ON THE □PPE□L OF DRUG P□TENT CH□LLENGES

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Administrative patent challenge proceedings, the most prominent form of which is inter partes review, have attracted much controversy. In particular, the pharmaceutical industry and its supporters have criticized the proceedings as unfairly biased toward canceling valuable drug patents. Yet there has been little empirical study of the impact of these administrative proceedings on drug patents or pharmaceutical markets.

In this Article, I review the universe of administrative challenges on drug patents that have proceeded through appeal to the Federal Circuit. I find that a large fraction of patents challenged this way are deemed unpatentable at both the agency and appellate levels, and that administrative cancellation of drug patents correlates closely with subsequent generic drug competition and reduced drug prices. The data suggests that these effects are not due to bias against patents, but rather because of the expertise of administrative adjudicators and the remarkably low quality of the drug patents challenged. Indeed, I find that nuanced aspects of these administrative proceedings, particularly at the appellate level, in fact are biased in the opposite direction—against patent challengers. These findings suggest that inter partes review and other administrative challenge proceedings likely serve an important purpose for lowering the costs of medicines, and those proceedings could potentially be improved.

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Introduction

It was called "a slimy legal trick,"[1] "sneaky, unscrupulous, and just plain wrong,"[2] one of the "biggest turkey deals of 2017,"[3] a "dubious precedent,"[4] and "a legal maneuver that has left may rubbing their eyes."[5] The foreign press described it as a "sleight of hand" and a "gimmick."[6] Even the seasoned Judge William C. Bryson of the Federal Circuit, sitting by designa-

1. Derek Lowe, *Allergan Pulls a Fast One*, Sci. Translational Med.: In Pipeline (Sept. 11, 2017), http://blogs.sciencemag.org/pipeline/archives/2017/09/11/allergan-pulls-a-fast-one.

2. Joe Nocera, *Allergan Patent Deal Isn't Just Unusual. It's Ugly*, Bloomberg View (Sept. 11, 2017), https://www.bloomberg.com/view/articles/2017-09-11/allergan-patent-deal-isn-t-just-unusual-it-s-ugly.

3. Allan Sloan, *The Biggest Turkey Deals of 2017*, Wash. Post, Nov. 19, 2017, at G2, G2, https://www.washingtonpost.com/business/economy/the-biggest-turkey-deals-of-2017/2017/11/17/f3c4238e-ca37-11e7-b0cf-7689a9f2d84e_story.html.

4. *Allergan's Restasis Patent Scuffle: An Ugly Sight for Sore Eyes*, Pharmafocus, Oct. 2017, at 1, http://edition.pagesuite-professional.co.uk/html5/reader/production/default.aspx?pubname=&edid=6585896d-c48f-4305-9b98-35f7a8baca4a&pnum=1.

5. Lisa M. Schwartz & Steven Woloshin, *A Clear-eyed View of Restasis and Chronic Dry Eye Disease*, 178 JAMA Internal Med. 181, 181 (2018); *see also* Michael McCaughan, *United We Stand vs. Divide and Conquer: Pharma in the Age of Trump*, Pink Sheet Pharma Intelligence (Jan. 8, 2018), https://pink.pharmaintelligence.informa.com/PS122256/United-We-Stand-Vs-Divide-And-Conquer-Pharma-In-The-Age-Of-Trump (finding it "hard to imagine a better way to undercut" the pharmaceutical industry); *Allergan's Restasis Patent Gamble Looks Increasingly Unlikely To Succeed*, Bus. Monitor Online, Oct. 24, 2017 (a "bold move [that] will ultimately end in failure"); David Crow, *Pharma Industry Faces Hypocrisy Charge over Patents*, Fin. Times (Nov. 1, 2017), https://www.ft.com/content/ad85104e-bd86-11e7-b8a3-38a6e068f464; *Allergan's Unusual Legal Tactic Attracts Political Scrutiny*, The Economist, Nov. 18, 2017, at 57, https://www.economist.com/news/business/21731418-how-native-american-tribes-can-perhaps-help-protect-patents-allergans-unusual-legal-tactic.

6. Chloé Hecketsweiler, *Allergan passe un accord avec une tribu indienne pour protéger ses brevets [Allergan Signs an Agreement with an Indian Tribe to Protect Its Patents]*, Le Monde (Sept. 19, 2017), http://www.lemonde.fr/economie/article/2017/09/19/allergan-passe-un-accord-avec-une-tribu-indienne-pour-proteger-ses-brevets_5187753_3234.html ("*tour de passe-passe*"); Von Roland Lindner, *Indianer als neue Patentwaffe [Indians as New Patent Weapon]*, Frankfurter Allgemeine Zeitung, Sept. 14, 2017, http://www.faz.net/aktuell/wirtschaft/agenda/indianer-als-neue-patentwaffe-15197794.html ("*Kniff*").

tion in the Eastern District of Texas, expressed "serious concerns about the legitimacy" of a transaction he called a "ploy" and an "artifice."[7]

The target of these raised eyebrows: pharmaceutical firm Allergan's attempt to save its billion-dollar patents on the dry eye drug Restasis.[8] In an administrative proceeding, the U.S. Patent and Trademark Office ("USPTO") had determined the patents in error.[9] Rather than defend the patents on the merits, Allergan sought to evade the challenge entirely by entering a sale-and-leaseback arrangement with an Native American tribe, exploiting the tribe's sovereign immunity to argue that the USPTO lacked jurisdiction.[10]

Allergan's ultimately unsuccessful sovereign-immunity ploy was just one facet of the pharmaceutical industry's attack on these administrative challenge proceedings, ongoing since they were created in 2011 as part of the America Invents Act ("AIA").[11] These administrative proceedings for reconsidering patent grants, the most significant being called inter partes review ("IPR"), responded to widespread concerns that invalid but in-force patents were harming legitimate competition and technological development.[12] Yet fearful that their big-ticket patents will be rendered worthless upon review, pharmaceutical firms and other critics of IPR have disparaged the process as a "death squad for patents,"[13] lobbied Congress to exempt

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7. Allergan, Inc. v. Teva Pharm. USA, Inc., No. 2:15-cv-1455, slip op. at 4 (E.D. Tex. Oct. 16, 2017) (opinion and order on joinder).

8. *See* Allergan PLC, Annual Report (Form 10-K), at F–72 (Feb. 15, 2019), https://www.abbvie.com/content/dam/abbvie-dotcom/uploads/PDFs/allergan/allergan-annual-report-form-10K-123118.pdf (noting ⊠1.261 billion in global revenues for Restasis).

9. *See* Saint Regis Mohawk Tribe v. Mylan Pharm., 896 F.3d 1322, 1324 (Fed. Cir. 2018).

10. *See id.*; Allergan PLC, Annual Report (Form 10-K), at 7 (Feb. 15, 2019), https://www.abbvie.com/content/dam/abbvie-dotcom/uploads/PDFs/allergan/allergan-annual-report-form-10K-123118.pdf.

11. *See* America Invents Act (AIA), Pub. L. No. 112-29, sec. 6(a), 125 Stat. 284, 299 (2011); *Saint Regis Mohawk Tribe*, 896 F.3d at 1327–29 (holding that the USPTO proceeding was more like an agency enforcement action to which sovereign immunity does not apply).

12. H.R. Rep. No. 112-98, at 45 (2011); *see* Joe Matal, *A Guide to the Legislative History of the America Invents Act: Part II of II*, 21 Fed. Cir. B.J. 539, 600–05 (2012) (describing historical events preceding enactment of post-grant challenges in the AIA).

13. *See, e.g.,* Jacob S. Sherkow, *On Generic Drugs, Patent "Death Squads" and the Oscars*, Forbes (Feb. 27, 2017), https://www.forbes.com/sites/jacobsherkow/2017/02/27/on-

drug patents from the proceeding,[14] launched multiple constitutional challenges against IPR,[15] and even invented legal evasions such as Allergan's idea that tribal sovereign immunity could skirt the statutory scheme.[16] The debate has not been all one-sided, of course: lawmakers, the generic drug industry, and public interest advocates have vigorously defended administrative patent challenges as an important tool for clearing out patents that prevent price-lowering generic competition, in an era of rising drug prices.[17]

Yet amidst this vigorous debate is little knowledge of what impact administrative patent challenges have had in the pharmaceutical space. The criticisms and defenses of IPR on drug patents have been largely based on anecdotes and theoretical expectations about the nature of drug patents and the challenge process.[18] Empirical studies of challenged drug patents

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generic-drugs-patent-death-squads-and-the-oscars/.

14. *See, e.g.*, Letter from James C. Greenwood, Biotechnology Innovation Org. & John J. Castellani, Pharm. Research & Mfrs. of Am., to Chuck Grassley et al., U.S. Cong. (July 15, 2015), https://www.ptabwatch.com/wp-content/uploads/sites/630/2015/09/Final_Joint_Phrma_Bio_Letter_on_IPR_071515.pdf; Hatch-Waxman Integrity Act of 2019, H.R. 990, 116th Cong. (2019).

15. *See, e.g.*, United States v. Arthrex, Inc., 141 S. Ct. 1970 (2021).

16. *See* Katie Thomas, *To Protect Patents, Allergan Sells Them to a Native American Tribe*, N.Y. Times, Sept. 8, 2017, at B3, https://www.nytimes.com/2017/09/08/health/allergan-patent-tribe.html (describing origins of the sovereign immunity deal).

17. *See, e.g.*, Letter from Patrick Leahy et al., U.S. Cong., to Andrew Hirshfeld, U.S. Patent & Trademark Office (Sept. 16, 2021), https://aboutblaw.com/ZFH; Ian Lopez, *Patent Tribunal Comes Under Fire in Congress Drug Cost Fight*, Bloomberg L. (Sept. 16, 2021), https://news.bloomberglaw.com/pharma-and-life-sciences/patent-tribunal-comes-under-fire-in-congress-drug-cost-fight; Kristi Martin, *Policymakers' Attention Turns to Drug Patents in the Debate on Prices*, Commonwealth Fund (Oct. 7, 2021), https://www.commonwealthfund.org/blog/2021/policymakers-attention-turns-drug-patents-debate-prices; Tahir Amin, *Addressing Drug Patent Abuse: Restoring The Role Of Inter Partes Review*, Health Aff. (Mar. 23, 2022), https://www.healthaffairs.org/do/10.1377/forefront.20220322.951082/; Ass'n for Accessible Meds., Inter Partes Review (IPR) Is Necessary to Lower Drug Prices by Ensuring that PTO Only Grants Patents that Reflect True Innovation (Mar. 2018), https://accessiblemeds.org/sites/default/files/2018-03/AAM-IssueBrief-InterPartesReview_0.pdf.

18. *See, e.g.*, Jonathan J. Darrow et al., *Will Inter Partes Review Speed US Generic Drug Entry?*, 35 Nature Biotechnology 1139 (2017); Meir Pugatch et al., U.S. Chamber of Commerce, Create: U.S. Chamber International Index (6th ed. Feb.

are not uncommon, but tend to focus on broad statistical summaries of the disputes and legal outcomes.[19] The literature lacks substantial consideration of the real-world effects of such challenges on the competitive space and drug prices.[20] Proponents on both sides of the debate are wont to point

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2018); Perry Cooper & Ian Lopez, *Drugmakers Undercut Rivals with New Patent Tactic as Law Shifts*, Bloomberg L. (Oct. 26, 2021), https://news.bloomberglaw.com/health-law-and-business/drugmakers-undercut-rivals-with-new-patent-tactic-as-law-shifts; Jennifer E. Sturiale, *Hatch-Waxman Patent Litigation and Inter Partes Review: A New Sort of Competition*, 69 Ala. L. Rev. 59 (2017); Francisco Javier Espinosa, *Big Pharma Versus Inter Partes Review: Why the Pharmaceutical Industry Should Seek Logical Hatch-Waxman Reform over Inter Partes Review Exemption*, 50 J. Marshall L. Rev. 7 (2017); Winston Zou, *Fixing the Hatch-Waxman Imbalance: A Proposed Solution to the Problem Created by Inter Partes Review*, 47 AIPLA Q.J. 635 (2019); Joanna Shepherd, *Disrupting the Balance: The Conflict Between Hatch-Waxman and Inter Partes Review*, 6 N.Y.U. J. Intell. Prop. & Ent. L. 14 (2016).

19. *See, e.g.*, Jonathan J. Darrow et al., *The Generic Drug Industry Embraces a Faster, Cheaper Pathway for Challenging Patents*, 17 Applied Health Econ. & Health Pol'y 47 (2018); Tulip Mahaseth, Maintaining the Balance: An Empirical Study on Inter Partes Review Outcomes of Orange Book Patents and its Effect on Hatch-Waxman Litigation (Nov. 29, 2018) (unpublished manuscript), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3188995; Feng-Chi Chen et al., *Interactions Between Inter Partes Review and Hatch-Waxman Litigations*, *in* July 9–11, 2019 IEEE Conf. on Computational Intelligence Bioinformatics & Computational Biology, https://ieeexplore.ieee.org/abstract/document/8791240; Corinne Atton & April Breyer Menon, *Seven Years of Orange Book Patent IPRs: Where Are We Now*, 284 Managing Intell. Prop. 23 (2019); Espinosa, *supra* note 18. My own prior research looks at the impact of IPR on drug prices, but only in the aggregate. *See* Charles Duan, Administrative Patent Challenges and Drug Prices (R St. Inst., Policy Study No. 264, Sept. 2022), https://www.rstreet.org/2022/09/21/administrative-patent-challenges-and-drug-prices/.

20. There are brief mentions of unpublished studies of the pricing impacts of administrative patent challenges. *See, e.g.*, Joseph Walker, *Drug-Industry Rule Would Raise Medicare Costs*, Wall St. J., Aug. 31, 2015, https://www.wsj.com/articles/drug-industry-bill-would-raise-medicare-costs-1441063248 (describing Congressional Budget Office study, "communicated orally to senate staffers," that "federal spending would increase by ⊠1.3 billion over 10 years because the exemption would delay the launch of certain generic products"); Sarah Karlin-Smith, *Patent Review: Not Super Effective in Speeding Early Generic Entry*, Politico: Prescription Pulse (Aug. 1, 2016), https://www.politico.com/tipsheets/prescription-pulse/2016/08/part-d-premiums-remain-stableptos-patent-review-isnt-speeding-many-genericsportman-calls-for-more-opioid-funding-215637 (describing financial analysts' report on impact of IPR on generic entry).

out the dearth of evidence on the effects of these patent challenges.[21]

In this Article, I seek to provide this real-world evidence by reviewing a corpus of administrative challenges to drug patents, to find trends in the nature of the patents challenged, the arguments presented, and the market effects that followed. As the title of this Article suggests, my focus is on proceedings that were appealed to the Federal Circuit, both because of the subject of the present Symposium and because appealed patent challenges tend to be well-briefed and have fully developed records to review.

My overall finding, giving rise to the double meaning of this Article's title, is that administrative challenges to drug patents ought to be appealing to the public interest and the proper functioning of the patent system. In the majority of appellate decisions reviewed where drug pricing data was available, the Federal Circuit affirmed a determination of unpatentability, and generic entry and lower prices almost always followed within a few years.[22] Commentators' fears that IPR tilts in favor of patent challengers[23] do not stand up to scrutiny, however: The Federal Circuit affirms decisions at an extremely high rate, with only three reversals on the merits out of thirty-two cases, two of which change the result toward unpatentability.[24]

Instead, the high rate of drug patent invalidation is likely due to two factors observed in the data. First, the administrative patent judges who decide these patent challenges are often experts in biochemistry and pharmaceutics, making them well-equipped to understand the patents at issue and the technical evidence before them. Second, the patents being challenged are distinctly questionable in terms of patentability. The patents in the appeals reviewed were all filed years or decades after the drug was initially discovered and patented, and covered subject matter seemingly distant from useful drug innovation: mandatory warning labels on drug canisters,[25] screw thread arrangements on autoinjector devices,[26] or combi-

21. *See* Greenwood & Castellani, *supra* note 14, at 3 (supporting exemption for pharmaceutical patents); Karlin-Smith, *supra* note 20 (noting report author's opposition to such legislation); Espinosa, *supra* note 18, at 340.

22. *See infra* Section III.A.

23. *See, e.g.*, Shepherd, *supra* note 18, at 34–41.

24. *See infra* Section III.C.

25. *See infra* Section III.C.1.

26. *See infra* Section III.A.3.

nations with well-known drugs.[27] In some cases, the patent owners ended up contradicting their own arguments in failed attempts to justify their patents.[28] The persistent assertions that pharmaceutical patents equate with valuable innovation are difficult to maintain in light of the patents actually being disputed in administrative challenges.

It is good news that administrative challenges appear primarily to eliminate flawed pharmaceutical patents to enable price-lowering generic competition. But there is cause for concern in the data as well. Affirmances of unpatentability determinations are by far the predominant outcome, but one would not know that from the Federal Circuit's publication record, which skews heavily toward reversals and patent-favorable outcomes.[29] This distorted record of published opinions could potentially lead policymakers to a misguided view of how administrative patent challenges interact with drug patents. Additionally, several appeals of drug patent challenges end up being dismissed for lack of Article III standing, always in favor of the patent owners.[30] Given commentators' and judges' criticisms of the Federal Circuit's standing analysis,[31] the application of that analysis to defeat drug patent challenges questionably limits the utility of the proceeding. Enhancing administrative patent challenges to best serve the public interest in accessible, affordable medicines will require addressing these challenges.

This Article proceeds as follows. Section I describes the ongoing policy debate over drug patents and lays out the nature of administrative patent challenges. Section II describes the data sources and methods used for the analysis in this Article. Section III then reviews Federal Circuit cases, categorized by the court's disposition on appeal. Finally, Section IV concludes with general observations about the cases considered.

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27. *See infra* Section III.A.5.

28. *See infra* Section III.B.1.

29. *See infra* text accompanying notes 136–138.

30. *See infra* Section III.D.1.

31. *See infra* notes 200–202 and accompanying text.

I. Background

As the subject of this Article is administrative challenges to drug patents, this Part provides background information first on drug patents and then on administrative patent challenges.

A. Drug Patents

Skyrocketing drug prices today certainly merit the term "crisis." Eight in ten surveyed Americans describe the cost of prescription drugs as "unreasonable,"[32] and the "rising price of prescription drugs was an important factor" to a majority of voters of all parties.[33] Unaffordability has harmed Americans, with nearly a third of surveyed adults reported not taking medicines as prescribed because of costs, and 29% of them reportedly became sicker as a result.[34] Indeed, researchers attribute between 112,000 and 125,000 deaths a year to patients who fail to take necessary medications because they cannot afford them.[35]

The most straightforward approach to overcoming this drug pricing problem is competition.[36] In the pharmaceutical space, the primary source of competition is generic drugs, which are approved to be therapeutically equivalent to their more expensive brand-name counterparts.[37] Because

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32. *See* Ashley Kirzinger et al., *KFF Health Tracking Poll—February 2019: Prescription Drugs*, Kaiser Fam. Found. (Mar. 1, 2019), https://www.kff.org/health-costs/poll-finding/kff-health-tracking-poll-february-2019-prescription-drugs/.

33. Coal. Against Patent Abuse & Morning Consult, Reforming the Patent System 1 (Nov. 2020), https://www.capanow.org/wp-content/uploads/2020/11/CAPA_Memo_MC.pdf.

34. *See* Kirzinger et al., *supra* note 32.

35. *See* Xcenda AmerisourceBergen, Modeling the Population Outcomes of Cost-Related Nonadherence: Model Report 13 tbl.6 (2020), https://www.cidsa.org/publications/xcenda-summary; Ass'n for Accessible Meds., Generic Drug Access & Savings in the U.S. 26 (2017), https://accessiblemeds.org/resources/blog/2017-generic-drug-access-and-savings-us-report.

36. *See* U.S. Gov't Accountability Office, GAO-18-40, Drug Industry: Profits, Research and Development Spending, and Merger and Acquisition Deals 47–50 (Nov. 2017), https://www.gao.gov/assets/690/688472.pdf (citing studies).

37. *See, e.g.*, Richard G. Frank, *The Ongoing Regulation of Generic Drugs*, 357 New Eng. J. Med. 1993, 1994–95 (2007), https://www.researchgate.net/profile/Richard-Frank-2/publication/5842975_The_Ongoing_Regulation_of_Generic_Drugs/links/

state laws enable pharmacies and patients to substitute generics for brand-name products,[38] the availability especially of a large number of generics can cut prices tremendously—over 95% in some cases, a U.S. Food and Drug Administration study finds.[39] The Government Accountability Office similarly concludes that generics cost on average 75% less than the brand-name equivalent, and substitution of generic drugs between 1999 and 2010 saved Americans more than ⊠1 trillion.[40]

Patents on drugs, as government-granted privileges of exclusivity over an invention for a limited time,[41] are a primary impediment to generic competition. Such a limit on competition is justified on the theory that the costs of drug development and commercialization require additional monetary incentives, which patents grant in the form of temporary monopoly power over the drug.[42] Most drugs are patented at the time of discovery, and often there are multiple patents on a single drug.[43]

Especially for the most profitable drugs, however, there are strong incentives to maintain this state of monopoly control well past the prescribed patent term of twenty years.[44] To do so, patent-holding drug manufacturers often turn to "secondary patents," filed potentially decades after initial

09e415065005652275000000/The-Ongoing-Regulation-of-Generic-Drugs.pdf.

38. *See* Jesse C. Vivian, *Generic-Substitution Laws*, 33 US Pharmacist 30 (2008), https://www.uspharmacist.com/article/generic-substitution-laws; Yan Song & Douglas Barthold, *The Effects of State-Level Pharmacist Regulations on Generic Substitution of Prescription Drugs*, 27 Health Econ. 1717 (2018).

39. Ryan Conrad & Randall Lutter, U.S. Food & Drug Admin., Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices 3 (Dec. 2019), https://www.fda.gov/media/133509/download.

40. *See* Gov't Accountability Office, Report GAO-12-371R, Drug Pricing: Research on Savings from Generic Drug Use (Jan. 31, 2012), https://www.gao.gov/assets/files.gao.gov/assets/gao-12-371r.pdf; U.S. Gov't Accountability Office, *supra* note 36, at 47–50.

41. 35 U.S.C. § 154(a)(2); § 271(a).

42. *See, e.g.,* Erin H. Ward et al., Cong. Research Serv., Report R46679, Drug Prices: The Role of Patents and Regulatory Exclusivities 3–4 (Feb. 10, 2021), https://crsreports.congress.gov/product/pdf/R/R46679.

43. *See* Lisa Larrimore Ouellette, *How Many Patents Does It Take to Make a Drug? Follow-On Pharmaceutical Patents and University Licensing*, 17 Mich. Telecomm. & Tech. L. Rev. 299, 314–15 & fig.2 (2010).

44. *See* 35 U.S.C. § 154(a)(2).

drug discovery and patenting.[45] These patents are typically directed not to the drug itself but to dosage regimes, drug formulations, inactive excipients used to package the drug, or methods of using the drug to treat new indications or conditions.[46] Such patents tend to be "weak" or "less solid" in that they are often later discovered to fail the statutory requirements for patentability.[47] Nevertheless, their existence is sufficient to preclude the entry of generic competitor products, and multiple surveys find that Americans overwhelmingly blame pharmaceutical patents and the firms that hold them for the unreasonable costs of drugs.[48]

The traditional means for challenging the validity of drug patents is through structured litigation under the Drug Price Competition and Patent Term Restoration Act ("Hatch–Waxman").[49] The process begins when a generic manufacturer seeks Food and Drug Administration ("FDA") approval of a product, at which time the generic manufacturer must certify that certain patents on the drug are invalid or not infringed.[50] That certi-

45. On secondary patents, see generally Kevin T. Richards et al., Cong. Research Serv., Report No. R46221, Drug Pricing and Pharmaceutical Patenting Practices 9, 16–19 (Feb. 11, 2020), https://www.everycrsreport.com/reports/R46221.html.

46. *See, e.g.*, Tahir Amin & Aaron S. Kesselheim, *Secondary Patenting of Branded Pharmaceuticals: A Case Study Of How Patents On Two HIV Drugs Could Be Extended For Decades*, 31 Health Aff. 2286 (2012); Amy Kapczynski et al., *Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of "Secondary" Pharmaceutical Patents*, 7 PLoS One No. e49470 (2012), https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0049470.

47. Competition Dir.-Gen., European Comm'n, Pharmaceutical Sector Inquiry: Final Report para. 504, at 192 (July 8, 2009), https://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf (quoting pharmaceutical firm); *see* C. Scott Hemphill & Bhaven N. Sampat, *When Do Generics Challenge Drug Patents?*, 8 J. Empirical Legal Stud. 613, 644 (2011); C. Scott Hemphill & Bhaven Sampat, *Drug Patents at the Supreme Court*, 339 Science 1386, 1387 (2013).

48. *See* Coal. Against Patent Abuse & Morning Consult, *supra* note 33, at 1; Kirzinger et al., *supra* note 32.

49. *See* Drug Price Competition and Patent Term Restoration Act (Hatch–Waxman), Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at Federal Food, Drug, and Cosmetic Act (FFDCA) § 505(j), 21 U.S.C. § 355).

50. *See* FFDCA § 505(j)(2)(A)(vii)(IV). The holder of those patents must have previously listed the patents in the FDA's compilation of drug approvals and exclusivities, known as the Orange Book. *See id.* § 505(b)(1)(viii); Food & Drug Admin., Approved Drug Products with Therapeutic Equivalence Evaluations (the Orange Book) (42d ed. 2022), https://www.fda.gov/media/71474/download.

fication enables the patent holder to bring patent infringement litigation against the generic manufacturer in district court, where the validity of the patent may be tested.[51]

Hatch–Waxman litigation presents a number of drawbacks that limit its efficacy for testing the validity of drug patents. First, it is time-consuming and expensive, often costing several million dollars to litigate.[52] Second, the structure of the litigation discourages invalidity challenges to a certain extent: The generic manufacturer can also argue to the district court that it does not infringe the patent, and has some incentives to jettison good invalidity arguments in favor of noninfringement positions.[53] Third, Hatch–Waxman litigation requires the generic firm first to make investments sufficient to compile an FDA-ready application for approval, meaning the firm is gambling on the litigation proving those investments worthwhile.[54] The cost of that gamble is exacerbated by the fact that the FDA cannot approve the generic's application for 30 months unless litigation completes before then,[55] preventing the generic firm from recouping at least some of its costs through sales during the "at-risk" litigation period.

B. Administrative Patent Challenges

Administrative patent challenge proceedings such as IPR are an alternative pathway for disputing the validity of issued patents. As enacted in the AIA, the procedure works as follows.[56] Any person (other than the patent owner) who wishes to challenge a patent may file a petition with the USPTO, paying the necessary fees and explaining the reasons why the challenged patent was erroneously granted.[57] After optional response fil-

51. *See* 35 U.S.C. § 271(e)(2)(A).

52. *See, e.g.*, Branka Vuleta, *25 Patent Litigation Statistics—High-Profile Feuds about Intellectual Property*, LegalJobs (Aug. 6, 2021), https://legaljobs.io/blog/patent-litigation-statistics/.

53. *See* Roger Allan Ford, *Patent Invalidity Versus Noninfringement*, 99 Cornell L. Rev. 71, 93–103 (2013).

54. *See* FFDCA § 505(j)(2) (listing required contents of a generic drug application).

55. *See id.* § 505(j)(5)(B)(iii).

56. Although the citations that follow related to IPR, a similar procedure applies to the other major proceeding, post-grant review. *See* 35 U.S.C. §§ 321–329.

57. *See* 35 U.S.C. § 311(a). Depending on which form of proceeding is used, there are limits on what grounds for error may be proffered in the petition, and also on the

ings from the patent owner, the Director of the USPTO decides whether to institute the proceeding.[58] If the Director decides in the negative, then the patent remains in force and the decision is not appealable.[59]

Otherwise, the proceeding moves to a trial before administrative patent judges of the Patent Trial and Appeal Board ("Board").[60] The Board may receive evidence, manage discovery, hear expert witness testimony, and hold oral hearings, ultimately so that it may render a final determination on the patentability of the patent at issue.[61] The Board's decision may then be appealed to the Federal Circuit.

Administrative challenges before the Board have a number of advantages that solve many of the difficulties described above with respect to Hatch–Waxman litigation. They are typically cheaper and shorter, because they lack the overhead of federal court litigation and do not deal with patent infringement issues.[62] Second, members of the Board are required to have training in science and engineering, making them particularly capable of understanding complex technical evidence that often arises in patent disputes.[63] Third, because anyone can petition for IPR at almost any time,

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timing of the petition. *See* 35 U.S.C. § 311(b)–(c).

58. *See* 35 U.S.C. § 314(a). Currently, the Director delegates this determination to the Patent Trial and Appeal Board ("Board").

59. *See* 35 U.S.C. § 314(d); Thryv, Inc. v. Click-To-Call Techs., LP, 140 S. Ct. 1367, 1373–74 (2020).

60. *See* 35 U.S.C. § 316(c).

61. *See* 35 U.S.C. § 316(a) (trial procedure); 35 U.S.C. § 318(a). There is a terminological nuance: Courts can declare patents "invalid" while the Board can hold them "unpatentable." The difference is immaterial for purposes of this Article. Additionally, on the view that a patent not declared invalid or unpatentable might be later held invalid or unpatentable, it is typical to say that a favorable ruling on a patent holds it "not invalid" or "not unpatentable." *See* Envirotech Corp. v. Al George, Inc., 730 F.2d 753, 672 (Fed. Cir. 1984) ("[A] court never 'declares' a patent valid . . . ."); Fromson v. Advance Offset Plate, Inc., 755 F.2d 1549, 1555 n.1 (Fed. Cir. 1985); John R. Allison et al., *Patent Quality and Settlement Among Repeat Patent Litigants*, 99 Geo. L.J. 677, 679 (2011). Again the difference is immaterial for this Article, so for simplicity I will use "patentable" to mean a Board determination in favor of a patent.

62. *See, e.g.*, Josh Landau, *Inter Partes Review: Five Years, Over $2 Billion Saved*, Pat. Progress (Sept. 14, 2017), https://www.patentprogress.org/2017/09/14/inter-partes-review-saves-over-2-billion/.

63. *See* 35 U.S.C. § 6(a) (requiring administrative patent judges to have "competent legal knowledge and scientific ability"); Matthew G. Sipe, *Experts, Generalists, Laypeople—*

the proceeding avoids the sunk-cost and 30-month stay problems identified above with respect to Hatch–Waxman litigation: A generic manufacturer thinking about manufacturing a drug can use IPR to dispute patents on the drug before making the investments to apply for approval. As a result, it is understandable that generic firms seeking to compete in drug markets would look to administrative patent challenges as a tool to enable their doing so.[64]

II. Methods

To investigate the nature and effects of administrative challenges of drug patents, this Article relies on four sources of data: information on Federal Circuit Appeals, information on administrative patent challenges, records of drugs associated with patents, and drug pricing data. For purposes of transparency, replicability, and follow-on research, all data used in this study is publicly available free of charge.

For the latter three items above, I rely on a USPTO database of Board determinations,[65] the National Average Drug Acquisition Cost ("NADAC") database produced by the Centers for Medicare and Medicaid Services,[66] the FDA's Orange Book data on approved drugs and patent exclusivities,[67] and the National Drug Code ("NDC") database of drug identifiers.[68] The nature of these databases and my methods of using them are described in my

and the Federal Circuit, 32 Harv. J.L. & Tech. 575, 578 (2019).

64. *See, e.g.*, Darrow et al., *supra* note 19.

65. *See PTAB API v2*, U.S. Pat. & Trademark Off. Open Data Portal (last updated June 3, 2022), https://developer.uspto.gov/api-catalog/ptab-api-v2.

66. *See* Ctrs. for Medicare & Medicaid Servs., Methodology for Calculating the National Average Drug Acquisition Cost (NADAC)for Medicaid Covered Outpatient Drugs (Jan. 2021), https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/ful-nadac-downloads/nadacmethodology.pdf (describing database).

67. *See* Food & Drug Admin., *supra* note 50. Because the FDA deletes outdated records in revised editions of the book, I retrieved historical copies as well.

68. *See* Food & Drug Admin., *National Drug Code Database Background Information* (Mar. 20, 2017), https://www.fda.gov/drugs/development-approval-process-drugs/national-drug-code-database-background-information. Again, the FDA deletes outdated NDC records, so I retrieved historical databases.

prior research.[69] Unless otherwise noted, these databases are the sources of drug approval, generic entry, and pricing information throughout the remainder of this Article.

The appeals data is drawn from Professor Jason Rantanen's *Compendium of Federal Circuit Decisions*.[70] Among other things, the database identifies the originating tribunal's docket number, such that appeals can be matched with the administrative proceedings database. Records of original docket numbers are somewhat incomplete, particularly for proceedings initiated before 2015, so I supplemented these records by hand. Still, it is possible that some relevant appeals were omitted from consideration. Since the database appears to be more complete for recent appeals, though, the results of this study ought to reflect current trends with reasonable accuracy.

III. Federal Circuit Cases

A. Affirmances of Unpatentability

By far, the most common Federal Circuit disposition of administrative drug patent challenges is to affirm a determination of unpatentability, with twenty-one appeals reaching that result. Indeed, the Federal Circuit often has little to say about these affirmances: Nine decisions were summary affirmances under Federal Circuit Rule 36 with no written opinion,[71] six opinions were designated nonprecedential,[72] and six were published and

69. *See* Duan, *supra* note 19, at 6–7.

70. *See The Compendium of Federal Circuit Decisions* (last visited Dec. 15, 2022), https://empirical.law.uiowa.edu/compendium-federal-circuit-decisions; Jason Rantanen, *The Landscape of Modern Patent Appeals*, 67 Am. U. L. Rev. 985 (2018) (discussing methodology and contents thereof).

71. *See* Mylan Labs. Ltd. v. Sanofi Mature IP, No. 2020-1302 (Fed. Cir. Jan. 15, 2021); Neurelis, Inc. v. Aquestive Therapeutics, Inc., No. 2021-1038 (Fed. Cir. Oct. 7, 2021); Fresenius Kabi USA, LLC v. Bass, 741 F. App'x 801 (Fed. Cir. 2018); Senju Pharm. Co. v. Akorn Inc., 733 F. App'x 1024 (Fed. Cir. 2018); *In re* NPS Pharm., Inc., 702 F. App'x 990 (Fed. Cir. 2017); Purdue Pharma LP v. Iancu, 760 F. App'x 1023 (Fed. Cir. 2019); United Therapeutics Corp. v. Steadymed Ltd., 702 F. App'x 990 (Fed. Cir. 2017); BioDelivery Scis. Int'l, Inc. v. RB Pharm. Ltd., 667 F. App'x 997 (Fed. Cir. 2016); Daiichi Sankyo Co. v. Accord Healthcare Inc., 706 F. App'x 679 (Fed. Cir. 2017).

72. *See* Icos Corp. v. Actelion Pharm., Ltd., 726 F. App'x 812 (Fed. Cir. 2018); Anacor Pharm., Inc. v. Flatwing Pharm., LLC, No. 2019-2264 (Fed. Cir. Aug. 27, 2020); Sanofi-

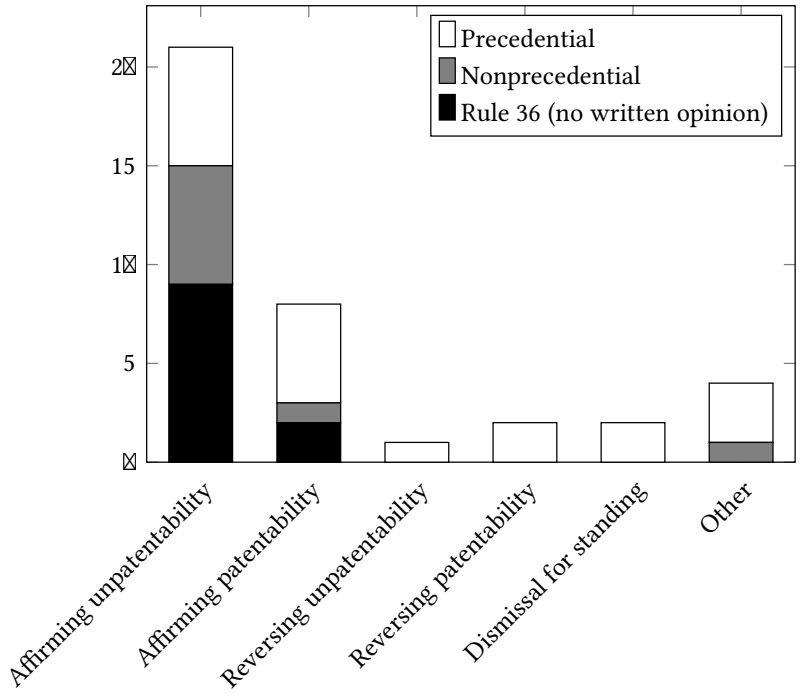

Figure 1: Federal Circuit dispositions of inter partes reviews of Orange Book patents, by outcome and precedentiality.

precedential.[73]

A few trends can be observed across these cases. First, the patents at issue tend to be secondary patents, covering not active ingredients of drugs but distribution safety protocols,[74] formulations to increase absorption in the human body,[75] dosing regimens,[76] and the like. As such, these patents remain in force after the initial patents on the drug have expired, effectively extending the duration of patent protection on the drug beyond the statutory 20-year term.[77] One might think that generic competitors could nevertheless enter the market after the initial drug patents expire by not using or working around the improvements in the later-filed secondary patents. Yet the secondary patents that come up in these cases are often difficult to work around in view of the regulatory approval process. The FDA is unlikely to approve a generic drug product that lacks adequate distribution safety protocols,[78] that absorbs differently into the body,[79] or that uses a different dose.[80] As a result, invalidation of these patents is often a necessary precursor to generic entry.

Most importantly, when these patents are deemed erroneous in an administrative challenge procedure, generic entry and substantial reduc-

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Aventis Deutschland GmbH v. Mylan Pharm. Inc., 791 F. App'x 916 (Fed. Cir. 2019); Sanofi-Aventis Deutschland v. Mylan Pharm. Inc., Nos. 2020-1871 etc. (Fed. Cir. Dec. 29 2021) (per curiam); Sanofi-Aventis Deutschland GmbH v. Mylan Pharm. Inc., No. 2020-2066 (Fed. Cir. Dec. 29, 2021); Sanofi-Aventis Deutschland v. Mylan Pharm., Inc., No. 2020-2071 (Fed. Cir. Dec. 29, 2021).

73. *See* Anacor Pharm., Inc. v. Iancu, 889 F.3d 1372 (Fed. Cir. 2018); Jazz Pharm., Inc. v. Amneal Pharm., LLC, 895 F.3d 1347 (Fed. Cir. 2018); Novartis AG v. Noven Pharm. Inc., 853 F.3d 1289 (Fed. Cir. 2017); Indivior UK Ltd. v. Dr. Reddy's Labs. SA, 18 F.4th 1323 (Fed. Cir. 2021); BTG Int'l Ltd. v. Amneal Pharm. LLC, 923 F.3d 1063 (Fed. Cir. 2019); Yeda Research & Dev. Co. v. Mylan Pharm., Inc., 906 F.3d 1031 (Fed. Cir. 2018).

74. *See Jazz Pharm.*, 895 F.3d at 1350–51.

75. *See Icos*, 726 F. App'x at ?.

76. *See Anacor Pharm.*, No. 2019-2264.

77. *See* 35 U.S.C. § 154(a)(2).

78. *See* Federal Food, Drug, and Cosmetic Act (FFDCA) §§ 505–1(i)(1)(C)(i), 21 U.S.C. §§ 355–1.

79. *See* Federal Food, Drug, and Cosmetic Act (FFDCA) § 505(j)(8)(B)(i), 21 U.S.C. § 355 (defining "bioequivalent" to require no significant difference in "the rate and extent of absorption").

80. *See* FFDCA § 505(j)(2)(iii) (requiring that "the route of administration, the dosage form, and the strength" of a generic drug be identical to the brand-name counterpart).

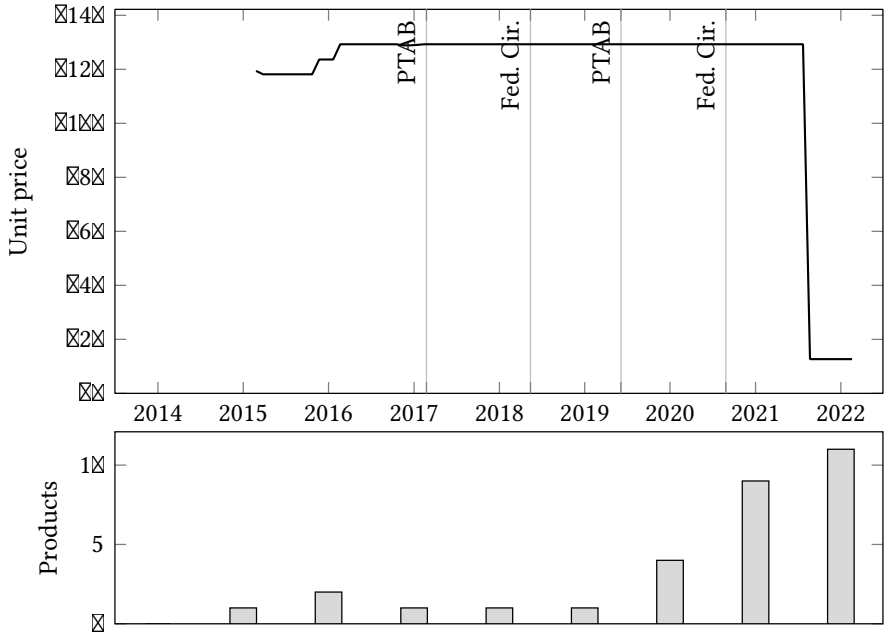

Figure 2: Unit price of tavaborole, 5%. The line shows the lowest price for the drug formulation in the previous 30-day period, as reflected in NADAC data. The bars show the number of products listed in the NDC directory for the formulation.

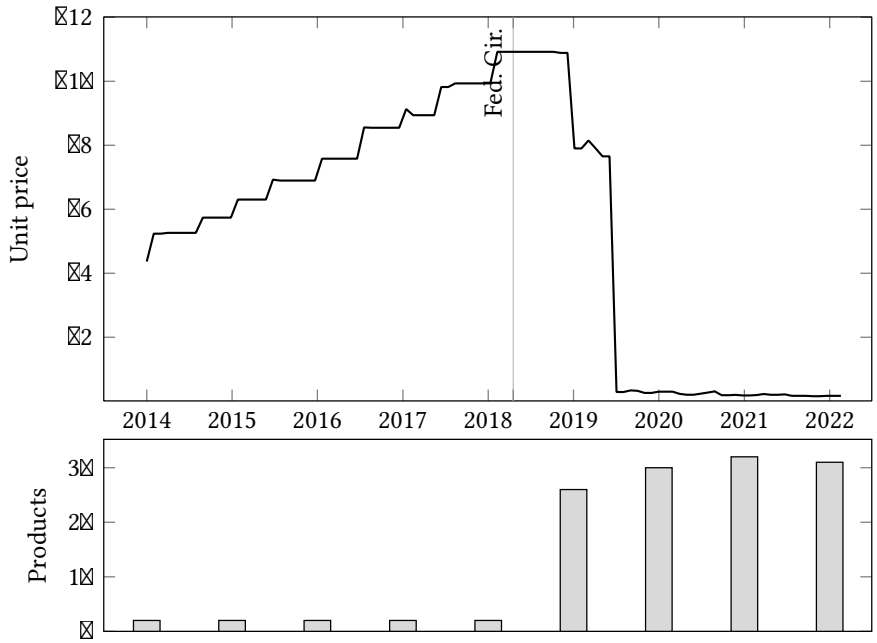

Figure 3: Unit price of tadalafil, 2.5mg. Dates of PTAB decisions omitted.

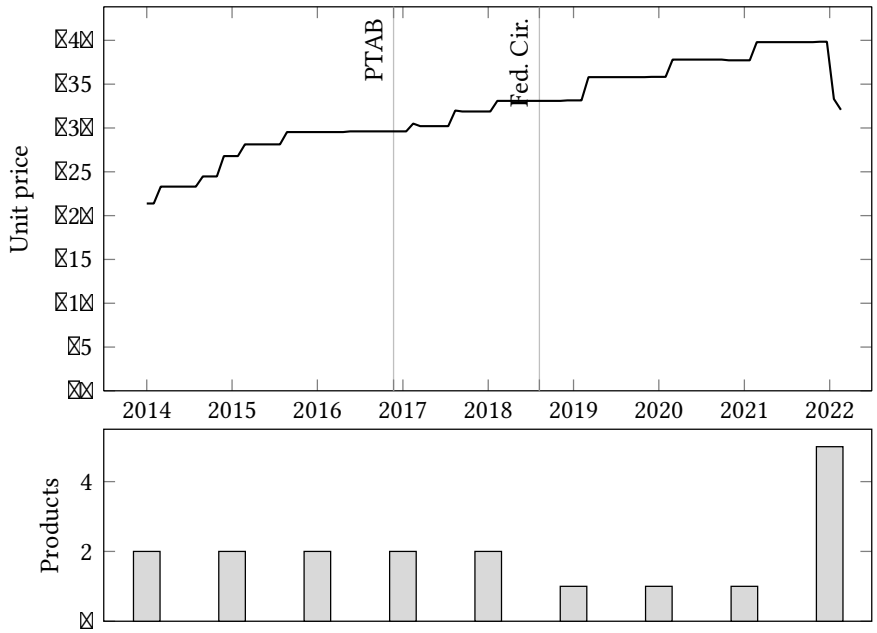

Figure 4: Unit price of difluprednate, 0.05%.

tions in price typically follow. Such benefits can be observed in every case where NADAC price data was available, a Federal Circuit affirmance of a the Board unpatentability decision, with one understandable exception.[81] Tavaborole, a topical antifungal medication, was challenged in two IPR proceedings in 2018 and 2020; its price went from ₹145.33 per milliliter in 2020 to ₹12.68 in 2021.[82] Tadalafil was the subject of a successful IPR challenge in 2018; over twenty generic products were approved in the next few years and the drug's price dropped from ₹8.94 per dose in 2017 to ₹0.14 in 2022.[83] A patent on difluprednate, an inflammation and pain reliever, was successfully challenged in 2018; generic entry was apparently delayed for unrelated reasons but has reduced prices from a high of ₹37.72 in 2020 down to ₹22.56 in 2022.[84]

To illustrate the effects of administrative challenges on drug patents further, several case studies are given in detail below.

1. Rivastigmine, Alzheimer's Disease

Use of rivastigmine to treat moderate dementia diseases was discovered in the 1980s,[85] but in 1998 the pharmaceutical company Novartis sought patents on delivery of that drug through a transdermal patch applied to the skin, which it sold under the name Exelon Patch.[86] The thrust of those patents was the combination of rivastigmine with an antioxidant in a transdermal patch, where rivastigmine alone in a patch was old knowledge and thus unpatentable.

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81. No reduction in price appears to occur after *Purdue Pharma*, but the drug at issue there is oxycodone, and public safety issues complicate generic entry. *See generally* Ctr. for Drug Evaluation & Research, Food & Drug Admin., General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products: Guidance for Industry (Nov. 2017), https://www.fda.gov/media/96643/download.

82. *See* Anacor Pharm., Inc. v. Iancu, 889 F.3d 1372 (Fed. Cir. 2018); Anacor Pharm., Inc. v. Flatwing Pharm., LLC, No. 2019-2264 (Fed. Cir. Aug. 27, 2020).

83. *See* Icos Corp. v. Actelion Pharm., Ltd., 726 F. App'x 812 (Fed. Cir. 2018).

84. *See* Senju Pharm. Co. v. Akorn Inc., 733 F. App'x 1024 (Fed. Cir. 2018).

85. *See In re* Rivastigmine Patent Litig., No. 1:05-md-1551, slip op. at 3–4 (S.D.N.Y. Sept. 22, 2005) (noting filing of patent application on the chemical).

86. *See* U.S. Patent No. 6,316,023 (issued Nov. 13, 2001); U.S. Patent No. 6,335,031 (issued Jan. 1, 2002).

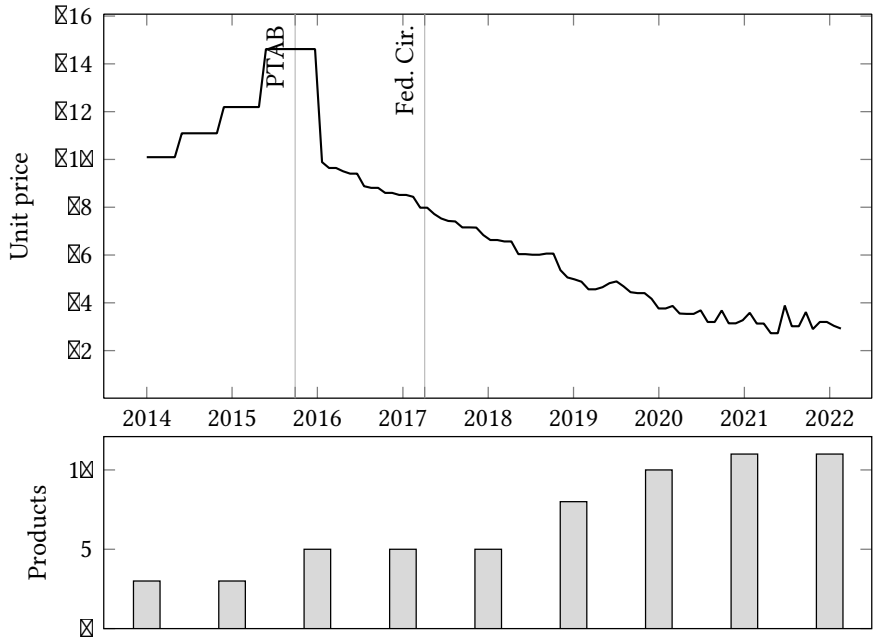

Figure 5: Unit price of rivastigmine, 4.6mg/24hr.

In *Novartis AG v. Noven Pharmaceuticals Inc.*, the Board found the combination obvious, and the Federal Circuit affirmed.[87] Since basic scientific principles taught that rivastigmine would degrade absent an antioxidant, the Board and the appellate court agreed that one with ordinary skill in organic chemistry would have come up with the same combination, rendering the patent in error.[88] Generic entry followed quickly, reducing prices by up to 75%.

Two years earlier, a district court had reached a seemingly opposite conclusion, refusing to deem the same patents invalid.[89] That result, though odd, in fact exemplifies the unique role of IPR. The district court admitted difficulty in understanding the expert opinions, conceding that "both arguments seem logical" and finding itself forced to "resolv[e] this dispute based on credibility" rather than scientific reasoning.[90] The Federal Circuit's own ambivalence about that result is perhaps reflected in the court's designation of its opinion as nonprecedential.[91]

That hesitancy contrasts starkly with the appellate court's confidence in the scientific accuracy of the IPR decision. There, the Federal Circuit praised the Board for citing "[a]mple record evidence from scholarly sources."[92] It further distinguished the contrary district court result on the grounds that the Board had a better-developed factual record—likely because the parties were willing to present the expert Board with scientific facts that would have been too technical for the district court.[93] Specialized expertise thus led the Board, and the Federal Circuit upon review, to receive a richer presentation of scientific facts from which to reach a better-reasoned result.

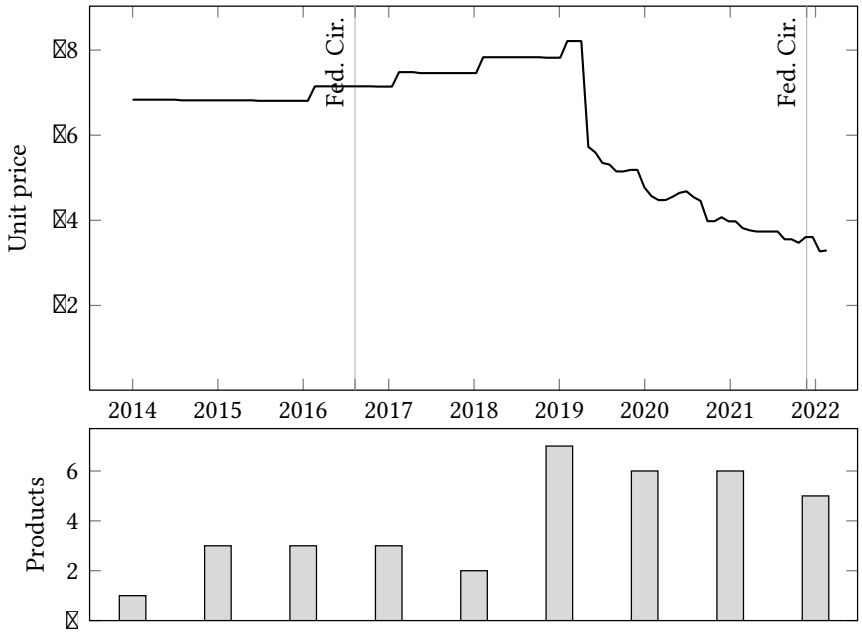

Figure 6: Unit price of buprenorphine hydrochloride, 8mg. Dates of PTAB decisions omitted.

2. Buprenorphine, Opioid Addiction

In 2008, British pharmaceutical firm Reckitt Benckiser reaped over £540 million on its blockbuster opioid addiction treatment buprenorphine/naloxone, sold under the brand name Suboxone.[94] But it stood to lose that revenue stream when the company's federal regulatory exclusivity expired in 2009, opening the drug to generic competition.[95] In an effort to maintain its monopoly position, Reckitt Benckiser devised a scheme to switch buprenorphine patients from a tablet-form medicine to a "sublingual film" designed to dissolve under the tongue; patents on the latter formulation would have prevented generic entry through at least 2023.[96] Despite no evidence that the latter formulation was an improvement and indeed some indications that it was more dangerous to children, Reckitt Benckiser and its corporate successor Indivior propounded numerous false advertisements and studies claiming that the sublingual film was safer for households with children.[97]

In July of 2020, Indivior pleaded guilty to fraud and agreed to a £290 million fine, following a £1.4 billion settlement by Reckitt Benckiser.[98] But the

87. *See* Novartis AG v. Noven Pharm. Inc., 853 F.3d 1289, 1291 (Fed. Cir. 2017).

88. *See id.* at 1295–96.

89. *See* Novartis Pharm. Corp. v. Par Pharm., Inc., 48 F. Supp. 3d 733, 736 (D. Del. 2015), *aff'd sub nom.* Novartis Pharm. Corp. v. Watson Labs., Inc., 611 F. App'x 988 (Fed. Cir. 2015) (nonprecedential).

90. *See id.* at 757.

91. *See Novartis Pharm.*, 611 F. App'x 988.

92. *See Novartis AG*, 853 F.3d at 1295.

93. *See id.* at 1293–94.

94. *See* Reckitt Benckiser Grp. PLC, Annual Report and Financial Statements 2008, at 20 (Mar. 2009) (applying currency exchange rate of 1.6).

95. *See id.* at 18; Rebecca L. Haffajee & Richard G. Frank, *Generic Drug Policy and Suboxone to Treat Opioid Use Disorder*, 47 J.L. Med. & Ethics 43, 44 (2019).

96. *See* Haffajee & Frank, *supra* note 95, at 45.

97. *See* Plea Agreement at Exh. B, paras. 18–26, at 5–8, United States v. Indivior Sols., Inc., No. 1:19-cr-16 (W.D. Va. July 27, 2020) (Doc. No. 427-5).

98. *See id.* at 3 tbl.; Press Release, U.S. Dep't of Justice, *Justice Department Obtains $1.4 Billion from Reckitt Benckiser Group in Largest Recovery in a Case Concerning an Opioid Drug in United States History* (July 11, 2019), https://www.justice.gov/opa/pr/justice-department-obtains-14-billion-reckitt-benckiser-group-largest-recovery-case.

scheme was successful in its legacy: Most buprenorphine users switched to the film formulation, and Indivior discontinued its own sales of the tablet.[99] Undoing the fraud, then, required undoing the patents that monopolized the film formulation through IPR. In the 2015 proceeding *BioDelivery Sciences International, Inc. v. RB Pharmaceuticals Ltd.*, the Board found error in one of Indivior's key patents on the sublingual film; the Federal Circuit affirmed.[100] A subsequent IPR proceeding considered Indivior's patent on relative weight percentages of the components of the sublingual film.[101] The Board held all but one claim unpatentable on the grounds that the patent did not disclose the relevant percentages until years after its original filing; the Federal Circuit affirmed on all grounds.[102]

In combination with other litigation on Indivior's other patents,[103] the IPR decisions opened the door to generic competition on Suboxone film as of 2019. At least thirteen generics are now approved for sale, and prices have dropped about 50% compared to the peak brand price. IPR created tremendous patient savings by enabling competition, despite a patent holder's brazen efforts to stifle it.

3. Insulin and Injector Pens

Glargine is a modern form of insulin, invented in the late 1980s, that releases itself slowly into the bloodstream, reducing the number of injections needed.[104] The 20-year patent term on glargine has long expired, and yet manufacturer and patent holder Sanofi has made extensive efforts to extend its monopoly position beyond the expected period. Many of these efforts have been met with challenges through IPR.

A first set of patents covered the combination of glargine with a "non-

99. *See* Haffajee & Frank, *supra* note 95, at 46, 48–49.

100. *See* BioDelivery Scis. Int'l, Inc. v. RB Pharm. Ltd., No. IPR2014-00325, slip op. at 2 (P.T.A.B. June 30, 2015) (final written decision), *aff'd without opinion*, 667 F. App'x 997 (Fed. Cir. 2016).

101. *See* Indivior UK Ltd. v. Dr. Reddy's Labs. SA, 18 F.4th 1323, 1325–26 (Fed. Cir. 2021).

102. *See id.* at 1329–30.

103. *See* Indivior Inc. v. Dr. Reddy's Labs., SA, 930 F.3d 1325, 1330–31 (Fed. Cir. 2019).

104. *See* U.S. Patent No. 5,656,722 col. 1, l. 9 (filed Sept. 12, 1994); Mark R. Sommerfeld et al., *In Vitro Metabolic and Mitogenic Signaling of Insulin Glargine and Its Metabolites* 1, *in* 5 PLoS One (2010), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2832019/ (describing date of invention and nature of glargine).

ionic surfactant" to prevent misfolding, or "non-native aggregation," of the glargine proteins.[105] The Board had little difficulty holding the combination obvious, given that aggregation is a known problem for insulins and nonionic surfactants were well-known insulin stabilizers; the Federal Circuit had little difficulty affirming.[106]

But generic entry was not immediately possible because Sanofi also held patents on the SoloStar injector pen device in which it distributed Lantus; regulatory approval required an equivalent generic injector.[107] To enable generic competition on glargine, then, several generic manufacturers initiated nearly a dozen IPR proceedings against Sanofi's SoloStar injector pen patents.[108]

Challenges to the SoloStar patents revealed how little innovation the product accounted for. The supposedly novel injector pen was strikingly similar to the many other insulin injectors earlier on the market, with only the minor changes to features such as screw threads that the Board deemed obvious to one of ordinary skill in mechanical engineering.[109] In an effort to overcome this outcome, Sanofi contended that the SoloStar had performed

105. Sanofi-Aventis Deutschland GmbH v. Mylan Pharm. Inc., 791 F. App'x 916, 4 (Fed. Cir. 2019).

106. *See id.* at 11.

107. On the use of device patents to block generic drug competition, see Reed F. Beall & Aaron S. Kesselheim, *Tertiary Patenting on Drug–Device Combination Products in the United States*, 36 Nature Biotechnology 142, 143 (2018).

108. *See* Mylan Pharm. Inc. v. Sanofi-Aventis Deutshland GmbH, IPR2018-01670 (P.T.A.B. Apr. 2, 2020); Mylan Pharm. Inc. v. Sanofi-Aventis Deutschland GmbH, IPR2018-01675 (P.T.A.B. May 29, 2020); Mylan Pharm. Inc. v. Sanofi-Aventis Deutschland GmbH, IPR2018-01676 (P.T.A.B. May 29, 2020); Mylan Pharm. Inc v. Sanofi-Aventis Deutschland GmbH, IPR2018-01677 (P.T.A.B. Dec. 19, 2018); Mylan Pharm. Inc. v. Sanofi-Aventis Deutschland GmbH, IPR2018-01678 (P.T.A.B. May 29, 2020); Mylan Pharm. Inc. v. Sanofi-Aventis Deutschland GmbH, IPR2018-01679 (P.T.A.B. May 29, 2020); Mylan Pharm. Inc v. Sanofi-Aventis Deutschland GmbH, IPR2018-01680 (P.T.A.B. May 29, 2020); Mylan Pharm. Inc. v. Sanofi-Aventis Deutschland GmbH, IPR2018-01682 (P.T.A.B. May 29, 2020); Mylan Pharm. Inc. v. Sanofi-Aventis Deutschland GmbH, IPR2018-01684 (P.T.A.B. May 29, 2020); Mylan Pharm. Inc. v. Sanofi-Aventis Deutschland GmbH, IPR2019-00122 (P.T.A.B. May 29, 2020); Pfizer Inc. v. Sanofi-Aventis Deutschland, IPR2019-00979 (P.T.A.B. Aug. 11, 2020).

109. *See, e.g., Mylan Pharm. Inc*, IPR2018-01677, at 34 (finding that "one of ordinary skill in the art would have reasonably expected the modified parts to perform the same function as before").

superiorly in the market compared to other insulin pens, but the evidence before the Board proved almost the opposite: The Board credited testimony that the SoloStar was "not recognized as an unusually good pen" and was "in a statistical tie" with a competitor.[110] Market demand for the SoloStar appeared to be driven by consumer preference not for the device but for the glargine inside it.[111] Not only did the Board find every challenged claim to be unpatentable, but also the Federal Circuit affirmed every such determination to the extent necessary to render the patents canceled, in brief unpublished opinions all issued the same day.[112]

The apparent lack of valuable innovation in the SoloStar pen is consistent with the view, also posited in an antitrust case that the First Circuit recently allowed to proceed, that the SoloStar patents were no more than an "effective extension of Sanofi's monopoly."[113] Mylan received approval for a biosimilar glargine product in 2020,[114] and marketed it at a price of ₹9.36 per milliliter compared to ₹27.21 for Sanofi's brand-name product.[115]

The price differences are consistent with Mylan's announced pricing of ₹147.98 for five pens compared to ₹425.31 for the Lantus SoloStar.[116] No-

110. *Id.* at 87–88.

111. *See id.* at 87, 103–05.

112. *See* Sanofi-Aventis Deutschland v. Mylan Pharm. Inc., Nos. 2020-1871 etc. (Fed. Cir. Dec. 29 2021) (per curiam); Sanofi-Aventis Deutschland GmbH v. Mylan Pharm. Inc., No. 2020-2066 (Fed. Cir. Dec. 29, 2021); Sanofi-Aventis Deutschland v. Mylan Pharm., Inc., No. 2020-2071 (Fed. Cir. Dec. 29, 2021).

113. *In re* Lantus Direct Purchaser Antitrust Litig., 950 F.3d 1, 2 (1st Cir. 2020).

114. *See* Letter from Patrick Archdeacon, U.S. Food & Drug Admin., to S. Wayne Talton, Mylan Pharm. Inc., *NDA Approval, NDA 210605* (June 11, 2020).

115. The price information had to be retrieved from the datasets manually because insulin is a biologic product rather than a small-molecule drug. As a result, insulin products are not consistently listed in the Orange Book like other drugs described in this Article, so my automated price computations were ineffective. Instead, my process was as follows. Sanofi's Lantus product was approved under New Drug Application 021081; Mylan's competing product was first approved under New Drug Application 210605 and subsequently under Biologics License Application 761201. I retrieved all NDC codes associated with these application numbers, and then used NADAC data from 2020 to identify prices associated with those NDC codes.

116. *See* Press Release, Mylan N.V., *Mylan and Biocon Biologics Announce Launch of Semglee (insulin glargine injection) in the U.S. to Expand Access for Patients Living with Diabetes* (Aug. 31, 2020), http://newsroom.mylan.com/2020-08-31-Mylan-and-Biocon-Biologics-Announce-Launch-of-Semglee-TM-insulin-glargine-injection-in-the-U-

tably, Mylan announced this 65% price cut while Federal Circuit appeals were pending on the SoloStar patents; the company stated it was "confident" that the appeals "will not affect commercialization."[117] That confidence reflects an ongoing recognition that the Board's inter partes review decisions are of such high quality—the Federal Circuit fully affirms the Board in 80% of appeals[118]—that pharmaceutical manufacturers are willing to stake millions in potential damages on at-risk launches based on those decisions.

4. Abiraterone, Prostate Cancer

Abiraterone acetate, used to treat prostate cancer, has been known since at least 1994, and patents on the compound expired about 2014.[119] Janssen Biotech markets and holds patents to a formulation called Zytiga, in which abiraterone is prescribed for use in combination with "a therapeutically effective amount of prednisone," a well-known steroid.[120]

In IPR, the Board deemed the combination patent erroneously obvious, and the Federal Circuit agreed in view of evidence that both abiraterone and prednisone were "individually considered promising prostate cancer treatments," and ordinary scientists had no reason to doubt that the two treatments would be more effective together.[121] Indeed, evidence before the Board showed that combining steroids with other anti-cancer treatments was not just "common practice" but indeed "the standard regimen" at the

S-to-Expand-Access-for-Patients-Living-with-Diabetes; Sanofi-Aventis U.S. LLC, How Much Should I Expect to Pay for Lantus? (Oct. 2019), https://www.lantus.com/-/media/EMS/Conditions/Diabetes/Brands/Lantus2/Consumer/Lantus-Pricing.pdf.

117. *See* Mylan N.V., *supra* note 116.

118. *See* Jason Rantanen, *The PTAB, the Director, and the Federal Circuit*, Fed Cir. Blog (Feb. 9, 2022), https://fedcircuitblog.com/2022/02/09/online-symposium-the-ptab-the-director-and-the-federal-circuit/.

119. *See Abiraterone Acetate*, 10 Drugs R & D 261 (2010); *A New Way to Treat Prostate Cancer: The Story of Abiraterone*, Inst. Cancer Res. (May 26, 2011), https://www.icr.ac.uk/news-features/latest-features/a-new-way-to-treat-prostate-cancer-the-story-of-abiraterone.

120. *See* BTG Int'l Ltd. v. Amneal Pharm. LLC, 923 F.3d 1063, 1066–67 (Fed. Cir. 2019).

121. *Id.* at 1074.

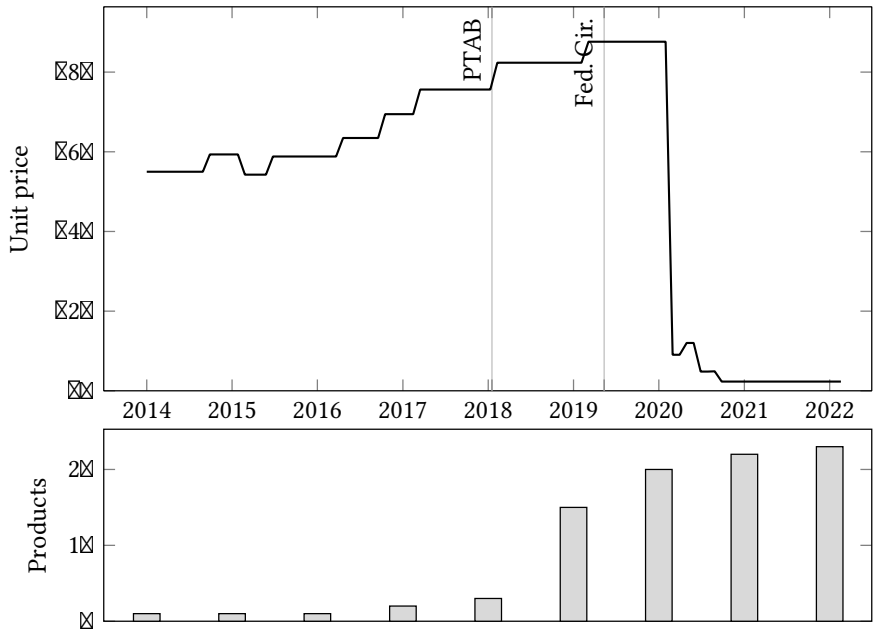

Figure 7: Unit price of abiraterone acetate, 250mg.

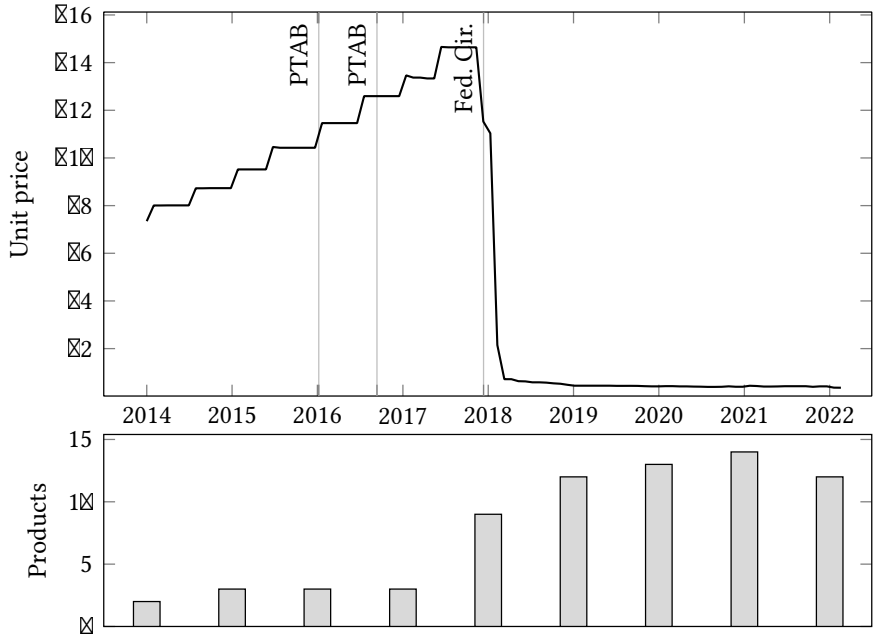

Figure 8: Unit price of prasugrel hydrochloride, 10mg.

time that Janssen's patent was applied for.[122]

Upon the Federal Circuit's conclusion that this obvious combination was unpatentable, generic competitors entered at a price of 2–19 per dose, compared to 88 for the brand. IPR thus enabled almost 98% savings on a drug that the World Health Organization lists as one of the "essential medicines for priority diseases" that constitute "minimum medicine needs for a basic health-care system."[123]

5. Prasugrel, Heart Disease

Prasugrel is an anti–blood clot drug used to treat cardiovascular disease; the brand formulation is Effient. The patent on the drug itself expired

122. *Id.* at 1074–75.

123. *See* World Health Org., Model List of Essential Medicines 32 (21st ed. 2019), https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf.

in 2017, but Daiichi Sankyo also held later-expiring patents on "methods of using Effient with aspirin," which effectively extended patent protection by six years.[124]

Since aspirin is a blood thinner that also limits blood clots, the Board in IPR concluded that the combination of aspirin and prasugrel was obvious.[125] Tracing prasugrel's predecessors, the Board found consistent use of aspirin in combination with increasingly powerful anti-clotting agents.[126] It concluded that an ordinary researcher "would have followed the rationale" of that prior art to "select[] the more potent, and preferred ADP-receptor blocking anti-platelet drug, i.e., prasugrel," as the predictable next choice for the combination.[127]

The Federal Circuit affirmed the Board's patentability determination without opinion.[128] The costs of the improper Effient patent extension were made apparent once generic competitors entered in 2017, at prices 97% below the brand cost.

6. Glatiramer, Multiple Sclerosis

Used to treat multiple sclerosis, glatiramer acetate has been available in generic form since at least 2016, but Yeda Pharmaceuticals held patents on a particular dosing regime of glatiramer acetate, which it marketed as Copaxone 40mg.[129] In inter partes review, Mylan challenged those patents as obvious in view of evidence that researchers had long been searching for higher-strength, less-frequent dosing regimes, for which a 40mg dose was the only reasonable choice according to the literature.[130] The Board agreed that the 40mg regime was obvious in view of this extensive evidence

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124. Eli Lilly & Co., Annual Report (Form 10-K), at 10 (Feb. 21, 2017). Eli Lilly markets Effient in the United States.

125. *See* Accord Healthcare Inc. v. Daiichi Sankyo Co., No. IPR2015-00864, slip op. at 22 (P.T.A.B. Sept. 12, 2016) (final written decision), *aff'd without opinion*, 706 F. App'x 679 (Fed. Cir. 2017).

126. *See id.* at 19.

127. *Id.*

128. *See Daiichi Sankyo*, 706 F. App'x 679.

129. *See* Yeda Research & Dev. Co. v. Mylan Pharm., Inc., 906 F.3d 1031, 1035–36 (Fed. Cir. 2018).

130. *See id.* at 1036–37.

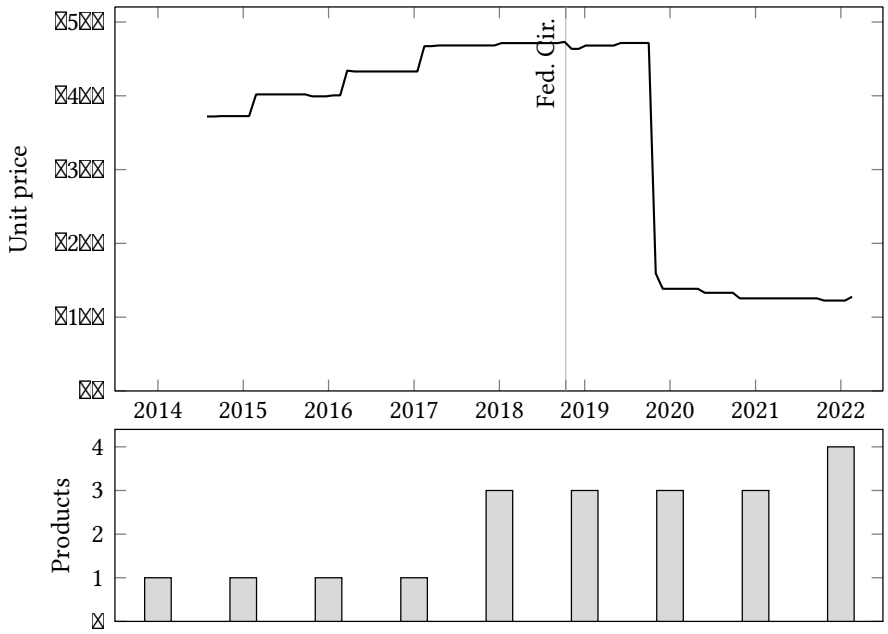

Figure 9: Unit price of glatiramer acetate, 40mg/ml. Dates of PTAB decisions omitted.

pointing to that regime, and the Federal Circuit affirmed.[131] Generic entry followed swiftly thereafter, reducing prices by about 75%.

Inter partes review here is notable because the same patents were declared invalid in parallel district court litigation;[132] a comparison of the cases reveals two important advantages of inter partes review. First, the administrative proceeding is speedier without sacrificing quality. District court litigation was filed in 2014 and resolved in January 2017, while IPR was sought in 2015 and completed in December 2016.[133] Second, while district court patent invalidation is limited to the particular patent claims asserted in the litigation, inter partes review can consider potentially all claims, including those that a patent holder may be keeping in reserve for future competitors.[134] Successful inter partes review thus enables a potentially wider range of generic competitors than district court litigation, and a wider range of competitors translates into lower prices overall.

B. Affirmances of Patentability

In eight cases, the Federal Circuit affirmed a wholly or partially unsuccessful Board challenge to a drug patent.[135] A number of trends are noteworthy here.

First, all but three of the Federal Circuit opinions here are published, precedential opinions, and only two are summary affirmances without an opinion (one of which affirms a mixed-result IPR with some claims can-

131. *See id.* at 1046.

132. *See* Teva Pharm. USA, Inc. v. Sandoz Inc. (*In re* Copaxone Consol. Cases), 906 F.3d 1013, 1015 & n.1 (Fed. Cir. 2018).

133. *See id.* at 1020; *Yeda Research & Dev.*, 906 F.3d at 1039–40.

134. *Compare Yeda Research & Dev.*, 906 F.3d at 1037 (challenging "all claims" of the Copaxone 40mg patents), *with Copaxone Consol. Cases*, 906 F.3d at 1021 (considering only select claims from those patents).

135. *See* Amerigen Pharm. v. UCB Pharma GmbH, 913 F.3d 1076, 1089 (Fed. Cir. 2019); ModernaTx, Inc. v. Arbutus Biopharma Corp., 18 F.4th 1364, 1377 (Fed. Cir. 2021); Par Pharm., Inc. v. Horizon Therapeutics, LLC 727 F. App'x 688 (Fed. Cir. 2018) (mem.); Teva Pharm. USA v. Corcept Therapeutics, Inc., 18 F.4th 1377, 1383 (Fed. Cir. 2021); Mylan Pharm. Inc. v. Research Corp. Techs., 914 F.3d 1366, 1377 (Fed. Cir. 2019); Neptune Generics, LLC v. Eli Lilly & Co., 921 F.3d 1372, 1378 (Fed. Cir. 2019); Mylan Pharm. Inc. v. Biogen MA Inc., No. 2020-1673 (Fed. Cir. Nov. 30 2021); Luitpold Pharm., Inc. v. Pharmacosmos A/S, 718 F. App'x 989 (Fed. Cir. 2018) (mem.).

celled and others not).[136] The discrepancy compared to affirmances of unpatentability, which were rarely published,[137] is consistent with other findings that the Federal Circuit skews its publication of opinions in favor of patent owners.[138]

Second, in every non-summary disposition, the Federal Circuit makes extensive use of the record and the technical literature developed before the Board, often delving deeply into biochemistry to evaluate determinations of nonobviousness.[139] This adds support to the proposition that the required scientific background of administrative patent judges deciding administrative patent challenges invites a fuller, more robust airing of the technologies at issue.[140]

In terms of effects on generic availability and drug prices, it is unsurprising that these affirmances of Board determinations of patentability generally do not lead to changes to either. There is one important exception, described below.

1. Dimethyl Fumarate: Multiple Sclerosis

In *Mylan Pharmaceuticals Inc. v. Biogen MA Inc.*, the Federal Circuit issued a brief unpublished opinion affirming the Board's determination of patentability for Biogen's patent on a 480-milligram dose of the multiple sclerosis drug dimethyl fumarate.[141] Yet the IPR determination had done important work even before that appeal was reached. In parallel litigation, affirmed by the Federal Circuit, the district court held Biogen's patent to be invalid for lack of written description, because the patent failed to con-

136. *See Mylan Pharm.*, No. 2020-1673; *Par Pharm.*, LLC 727 F. App'x 688; Pharmacosmos A/S v. Luitpold Pharm., Inc., No. IPR2015-01490, slip op. at 51 (P.T.A.B. Jan. 4, 2017) (Paper No. 54), *aff'd*, 718 F. App'x 989.

137. *See supra* notes 71–73 and accompanying text.

138. *See* Paul Gugliuzza & Mark A. Lemley, *Can a Court Change the Law by Saying Nothing?*, 71 Vand. L. Rev. 765, 767 (2018).

139. *See, e.g., Amerigen Pharm.*, 913 F.3d at 1086–89 (discussing Board findings on "toxicity, bioavailability, receptor affinity, pharmacokinetics, and pharmacodynamics" of compounds); *Mylan Pharm.*, 914 F.3d at 1375 (discussing chemistry of potential modifications to drug compounds).

140. *See supra* Section III.A.1.

141. *See Mylan Pharm.*, No. 2020-1673, slip op. at 2.

template the 480-milligram dose with specificity.[142]

To support this finding of invalidity, the district court relied heavily on the Board's decision, using Biogen's assertions and arguments in that proceeding to better interpret the scope and purport of the patent.[143] Biogen had argued to the Board that the 480-milligram dose was an unexpected result of a study it conducted in 2011.[144] Yet Biogen had argued before the district court that the dose was contemplated in a 2007 patent application that gave rise to its patent.[145] The contradiction between these two arguments before different tribunals made it clear to both the district court and the Federal Circuit that the patent could not stand.[146]

Invalidation of Biogen's dimethyl fumarate patent quickly enabled generic entry. Although there is insufficient pricing data in the NADAC, the Orange Book shows that two drug products were approved in 2019, twenty-four were approved in 2020, and twenty-eight in 2022. Even though IPR did not result in cancellation of a drug patent in this case, it laid the interpretive groundwork that helped to secure the patent's later invalidation and subsequent generic competition.

C. Reversals

The Federal Circuit has reversed or vacated Board decisions on drug patents only three times, all published, once with the appellate court favoring patentability and twice against. This remarkably low rate of error is consistent with other findings that IPR decisions and the Board decisions generally are affirmed at a high rate.[147]

In one case, the Federal Circuit held that the Board had erroneously disapproved a patent based on a claim construction that focused too much

142. *See* Biogen Int'l GmbH v. Mylan Pharm. Inc., No. 1:17-cv-116, slip op. at 45 (N.D.W.V. June 18, 2020) (mem.), *aff'd*, 18 F.4th 1333 (Fed. Cir. 2021).

143. *See, e.g., id.* at 40 n.20.

144. *See id.* at 10, 43–44.

145. *See id.* at 39–40.

146. *See id.* at 45; *Biogen II*, 18 F.4th at 1343–44.

147. *See, e.g.*, Daniel F. Klodowski & Audrey J. Parker, *Federal Circuit PTAB Appeal Statistics for September 2022*, At PTAB Blog (Jason E. Stach & Elliot C. Cook eds., Finnegan, Henderson, Farabow, Garrett & Dunner, LLP Nov. 1, 2022), https://www.finnegan.com/en/insights/blogs/at-the-ptab-blog/federal-circuit-ptab-appeal-statistics-for-september.html; Rantanen, *supra* note 118.

on the patent's literal definition of a term and not enough on inferences from the patent text and prosecution history.[148] In another, the appellate court vacated a finding of patentability on the grounds that the Board had erroneously failed to consider expert witness testimony and test data evidence.[149] The third case is described in more detail below.

1. Nitric Oxide: Neonatal Respiratory Failure

Praxair Distribution, Inc. v. Mallinckrodt Hospital Products IP Ltd., the third case involving Federal Circuit correction of a Board error on the merits, dealt with nitric oxide, a gas that treats insufficient blood oxygen levels.[150] Although the drug has been known and studied since the early 1990s,[151] the drug's sole manufacturer Mallinckrodt obtained a patent dealing with potential side effects for patients with a preexisting condition called left ventricular dysfunction.[152] Rather than proposing a novel method of treatment or diagnosis however, the patent covered nothing more than providing nitric oxide with a warning label about left ventricular dysfunction.[153]

Had Mallinckrodt's warning-label patent stood, it would have pushed the company's patent protection drug out until 2029,[154] effectively eliminating generic competition on the decades-old drug since the FDA would not approve a product without an adequate warning label.[155] The patent would exemplify the phenomenon of "mandatory infringement" that can

148. *See* Kaken Pharm. Co. v. Iancu, 952 F.3d 1346, 1351–54 (Fed. Cir. 2020).

149. *See* Altaire Pharm., Inc. v. Paragon Bioteck, Inc., 889 F.3d 1274, 1284–87 (Fed. Cir. 2018). The parties subsequently settled, and the Federal Circuit vacated the remand. *See* Altaire Pharm., Inc. v. Paragon Bioteck, Inc., No. 2017-1487 (Fed. Cir. Oct. 2 2018) (per curiam).

150. *See* Praxair Distribution, Inc. v. Mallinckrodt Hosp. Prods. IP Ltd., 890 F.3d 1024, 1027 (Fed. Cir. 2018).

151. *See id.* at 1029 n.4 (citing Evan Loh et al., *Cardiovascular Effects of Inhaled Nitric Oxide in Patients with Left Ventricular Dysfunction*, 90 Circulation 2780 (1994)).

152. *See id.* at 1028; Methods of Distributing a Pharmaceutical Product Comprising Nitric Oxide Gas for Inhalation, U.S. Patent No. 8,846,112 col. 1, ll. 54–63 (filed Nov. 21, 2012).

153. *See* '112 Patent col. 14, ll. 41–42.

154. The patent's priority date was June 30, 2009. *See id.* col. 1, ll. 9–17.

155. *See* Federal Food, Drug, and Cosmetic Act (FFDCA) § 505(j)(2)(v), 21 U.S.C. § 355.

fundamentally distort competition and innovation incentives, as I have described in other research.[156]

The Board easily saw through this anticompetitive strategy when a potential generic entrant challenged Mallinckrodt's patent. Applying the "printed matter doctrine" of patent law,[157] the Board gave the patent's recitations about labeling "no patentable weight" and held all the claims unpatentable, except for one claim that added several diagnostic steps.[158] The Federal Circuit affirmed the Board's unpatentability findings, and reversed to hold the remaining claim also unpatentable.[159] In view of this result in combination with other litigation,[160] the FDA approved a generic nitric oxide product in 2018.[161]

D. Dispositions on Non-Merits Issues

Six appeals of administrative drug patent challenges have dealt primarily with issues unrelated to the merits of the challenged patent. One related to a dispute over attorney fees,[162] one involved the burden of proof for amending claims during IPR,[163] and one considered the Federal Circuit's statutory jurisdiction after the Board denied institution of an IPR.[164] These fact-specific issues are unlikely to provide generalizable information about

156. *See* Charles Duan, *Mandatory Infringement*, 75 Fla. L. Rev. (forthcoming 2023) (manuscript at 19–22), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4193947.

157. *See, e.g.*, AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1064–65 (Fed. Cir. 2010) (quoting *In re* Ngai, 367 F.3d 1336, 1339 (Fed. Cir. 2004) (per curiam)).

158. Praxair Distribution, Inc. v. Mallinckrodt Hosp. Prods. IP Ltd., No. IPR2015-00529, slip op. at 29–30 (P.T.A.B. July 7, 2016); *see id.* at 40–42.

159. *See* Praxair Distribution, Inc. v. Mallinckrodt Hosp. Prods. IP Ltd., 890 F.3d 1024, 1038–39 (Fed. Cir. 2018).

160. *See* INO Therapeutics LLC v. Praxair Distribution Inc., 782 F. App'x 1001 (Fed. Cir. 2019) (nonprecedential).

161. *See* Letter from Vincent Sansone, U.S. Food & Drug Admin., to Amy Kniefel, ICON Clinical Research LLC, *ANDA Approval, ANDA 207141* (Oct. 2, 2018), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/207141Orig1s000Ltr.pdf.

162. *See* Amneal Pharm. LLC v. Almirall, LLC, 960 F.3d 1368, 1372–73 (Fed. Cir. 2020).

163. *See* Sanofi Mature IP v. Mylan Labs. Ltd., 757 F. App'x 988, ? (Fed. Cir. 2019).

164. *See* BioDelivery Scis. Int'l v. Aquestive Therapeutics, Inc., 935 F.3d 1362, 1366 (Fed. Cir. 2019), *reh'g en banc denied* BioDelivery Scis. Int'l v. Aquestive Therapeutics, Inc., 946 F.3d 1382 (Fed. Cir. 2020).

administrative drug patent challenges overall.[165]

The remaining three cases have dealt with constitutional standing to appeal and sovereign immunity, and are discussed below.

1. Appellate Standing

Under current Supreme Court precedent, a federal court may adjudicate a dispute only if a party to the dispute has "standing," namely a concrete injury that the court can redress with appropriate relief.[166] Standing is not required to challenge a patent before the Board,[167] but appealing an agency decision to a federal court requires a separate showing of standing.[168] A patent owner obviously has standing to appeal a Board determination of unpatentability,[169] but in several cases the Federal Circuit has held patent challengers to lack standing on the grounds that the challengers are not concretely harmed by the Board's failure to cancel a patent.[170] Even companies making research and development expenditures in the same technological field of a patent may lack standing, under current Federal Circuit law, absent "evidence that these expenses were caused by the [relevant] patent."[171]

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165. In particular, *BioDelivery Sciences* involved the Federal Circuit resolving an unusual timing situation, in which the Supreme Court decided an issue in the midst of the IPR proceeding. *See id.* at 1364–65. Similarly, *Sanofi Mature IP* considered the Board's approach to claim amendments in view of an intervening en banc Federal Circuit decision on that same question. *See* 757 F. App'x at ?.

166. *See, e.g.,* Spokeo, Inc. v. Robins, 578 U.S. 330, 338 (2016) (citing Lujan v. Defs. of Wildlife, 504 U.S. 555, 560–61 (1992); Friends of the Earth, Inc. v. Laidlaw Envtl. Servs. (TOC), Inc., 528 U.S. 167, 180–81 (2000)).

167. *See* 35 U.S.C. § 311(a) (permitting "a person who is not the owner of a patent" to petition for institution of IPR); Cuozzo Speed Techs., LLC v. Lee, 579 U.S. 261, 279 (2016).

168. *See, e.g.,* Sierra Club v. Envtl. Prot. Agency, 292 F.3d 895, 899 (D.C. Cir. 2002).

169. *See, e.g.,* Pers. Audio, LLC v. Elec. Frontier Found., 867 F.3d 1246, 1250 (Fed. Cir. 2017).

170. *See, e.g.,* Consumer Watchdog v. Wis. Alumni Research Found., 753 F.3d 1258, 1263–64 (Fed. Cir. 2014); Apple Inc. v. Qualcomm Inc., 17 F.4th 1131, 1137–38 (Fed. Cir. 2021).

171. Gen. Elec. Co. v. United Techs. Corp., 928 F.3d 1349, 1354 (Fed. Cir. 2019). *But see id.* at 1357–58 (Hughes, J., concurring) (questioning whether the Federal Circuit's "patent-specific treatment of competitor standing is out of step with its application in other areas").

Two appeals of administrative drug patent challenges have been dismissed for lack of standing.[172] In *Argentum Pharmaceuticals LLC v. Novartis Pharmaceuticals Corp.*, several generic drug manufacturers petitioned for IPR on Novartis's patent on a multiple sclerosis drug, which the Board found not unpatentable.[173] All but one of the petitioners settled.[174] The remaining petitioner apparently did not intend to make the drug or seek FDA approval of it except through a business partner, leading the Federal Circuit to conclude that the remaining petitioner itself lacked a sufficiently concrete injury to satisfy standing.[175] Similarly in *ModernaTx, Inc. v. Arbutus Biopharma Corp.*, the Federal Circuit dismissed an appeal of an IPR decision upholding an RNA technology patent, for lack of standing.[176] In that case, the IPR petitioner Moderna held a paid-up license to the patent, leading the court to conclude that Moderna suffered no injury from the Board's failure to cancel the patent.[177]

2. Cyclosporin (and Sovereign Immunity)

Cyclosporin, as an ophthalmic emulsion, is used for the treatment of dry eye.[178] Allergan manufactures a cyclosporin product under the brand name Restasis, and holds a portfolio of patents on the emulsion formulation.[179] The portfolio consisted of a "first wave" of now-expired patents dat-

172. There have also been cases where the patent challenger was held to have standing. *See, e.g.*, Altaire Pharm., Inc. v. Paragon Bioteck, Inc., 889 F.3d 1274, 1282–84 (Fed. Cir. 2018); ModernaTx, Inc. v. Arbutus Biopharma Corp., 18 F.4th 1364, 1372 (Fed. Cir. 2021); Amerigen Pharm. v. UCB Pharma GmbH, 913 F.3d 1076, 1083 (Fed. Cir. 2019).

173. *See* Argentum Pharm. LLC v. Novartis Pharm. Corp., 956 F.3d 1374, 1375 (Fed. Cir. 2020).

174. *See id.* at 1375 & n.1.

175. *See id.* at 1377–78.

176. *See* ModernaTx, Inc. v. Arbutus Biopharma Corp., 18 F.4th 1352, 1354 (Fed. Cir. 2021).

177. *See id.* at 1362. The Board also held some of the patent's claims unpatentable; the Federal Circuit affirmed that result. *See id.* at 1362–64.

178. *See* Mylan Pharm. Inc. v. Saint Regis Mohawk Tribe, No. IPR2016-01129, slip op. at 6 (P.T.A.B. Sept. 27, 2019).

179. *See id.* at 4–5.

ing back to 1995, and a "second wave" of patents filed beginning in 2003.[180] Mylan, the potential generic entrant, challenged the second-wave patents in several IPR proceedings, and was also sued on those patents in district court.[181]

The district court in this case managed to issue its decision before the IPR proceedings completed, with Judge Bryson of the Federal Circuit (sitting by designation) holding that "Allergan is not entitled to renewed patent rights for Restasis in the form of a second wave of patent protection."[182] Yet Judge Bryson could not adjudicate the entire second-wave patent portfolio because prior to that judgment, Allergan had given the generic defendants in that case covenants not to sue on two of its patents, thereby insulating them from invalidation.[183] These two patents remained intact, able to prevent generic competition beyond the generic firms in the litigation.

Attention thus turned to the pending IPR proceedings on the two remaining patents, which were able to proceed despite the covenant not to sue by virtue of being an agency proceeding.[184] In both proceedings, the Board held that the patents were indistinguishable from those invalidated in district court and therefore were unpatentable.[185] Rather than defend its

180. *See* Allergan, Inc. v. Teva Pharm. USA, Inc., No. 2:15-cv-1455, slip op. at 7–10, 18–19 (E.D. Tex. Oct. 16, 2017) (findings of fact and conclusions of law), *aff'd without opinion*, 742 F. App'x 511 (Fed. Cir. 2018).

181. *See Mylan Pharm.*, No. IPR2016-01129, slip op. at 4–5 (summarizing litigation); *Allergan*, No. 2:15-cv-1455, slip op. at 23.

182. *Allergan*, No. 2:15-cv-1455, slip op. at 135. The IPR proceedings were delayed largely because of the extra briefing required on the sovereign immunity issue described below.

183. *See Allergan*, No. 2:15-cv-1455, slip op. at 29; Super Sack Mfg. Corp. v. Chase Packaging Corp., 57 F.3d 1054, 1058 (Fed. Cir. 1995) ("[A] patentee defending against an action for a declaratory judgment of invalidity can divest the trial court of jurisdiction over the case by filing a covenant not to assert the patent at issue against the putative infringer . . . .").

184. More specifically, a covenant not to sue deprives a court of an Article III case or controversy in which to adjudicate patent validity. *See Super Sack Mfg.*, 57 F.3d at 1058. However, Article III does not govern administrative agency proceedings. *See* Oil States Energy Servs., LLC v. Greene's Energy Grp., LLC, 138 S. Ct. 1365, 1373 (2018).

185. *See Mylan Pharm.*, No. IPR2016-01129, slip op. at 24; Mylan Pharm. Inc. v. Saint Regis Mohawk Tribe, No. IPR2016-01130, slip op. at 26 (P.T.A.B. Sept. 27, 2019).

patents on the merits, Allergan attempted a different strategy to insulate its patents from cancellation: It transferred the patents to an American Indian tribe, and argued before the Federal Circuit that the tribe's sovereign immunity precluded the Board's review.[186] In a closely watched appeal, the court rejected this sovereign immunity claim, holding that "IPR is more like an agency enforcement action than a civil suit brought by a private party," such that "tribal immunity is not implicated."[187] With Allergan's gambit put to rest, the door was open to competition, with Mylan receiving approval for a generic cyclosporin emulsion in February 2022.[188]

IV. Observations

The following are several observations based on the cases described above.

A. Effect on Generic Entry and Drug Prices

Most notably, cancellation of a drug patent through an administrative challenge frequently resulted in subsequent generic entry and lower prices. This Article thus directly answers the often-repeated claim that "there is no evidence that IPRs will allow generic and biosimilar companies to bring products to market more quickly."[189]

In every case but one where the challenged patent was deemed unpatentable and NADAC data was available, prices dropped significantly as a result of subsequent generic entry.[190] Even where pricing data was unavailable, I was able to identify generic drug approvals indicating a likely increase in competition.[191]

To be sure, it is possible that if administrative patent challenges did not

186. *See* Saint Regis Mohawk Tribe v. Mylan Pharm., 896 F.3d 1322, 1324 (Fed. Cir. 2018).

187. *Id.* at 1327.

188. *See* Letter from Edward M. Sherwood, U.S. Food & Drug Admin., to Wayne Talton, Mylan Pharm. Inc., *ANDA Approval, ANDA 205894* (Feb. 2, 2022), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/205894Orig1s000ltr.pdf.

189. *See* Greenwood & Castellani, *supra* note 14, at 3.

190. *See supra* Section III.A. The exception, as noted above, was for oxycodone. *See supra* note 81.

191. *See supra* Section III.C.1.

exist, the same price-lowering results would have resulted from Hatch–Waxman litigation. But there are several reasons to doubt this. Virtually all of the patents considered in this survey were densely complex and technical. In at least the rivastigmine case, the Board's technical expertise advantage led to an observably better understanding of the patent, suggesting that expertise is an important factor in proper adjudication of drug patents. And the dimethyl fumarate case suggests that even when the Board upholds a patent, the contents of the proceeding can assist district courts in understanding and evaluating issues.[192] Even when district court litigation is copending, administrative patent challenges appear to play an important role in achieving outcomes that enable generic entry and lower drug prices for Americans.

B. Lack of Evidence of Bias Against Patent Owners

A large fraction of the appeals considered in this Article resulted in patents being determined unpatentable in whole—twenty-three appeals out of thirty-two that were decided on the merits. Yet close examination of these appeals resists the simple conclusion, drawn by many, that a high rate of patent cancellation means bias against patentees.[193]

For one thing, the Board plainly does not deem every drug patent it sees unpatentable—it reached the opposite conclusion in ten cases. Furthermore, the overwhelming majority of decisions were affirmed by the Federal Circuit, and of the only three reversals, two of them found that the Board erred in the direction of patentability. To the extent that the Board's decisions are biased against drug patent holders, these cases would suggest that the Federal Circuit is in near-total agreement and perhaps even more biased against patent holders, an unlikely scenario given most opinions about the Federal Circuit.

It is possible, of course, that the bias against patent owners in administrative patent challenges arises from the structure of the proceedings, in particular the different burdens of proof used before the Board compared to district courts.[194] But the evidence gives several reasons to doubt this

192. *See supra* Section III.B.1.

193. *See, e.g.*, Shepherd, *supra* note 18; Zou, *supra* note 18; PUGATCH ET AL., *supra* note 18, at 8.

194. *See* Shepherd, *supra* note 18, at 35.

possibility as well. Almost all of the decisions reviewed turned on a question of obviousness, the ultimate determination of which is a matter of law that the Federal Circuit reviews de novo. Furthermore, to the extent that a procedural difference gives rise to a substantive difference in outcome, Federal Circuit judges have been far from shy about shining a spotlight on such discrepancies.[195] That no Federal Circuit judge has criticized any of the administrative proceedings studied for inequities suggests that the court does not perceive any.[196]

C. Problematic Nature of Patents Challenged

Instead, the better explanation for the high rate of patent cancellation before the Board is simply that the patents brought before it were wrongly granted and worthy of being cancelled. This is as basic economics would predict—a generic manufacturer would not put up thousands of dollars in legal fees and risk legal estoppel to challenge a patent unless it was reasonably certain the patent was invalid—but the review of cases empirically confirms the low quality of challenged drug patents.

All of the patents invalidated in this study were secondary patents on formulations or uses of drugs. In most cases, the innovations were not just incremental but largely unsurprising—screw threads, warning labels, safety procedures, and adding aspirin to avoid blood clots. Indeed, these patents are not mere follow-on modifications to drugs, but tend to be carefully selected features that generics cannot easily work around due to the FDA approval process. In other research I have theorized that these kinds of "mandatory infringement" patents, which competitors must infringe in order to satisfy a regulatory mandate, create economic distortions that

195. *See* PPC Broadband, Inc. v. Corning Optical Commc'ns RF, LLC, 815 F.3d 734, 741–43 (Fed. Cir. 2016) (emphasizing difference in claim constructions depending on standards applied).

196. Notably, as I have observed elsewhere, the Federal Circuit's analysis of the non-applicable claim construction in *PPC Broadband* is wholly advisory and arguably improper under Article III. *See* Brief of *Amicus Curiae* Public Knowledge at 30–31, Cuozzo Speed Techs., LLC v. Lee, 579 U.S. 261 (Mar. 29, 2016) (No. 15-446), https://www.scotusblog.com/wp-content/uploads/2016/03/15-446_amicus_resp_PublicKnowledge.authcheckdam.pdf. That only goes to show how far the Federal Circuit is willing to go to call out policy problems it perceives.

undermine incentives to develop high-quality innovations.[197] The consistently minimal innovation in administratively challenged drug patents appears to confirm this theory.

To be sure, in the cyclosporin and dimethyl fumarate cases the patent owner argued that the specific changes in the challenged secondary patent were unexpectedly beneficial, backing up those arguments with credible experimental evidence.[198] Yet in both of these cases, those arguments backfired as the patent owner had tried to backdate the supposedly unexpected invention to prior to its discovery. That illustrates a different form of low-quality patent, obtained through manipulation of the patent prosecution process.

Given the truly questionable nature of the many patents reviewed in this Article, what is surprising is not that drug patents are invalidated by administrative challenges but that so these questionable patents exist in the first place. The existence of administrative challenges is perhaps symptomatic of larger issues with patent law and examination practice that allow for such patents not only to come into existence but to have dramatic effects on the availability and prices of lifesaving drugs.[199]

D. Possible Biases Against Challengers

Contrary to suppositions that administrative challenge proceedings introduce biases against drug patent holders, the surprising finding of this Article is that the proceedings at least at the appeal stage appear somewhat biased against patent *challengers*. This bias manifests in two ways.

First, the Federal Circuit's opinion publication practices skew heavily away from affirmances of Board holdings of unpatentability, which are often issued summarily without opinion. There are almost twice as many unpatentability affirmance decisions as there are patentability affirmances and reversals combined (twenty-one compared to eight plus three), and yet from the published opinion record it would seem unpatentability affir-

197. *See* Duan, *supra* note 156, at ?.

198. *See supra* Section III.D.2; *supra* Section III.B.1.

199. *See generally* Exec. Order 14036, Promoting Competition in the American Economy, 86 Fed. Reg. 36987, 36988 (July 9, 2021) ("And too often, patent and other laws have been misused to inhibit or delay—for years and even decades—competition from generic drugs and biosimilars, denying Americans access to lower-cost drugs.").

mances are in the minority (six compared to five plus three).

The true record shows that the vast majority of challenged drug patents are rightly held unpatentable and that only 9% of Board decisions are reversed. But scholars and commentators who typically focus on published opinions might reach the mistaken conclusion that a substantial of challenged drug patents are valid and that the Board is reversed over 21% of the time. These misleading statistics could easily feed into an erroneous perception that patent challengers are using administrative procedure to harass drug innovators' valuable patents, a perception that the correct statistics plainly do not support.

Second, the Federal Circuit's application of Article III standing law to prevent patent challengers from appealing adverse Board decisions again skews in favor of patent holders. In both of the standing cases discussed previously,[200] the patent challengers supposedly lacking standing both had specific plans to develop commercially important drug products that potentially infringed the patents at issue; indeed in the *ModernaTx* case the future product in question was Moderna's COVID-19 vaccine.[201] If the Federal Circuit's application of standing law is correct, then that result would be merely unfortunate, but commentators and even one Federal Circuit judge have criticized the court's jurisprudence as an "overly rigid and narrow standard for Article III standing."[202] An erroneous standing rule that bars product-developing firms from the appeal stage of patent challenges does not only render the process unfairly tilted against patent challenges, but also could potentially impede the introduction of new vaccines and treatments of value to the public.

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200. *See supra* Section III.D.1.

201. *See* ModernaTx, Inc. v. Arbutus Biopharma Corp., 18 F.4th 1352, 1360–61 (Fed. Cir. 2021); *see also* Argentum Pharm. LLC v. Novartis Pharm. Corp., 956 F.3d 1374, 1377 (Fed. Cir. 2020).

202. Gen. Elec. Co. v. United Techs. Corp., 928 F.3d 1349, 1355 (Fed. Cir. 2019) (Hughes, J., concurring); *see also* Sapna Kumar, *Standing Against Bad Patents*, 32 Berkeley Tech. L.J. 87, 136 (2017) (characterizing Federal Circuit standing law as "artificially constraining the class of people that can challenge the PTO's actions").

Conclusion

Using publicly available data on patent adjudication, FDA approvals, and drug prices, this Article identifies a correlation between administrative patent challenge procedures such as IPR and lower drug prices due to generic entry. It uses empirical data to respond to criticisms about the application of these challenge procedures to drug patents, and it identifies areas in which the procedures can be improved to better serve the purposes of a well-crafted patent system that avoids abuse and enables appropriate competition.

What I, at least, have found most surprising from this study is the sheer extent of the tactics that drug companies seem willing to undertake in order to defeat generic competition and maintain ongoing patent protection for their products. Besides selling off patents to an American Indian tribe in a failed attempt to rent a share of sovereign immunity, the patent-holding drug companies described in this Article have pushed minimally inventive improvements into million-dollar patent portfolios, made two-faced arguments to federal tribunals, and exploited the administrative safety system by patenting regulatory requirements. To the extent that administrative patent challenges and other reforms to the law chip away at companies' ability to avail themselves of these shenanigans, one hopes that those companies go back to seeking out monopoly profits the old-fashioned way—by inventing better products.