of clamping down even more firmly on patentability standards, then the biologics industry may face an even more difficult challenge in procuring patent rights. Judicial opinions with respect to the patent disclosure doctrines of enablement and written description, whether from the Federal Circuit or Supreme Court, will remain an important component of the balance between innovation and access going forward.

IV. CONCLUSION

Predictive writing is fraught with peril. Despite this essential difficulty, *Biologics: The New Antitrust Frontier* qualifies as an important piece of scholarship that will guide antitrust enforcement within this burgeoning market. This Article has attempted to supplement Carrier and Minniti with additional observations with respect to the food and drug laws, industry practices, and the patent law.

Any discussion of this topic needs to close with a recognition of an important reality: Our experience implementing the standards developed in *FTC v. Actavis, Inc.*¹¹² remains slight. Until the lower courts have had a greater opportunity to develop the antitrust standards announced in *Actavis* within the small-molecule setting, our ability to forecast forthcoming responses in the biologics market remains diminished. In this sense, the set of antitrust issues that Carrier and Minniti speak of do not yet stand beyond our current borders. Rather, the antitrust frontier remains within.

110. *Id.* at 1378.

111. Sarah A. Kagan, *Intellectual Property Alert: Federal Circuit Discredits Special Disclosure Rule for Antibodies*, BANNER & WITCOFF, LTD (Oct. 31, 2017), https://bannerwitcoff.com/wp-content/uploads/2017/10/ALERT-Amgen-v.-Sanofi-Fed.-Cir.Kagan_.pdf.

112. 133 S. Ct. 2223 (2013).