

UIC School of Law

UIC Law Open Access Repository

UIC Law Open Access Faculty Scholarship

2018

Biologics as the New Antitrust Frontier: Reflections, Riposte, and Recommendations, 2018 U. Ill. L. Rev. Online 209 (2018)

Daryl Lim

John Marshall Law School, daryllim@uic.edu

Follow this and additional works at: <https://repository.law.uic.edu/facpubs>



Part of the [Antitrust and Trade Regulation Commons](#)

Recommended Citation

Daryl Lim, *Biologics as the New Antitrust Frontier: Reflections, Riposte, and Recommendations*, 2018 U. Ill. L. Rev. Online 209 (2018)

<https://repository.law.uic.edu/facpubs/691>

This Article is brought to you for free and open access by UIC Law Open Access Repository. It has been accepted for inclusion in UIC Law Open Access Faculty Scholarship by an authorized administrator of UIC Law Open Access Repository. For more information, please contact repository@jmls.edu.

BIOLOGICS AS THE NEW ANTITRUST FRONTIER: REFLECTIONS, RIPOSTE, AND RECOMMENDATIONS

Daryl Lim[†]

I. INTRODUCTION

History reminds us that without regulation, the strong do what they will and the weak suffer what they must.¹ Self-interest drives incumbents to entrench their dominance and thwart challenge.² Congress enacts laws to protect the process of competition in the marketplace from the tyranny of corporate might.³ In turn, courts attempt to give effect to those policies while safeguarding the incentive of incumbents and entrants to invest and innovate.⁴ The challenge of walking that tightrope at each technological frontier remains the same—whether dealing with sewing machines,⁵ computer operating systems,⁶

[†] Associate Professor and Director, Center for Intellectual Property, Information and Privacy Law, The John Marshall Law School. I am grateful to Bradley Williams, Collin Stitch, and the rest of the Editorial Board of the University of Illinois Law Review for their excellent work in bringing this article to print. Paras Shah provided outstanding research assistance.

1. THUCYDIDES, HISTORY OF THE PELOPONNESIAN WAR 5.89.1 (Richard Crawley trans.) (1910) (“[R]ight, as the world goes, is only in question between equals in power, while the strong do what they can and the weak suffer what they must.”).

2. See U.S. DEP’T OF JUSTICE, SINGLE-FIRM CONDUCT AND SECTION 2 OF THE SHERMAN ACT: AN OVERVIEW 8 (2008), https://www.justice.gov/sites/default/files/atr/legacy/2008/09/12/236681_chapter1.pdf (describing how antitrust law prevents firms from “taking steps to entrench their existing monopoly power, through means incompatible with the competitive process”).

3. United States v. Topco Assocs., Inc., 405 U.S. 596, 610 (1972) (“Antitrust laws in general, and the Sherman Act in particular, are the Magna Carta of free enterprise. They are as important to the preservation of economic freedom and our free-enterprise system as the Bill of Rights is to the protection of our fundamental personal freedoms. And the freedom guaranteed each and every business, no matter how small, is the freedom to compete—to assert with vigor, imagination, devotion, and ingenuity whatever economic muscle it can muster.”).

4. See Atari Games Corp. v. Nintendo of Am., Inc., 897 F.2d 1572, 1576 (Fed. Cir. 1990) (“[T]he aims and objectives of patent and antitrust laws . . . are actually complementary, as both are aimed at encouraging innovation, industry, and competition.”).

5. See United States v. Singer Mfg. Co., 374 U.S. 174 (1963).

6. See United States v. Microsoft Corp., 253 F.3d 34 (D.C. Cir. 2001).

small-molecule drugs,⁷ or biologics.⁸ In each case, courts must operationalize antitrust precedent by adapting them to the technology before them and providing meaningful public guidance.⁹

Michael Carrier and Carl Minniti (“the Authors”) offer a commanding survey of how antitrust policy and precedent interface with the competitive dynamics of biologics.¹⁰ Biologics lie at the frontier of medical science, dangling succor for those who can afford their hefty price tags.¹¹ For instance, a conventional rheumatoid arthritis treatment currently costs \$300 annually, while its biologic alternative can cost \$200,000.¹² The biologics market itself will be worth about \$400 billion worldwide by 2020, a dramatic tenfold increase in just ten years.¹³

In an age of divisive politics, there has been a surprising amount of consensus on the soaring cost of healthcare and the need to contain it.¹⁴ But small-molecule (“SM”) drugs are costly to develop and biologics even more so—averaging \$800 million for SM drugs and \$2 billion for biologics.¹⁵ The Hatch-Waxman Act (“HWA”)¹⁶ was designed to incentivize innovation by authorizing the extension of patent terms to account for clinical trials and the post-trial FDA approval process,¹⁷ nonpatent market exclusivity,¹⁸ and a thirty-month

7. See *FTC v. Actavis, Inc.*, 570 U.S. 136 (2013).

8. See, e.g., Michael A. Carrier, *Sharing, Samples, and Generics: An Antitrust Framework*, 103 CORNELL L. REV. 1 (2017); see also Joanna M. Shepherd, *Biologic Drugs, Biosimilars, and Barriers to Entry*, 25 HEALTH MATRIX 139, 142 (2015).

9. Michael A. Carrier & Carl J. Minniti III, *Biologics: The New Antitrust Frontier*, 2018 U. ILL. L. REV. 1, 4 [hereinafter Carrier & Minniti] (“Antitrust finds itself at a unique and crucial moment: poised at the precipice of a new industry but able to draw on decades of case law in an analogous setting that has addressed issues of competition and innovation.”).

10. *Id.*

11. Julie D. Polovina, *Mutant Biologics: The 2010 Health-Reform Legislation’s Potential Impact on Reducing Biologic Research and Development Costs*, 100 GEO. L.J. 2291, 2293 (2012) (describing how biologics may combat cancers, HIV/AIDS, hepatitis C, and autoimmune disorders, as well as heart disease and stroke” by replacing or enhancing natural proteins produced by the body); Martina Weise et al., *Biosimilars: What Clinicians Should Know*, 120 BLOOD 5111, 5111 (2012) (describing biologics as large, complex molecules derived from living organisms—while a small-molecule drug may contain a hundred atoms per molecule, biologics can contain tens of thousands per molecule); see also Polovina, *supra* note 11, at 2296 (“[H]igh manufacturing and R&D expenses result in biologics being one of the most expensive pharmaceutical therapies available to consumers.”).

12. See JUDITH A. JOHNSON, CONG. RESEARCH SERV., *FDA REGULATION OF FOLLOW-ON BIOLOGICS 1* (2010) (estimating common biologics range from \$37,000 for Herceptin (breast cancer) to \$200,000 for Cerezyme (Gaucher’s disease)).

13. See Carrier & Minniti, *supra* note 9, at 4.

14. Daryl Lim, *Antitrust and the Mylan Conspiracy*, JURIST-ACAD. COMMENT. (Jan. 20, 2017), <http://www.jurist.org/forum/2017/01/antitrust-and-the-mylan-conspiracy.php>.

15. See Andrew Jack, *Big Drug Groups Urged to Buy in Test Products*, FIN. TIMES (Jan. 31, 2010), <https://www.ft.com/content/2ed73272-0eb6-11df-bd79-00144feabdc0> (stating that it now takes up to \$2 billion to develop a new biologic).

16. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 21 U.S.C. § 355 (2012)).

17. 35 U.S.C. §§ 156(c), (g)(6) (2012)(stating that the approval process takes up to 5 years, giving patentees a minimum of 14 years of patent protection post-grant).

stay of FDA approval on a generic's drug.¹⁹ The Biologics Price Competition and Innovation Act ("BPCIA") similarly contains exclusivity provisions to reward innovation in developing biologics and encourage future research and development.²⁰ These provisions include a four-year freeze on any follow-on biologic ("FOB") manufacturer filing an application for entry until after approval of the reference biologic ("RB"),²¹ and a twelve-year freeze to prevent the FDA from approving FOBs who rely on the RB's data.²² With many SM blockbuster drugs losing their patent protection within the next decade, up to half of drug companies' revenues will come from biologics.²³ What, if any, is the role of antitrust law at this new frontier?

The Authors note that antitrust law has a remedial role where the preexisting regime is ineffective in curbing anticompetitive abuses.²⁴ And here, they argue that "[t]he BPCIA framework offers a textbook example of a regime in which the regulatory agency is without power to remedy anticompetitive conduct."²⁵ The Authors assess the risks of antitrust concerns arising in six areas: patent settlements, product hopping, regulatory abuse (including the Risk Evaluation and Mitigation Strategy or REMS program),²⁶ citizen petitions, disparagement, and collusion. Compared with SM drugs, they conclude that anticompetitive conduct in biologics will be more prevalent in four areas (disparagement, citizen petitions, collusion, and regulatory abuse), and less prevalent in two areas (product hopping and reverse-payment settlements). In each case, they provide an antitrust framework to assess those issues. This Response discusses three of those issues: patent settlements, product hopping, and regulatory abuse (including REMS). It reflects on the Authors' observations, weaving in ripostes and recommendations where appropriate.

With patent settlements, as the Authors note, the *Actavis* framework will continue to be applicable in situations where RBs pay FOBs to stay out of their markets.²⁷ The Authors' optimism that reverse payments will be less likely,

18. 35 U.S.C. §§ 156(c), (g)(6) (2012) (stating that the nonpatent market exclusivity lasts 3 years for new clinical investigations essential to approval); 35 U.S.C. §§ 355(j)(5)(F)(ii) (2012) (stating that the nonpatent market exclusivity lasts 5 years for formulations with new active ingredients).

19. 21 U.S.C. § 355(j)(5)(B)(iii).

20. Pub. L. No. 111-148, 124 Stat. 804 (codified as amended at 42 U.S.C. § 262 (2012)).

21. § 262(k)(7)(B).

22. § 262(k)(7)(C).

23. See Carrier & Minniti, *supra* note 9, at 9.

24. *Id.* at 36 ("Behavior like pay-for-delay settlements, multiple 30-month stays, and fraudulent patent listings are textbook examples of a regulatory regime not effectively being enforced, which necessitates a role for antitrust. Because the FDA is not able to address anticompetitive schemes, antitrust law must fill the void.").

25. *Id.* at 47.

26. For a background on REMS, see *id.* at 46–52.

27. *FTC v. Actavis, Inc.*, 570 U.S. 136 (2013); Carrier & Minniti, *supra* note 9, at 24 ("The [*Actavis*] Court relied on an array of previous cases to confirm that its precedents "make clear that patent-related settlements can sometimes violate the antitrust laws. . . . [W]e believe the setting of complex pharmaceutical regulation under the BPCIA easily offers sufficient similarities to the Hatch-Waxman Act to allow application of *Actavis*'s broad principles.").

however, should be tempered. Factors including the ability for FOBs to offer interchangeable therapies over time, the likelihood that FOBs must disclose manufacturing trade secrets during BPCIA litigation, and the real and present threat of patent revocation in post-grant proceedings both individually and may cumulatively result in a higher incidence of reverse payments than the Authors predict. At the same time, the lack of automatic reporting obligations will make anticompetitive biologic settlements more difficult to detect than those in the SM space.²⁸

With product hopping, the Authors are similarly optimistic. RBs are less likely to reformulate biologics; FOBs must price their biologics higher, making it less attractive for RBs to engineer “hard switches”; state substitution laws do not apply to biosimilars; and the BPCIA does not provide additional exclusivity for minor reformulations. As with the reverse-payments scenario, however, interchangeable FOB therapies will become the norm over time.²⁹ The primacy of process innovation in biologics will make reformulation easier than in the SM space.³⁰ *Actavis* also cautions against the Authors’ suggestion that RBs who enter with a reformulated biologic after a FOB should qualify for a safe harbor. Rather, the rule of reason should still be applied, though that analysis may be concluded in a “twinkling of an eye.”³¹

Finally, as the Authors note, regulatory abuse (including REMS) will continue to raise antitrust concerns. In this regard, the Response amplifies the Authors’ analysis of refusals to deal in biologic samples for REMS purposes, as well as their analogies to patent assertion entities and standard essential patents, explain how each of these can inform the antitrust analysis in the biologics space.³² The Response also discuss why and how patent misuse can be used as a policy lever to address regulatory abuses, and why the cumulative nature of innovation in the biologics space makes patent misuse a particularly apt response.³³

II. PATENT SETTLEMENTS

The SM generic drug market in the United States is worth \$74.5 billion, due in part to the HWA, which spurred a flood of generics (88% of all prescriptions—up from 19% in 1984, the year of the Act), and brought the average price of a generic down from \$44 to \$8 by 2015.³⁴ The BPCIA, passed as part

28. Carrier & Minniti, *supra* note 9, at 24

29. *See infra* Part III.

30. *See infra* Part III.

31. *Am. Needle, Inc. v. Nat’l Football League*, 560 U.S. 183, 203 (2010) (“[T]he Rule of Reason may not require a detailed analysis; it can sometimes be applied in the twinkling of an eye.”).

32. *See infra* Part IV.

33. *See infra* Part IV.

34. Carrier & Minniti, *supra* note 9, at 11 (“In 1984, Congress enacted the Hatch Waxman Act. In doing so, the legislature sought to increase generic competition and foster innovation in the pharmaceutical indus-

of the Affordable Care Act (“ACA”) during the Obama Administration, mirrors the HWA by carving out an abbreviated approval pathway for FOBs,³⁵ and is expected to save consumers \$250 billion in costs over ten years.³⁶ The HWA and BPCIA both provide dispute resolution pathways, and feuding parties may opt to use them or settle rather than litigate matters to their conclusion.³⁷ In some instances, the patentee pays its generic rival, who in turn agrees to stay out of the patentee’s market.³⁸

Reverse payments, so called because the settlement money flows from the incumbent to the potential generic seeking to challenge the brand’s dominance under the guise of patent settlements, have received unparalleled antitrust attention in recent years.³⁹ These settlements keep prices at monopoly levels by blocking subsequent challenges of the brand’s patent.⁴⁰ In 2013, the Supreme Court held that such settlement agreements could have “significant anticompetitive effects” and held such payments were not immune from antitrust scruti-

try.”); *see also* GENERIC PHARM. ASSOC., *GENERIC DRUG SAVINGS IN THE U.S.* 1 (2015), http://www.gphaonline.org/media/wysiwyg/PDF/GPhA_Savings_Report_2015.pdf; IMS INST. FOR HEALTHCARE INFORMATICS, *MEDICINES USE AND SPENDING IN THE U.S.: A REVIEW OF 2015 AND OUTLOOK TO 2020* 4 (2016), https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/medicines-use-and-spending-in-the-us-2016.pdf?la=en&hash=88D3165AB5704A57CC6DC715D85989F5BD781C38&_=1520267312794.

35. *See* 42 U.S.C. § 262(k). Congress established such “a biosimilars pathway balancing innovation and consumer interests.” Biologics Price Competition and Innovation Act, Pub. L. No. 111-148, § 7001(b), 124 Stat. at 804. Biocomparability is derived from similarity, toxicity immunogenicity, pharmacokinetics, or pharmacodynamics studies to determine if a biologic is “highly similar to the reference product notwithstanding minor differences in clinically inactive components” and “there are no clinically meaningful differences between the [biosimilar] and the reference product in terms of safety, purity, and potency of the product.” § 262(i)(2)(A)–(B). Interchangeability requires additional proof that they “produce the same clinical result as the reference product in any given patient,” and can be switched between the FOB and originator without presenting any ancillary safety or efficacy risks. 42 U.S.C. § 262(k)(4)(A)(ii). Interchangeable FOBs can be automatically substituted by pharmacists without intervention by the prescribing physician. 42 U.S.C. § 262(i)(3); *see also* Richard A. Epstein, *The Constitutional Protection of Trade Secrets and Patents Under the Biologics Price Competition and Innovation Act of 2009*, 66 *FOOD & DRUG L.J.* 285, 285 (2011) (“The Biologics Price Competition and Innovation Act of 2009 is for the field of pharmaceutical products the single most important legislative development since passage of the [Hatch-Waxman Act], on which portions of the [BPCIA] are clearly patterned.”); Darren S. Tucker & Gregory F. Wells, *Emerging Competition Issues Involving Follow-On Biologics*, 29 *ANTITRUST MAGAZINE* 100, 105 n.7 (2014) (noting that since the Affordable Care Act (ACA) contains no express severability provision, “whether the BPCIA would survive a successful challenge to the ACA is an open question.”).

36. Sabrina Tavernise & Andrew Pollack, *F.D.A. Approves Zarxio, Its First Biosimilar Drug*, *N.Y. TIMES* (Mar. 6, 2015), <https://www.nytimes.com/2015/03/07/health/fda-approves-zarxio-first-biosimilar-drug.html>; *see also* Kate S. Gaudry, *Exclusivity Strategies and Opportunities in View of the Biologics Price Competition and Innovation Act*, 66 *FOOD & DRUG L.J.* 587, 598–600 (2011). A biosimilar application may only be submitted 4 years after the reference product was first licensed, § 262(k)(7)(B), and approval of a biosimilar application may only be made effective 12 years after the reference product was first licensed. § 262(k)(7)(A). Biosimilars can use clinical data from their reference products to obtain FDA approval and enter the market after the reference product’s 12-year exclusivity period expires, regardless of patent protection.

37. *Carrier & Minniti*, *supra* note 10, at 11–14, 16–18.

38. *Id.* at 19 n.169.

39. *Id.* at 19 (“For the past two decades, no antitrust issue in the pharmaceutical industry has received as much attention among courts and commentators as settlements.”).

40. *See* *FTC v. Actavis, Inc.*, 570 U.S. 136 (2013).

ny.⁴¹ This is consistent with antitrust precedent condemning naked horizontal agreements among rivals to fix prices, or to restrict their output.⁴²

The Court rejected the “scope of the patent” approach adopted by some lower courts, which immunize the settlements from antitrust scrutiny as long as they fell within the patents’ temporal and claim scope.⁴³ Instead, factors such as the size of the payment from brand to generic could be compared to litigation costs as a proxy to determine whether the settlement violated antitrust laws.⁴⁴ Significantly, the Court held that both patent and antitrust policies were relevant in delineating that patent scope.⁴⁵ Lower courts in subsequent cases have held that *Actavis* should be interpreted to cover non-cash payments.⁴⁶ Here the Authors aptly describe how *Actavis* should be applied to biologics: RBs should not be able to pay FOBs to gain additional delay with consideration not available as a direct consequence of winning the lawsuit.⁴⁷

The Authors observe that “payment to avoid the risk of biosimilar competition presents the same concerns highlighted in *Actavis*.”⁴⁸ Like the HWA, BPCIA litigation will usually begin before the FOB enters the market.⁴⁹ Also like the HWA, the BPCIA provides for first-filer exclusivity for the first interchangeable biologic, for one year rather than 180 days.⁵⁰ Since RBs have no actual damages and no risk of their patents being declared invalid, and since FOB entry significantly reduces the profits of high-margin biologics, they naturally see compensation as a natural part of their risk mitigation strategy.⁵¹ The Authors argue that “[t]he biologic manufacturer is entitled to rely on its patent to exclude a generic. But it should not be able to pay a biosimilar to gain additional delay.”⁵² According to them, the touchstone is “whether the biologic manufacturer conveys a type of consideration not available as a direct conse-

41. *Id.* at 158.

42. *United States v. Line Materials Co.*, 333 U.S. 287, 312 (1948) (“As the Sherman Act prohibits agreements to fix prices, any arrangement between patentees runs afoul of that prohibition and is outside the patent monopoly.”).

43. 570 U.S. at 146–47.

44. *Id.* at 154–57.

45. *Id.* at 148 (“[I]t was ‘incongruous’ to determine antitrust legality by measuring the settlement’s anti-competitive effects solely against patent law policy, rather than by measuring them against procompetitive antitrust policies as well.”).

46. *See e.g.*, *King Drug Co. of Florence v. Smithkline Beecham Corp.*, 791 F.3d 388 (3d Cir. 2015).

47. *Carrier & Minniti*, *supra* note 9, at 25; *see also id.* at 25–26 (citing as examples access to “manufacturer direct” distribution channels, reimbursement agreements, and forgiveness of damages).

48. *Carrier & Minniti*, *supra* note 9, at 24; *see also Tucker & Wells*, *supra* note 35, at 102 (“There is language in the *Actavis* decision that could be read to suggest that the decision should apply to reverse-payment settlements occurring under the BPCIA, which is undoubtedly the position that the FTC will take.”).

49. *Carrier & Minniti*, *supra* note 9, at 16–18.

50. *Id.* at 15.

51. *Id.* at 25.

52. *Id.*

quence of winning the lawsuit.”⁵³ Evidence of non-cash payments include biosimilar applicants access to distribution or reimbursement networks.⁵⁴

At the same time, the Authors predict that “there will be fewer reverse-payment settlements between biologics and biosimilars.”⁵⁵ They provide three reasons for this. First, there is a smaller price difference between biologic manufacturers and biosimilars because of higher development costs and fewer entrants.^{56 57} Further, a first filer can delay entry of subsequent applicants of interchangeable biologics but there is no first-filer exclusivity for biosimilars.⁵⁸ Since there are no interchangeable biologics currently available, other FOBs can still enter the market. Second, the Authors predict that notoriety of both the biologic and its manufacturer may induce consumers to pay more to avoid switching costs.⁵⁹ These costs include “prescriber and patient education, consumer reluctance, and more uncertain FDA approval,”⁶⁰ which generics avoid because of state substitution laws and the identical chemicals used.⁶¹ Third, the Authors predict that the increasing prevalence of administrative post-grant proceedings make it less likely biosimilar makers will want to enter into settlements with reference to biologic makers since they can “clear the field” of suspect patents before filing a biosimilar application.⁶² They note that “biosimilar makers may be less willing to settle because of their significant expenditures and because they wish to satisfy shareholder expectations of launching lucrative biosimilars.”⁶³ The Authors’ predictions are correct, but only to an extent.

As to their first and second observations, the price differential is likely to widen as the cost of replicating RBs falls and interchangeable biologics replace biosimilars as the predominant alternative to RB. DNA sequencing and manipulation techniques have steadily become cheaper and more effective in recent

53. *Id.*

54. *Id.* (describing access to a “manufacturer direct” channel which, in selling directly to purchasers (e.g., specialty pharmacies and large hospitals), removes the “middleman,” or providers who pool resources to maximize economies of scale in drug purchasing and sometimes function as distributors, gaining control over products offered to downstream purchasers”).

55. *Id.* at 21.

56. *Id.* (“[G]iven high development costs and a more finite universe of potential biosimilar entrants, the price likely will not fall as significantly upon biosimilar entry, which may reduce biologics’ urgency to enter into settlements.”); *see also id.* at 10 (“[W]hile the entry of multiple small-molecule generics results in significant price erosion (50% with 2 generics and 75% with at least 6), we predict that the reductions may be more modest given attempts to recoup biosimilar development costs, which greatly exceed those incurred by generics.”); Henry G. Grabowski et al., *Entry and Competition in Generic Biologics*, 28 *MANAGERIAL AND DECISION ECON.* 439 (2007).

57. Tucker & Wells, *supra* note 35, at 102.

58. Carrier & Minniti, *supra* note 9, at 15.

59. *Id.* at 22.

60. *Id.*

61. *Id.*

62. *Id.* at 22 (“While IPR tactics have increasingly been employed in the small-molecule setting, patent challenges to biologics at the Patent Office have been used more frequently, quickly becoming the norm.”).

63. *Id.* at 24.

times.⁶⁴ Better replication techniques will minimize immunogenicity making switching costs less significant. Other factors the Authors cite in predicting biologics reverse payments are less likely compared to SM will similarly be muted as technological advances make interchangeable biologics more commonplace over time. These include the concomitant value of the RB's name strength, prescriber and patient education, consumer reluctance, and more uncertain FDA approval.⁶⁵

As the dynamics of the biologics market begin to mirror the SM space, so will the temptation for makers of interchangeable biologics and RBs to engage in reverse payments. Interchangeable FOBs enjoy twice the length of exclusivity compared to their SM counterparts. The ability for RBs and FOBs to divide up a broader swath of exclusivity would make it at least as compelling to enter into a reverse-payment settlement agreement than under in the SM, and arguably more so. Further, as the Authors rightly note, litigating under the BPCIA framework would require the biosimilar applicant to provide the sponsor with its manufacturing know-how, including its proprietary trade secrets.⁶⁶ The arms race lies not merely in the research and development of the biologic itself, but in the relative superiority of manufacturing processes. FOBs would want to avoid disclosing their knowhow to RBs if possible. Indeed, as the Authors themselves note, "the product is the process."⁶⁷ Settlement allows them to short-circuit the formal dispute resolution and avoid disclosing their trade secrets.

The Authors downplay the possibility of anticompetitive harm citing public access to the settlement agreement "upon written request, payment of a specified fee, and with a showing of good cause,"⁶⁸ but that suggestion assumes members of the public would have the interest, knowledge, resources, and sufficient diligence to do so in any meaningful way. Patent settlements under the BPCIA are not reportable to the Federal Trade Commission ("FTC") as they are under the HWA, creating an opaqueness that makes biologic patent settlements harder to detect and arrest in this space than in the SM space.⁶⁹

The Authors' observation that post-grant reviews will result in fewer reverse payments overlooks the leverage Inter Partes Review ("IPR") gives FOBs against RBs, who may be willing to pay large sums to challenge to their pa-

64. For instance, the cost of sequencing DNA fell from \$1 million a gene to just over \$1,000 over fifteen years. *The Cost of Sequencing a Human Genome*, NAT'L GENOME RES. INST., <https://www.genome.gov/27565109/the-cost-of-sequencing-a-human-genome> (last visited Mar. 21, 2018); see also Luke Dormehl, *CRISPR Gene Editing May Have Just Become a Whole Lot More Accurate*, DIGITAL TRENDS, (Jan. 22, 2018, 1:37 PM), https://www.digitaltrends.com/cool-tech/mcgill-crispr-90-percent-breakthrough/?utm_source=sendgrid&utm_medium=email&utm_campaign=daily-brief.

65. Carrier & Minniti, *supra* note 9, at 22.

66. *Id.* at 24. ("[B]ecause a biosimilar's manufacturing processes are proprietary trade secrets, applicants could be tempted to enter into settlements to avoid disclosing sensitive information.")

67. *Id.* at 7 (citing James T. O'Reilly & Katharine A. Van Tassel, Food and Drug Administration § 13:135 n.16 (Thomson Reuters, 4th ed. 2016)).

68. *Id.* at 23 (citing 35 U.S.C. § 317(b)).

69. Tucker & Wells, *supra* note 35, at 101.

tents. The Authors note the empirical evidence that “early trends in BPCIA litigation have revealed multiple biosimilar makers filing IPR petitions on the same patents.”⁷⁰ The Authors themselves aptly note these IPR challenges could pose antitrust issues in the form of vexatious litigation.⁷¹

The Patent Trial and Appeal Board (“PTAB”) provides an administrative forum that allows FOBs to challenge the validity of patents granted to RBs. Once a patent enters the IPR process, it faces a 70% chance of invalidation by the PTAB.⁷² As Erik Hovenkamp and Jorge Lemus cautioned in the SM space:

[The] PTAB may be exploited as a convenient platform for reaching potentially-anticompetitive “reverse payment” settlements. . . . [O]ur empirical analysis shows that many PTAB petitions involving drug-related patents are settled – about 38%. Of those trials that settle, about 75% meet our criterion for inferring reverse payment. Curiously, about half of these settlements occur after a decision to institute the petition. It seems unlikely that a generic firm would settle for nothing right after the judge signals that it has a good chance of prevailing on final judgment, so the inference of reverse payment is particularly strong in these settlements.⁷³

Hovenkamp and Lemus provide two reasons for this phenomenon. First, the PTAB provides a convenient venue for facilitating reverse payment deals because they are administered by officials without antitrust jurisdiction but who have the same ability as Article III judges to invalidate patents. Second, while parties have an obligation to report their patent settlements to the FTC for anti-

70. Carrier & Minniti, *supra* note 9, at 22.

71. *Id.* at 23 n.208 (“An issue lying outside the scope of this Article worth attention in the coming years involves the antitrust implications of agreements with payment settling IPR challenges. . . . The reason is that if the generic were to maintain its challenge after institution (i.e., the critical, initial step a petitioner must meet to continue an IPR challenge), it will have already demonstrated a reasonable likelihood of showing that the challenged claims are unpatentable. . . . For that reason, the generic can use this leverage of potential patent invalidation as a means to obtain a settlement.”) (citations omitted).

72. Gene Quinn & Steve Brachmann, *Patent Killing Fields of the PTAB: Erasing Federal District Court Verdicts on Patent Validity*, IPWATCHDOG (Jan. 14, 2018), <http://www.ipwatchdog.com/2018/01/14/patent-killing-fields-ptab-erasing-federal-district-court-verdicts-patent-validity/id=92375/> (“82.5% of patents reviewed by PTAB in a final written decision are found defective. 69% of cases reaching a final written decision by the PTAB have all claims invalidated. 5% of patents reviewed by the PTAB are disclaimed by the patent owner, which makes them unenforceable.”); see also Gene Quinn, *Why is PTAB Spending Precious Resources Killing Good Patents*, IPWATCHDOG (Jan. 16, 2018), <http://www.ipwatchdog.com/2018/01/16/ptab-killing-good-patents/id=92094/> (“At a minimum, what the PTAB is doing with respect to good patents previously adjudicated as valid raises very serious questions about an overactive, even rogue tribunal that seems to have a vendetta against patent owners and patents, regardless of whether those patents are good or bad.”)

73. Erik Hovenkamp & Jorge Lemus, *Reverse Payment Settlements and Holdup Under PTAB*, IPWATCHDOG (July 31, 2016), <http://www.ipwatchdog.com/2016/07/31/reverse-payment-settlements-and-holdup-under-ptab/id=71404/>; see also *id.* (“[T]he parties obtain a consent decree holding the patent valid and infringed (and enjoining the generic firm). This has a strong claim-preclusive effect that will keep the generic firm out of the market until the patent expires. The consent decree does not provide for a reverse payment, however, which ensures that a federal judge will not challenge it on antitrust grounds. But the parties can still achieve reverse payment by relegating it to the PTAB settlement, where the judge has no authority to enforce the antitrust laws. The result of this bifurcated settlement appears to be a de facto pay for delay agreement that lasts for the full remainder of the patent term.”).

trust review, they may simply report a PTAB consent decree stating the patent is valid and would be infringed by the proposed generic to circumvent the disclosure of the terms of their settlement.⁷⁴ There is no apparent reason to conclude that the result for biologics on this issue would be any different.

Ultimately, the value to shareholders is the value of a company's assets and liabilities, whether that company is an RB or FOB. If the value the settlement brings outweighs the rewards of seeing the challenge through, it is in the interest of shareholders on both sides to condone the reverse payment, with their decision adjusted only by the risk of detection and penalties if caught. Indeed, the litigation costs for biosimilar makers are higher than generics because they must do more substantial pre-application investigations to identify applicable patents.⁷⁵ Accordingly, the incentive to avoid litigation (and thus settling) is greater. It might be that there are good reasons why a settlement which allows parties to enter a truce under the HWA or BPCIA should be honored. If so, the obligation remains on those best placed to provide reasons to aid the court in that determination – the settling parties themselves. Accordingly, anti-competitive reverse payments in the biologics space remains a real and present threat and should be treated as such.

III. PRODUCT HOPPING

“Product hopping” occurs when brands switch drug formulations to delay a FOB's entry, for example by evading state drug product substitution laws in the SM space.⁷⁶ These laws allow or require pharmacies to substitute generic versions of brand prescriptions.⁷⁷ Courts have distinguished between anticompetitive “hard switches,” where the brand company removes the original drug from circulation, and generally permissible “soft switches,” where the original drug remains on the market.⁷⁸ The touchstone is whether consumers are deprived of coercive tactics.⁷⁹ Hard switches also reveal that patentees may be willing to sacrifice short-term profits to achieve this goal.⁸⁰ The threshold is not absolute foreclosure, but substantial foreclosure stemming from cost-efficient

74. *Id.* (“After all, a PTAB settlement simply says that the parties agree to terminate the IPR – it need not declare the patent valid – and this arguably does not relate to manufacture or sales.”).

75. *Carrier & Minniti*, *supra* note 9, at 26.

76. *See New York ex rel. Schneiderman v. Actavis PLC*, 787 F.3d 638, 643–46 (2d Cir. 2015).

77. *Id.*

78. *Id.* at 654.

79. *Id.* at 654 (“Neither product withdrawal nor product improvement alone is anticompetitive [but] . . . when a monopolist combines product withdrawal with some other conduct, the overall effect of which is to coerce consumers rather than persuade them on the merits . . . and to impede competition . . . its actions are anticompetitive under the Sherman Act.”).

80. *Id.* at 658 (“[I]n deciding to take IR off the market, Defendants were willing to give up profits they would have made selling IR—Forest’s best-selling drug. . . . This ‘willingness to forsake short-term profits to achieve an anticompetitive end’ is indicative of anticompetitive behavior.” (quoting *In re Adderall*, 754 F.3d 128, 135 (2d Cir. 2014))).

channels for competition.⁸¹ Evidence that patentees sought to block competition will likely be probative of anticompetitive harm.⁸² Significantly, where courts determine that a patentee's procompetitive justifications are pretextual, they will likely refuse to weigh them against the anticompetitive harms or simply conclude that those benefits outweigh the harms.⁸³ From a dynamic efficiency perspective, the heuristic also leads courts to conclude that antitrust scrutiny would not harm innovation incentives.⁸⁴

The Authors argue that product hopping would be rarer in the biologics context because: (1) the size and complexity of biologics would make it more difficult for RBs to reformulate them compared to SM drugs;⁸⁵ (2) FOBs would also find it more difficult to offer interchangeable products, with smaller price cliffs making it less attractive for RBs to engineer "hard switches";⁸⁶ (3) RBs "also should experience less urgency to switch the market to a reformulated version because of the absence of state substitution laws, which could have shifted the emphasis from biosimilar marketing to price-conscious pharmacists";⁸⁷ and (4) the BPCIA, unlike the HWA, does not provide additional regulatory exclusivity for reformulations unless they change the biologics' safety, purity, or potency.⁸⁸

As with patent settlements, improved manufacturing know-how will result in more interchangeable FOBs, which will in turn diminish the extent that rea-

81. *Id.* at 655–56 ("For there to be an antitrust violation, generics need not be barred 'from all means of distribution' if they are 'bar[red] . . . from the cost-efficient ones' . . . [with] competition through state drug substitution laws [being] the only cost-efficient means of competing available to generic manufacturers. . . . Moreover, as the district court found, additional expenditures by generics on marketing would be impractical and ineffective because a generic manufacturer promoting a product would have no way to ensure that a pharmacist would substitute its product, rather than one made by one of its generic competitors.").

82. *Id.* at 658; *see also id.* at 661 n.36 (noting that the harm was significant because "consumers would pay almost \$300 million more," third-party payers "would pay almost \$1.4 billion more," and Medicare and its beneficiaries would pay "a minimum of \$6 billion over the next ten years.").

83. *Id.* at 658 ("Because we have determined that Defendants' procompetitive justifications are pretextual, we need not weigh them against the anticompetitive harms. But in any event, New York has shown that whatever procompetitive benefits exist are outweighed by the anticompetitive harms.").

84. *Id.* at 659.

85. *Carrier & Minniti, supra* note 9, at 28 ("In contrast to the straightforward reformulations that characterize small-molecule drugs, biologics are larger and more complex, which reduces the frequency of reformulations.").

86. *Id.* at 29 ("[D]evelopment costs and lack of identity between biologics and biosimilars make it less likely that the market will experience the dramatic price reductions that have been observed in the small-molecule setting and that have motivated product hopping."); *see also Tucker & Wells, supra* note 35, at 102 ("Existing state generic substitution laws do not apply to FOBs. To date, more than 20 states have considered 25 and six states have passed 26 new pieces of biologic substitution legislation. Substitution laws enacted to date impose various conditions not found in the generic pharmaceutical context, including requiring that pharmacists notify prescribers and/or patients when a substitution has been made. In addition, there are typically weaker reimbursement incentives to switch to FOBs compared to generic pharmaceuticals. Finally, concerns about the safety and efficacy of FOBs—whether well-founded or not—may lead to consumer or physician resistance to FOBs.").

87. *Carrier & Minniti, supra* note 9, at 29–30.

88. *Id.* at 29 ("By not offering additional exclusivity periods—which are stronger than patents in preventing the agency from receiving or granting applications—the regulatory structure offers less incentive to engage in product hopping.").

sons (1), (2) and (3) are true. Further, it will be easier for both BPs and FOBs to create better manufacturing processes than to develop better formulations that qualify for product patents.⁸⁹ As for reason (4), while the BPCIA precludes both the twelve-year data exclusivity period and the four-year application exclusivity period from applying to minor changes to “new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength,” minor structural modifications that change safety, purity, or potency even to a small degree may entitle RBs to a twelve-year period of data exclusivity for the reformulation.⁹⁰ Further, biologics, like SM drugs, may benefit from additional patents regardless of whether they qualify for additional regulatory exclusivity under the BPCIA if they qualify for the criteria imposed by patent law such as whether they are new, nonobvious, and qualify as statutory subject matter.⁹¹ Thus, while the Authors correctly conclude that reason (3) “supports a modestly reduced incentive to make inconsequential product changes,” the impact on process innovation, which the Authors acknowledge is much more significant in the case of biologics, needs to be part of the equation when predicting whether product hopping in biologics will be more or less likely than in the SM space.⁹²

The Authors also propose applying a “no-economic sense” test “that asks whether conduct allegedly maintaining a monopoly by excluding nascent competition likely would have been profitable if such competition flourished and the monopoly was not maintained.”⁹³ They go on to carve out a safe harbor for biologic manufacturers based on whether the biosimilar enters the market before the manufacturer introduces its reformulated version.⁹⁴ While “introduction of reformulation before generic entry “nearly eliminates both price competition and quality competition as between the original and new products,”⁹⁵ it does not follow that biologic manufacturers should be immunized from anti-trust scrutiny.

As the adage goes, “low crime doesn’t mean no crime.”⁹⁶ Indeed, *Actavis* points in the opposite direction.⁹⁷ The better approach is that entry of the RB’s

89. Tojo Jose, *What is the Difference between Product Patent and Process Patent?*, INDIANECONOMY.NET (Dec. 17, 2015), <http://www.indianeconomy.net/splclassroom/98/what-is-the-difference-between-product-patent-and-process> (“There is high tendency for competitors to reengineer the original invention by discovering a new process with less strain and investment.”).

90. 42 U.S.C. § 262(k)(7).

91. Tucker & Wells, *supra* note 35, at 104 (“Given the likely time and difficulty to obtain approval for an interchangeable FOB (particularly compared to the burden of showing that generic pharmaceuticals are bio-equivalent), biologic manufacturers may have a strong incentive to pursue such a strategy.”).

92. Carrier & Minniti, *supra* note 9, at 29.

93. *Id.* at 31.

94. *Id.* at 29-30.

95. Steve D. Shadowen et al., *Anticompetitive Product Changes in the Pharmaceutical Industry*, 41 RUTGERS L.J. 1, 51 (2009).

96. SUSAN SIM, MAKING SINGAPORE SAFE: THIRTY YEARS OF THE NATIONAL CRIME PREVENTION COUNCIL 25 (2011).

97. *FTC v. Actavis*, 133 S. Ct. 2223, 2230–31 (2013) (“[T]o refer, as the Circuit referred, simply to what the holder of a valid patent could do does not by itself answer the antitrust question.”).

reformulated product prior to the FOB's entry should be merely one factor courts and agencies consider. Alarm bells should ring if the new formulation lacks significant medical benefits over the single drug alone, is timed to coincide with the expiration or invalidation of a patent, or if the RB withdraws sale of the original drug.⁹⁸ The burden should then shift to the innovator to show a benefit that justifies the formulation. It may be that the conduct is likely to survive the rule of reason without a detailed analysis and "can sometimes be applied in the twinkling of an eye."⁹⁹ It makes no sense to immunize anticompetitive behavior because of the risk that some cases might prove tough to decide. The proper standard requires sensitivity to innovation concerns, not abdication of judicial oversight.¹⁰⁰

IV. REGULATORY ABUSE (INCLUDING REMS)

The Authors point out that the BPCIA could be subject to multiple forms of regulatory abuse by RBs, pointing to tactics like submarine patents,¹⁰¹ using shell companies to circumvent BPCIA disclosure obligations, or refusing FOBs access to samples for REMS clearance.¹⁰² Each of these, they argue, may give rise to an antitrust violation. The Authors point out that such monopolistic conduct would likely violate antitrust laws,¹⁰³ and, once again, unlike a regime without monitoring mechanism and financial or other penalties, can satisfactorily help rivals and consumers that have been harmed in a way that the FDA or BPCIA currently cannot.¹⁰⁴

As for shell companies, the Authors draw parallels between shell licensing and patent assertion entity ("PAE") conduct, where PAEs were used to obscure the identities of patent holders when negotiating with prospective licensees.¹⁰⁵ This results in "defendants not knowing how to 'identify the beneficial

98. HERBERT HOVENKAMP ET AL., § 15.03: PRIVATE EFFORTS TO MANIPULATE REGULATORY FRAMEWORKS AS ANTITRUST VIOLATIONS, *in* IP AND ANTITRUST: AN ANALYSIS OF ANTITRUST PRINCIPLES APPLIED TO INTELLECTUAL PROPERTY LAW (2017).

99. *Am. Needle, Inc. v. NFL*, 560 U.S. 183, 203 (2010).

100. *See* HOVENKAMP ET AL., *supra* note 98.

101. *Carrier & Minniti*, *supra* note 9, at 38 ("Submarine patents involve an applicant's use of silent delay tactics at the PTO, aimed at obtaining issuance of a patent years after the initial filing, but still with the legal right to surprise a mature market.").

102. *Id.* at 43 (noting that this evasion "contravenes the intent of the BPCIA and raises significant competitive concerns. Phase-One litigation is designed to provide significant control to the biosimilar applicant over patent resolution"); *see also id.* at 41 ("If a manufacturer is able to conceal relevant patents until years after Phase-One litigation is completed, a biosimilar applicant is exposed to a higher liability concern than it expected when agreeing on the patents to litigate during the patent dance. That raises the potential for delayed entry and an evasion of the BPCIA.").

103. *Id.* at 45 ("the use of submarine patents and shell-licensed patents would appear to be anticompetitive conduct that in the context of the BPCIA—with its intricately-choreographed moves and countermoves between the parties, lack of certification requirement, and windfall from late-filed patents—makes no sense other than by harming rivals.").

104. *Id.* at 36–37.

105. *Id.* at 42–43.

party or true party-in-interest,’ or even if they ‘already ha[ve] a license’ through earlier deals with related entities.”¹⁰⁶ More objectionable is that “the biosimilar was never afforded an opportunity to contest that patent during Phase-One litigation, when final rulings (as opposed to tentative preliminary injunction determinations) on infringement could have been completed,”¹⁰⁷ as the BPCIA intended.¹⁰⁸

Courts have opined that PAEs who used shell companies to inflict an onslaught of lawsuits and corral alleged infringers who had sunk costs into adopting a technology into settling for inflated royalties may well violate antitrust law.¹⁰⁹ One court found that a PAE had demanded banks take a license from it on the pain of “ceaseless litigation” through “a carefully orchestrated campaign of patent aggregation, concealment and sham litigation.”¹¹⁰ The PAE did so by acquiring 3,500 patents with dubious claims on existing products in financial-services.¹¹¹ An alternative license would not eliminate the threat of ceaseless litigation.¹¹² As with RBs, high entry barriers based on the patentee’s control over essential patents prevented rivals from expanding their output to challenge the patentee’s high prices.¹¹³ And significantly, the patentees there “concealed and obfuscated [their] patent holdings” so that it was “practically impossible for targets” to assess the portfolio and take steps to avoid infringement.¹¹⁴ Leveraging on sunk costs in bad faith has been a recurrent theme in the holdup narrative, both in the tech and biopharma space, and patentees should find themselves vilified regardless of the form that the holdup attempt takes.

As for REMS, generics and FOBs can use results from earlier clinical trials done by the brand to show bioequivalence—but only if they can access the brand’s sample.¹¹⁵ REMS prevent FOBs from getting their supplies from the REMS’ distributors and wholesalers, making RBs the only source for samples.¹¹⁶ RBs refuse to sell samples despite FOBs willing to buy them at prevail-

106. *Id.* at 42.

107. *Id.* at 42–43.

108. *Id.* at 43 (“As a result, the biosimilar maker could face significant liability for patents it never had the chance to challenge in the stage of the process at which such challenges were anticipated. Conducting an infringement analysis is costly and time-consuming, which is why eight years of exclusivity are allocated to the resolution of these issues.”).

109. *Intellectual Ventures I, LLC v. Capital One Fin. Corp.*, 99 F. Supp. 3d 610 (D. Md. 2015) (describing how PAE acquired 3,500 patents and asserted them through 2,000 shell companies.).

110. *Id.* at 623.

111. *Id.* at 621.

112. *Id.* at 623.

113. *Id.* at 624.

114. *Id.* at 626.

115. *Carrier & Minniti*, *supra* note 9, at 46–47.

116. Lauren Battaglia, *Risky Conduct with Risk Mitigation Strategies? The Potential Antitrust Issues Associated with REMS*, ANTITRUST HEALTH CARE CHRON. 28 (2013); *see also* *Carrier*, *supra* note 8, at 10. (“A generic company cannot use a foreign sample as a substitute because the FDA does not consider this to be the same drug product for bioequivalence testing purposes. And even if a generic has “the exact recipe of a brand formulation,” it “cannot manufacture its own version” because only the brand version constitutes the “reference listed drug” under the Hatch-Waxman Act.”).

ing market prices,¹¹⁷ even with the generic offering to indemnify the brand in one case.¹¹⁸ Refusal thwarts the pathway to generic competition carved out by legislation like HWA, BPCIA, and state substitution laws.¹¹⁹ In the SM space, REMS blockages have affected more than 100 generic firms and raised healthcare costs by at least \$5 billion annually.¹²⁰

While companies may generally choose their business partners,¹²¹ anti-trust law condemns conduct by businesses who sacrifice short-run profits and goodwill to sink rivals by refusing access to the resources they own.¹²² Courts frown on obstructive behavior of this sort with refusals to deal at retail prices revealing “a distinctly anticompetitive bent.”¹²³ Ceasing prior dealing also provides circumstantial evidence of anticompetitive intent and a lack of legitimate business justification.¹²⁴ As the Authors note, FOBs face high entry barriers due to the difficulty in developing substitutes because they lack access to proprietary manufacturing process and immunogenicity.¹²⁵ And, like generics, the

117. Transcripts of Motions Hearing at 52, *Actelion Pharms., Ltd. v. Apotex Inc.*, 2013 U.S. Dist. LEXIS 135524, at 49 (noting that “[t]he generics have offered to pay retail published price or, frankly . . . any price that was within the realm of reasonableness”); *Natco Pharma Ltd. v. Gilead Scis., Inc.*, 2015 U.S. Dist. LEXIS 131058, *6 (Minn. 2015) (offering to pay the market rate and shipping costs).

118. Plaintiff Mylan Pharms.’ Brief in Opposition to Celgene’s Motion to Dismiss at *13–14, *Mylan Pharms. Inc. v. Celgene Corp.*, Civ. Action No. 2:14-cv-02094-ES-MAH, 2014 U.S. Dist. Ct. Briefs LEXIS 1435 (D.N.J. June 16, 2014). ??? Unsure about this cite.

119. Carrier, *supra* note 8, at 3 (“Regulations such as the federal Hatch-Waxman Act and state substitution laws foster widespread generic competition. But these regimes can only be effectuated through generic entry. And that entry can take place only if a generic can use a brand’s sample to show that its product is equivalent.”); Tucker & Wells, *supra* note 35, at 103 (“The key factors leading to concerns under the Hatch-Waxman Act—the need for samples of the branded product to submit a generic/FOB application, the inability to procure product samples from ordinary distribution channels due to the REMS, and the branded firm’s refusal to sell directly to the generic/FOB firm—are the same under the BPCIA.”).

120. Carrier, *supra* note 8, at 1 (“More than 100 generic firms have complained that they have not been able to access needed samples. One study of 40 drugs subject to restricted access programs found that generics’ inability to enter increased U.S. healthcare costs by more than \$5 billion a year.”).

121. *United States v. Colgate & Co.*, 250 U.S. 300, 307 (1919).

122. *Verizon Commc’ns Inc. v. Law Offices of Curtis V. Trinko, LLP*, 540 U.S. 398, 409 (2004) (“The unilateral termination of a voluntary (and thus presumably profitable) course of dealing . . . suggested a willingness to forsake short-term profits to achieve an anticompetitive end.”); *Aspen Skiing Co. v. Aspen Highlands Skiing Corp.*, 472 U.S. 585, 610–11 (1985) (finding the defendant “willing to sacrifice short-run benefits and consumer goodwill in exchange for a perceived long-run impact on its smaller rival.”); *Otter Tail Power Co. v. United States*, 410 U.S. 366, 378 (1973) (requiring access to rivals where the firm was already providing the service, where the refusal was “to prevent municipal power systems from eroding its monopolistic position.”).

123. *Trinko*, 540 U.S. at 409.

124. Carrier & Minniti, *supra* note 9, at 48.

125. *Id.* at 8 (“If variability in biologic development and immunogenicity is a concern for the biologic manufacturer in making its own product, a follow-on maker will confront even higher hurdles. While these entities can rely on patent disclosures and other materials in the public domain, they will lack access to critical information that the biologic manufacturer protects as a trade secret. Because biologics are “so closely defined by their manufacturing process,” this secrecy blocks competition. Finally, the effects of complexity and secrecy are exacerbated by the difficulty even of analyzing a protein’s structure. The ability to use analytic techniques to demonstrate clinical comparability is more limited than for small-molecule drugs, with biosimilars not able to show that its product is identical to the biologic product.”).

FDA cannot compel samples and the BPCIA does not provide a remedy for anticompetitive abuses.¹²⁶

Concerns that stymied intervention: chilling innovation incentives, onerous oversight by courts, and the risk of collusion, are absent. First, the BPCIA itself envisions generic access to piggyback on the brand's results.¹²⁷ Since the RB is already or will soon be on the market, providing a sample requires only marginal effort, and the general availability of the drug suggests the refusal was intended to harm potential rivals.¹²⁸ Lack of prior dealing with the generic is likely no excuse.¹²⁹ Indeed, given the REMS setting, it would be unlikely that any prior dealing could have existed.¹³⁰ Courts have brushed aside product liability concerns.¹³¹ And, rightly so, since brands control generic REMS can implement steps needed to ameliorate any risks.¹³² Second, the terms for the sample are set if already available, and if not, would require a one-time sale.¹³³ Third, generics have no incentive to collude with the brand—one seeks expedited entry, and the other resents it.¹³⁴ The RB's intent reveals whether its justifications are “pretextual,” a death knell for the defendant's case in antitrust parlance.¹³⁵

To the antitrust responses outlined above, this Response adds one more policy tool that courts may use—patent misuse.¹³⁶ Patent misuse is an affirmative defense that finds its roots in the equitable doctrine of “unclean hands.”¹³⁷ Courts will not enforce a patent if the patentee had acted inequitably, and the patent remains unenforceable until the baleful effects of the patentee's conduct

126. *Id.* at 47 (citing Transcript of Motions Hearing, *Actelion Pharm. Ltd. v. Apotex, Inc.*, 2013 WL 5524078 (D.N.J. Oct. 17, 2013)).

127. *Id.* at 27.

128. *Carrier*, *supra* note 8, at 41 (“[T]he ready availability of samples offers additional evidence that the refusal to provide them to generics constitutes behavior that makes sense only by harming rivals.”).

129. *In re Thalomid and Revlimid Antitrust Litigation Civil, No. 14-6997 (KSH) (CLW)*, 2015 WL 9589217, at *21 (D.N.J. Oct. 29, 2015) (denying a motion to dismiss).

130. *Carrier*, *supra* note 8, at 52 (“REMS programs involve new drugs that have not previously been on the market, precluding a preexisting relationship between the brand and generic. The generic, by definition, is seeking a sample of the drug to enter the market. Because the sale of samples is likely to be a one-time event, if the generic had previously engaged with the brand, it would not need a sample.”).

131. *Id.* at 18 (“The court also rejected a defense based on product liability concerns, stating that “[t]he possibility that [a brand] could be liable for a generic drug's harm is . . . not a legitimate justification that would support its refusal to supply generic manufacturers with samples.”).

132. U.S. FOOD & DRUG ADMIN., *A Brief Overview of Risk Evaluation & Mitigation Strategies (REMS)* 4, <http://www.fda.gov/downloads/UCM328784.pdf>.

133. *Id.*

134. *Id.*

135. *In re Thalomid & Revlimid Antitrust Litig., No. CV146997KSHCLW*, 2015 WL 9589217, at *15 (D.N.J. Oct. 29, 2015) (finding that “motivation is central”).

136. See generally DARYL LIM, *PATENT MISUSE AND ANTITRUST LAW: EMPIRICAL, DOCTRINAL AND POLICY PERSPECTIVES* (2013).

137. *U.S. Gypsum Co. v. Nat'l Gypsum Co.*, 352 U.S. 457, 465–66 (1957); *Morton Salt Co. v. Suppiger Co.*, 314 U.S. 488, 493 (1942) (noting that the key question is whether “[e]quity may rightly withhold its assistance from such a use of the patent right by declining to entertain a suit for infringement . . . until . . . the improper practice has been abandoned and [the] consequences of the misuse of the [copyright] have been dissipated.”. For a detailed study of patent misuse, see LIM, *supra* note 136).

have been purged.¹³⁸ Patent misuse thus acts as a public injunction against abuses of the privileges granted under patent law.¹³⁹ Similar defenses include patent exhaustion,¹⁴⁰ and the defense of fair use in copyright law.¹⁴¹ Courts may find against RBs for patent misuse through declaratory judgments.¹⁴² While FOBs in patent infringement suits are normally reactive parties in the litigation process, they can proactively neutralize an RB's advance with declaratory judgments.¹⁴³

Patent misuse stands apart from antitrust law because it draws its vitality from patent policy.¹⁴⁴ Patent policy guides patent law in keeping owners within the boundaries of what they offer to society.¹⁴⁵ It is concerned about whether the patent is used to subvert technological progress.¹⁴⁶ At stake is not merely the private right of the defendant, but more importantly, the public interest.¹⁴⁷ Indeed, the Supreme Court forged patent misuse as a tool to prevent abuses of the patent system, "regardless of a demonstrable effect on competition."¹⁴⁸ Unlike an antitrust plaintiff, a defendant alleging misuse generally need not show that the patentee possessed market power or caused anticompetitive effects.¹⁴⁹ Unlike antitrust law, the effect of the patentee's conduct on market competition is incidental rather than a necessary part of liability. It begins with the premise that the patent grant is not a property right as such, but a privilege conferred by the patent office to promote technological progress.¹⁵⁰ In this regard, misuse may be analogized to the fair use defense in copyright law. Like patent misuse,

138. U.S. Gypsum, 352 U.S. at 465–66.

139. See *Syndicate Sales, Inc. v. Floral Innovations, Inc.*, No. 1:11-CV-00465-SEB-DKL, 2012 WL 4477691, at *2 (S.D. Ind. Sept. 28, 2012).

140. *Bowman v. Monsanto Co.*, 133 S. Ct. 1761, 1763 (2013).

141. See, e.g., *Cambridge Univ. Press v. Patton*, 769 F.3d 1232, 1238 (11th Cir. 2014); *In re Morton-Norwich Prods., Inc.*, 671 F.2d 1332 (C.C.P.A. 1982).

142. *Inamed Corp. v. Kuzmak*, 275 F. Supp. 2d 1100, 1124 (C.D. Cal. 2002); *Powertech Tech., Inc. v. Tessera, Inc.*, 2012 U.S. Dist. LEXIS 113194, at *13–18 (N.D. Cal. Aug. 10, 2012) (citing *B. Braun Med., Inc. v. Abbott Labs.*, 124 F.3d 1419, 1428 (Fed. Cir. 1997) (noting that the district court could enter a declaratory judgment that the patent was unenforceable due to misuse)).

143. See e.g., *Cty. Materials Corp. v. Allan Block Corp.*, 502 F.3d 730, 732 (7th Cir. 2007).

144. *Morton Salt Co. v. G. S. Suppiger Co.*, 314 U.S. 488, 492 (1942) ("[T]he public policy which includes inventions within the granted monopoly excludes from it all that is not embraced in the invention. It equally forbids the use of the patent to secure an exclusive right or limited monopoly not granted by the Patent Office and which it is contrary to public policy to grant.").

145. *Id.*

146. See HOVENKAMP ET AL., *supra* note 98.

147. See *Morton Salt*, 314 U.S. at 493 ("[A]dditional considerations must be taken into account where maintenance of the suit concerns the public interest as well as the private interests of suitors. Where the patent is used as a means of restraining competition with the patentee's sale of an unpatented product, the successful prosecution of an infringement suit even against one who is not a competitor in such sale is a powerful aid to the maintenance of the attempted monopoly of the unpatented article, and is thus a contributing factor in thwarting the public policy underlying the grant of the patent.").

148. *Kimble v. Marvel Entm't, LLC*, 135 S. Ct. 2401, 2413 (2015).

149. *Id.* ("The patent laws—unlike the Sherman Act—do not aim to maximize competition (to a large extent, the opposite). And the patent term—unlike the 'restraint of trade' standard—provides an all-encompassing bright-line rule, rather than calling for practice-specific analysis.").

150. See *United States v. Paramount Pictures, Inc.*, 334 U.S. 131, 158 (1948) ("The copyright law, like the patent statutes, makes reward to the owner a secondary consideration.").

fair use is “an open-ended and context-sensitive inquiry.”¹⁵¹ Both fair use and patent misuse are rooted in intellectual property policy despite patent misuse’s inquiry into aspects of market competition.¹⁵²

Patent misuse is particularly well suited for regulatory abuses for two reasons. First, the bad faith element. For instance, patent misuse has been raised in relation to the failure of defendants to disclose patents under obligations with standard setting organizations (“SSOs”).¹⁵³ Similarly, patentees who use their standard essential patents in a manner contrary “to obtain or to coerce an unfair commercial advantage,” may find courts refusing to aid such misuse.¹⁵⁴ The BPCIA, like SSO rules, require disclosure and good faith negotiations.¹⁵⁵ In each instance, patent policy seeks to reward the patentee’s technological contribution to society. Patent ambush severs the cord between the value of that contribution and the patentee’s reward, and patent misuse seeks to correct that.

Second, patent misuse is particularly concerned about abuse that impacts innovation. In the biologics space, innovation is cumulative, owing to its focus on process innovation.¹⁵⁶ The essence of biologics innovation thus lies in the manufacturing process because their characteristics and properties depend on the process.¹⁵⁷ Biologic manufacturers frequently change manufacturing processes from development to post-approval to increase scale, product stability, and comply with regulatory requirements.¹⁵⁸ Gamesmanship that stifles FOB access to samples for REMS approval harms their ability to innovate in the biologic manufacturing processes and compete with RBs.¹⁵⁹ Consumers are

151. *Blanch v. Koons*, 467 F.3d 244, 251 (2nd Cir. 2006).

152. 17 USC § 107(4) (2012).

153. *See, e.g., Hynix Semiconductor, Inc. v. Rambus Inc.*, 609 F. Supp. 2d 988, 1030 (N.D. Cal. 2009).

154. *Id.*

155. *Carrier & Minniti, supra note 9*, at 37. For a discussion of SSO obligations and how antitrust and patent misuse applies, see Daryl Lim, *Standard Essential Patents, Trolls and the Smartphone Wars: Triangulating the End Game*, 119 PENN STATE L. REV. 1 (2014).

156. Eric Lawrence Levi, *Using Data Exclusivity Grants to Incentivize Cumulative Innovation of Biologics’ Manufacturing Processes*, 66 AM. U. L. REV. 911, 956 (2017) (“Cumulative innovation is particularly applicable to biologics and biosimilars manufacturing processes during the current rapid growth of the biosimilars market. Cumulative innovation includes better processes for manufacturing a similar drug and safer, more efficacious drugs from more controlled manufacturing processes.”).

157. *How Do Drugs and Biologics Differ?*, BIOTECH INNOVATION ORG., <https://www.bio.org/articles/how-do-drugs-and-biologics-differ>.

158. Nanna Aaby Kruse, *Manufacturing Processes Changes, Biologic Product Comparability and Post Approval Changes*, EURO. MED. AGENCY (Apr. 16, 2015), http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2015/05/WC500187356.pdf (“Manufacturers of biotechnological/biological products frequently make changes to manufacturing processes of products both during development and after approval. Reasons for such changes include improving the manufacturing process, increasing scale, improving product stability, and complying with changes in regulatory requirements.”).

159. *Carrier & Minniti, supra note 9*, at 46-47 (“A central concern is that biologic manufacturers can exploit REMS to prevent biosimilars from entering the market. Generics and biosimilars must have access to samples to reach the market. Typically, these parties can acquire samples from distributors or wholesalers. But when REMS programs foreclose this route, brands and biologics offer the only option. And when there is no access to samples, generics and biosimilars must replicate the original trials. Such conduct contravenes the FDAAA, which makes clear that ETASU measures cannot be used to ‘block or delay’ follow-on applications. And it undercuts the Hatch-Waxman Act and BPCIA, which are based on follow-on competition.”).

harm as implementers abandon product development once costs and the uncertainty of rights clearances mount, leaving them with only the costlier RBs.

V. CONCLUSION

Despite the BPCIA's thoughtful construction, antitrust law has a gap-filling role. No solution is watertight and each piece is a compromised fit at best.¹⁶⁰ RBs are not malefactors any more than FOBs are angels. Like a referee calling out strikes, antitrust law simply provides a marker to identify and penalize behaviors that run contrary to expectations of good gamesmanship when competing.

The Authors present a comprehensive analysis of the competitive dynamics in biologics—the next frontier of the drug industry's evolution, and how antitrust law can remedy anticompetitive harm if they occur. This Response has focused on three areas the Authors identify—patent settlements, product hopping, and regulatory abuses (including REMS), and by reflection, riposte, and recommendations, responded to the Authors' analyses.

As with the BPCIA, the cumulative sum of our efforts will draw responses from others whose vantage points are informed by their own experiences and insights.¹⁶¹ Similarly, new insights from areas such as behavioral economics may eventually be adapted to refine traditional antitrust analysis and develop creative responses to anticompetitive behavior in the biologics space.¹⁶² The enterprise of developing a coherent understanding of biologics and its antitrust implications has only begun, but in all our endeavors, we can be grateful to the Authors for helping point the way.

160. Epstein, *supra* note 35, at 327 (“It would be foolish to defend the Biosimilars Act on the ground that it offers a perfect reconciliation of the various interests. No statute that seeks to deal with such a complex subject matter can claim to achieve that high level of perfection.”).

161. See, e.g., Erika Lietzan, *A Solution in Search of a Problem at the Biologics Frontier*, 2018 U. ILL. L. REV. ONLINE 19; Jacob S. Sherkow, *The Science of Substitution: A Response to Carrier and Minniti*, 2018 U. ILL. L. REV. ONLINE 81.

162. See Daryl Lim, *Retooling the Patent-Antitrust Intersection: Insights from Behavioral Economics*, 69 BAYLOR L. REV. 124, 144 (2017) (discussing how behavioral economics can be used to evaluate procompetitive justifications in the biopharma space.).