POST-GRANT ADJUDICATION OF DRUG PATENTS: AGENCY AND/OR COURT?

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ABSTRACT

The America Invents Act of 2011 (AIA) created a robust administrative system—the Patent Trial and Appeal Board (PTAB)—that provides a route for challenging the validity of granted patents outside of district courts. Congress determined that administrative adjudication of the validity of initial patent grants could be cheaper and more scientifically accurate than district court adjudication of such validity.

For private economic value per patent, few areas of technology can match the biopharmaceutical industry. This is particularly true for small-molecule drugs. A billion-dollar drug monopoly may be protected from competition by a relatively small number of patents. Accordingly, the social cost of invalid patents—and, by extension, the potential benefit of PTAB review—is particularly acute for small molecule drugs. Conversely, if the PTAB is overly assertive and improperly targets high-quality patents, we may observe problematic reductions in innovation incentives. Thus, empirical research on how PTAB review is functioning in the area of drug patents is important.

To investigate PTAB review of drug patents empirically, this Article uses several novel datasets, which are made publicly available, to study the respective roles of the PTAB and the district courts. Our empirical findings indicate that the PTAB's role in adjudicating small-molecule patents has been substantially more modest than for other types of patents. Moreover, there is little evidence that the PTAB targets categories of small-molecule patents

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that are generally considered high quality. There is also no evidence that the PTAB targets small-molecule patents held by small entities. However, PTAB challenges may not differentiate as finely among different categories of patents as district court challenges. The Article concludes by discussing legal reforms policymakers could implement if they were interested in encouraging a more active role for the PTAB in policing the validity of small-molecule drug patents. The case for these reforms is bolstered by data showing that the PTAB is used more frequently for biologics patents, where litigation currently operates differently than for small molecule drugs. The Article also discusses how ex post determination of drug patent validity at the PTAB could be structured in comparison to more rigorous ex ante patent application examination.

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I. INTRODUCTION

The America Invents Act of 2011 (AIA) created a robust administrative system—the Patent Trial and Appeal Board (PTAB)—that provides a route for challenging the validity of granted patents outside of district courts.[1] Congress determined that administrative adjudication of the validity of the initial patent grant could be cheaper and more scientifically accurate than district court adjudication of such validity.[2]

1. Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284–341 (codified as amended in scattered sections of 35 U.S.C.).

2. *See generally* Saurabh Vishnubhakat, Arti K. Rai & Jay P. Kesan, *Strategic Decision Making in Dual PTAB and District Court Proceedings*, 31 BERKELEY TECH. L.J. 45, 51–55 (2016) (discussing this standard "substitution" justification for implementing administrative post-grant review). The substitution justification generally requires that the district court stay Article III litigation pending the outcome of the PTAB proceeding. When district courts do not issue stays, the benefits of substitution can be thwarted by duplication and inconsistency. Senators Patrick Leahy and John Cornyn have introduced legislation that attempts to prescribe more district

However, as demonstrated by the six U.S. Supreme Court cases it has already generated,[3] the PTAB has proved quite provocative. As it happens, the creation of the PTAB coincided with what some analysts argue has been a rise of "anti-administrativism" at the Supreme Court.[4] In the case of the PTAB, specific reasons for controversy have ranged from disputes over whether patents represent the types of public rights amenable to administrative adjudication,[5] to questions regarding the extent to which Congress has precluded Article III review of administrative determinations.[6]

At least in part, the high-dollar value associated with patent cases provides the fuel for this legal fire. As Justice Brett Kavanaugh noted at oral argument in the most recent of the Supreme Court challenges, Arthrex, billions of dollars may turn on the PTAB's decisions.[7]

Although Justice Kavanaugh's remarks did not single out the biopharmaceutical industry, in terms of private economic value per patent, few areas of technology can match it. Particularly for small-molecule drugs that are generally taken orally (as contrasted with large-molecule biologic proteins, which generally must be injected), a billion-dollar drug monopoly may be protected from competition by a relatively small number of patents.[8]

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court stays by codifying a standard four-part test. Restoring the America Invents Act, S. 2891, 117th Cong. (2021). This test was codified in the context of the now-expired post-grant review of covered business method (CBM) patents, and the data show that it strongly counseled in favor of stays. *See* Joel Sayres & Julie Wahlstrand, *To Stay or Not to Stay Pending IPR? That Should be a Simpler Question*, 17 CHI.-KENT J. INTELL. PROP. 52, 63 (2018) (discussing the four-part CBM test).

3. Cuozzo Speed Techs., LLC v. Lee, 136 S. Ct. 2131 (2016); Oil States Energy Servs., LLC v. Greene's Energy Grp., LLC, 138 S. Ct. 1365 (2018); SAS Inst., Inc. v. Iancu, 138 S. Ct. 1348 (2018); Return Mail, Inc. v. U.S. Postal Serv., 139 S. Ct. 1853 (2019); Thryv, Inc. v. Click-To-Call Techs. LP, 140 S. Ct. 1367 (2020); United States v. Arthrex, Inc., 141 S. Ct. 1970 (2021).

4. *See, e.g.*, Gillian Metzger, *1930's Redux: The Administrative State Under Siege*, 131 HARV. L. REV. 1 (2017).

5. *See Oil States*, 138 S. Ct. at 1373.

6. *See Cuozzo*, 136 S. Ct. at 2141–42.

7. Transcript of Oral Argument at 22, *Arthrex*, 141 S. Ct. 1970 (Nos. 19-1434, -1452, -1458).

8. To be sure, issues of patent quantity are also salient as well. The number of patents per approved branded small-molecule drug has increased noticeably over the years. A study by C. Scott Hemphill and Bhaven N. Sampat, *When Do Generics Challenge Drug Patents?*, 8 J. EMPIRICAL LEGAL STUD. 613 (2011), computed mean and median patent numbers for each three-year FDA approval cohort between 1985 and 2002. Between the first cohort (1985–87) and the last (2000–02), the average number of patents per drug increased from 1.9 to 3.9, and the median number of patents increased from 1.5 to 2.5. *Id.* at 619–20. A commercial firm that extended the Hemphill and Sampat analysis through 2014 determined that the average number of patents per drug in the 2012–14 cohort was 6.1, and the median number of patents was 4.0. *Patent Proliferation: A 30-Year Increase in the Number of Patents Per Drug*, ONPOINT ANALYTICS

Accordingly, the social costs of invalid patents—and, by extension, the potential benefits of PTAB review—are particularly acute in the biopharmaceutical industry. Conversely, if the PTAB is overly assertive and improperly targets high-quality patents, we may observe problematic reductions in innovation incentives.[9]

To investigate PTAB review of drug patents empirically, this Article uses several novel datasets to study the respective roles of the PTAB and the district courts in patent invalidity proceedings. Analysis of contemporaneous district court litigation is particularly important because, prior to the AIA, Congress set up court-centric mechanisms for testing therapeutic patent validity. These court-centric mechanisms appear in the Hatch-Waxman Act of 1984 ("Hatch-Waxman"),[10] and the Biologics Price Competition and Innovation Act of 2010 (BPCIA), which was eventually passed as a portion of the Affordable Care Act.[11]

Indeed, some biopharmaceutical patentees argue that the PTAB improperly disturbs these court-centric mechanisms. Critics have sought legislation that exempts biopharmaceutical patents from PTAB review.[12] Critics have also lauded the PTAB's increased refusal to institute proceedings,[13]

(Sept. 12, 2016), https://onpointanalytics.com/pharma/patent-proliferation; *see also* Robin Feldman, *May Your Drug Price Be Evergreen*, J.L. & BIOSCIENCES 590, 631 (2018) (documenting increase in quantity of "added" patents per drug between 2005 and 2015). These single digit figures are nonetheless several orders of magnitude smaller than those found for products in the information and communications technology industries. Indeed, the number of patents per small-molecule drug can be more than an order of magnitude smaller than the number of patents per large-molecule biologic, particularly for blockbuster biologics. *See, e.g.*, Victor L. van de Wiele, Aaron S. Kesselheim & Ameet Sarpatwari, *Barriers to US Biosimilar Market Growth: Lessons from Biosimilar Patent Litigation*, 40 HEALTH AFFS. 1198, 1201 (2021) (identifying 80 to over 100 patents covering biologics like Roche/Genentech's bevacizumab (Avastin), rituximab (Rituxan), trastuzumab (Herceptin) and Abbvie's adalimumab (Humira)).

9. For present purposes, we assume that accurate application of existing patent validity standards will generally incentivize socially desirable innovation.

10. Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in 21 U.S.C. §§ 301, 355, 360cc).

11. Pub. L. No. 111-148, 124 Stat. 119–1025 (codified as amended in scattered sections of 42 U.S.C.).

12. In 2018, Senator Orrin Hatch, one of the namesakes of Hatch-Waxman, proposed legislation that exempted biopharmaceutical patents from generic or biosimilar challenge by barring those firms from challenging patents at the PTAB. *See* Ryan Davis, *PTAB's Doors Would Be Closed to Generics Under Hatch Bill*, LAW360 (June 20, 2018), https://www.law360.com/ip/articles/1054276/ptab-s-doors-would-be-closed-to-generics-under-hatch-bill (discussing proposed Hatch-Waxman Integrity Act of 2018, S. 3738, 115th Cong. (2018)).

13. *See* Christina Schwarz & Laura Fishwick, *PTAB Trends: More Orange Book Patents are Surviving the "Death Squad,"* IP WATCHDOG (Jan. 23, 2019), www.ipwatchdog.com/2019/01/23/ptab-trends-orange-book-patents-surviving-death-squad (discussing the positive reaction of patent owners to this development).

assuming (erroneously, as it happens)[14] that this development also applies to biopharmaceutical patents.

Conversely, generic firms and consumer advocates argue that district courts lack expertise in evaluating biopharmaceutical patents. In this view, an expert body, such as the PTAB, that polices erroneously issued biopharmaceutical patents is necessary to ensure that the exclusivity duration provides commensurate innovation-benefit to the public.[15] These groups express alarm at the possibility of a diminished role for the PTAB. Indeed, the Second Look at Drug Patents Act of 2020,[16] a bipartisan bill co-sponsored by Senators Patty Murray and John Cornyn, would require the Federal Drug Administration (FDA) and the U.S. Patent and Trademark Office (USPTO) to work together, notifying the public about small-molecule patents blocking generic entry that could be challenged through PTAB review.

These arguments have, however, often played out in a relative absence of data regarding the PTAB's involvement in biopharmaceutical patents, particularly relative to the district courts and to other types of patents. As one step in addressing the data gap, this Article focuses on patents that cover FDA-approved small molecules. Because the majority of these small-molecule patents are listed on the transparent, publicly accessible, central repository known as the Orange Book (OB),[17] these patents represent a more tractable empirical target than biologics patents.[18] Even for OB patents, however, much

14. In ongoing work, one of the Article's authors (SV) found that the PTAB's emerging framework of discretionary denials under the so-called *NHK-Fintiv* doctrine has *not* been applied to small-molecule patents to any meaningful degree. *See generally* NHK Spring Co. Ltd. v. Intri-Plex Techs. Inc., No. IPR2018-00752, 2018 WL 4373643 (P.T.A.B. Sept. 12, 2018) (precedential); Apple Inc. v. Fintiv Inc., No. IPR2020-00019, 2020 WL 2126495 (P.T.A.B. Mar. 20, 2020) (precedential). Specifically, in the total population of institution decisions decided under the *NHK-Fintiv* framework, just under 3.5% (16 out of 461) involved a patent on an FDA-approved small molecule, and only 0.65% (3/461) both involved this type of small-molecule patent *and* resulted in a discretionary *denial* under *NHK-Fintiv*. Instead, as this Article discusses, the roots of the PTAB's modest role lie elsewhere. Saurabh Vishnubhakat, *Patent Office Discretion and Agency Underreach* (working paper on file with author).

15. *See, e.g.*, Brief of the Coalition Against Patent Abuse as Amicus Curiae in Support of No Party 8–21,United States v. Arthrex, Inc., 141 S. Ct. 1970 (2021) (Nos. 19-1434, -1452, -1458) (arguing that the case studies presented show that PTAB decisions are more scientifically expert than district court decisions and are also correlated with generic entry and reduced prices).

16. S. 4253, 116th Cong. (2020).

17. The OB does not, however, list patents on non-FDA approved uses of metabolites, intermediates, and "process[es]" (i.e., manufacturing processes). 21 C.F.R. § 314.53(b)(1) (2019).

18. Although this Article focuses on small molecules, Part V, *infra*, does compare and contrast the Hatch-Waxman regime with the biologics regime, bringing in empirical findings on litigated biologics patents.

of the empirical discussion thus far has focused on litigation outcomes at the PTAB or the overlap in PTAB and district court litigation.[19]

This Article uses a somewhat different lens, assessing OB patents as a whole. The primary lens focuses further upstream than litigation outcomes and is somewhat less subject to selection effects. Specifically, this Article identifies all relevant OB-listed patents and can therefore drill down on parties' ex ante decisions to litigate OB patents and to litigate different types of OB patents in different fora.[20]

In general, this Article finds that, although OB patents are highly litigated, there are significant[21] differences in OB and non-OB patent litigation at the PTAB and in district court. For example, although most OB and non-OB patents challenged at the PTAB are also litigated in district court, the percentage of patents litigated solely at the PTAB is significantly lower for OB patents than for non-OB patents. The rate of PTAB challenge for OB patents with a parallel challenge in district court is significantly lower than for non-OB patents with a parallel district court challenge.

This Article discusses the extent to which these differences may reflect the influence of the Hatch-Waxman incentive scheme for challenging patents. This scheme provides both challengers and patentees incentives to stay in district court, even if administrative proceedings are cheaper and more accurate from a societal perspective.[22]

In addition, the literature has organized OB patents by scientific categories. This Article follows other scholars in differentiating between "primary" patents on active ingredients and "secondary" patents on methods of use,

19. *See, e.g.*, Michelle Ankenbrand & Jason Repko, *Orange Book Patent/Biologic Patent Study and District Court Pharma Litigation Study*, U.S. PAT. AND TRADEMARK OFF. (July 18, 2019), https://www.uspto.gov/sites/default/files/documents/Boardside%20Chat%20-%20Orange%20Book%20and%20Biologics%20%282019-07-11%29-IQ_807521-Final.pdf.

20. This Article takes the patent as its unit of analysis. A companion paper, Erik Hovenkamp, Jorge Lemus, Arti Rai, & Saurabh Vishnubhakat, *Drug Settlements and Generic Entry: Has the PTAB Made a Difference*, __ NATURE BIOTECHNOLOGY __ (forthcoming) examines what effect, if any, the PTAB is having at the drug level—specifically, on the timing of generic entry relative to originator product launch. That paper builds on prior work done by two of the authors (EH and JL) on the role of settlements at the PTAB. *See* Erik Hovenkamp & Jorge Lemus, *Delayed Entry Settlements at the Patent Office*, 54 INT'L REV. L. & ECON. 30 (2018) (investigating whether monopolist-patentees and their prospective rivals are using the PTAB as a platform for striking settlements that delay the rivals' entry).

21. By "significant" we mean statistically significant at the $p < 0.05$ level. *See infra* Part IV.

22. *See infra* Section II.A.

formulations, or other ancillary features.[23] Because secondary patents may be filed after the primary patent, they can extend a drug's patent life.[24] Moreover, secondary patents may extend patent life unduly because they are may be less scientifically innovative, and hence more likely to be invalid under conventional standards of patent law,[25] compared to primary patents. Critics also charge that even when secondary patents don't extend patent life,[26] they expand the roster of patents that potential generic entrants have to address.

Past analyses of the PTAB's role that differentiate by category of OB patent have either not reported their methodology for categorization, or have relied on patentees' self-reported categorization necessary to comply with FDA regulations. In contrast, we perform our own categorization and compare it to patentees' self-reported categorization. We then use our categorization to determine relative rates of litigation at the PTAB and the district court for different scientific categories of OB patents.

The calculations reveal that active-ingredient patents are significantly less likely to be challenged, whether at the PTAB or in district court, than secondary patents. Additionally, we do not find any significant difference between challenge rates of different types of patents at the PTAB compared to district court.

Furthermore, unlike the prior literature on the PTAB, this Article codes patents not only by scientific category but also by whether they represent an original-patent filing or a continuation. Specifically, the Article separates out continuations because such patents do not, at least in principle, extend a patent's life beyond the term allowed by the parent patent application. Critics argue, however, that continuations can be used to undermine the notice

23. *See, e.g.*, Amy Kapczynski, Chan Park, & Bhaven Sampat, *Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of "Secondary" Pharmaceutical Patents*, 7 PLOS ONE 1 (2012); C. Scott Hemphill & Bhaven N. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 31 J. HEALTH ECON. 327, 329–30 (2012) (using the terminology of patent with at least one "active ingredient" claim to denote what this Article calls a primary patent).

24. Kapczynski et al., *supra* note 23, at 2.

25. Particularly at the international level, there is vigorous debate on whether patent law should treat secondary patents as a different class from other patents. *See generally* Christopher Holman, Timo Minssen, & Eric M. Solovy, *Patentability Standards for Follow-on Pharmaceutical Innovation*, 37 BIOTECHNOLOGY L. REPT. 131 (2018) (arguing that because secondary patents can often be innovative, they should not be treated differently). Because the Article assumes the application of conventional legal standards, this issue is not addressed. In other work, one of the authors (AKR) endorsed nonobvious secondary patents that meet conventional patent law standards. *See* Arti K. Rai & Grant Rice, *Use Patents Can be Useful*, 6 SCI. TRANSLATIONAL MED. 248 (2014).

26. As discussed herein, see *infra* Section III.C, when secondary patents are filed as continuations, they do not extend patent life.

function of the parent patent by extending patent scope beyond that of the parent.[27] Continuations also increase search costs for generic entrants by adding to the total roster of patents.

This Article finds that continuations make up a substantial proportion of secondary OB patents. And continuation patents on non-active ingredients are significantly more likely to be challenged than either non-continuations or continuations on active-ingredient patents.

Finally, the regression framework, which examines correlations between litigation frequency and scientific category, continuation status, and small-entity status, is generally consistent with the results achieved through descriptive statistics. For example, even controlling for potential confounding factors such as examiner art unit and issue year, method-of-use patents and continuation patents are more likely to be challenged in district court. However, the regression does not find these effects at the PTAB.

Notably, small-entity status is negatively correlated with likelihood of challenge, both at the PTAB and in district court. To the extent that policymakers are concerned about small-entity patent owners being particularly vulnerable to PTAB challenge, this Article indicates that such concern may be misplaced—small-entity status is correlated with a reduced likelihood of challenge.

In sum, this Article shows that the PTAB's role in adjudicating OB patents has been substantially more modest than for non-OB patents. Moreover, there is little evidence that the PTAB targets active-ingredient patents disproportionately. However, our regression framework does indicate that, while method-of-use and continuation patents are more likely to be challenged in district court than active-ingredient patents, this is not the case at the PTAB.

Relying on this data, the Article concludes by discussing paths policymakers could take if they were interested in a more active role for the PTAB in policing the validity of OB patents. The Article also discusses policy choices between ex post review by the PTAB or the courts, and more rigorous ex ante review.

Part II of the Article provides the statutory and regulatory background for the strategic positioning adopted by originators and generic entrants. It also discusses the existing literature. Part III presents data collection, classification, and empirical strategy. Part IV presents results. Part V provides a discussion and some conclusions.

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27. *See generally* Mark A. Lemley & Kimberly A. Moore, *Ending Abuse of Patent Continuations*, 84 BOSTON U. L. REV. 63 (2004) (examining efforts undertaken to control the problems associated with continuation patents).

II. BACKGROUND

A. STATUTORY AND REGULATORY

The AIA, whose relevant provisions came into force on September 16, 2012, implemented several new mechanisms to conduct post-grant administrative review of patents. As noted, *supra* Part I, Congress determined that post-grant administrative review had the potential to correct errors more cheaply and accurately than district court litigation.

Moreover, absent a relatively cheap forum for challenging validity, even infringing defendants that thought a patent was weak might not expend resources to challenge it. This is because Supreme Court case law builds asymmetric incentives to litigate validity into patent doctrine. Under estoppel doctrine in patent law, a challenger that successfully invalidates a patent provides a public good: the challenger not only benefits, but so do all other potential competitors, who can free ride off the challenger's efforts.[28] Conversely, the challenger who loses is uniquely estopped from challenging the patent again, while the patent remains in force.[29] The result is fewer patent validity challenges than might be socially optimal, just as any public good is likely to be undersupplied. Although some of this public good problem may also exist in the administrative context,[30] the possibility of collective action through joinder and the reduced cost of administrative proceedings likely reduces its scale.[31]

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28. *See* Blonder Tongue Laby's, Inc. v. Univ. of Ill. Found., 402 U.S. 313, 350 (1971) (holding that a finding of patent invalidity creates nonmutual-defensive collateral estoppel, such that a patent that is invalid against one party is invalid against the world).

29. A separate statutory change created by the AIA arguably exacerbates this problem by restricting lawsuits against individual accused infringers, thereby making it harder to form joint defense agreements. *See* 35 U.S.C. § 299. The ability to form such joint defense agreements is contested even where accused infringers are, indeed, joined as co-defendants. *See* Joseph Scott Miller, *Joint Defense or Research Joint Venture? Reassessing the Patent-Challenge-Bloc's Antitrust Status*, 2011 STAN. TECH. L. REV. 5, 16–19 (2011) (arguing that such agreements are proper under antitrust law). The reduced likelihood of such co-defendant joinder under the AIA makes joint-defense agreements even harder to justify and less likely to arise.

30. *See* John R. Thomas, *Collusion and Collective Action in the Patent System: A Proposal for Patent Bounties*, 2001 U. ILL. L. REV. 305, 308–09 (2001). *But see* Stuart M. Benjamin & Arti K. Rai, *Who's Afraid of the APA? What the Patent System Can Learn from Administrative Law*, 95 GEO. L.J. 269, 323–27 (2007) (noting that administrative review relying on *Chevron* deference by the courts, rather than estoppel against the patent challenger, could substantially reduce collective-action problems).

31. *See* Vishnubhakat et al., *supra* note 2, at 74–75, 102–03 (discussing the incentives and empirically observed patterns of strategic joinder between previously sued and non-sued parties and across technology sectors).

This Article focuses on inter partes review (IPR), which has proved, by far, to be the most popular type of post-grant administrative review. A petition for IPR can be filed at any time nine months after patent issue and is also available retrospectively against patents issued prior to the AIA. To be granted institution, the petition must establish "a reasonable likelihood that the requester would prevail with respect to at least 1 of the claims challenged in the request."[32] The PTAB decides on institution within six months of the petition filing[33] and makes a final decision on validity no more than one year after initiation of post-grant review.[34]

Notably, IPRs have no standing requirement. Accordingly, they are available to anyone other than the patent holder, so long as the challenger meets two conditions: 1) it has not previously challenged the patent in a civil action;[35] and 2) if the challenger has been sued in district court, it files an IPR within one year of being served with the district court complaint.[36]

As these limits on petitioning indicate, Congress intended the IPR process to interact efficiently with district court litigation. District courts, meanwhile, have the discretion to stay existing infringement litigation pending the outcome of an IPR.[37] In determining whether to issue a stay, courts generally consider three factors: 1) the potential for prejudice or tactical disadvantage against the nonmoving party; 2) how far along the district court litigation is; and 3) the likelihood a stay could simplify the pending litigation.[38]

The AIA also intersects with two specific statutory schemes challenging the validity of biopharmaceutical patents in district court—Hatch-Waxman and the BPCIA. Hatch-Waxman, enacted in 1984, covers small molecules, while the BPCIA, enacted in 2010, governs large-molecule biologics, which are more scientifically complex.[39]

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32. 35 U.S.C. § 314(a).

33. *See* U.S. PAT. & TRADEMARK OFF., AIA TRIALS 7 (2019),https://www.uspto.gov/sites/default/files/documents/What%20are%20AIA%20trials%20for%20website%2010.24.19.pdf.

34. 35 U.S.C. § 316(a)(11).

35. *Id.* § 315(a)(1). A counterclaim does not count as a civil action. *Id.* § 315(a)(3).

36. *Id.* § 315(b).

37. *See, e.g.*, Nichea Corp. v. Vizio, Inc., 2018 WL 2448098, at *3 (C.D. Cal. May 21, 2018).

38. *See id.* at *1. However, one of the authors of the AIA recently concluded that district courts need to be more aggressive in granting stays, otherwise efficiencies will not be realized to the extent originally contemplated. *See* Restoring the America Invents Act, S. 2891, 117th Cong. (2021).

39. *See generally* W. Nicholson Price II & Arti K. Rai, *Manufacturing Barriers to Biologics Competition and Innovation*, 101 IOWA L. REV. 1023 (2016) (examining the problem of secret biologics manufacturing processes).

Both Hatch-Waxman and the BPCIA allow competitors to rely on clinical trial data generated by a branded-originator firm. Hatch-Waxman also requires that the branded-drug manufacturer seeking FDA approval submit to the agency a list of all patents claiming the drug or a method of using such drug "with respect to which a claim of patent infringement could reasonably be asserted" if an unlicensed person manufactured, used, or sold the drug.[40] These patents are then listed on the OB.

The FDA has interpreted Hatch-Waxman to mean that branded firms must list the following categories of patents on the OB: active-ingredient patents (which it calls "drug substance" patents); formulation and composition patents (which it calls "drug product" patents); and method-of-use patents.[41] The OB annual edition contains all patents active as of December 31 of the preceding year that branded firms assert cover their marketed drugs. For example, the 2012 annual edition contains all patents active as of December 31, 2011.

To market its drug, a generic firm must file a so-called Paragraph IV certification, stating that all relevant OB patents are invalid or not infringed.[42] Because this certification creates an act of constructive infringement, the originator is entitled to sue in district court within forty-five days. The first generic entity that files a Paragraph IV certification is entitled to a 180-day period of exclusive marketing.[43] Notably, this 180-day period is intended to incentivize generic firms to challenge an invalid patent, providing a public good.[44] As currently construed, however, the 180-day period remains with the challenger even if the challenger decides to settle, thereby blocking generic entry until 180 days after another generic firm invalidates the patent.[45]

40. 21 U.S.C. § 355 note (Any Information or Documentary Material that May Have Been Filed Pursuant to The Pharmaceutical Agreement Notification). Patents on manufacturing, packaging, intermediates, and metabolites are not supposed to be submitted. The FDA does not, however, audit any OB listings. To the contrary, in the more than thirty-five years since the enactment of Hatch-Waxman, the FDA has disavowed performing anything other than a ministerial role with respect to patents. For a recent statement of this disavowal, see Listing of Patent Information in the Orange Book, 85 Fed. Reg. 33169, 33170 (2020).

41. 21 C.F.R. § 314.53 (2019).

42. *See Paragraph IV Drug Product Applications: Generic Drug Patent Challenge Notifications*, FDA (Apr. 20, 2021), https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/paragraph-iv-drug-product-applications-generic-drug-patent-challenge-notifications.

43. *Id.*

44. Thomas, *supra* note 30, at 336–37.

45. For this reason, critics argue that the 180-day incentive does not currently promote competition. *See* C. Scott Hemphill & Mark A. Lemley, *Earning Exclusivity: Generic Drug Incentives and the Hatch-Waxman Act*, 77 ANTITRUST L.J. 947, 953–55 (2011).

Moreover, challenging an OB patent solely through the IPR procedure does not confer any exclusivity on the challenger.

Once the generic manufacturer files a Paragraph IV certification, the patent owner can not only to sue for patent infringement but also receives an automatic 30-month stay of the generic drug's FDA approval process, pending district court consideration of the suit.[46] The stay can be terminated only if the district court enters judgment saying the patent claims at issue in the suit are invalid or not infringed.[47]

The automatic 30-month stay creates a challenge for would-be generic entrants that hope to use the PTAB's relatively expedited procedures. A PTAB determination of invalidity lifts a stay only if the district court chooses to enter judgment for the defendant.[48] Moreover, under current case law, the district court is only required to enter judgment if PTAB determinations are affirmed by the Court of Appeals for the Federal Circuit, the court with exclusive appellate jurisdiction over patent claims.[49] Likewise, the 180-day marketing-exclusivity incentive attaches only if the patent challenger makes itself vulnerable to a district court infringement suit via a Paragraph IV certification.[50]

B. EXISTING LITERATURE

The existing OB-patent literature that examines choice of litigation forum focuses on PTAB outcomes and whether OB patents are also being litigated in district court. Studies find that OB patents challenged at the PTAB generally fare better than non-OB patents. A USPTO 2019 study, examining PTAB litigation from September 16, 2012 to November 30, 2018, found that the agency instituted review of petitioner challenges at a rate of 64% for OB patents, relative to an overall institution rate of 66%.[51] The study also found that, in cases that made it to a final written decision, 52% of instituted claims were held to be patentable—i.e., were vindicated.[52] This compared with only 19% of instituted claims held patentable overall.[53] Similarly, a 2018 Ropes & Gray study analyzing from September 16, 2012, to May 1, 2018, determined

46. FDA, *supra* note 42.
47. 21 U.S.C. § 355(j)(5)(B)(iii)(I).
48. *Id.*
49. *See* Fresenius USA, Inc. v. Baxter Int'l, Inc., 721 F.3d 1330, 1334 (Fed. Cir. 2013) (holding that Federal Circuit affirmance of USPTO claim cancellation "extinguishes the underlying basis for suits based on the patent").
50. 21 U.S.C. § 355(j)(5)(B)(iv).
51. Ankenbrand & Repko, *supra* note 19, at 18.
52. *Id.* at 20.
53. *Id.*

that, for OB patents, at least one challenged claim in the patent survived in 51% of final written decisions.[54] In contrast, for non-OB patents, at least one challenged claim survived in only 35% of final written decisions.[55] A 2019 study from September 16, 2012, and April 24, 2017, determined that, of the 198 OB patents challenged, only 25 patents had all challenged claims invalidated.[56]

Analysts also find that OB patents litigated at the PTAB are generally also litigated in district court. For example, the 2021 USPTO study of OB patents determined that of 91% of OB patents challenged at the PTAB were also challenged in district court.[57]

Some analyses also look at different categories of patents. For example, one study determined that, of the twenty-five patents for which all challenged claims were invalidated at the PTAB, only two were listed by the branded firm as active-ingredient patents on the OB.[58] The Ropes & Gray analysis found that at least one challenged claim in active-ingredient patents generally survived, whether they were challenged at the PTAB or in district court.[59] Meanwhile, formulation and method-of-treatment claims were less likely to survive, though somewhat more likely at the PTAB than in district court.[60] The Ropes & Gray study did not, however, discuss its methodology for classifying patents.

Finally, although the PTAB is still a relatively young institution, analysts have looked at litigation trends over time. According to USPTO data, both absolute numbers and percentages of petitions challenging OB patents peaked in fiscal years 2015 and 2016 (at 133 and 127, or 7% and 7.5% of total AIA petitions). The 2015–16 period was arguably a one-time blip, however, as certain hedge funds thought at the time (incorrectly, as it happened) that simply filing a challenge at the PTAB might result in stock price drops that they could exploit by shorting the stock.[61] Both before and after that time

54. Filko Prugo, Scott McKeown & Jon Tanaka, *Insight: Orange, Purple Book Patentees Hone PTAB Survival Skills*,17 BNA PAT. TRADEMARK & COPYRIGHT J. 0, 2 (2018).

55. *Id.*

56. Jonathan J. Darrow, Reed F. Beall, & Aaron S. Kesselheim, *The Generic Drug Industry Embraces a Faster, Cheaper Pathway for Challenging Patents*, 17 APPLIED HEALTH ECON. & HEALTH POL'Y 47, 51 (2019).

57. Ankenbrand & Repko, *supra* note 19, at 11.

58. Darrow et al., *supra* note 56, at 51.

59. Prugo et al., *supra* note 54, at 2.

60. *Id.*

61. *See* Joseph Walker & Rob Copeland, *New Hedge Fund Strategy: Dispute the Patent, Short the Stock*, WALL ST. J. (Apr. 7, 2015, 7:24 PM), https://www.wsj.com/articles/hedge-fund-manager-kyle-bass-challenges-jazz-pharmaceuticals-patent-1428417408 (discussing practice

period, PTAB use has been substantially more modest, covering only about 2–4% of all AIA petitions.[62]

III. SOURCES OF DATA AND DATA COLLECTION

A. COLLECTION AND CLASSIFICATION

We began by establishing a dataset of all patents listed on the OB during any of the ten annual editions published between January 2010 and January 2019.[63] From 2010 to 2016, we relied on OB data extracted by Professor Heidi Williams and made publicly available on the National Bureau of Economic Research's (NBER) website.[64] From 2017 to 2019, we used Professor Williams's procedure to extract relevant information from PDFs of OB editions generously provided to us by Professor Erika Lietzan.

This resulted in a dataset of 5,842 unique patents, which we compared to classifications for OB patents that we purchased from a third-party vendor (PharmaIntelligence/Medtrack). For two reasons, one involving data limitations and the other involving limitations of the vendor's approach, we substantially reworked the vendor's approach.[65]

Our approach[66] first looks at all of the claims in a patent. If at least one claim is directed to[67] the two-dimensional structure of a chemical that was not

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of filing and publicizing patent challenges against pharmaceutical companies while also betting against their shares).

62. U.S. PAT. & TRADEMARK OFF., PTAB ORANGE BOOK PATENT/BIOLOGIC PATENT STUDY 3 (2021), https://www.uspto.gov/sites/default/files/documents/PTABOBbiologicpatentstudy8.10.2021draftupdatedthruJune2021.pdf.

63. As we discuss below, for analyses that involved a comparison of PTAB litigation with district court litigation, we needed only a subset of this data.

64. *Orange Book Patent and Exclusivity Data—1985–2016*, NAT'L BUREAU ECON. RSCH., https://www.nber.org/research/data/orange-book-patent-and-exclusivity-data-1985-2016 (last visited Nov. 11, 2021).

65. For example, at the outset, we determined that about 555 (10%) of patents in our OB patent dataset had not been classified by the vendor. Further, our detailed quality check of the vendor classifications determined that, although the classifications generally appeared sound for product and method-of-use patents, the vendor's distinctions drawn to create other classes were far less clear. Accordingly, one of the authors (AKR) and several research assistants with advanced degrees in the biochemical sciences iterated over multiple samples of the 5,842 unique patents. Through such iteration, we were able to identify a relatively straightforward approach that produces replicable classifications. We used this approach to classify the 555 unclassified patents and to reformulate the vendor's classifications.

66. Our approach is based on an approach taken, and validated, by C. Scott Hemphill and Bhaven N. Sampat in several articles on secondary patenting. *See, e.g.*, *supra* note 23.

67. By "directed to," we mean the claim is to the product. Claims to methods of use or formulation can sometimes include chemical structure. This chemical structure is, however, not the invention to which the claim is "directed."

disclosed in prior non-provisional applications, then we classify the patent as being directed to an active ingredient. We categorize such patents as product patents even if the patent also includes claims not directed to a product. The benefit of this approach to product patent classification is that it results in a bright-line rule with a clear application. Our approach is also consistent with the conventional understanding that patents containing active-ingredient claims may include claims drawn to other features.[68] Conversely, when a patent does not include any claim directed to a chemical compound, it cannot reasonably be viewed as anything other than secondary.

For secondary patents, one specific category of interest was new method-of-use patents. Method-of-use patents differ from other patent categories because Congress has permitted generic firms to use a limited drug label (colloquially known as a "skinny label") to avoid infringing patents on new uses found by originators. Skinny labeling is available as a path to generic entry so long as the drug has already been approved by the FDA for one use, and the patent that is blocking generic entry is the additional method-of-use patent with a later expiration date.[69] Accordingly, such patents have not always, at least historically,[70] blocked generic entry like other types of patents. If the patent did not contain any product claims, and the majority of claims were directed to a method of use, then we classified it as a method-of-use patent.

Finally, the literature discusses a variety of other types of secondary patent claims, including: claims directed to dosage forms or other formulations; salts; enantiomers; esters; and polymorphs or other crystalline structures. These types of patents can extend patent life on a drug. Additionally, in cases where the patent covers a variation on a prior approved drug that requires the filing of an additional "new drug application" (NDA) at the FDA, a secondary patent can undergird the practice of "product hopping."[71]

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68. Hemphill & Sampat, *supra* note 23, at 329 ("[A] patent with both active ingredient and non-active ingredient claims counts as an AI patent.").

69. *See* Arti K. Rai, *Use Patents, Carve-Outs, and Incentives: A New Battle in the Drug-Patent Wars*, 367 NEW ENG. J. MED. 491, 491 (2012) (discussing FDA carve-outs for patented uses from the generic label). Skinny labeling is not possible if the use patent covers the only FDA-approved use for the drug.

70. Recent Federal Circuit decisions have called into question the viability of skinny labeling. *See, e.g.*, GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 7 F.4th 1320 (Fed. Cir. 2021) (rehearing).

71. A firm engages in product hopping when it moves its customers from one branded drug that will shortly face generic entry due to patent expiry to a branded variation that has additional remaining patent life. *See generally* Michael A. Carrier & Steve D. Shadowen, *Product Hopping: A New Framework*, 92 NOTRE DAME L. REV. 167, 171 (2016) (describing benefits of product hopping).

However, we determined that these "other" claims were often found together in patents. Further, we were not particularly concerned with these distinctions among the various categories. Accordingly, we classified patents that predominantly contained these claims, and did not contain a product claim, as "secondary-other."

In contrast to our study, some of the existing analyses rely on patentees' self-reported OB classifications. To compare our analyses to those existing analyses, we compared our classifications against the OB classifications. As noted earlier, the FDA instructs applicants to classify their OB patents into one or more of three categories: "drug substance" (DS); "drug product" (DP); or "method-of-use" (UC). Somewhat confusingly for present purposes, the FDA states that the DS label denotes patents on active ingredients (what we are calling "product" patents).[72] Meanwhile, the DP label denotes a finished dosage form, such as a tablet, capsule, or solution (what we are calling "secondary-other" patents).[73]

Accordingly, the OB allows eight potential permutations for a given patent.[74] Moreover, as shown in Table 1, OB patent owners avail themselves of all available permutations, including the "uninformative" permutation of DS=0, DP=0, and UC=0. To some extent, this phenomenon arises because patents contain claims directed to different types of subject matter. But a casual approach to patent identification may also be encouraged by the FDA's longstanding position that it does not audit in any way the information that is put on the OB.[75]

Our investigation further determined that a given patent was sometimes classified in the OB not simply into one of the eight permutations but into several conflicting permutations. Once we limited ourselves to unique permutations, we were left with 5,495 patents. We could match all but eleven of these patents with our classifications. Table 1 shows the comparison for the 5,484 remaining patents.

72. 21 C.F.R. § 314.3(b) (2016).

73. *Id.*

74. *See infra* Table 1.

75. Rebecca S. Eisenberg & Daniel A. Crane, *Patent Punting: How FDA and Antitrust Courts Undermine the Hatch-Waxman Act to Avoid Dealing with Patents*, 21 MICH. TELECOMM. & TECH. L. REV. 197, 211 (2015).

Table 1. Comparison of Our Classification with OB Classifications

alt	product	method-of-use	other	Total
DS=1 & DP=1 & UC=1	254	21	91	366
DS=1 & DP=1 & UC=0	212	2	155	369
DS=1 & DP=0 & UC=1	20	9	10	39
DS=1 & DP=0 & UC=0	105	1	85	191
DS=0 & DP=1 & UC=1	10	121	625	756
DS=0 & DP=1 & UC=0	17	37	1,571	1,625
DS=0 & DP=0 & UC=1	38	1,558	228	1,824
DS=0 & DP=0 & UC=0	46	20	248	314
Total	702	1,769	3,013	5,484

In general, the heavy use of multiple classifications by OB-patent owners meant that our approach yielded a smaller number of patents in each category. For active-ingredient patents, one additional reason for the smaller number may be that FDA regulations suggest that patents on polymorphs of the active ingredient are also "drug substance" patents.[76] In contrast, our approach counts patent claims drawn to polymorphs as "secondary-other."

As Table 1 shows, 39.8% (374/965) of patents with a DS=1 classification in the OB are not classified as active-ingredient patents under our approach. Meanwhile, only 15.8% (111/702) of patents classified as active-ingredient patents fail to secure a DS=1 label. The overlap between the two approaches, constituting 591 patents, is substantial but far from complete.

Most of the patents (88.1%) (1,558/1,769) that we classified as method-of-use patents were designated as only method-of-use in the OB. On the other hand, the OB encompassed a much larger total number of patents (2,985) in the method-of-use category.

With DP=1, the numbers tended to be most similar between the categorizations. A total of 3,116 patents were listed as DP=1, and a total of 3,013 we classified as "secondary-other." Moreover, 2,442 patents are classified as both DP=1 in the OB and "secondary-other."

In general, our approach errs conservatively as to what constitutes an active-ingredient patent. By contrast, self-categorization by patentees on the

76. *See* 21 C.F.R. § 314.53 (2019) (indicating that a polymorph may be "the same active ingredient"); *see also* Listing of Patent Information in the Orange Book, 85 Fed. Reg. 33169, 33170–71 (discussing "drug substance patents that claim only a polymorph of the active ingredient").

OB listings may be overinclusive, particularly if the goal is to divide to conform to patent practice—that is, the first patent filed by the originator typically claims the active ingredient, though it may also contain claims to methods of use and perhaps even formulations. Additionally, in at least one circumstance, the FDA's regulations encourage overinclusion by suggesting that patents on polymorphs should be classified as active-ingredient patents.

B. LITIGATION DATA

We drew our data on PTAB litigation from Unified Patents and our data on district court case resolution from Lex Machina. The Unified Patents data[77] are publicly available and the Lex Machina data[78] are generally accessible upon request to academics. Additionally, all replication data and code for the Article are available at Harvard Dataverse.[79] Accordingly, our results are amenable to replication.

In the remainder of the Article, we focus on patents litigated either at the PTAB, in district court, or both. Because defendants could file a PTAB challenge only after the AIA went into effect, we focus on district court cases in Lex Machina filed on or after September 16, 2011, and through December 31, 2019. We similarly restrict our PTAB data to petitions filed since the PTAB began functioning on September 16, 2012, and through December 31, 2019.

Although our litigation data are highly granular with respect to date, our OB data are collected on an annual basis. Accordingly, we have a mismatch: we must either start with an OB edition (2011) that includes patents that expired before September 16, 2011, or with an annual edition (2012) that omits patents that expired between September 16, 2011, and December 31, 2011. Because the 2012 edition hews more closely to our desired time period, we run our litigation analyses starting with that edition. By dropping the 2010 and 2011 editions, we reduce the number of OB patents analyzed to 4,718.

77. *Free Patent Dispute Updates*, UNIFIED PATS., https://www.unifiedpatents.com/docket (last visited Nov. 17, 2021).

78. *Public Interest*, LEX MACHINA, https://lexmachina.com/public-interest (last visited Nov. 17, 2021).

79. Arti K. Rai, Saurabh Vishnubhakat, Jorge Lemus, & Erik Hovenkamp, *Replication Data for: Post-Grant Adjudication of Drug Patents: Agency and/or Court?*, HARV. DATAVERSE, https://doi.org/10.7910/DVN/YCMKVU (last visited Nov. 17, 2021).

C. CONTINUATION CLASSIFICATION

We also divided patents by whether they issued from a continuation application.[80] The USPTO prosecution history of each application contains its continuity record, including any earlier-filed ("parent") applications to which it claims priority as well as any later-filed ("child") applications that themselves claim priority to it.[81] Although continuation applications do not, at least in principle, extend the effective life of a patent beyond the parent patent application's term. Critics argue that continuations can be used to undermine the notice function of the parent patent by improperly extending patent scope beyond that of the parent.[82] Continuations also add to the total roster of patents with which a potential generic entrant must contend.

The use of continuations is part of a broader set of practices built around tradeoffs in patent priority, term, and breadth/scope. There is a tradeoff between the pursuit of priority by being first in time and the desire to maximize both the scope of patent claims and the patent's term. In general, the USPTO allocates priority from the patent application's filing date,[83] starting the 20-year clock to when the patent, if it is issued, will eventually expire.[84]

Meanwhile, patent scope is supposed to be limited by the application's disclosure, which adequately enables and describes all subject matter covered by the claims.[85] Thus, even if an applicant makes broadening amendments to claims, the claims cannot, at least in principle, exceed what can be properly supported by the disclosure, which is fixed at the filing date and cannot be amended.

Continuation practice relies on this dynamic by allowing an application to enjoy the same priority as the parent application. Because the continuation application is legally assigned the same "effective" filing date as the parent

80. We did not count divisional applications as continuations. Unlike true continuations, divisional applications arise when the USPTO determines that more than one invention is claimed in a given application. 35 U.S.C. § 121.

81. The prosecution history for a patent can be obtained by visiting *Public Patent Application Information Retrieval (PAIR)*, U.S PAT. & TRADEMARK OFF., https://portal.uspto.gov/pair/PublicPair (last visited Nov. 17, 2021).

82. *See*, *e.g.*, Lemley & Moore, *supra* note 27 (examining efforts undertaken to control the problems associated with continuation patents); Mark A. Lemley, *Ten Things to Do About Patent Holdup of Standards (And One* Not *To)*, 48 B.C. L. REV. 149 (2007) (same as applied to standard patents); Gary C. Ganzi, *Patent Continuation Practice and Public Notice: Can They Coexist?*, 89 J. PAT. & TRADEMARK OFF. SOC'Y 545 (2007) (discussing reasons supplied by patent owners on why continuations should be issued and the effect of those reasons on public notice).

83. *See* 35 U.S.C. § 119.

84. *Id.* § 154(a)(2).

85. *Id.* § 112(a).

application,[86] the later-filed application avoids intervening technological developments that might otherwise defeat patentability.

In principle, this legal fiction is permitted only because the later-filed application must also contain the same disclosure—and, hence, the same outer limit on patent scope—as the parent application. However, if the USPTO does not sufficiently enforce the statutory disclosure requirements of enablement[87] and written description,[88] an applicant can enjoy the benefit of earlier priority, claiming more than the earlier disclosure supports, to the detriment of public notice and the public domain.[89]

We include in our analysis not only full continuations but also continuations-in-part (CIPs), which can add new material, though that material is not given the same priority date as the parent application. We choose to treat CIPs in the same category as ordinary continuations for two reasons. First, because CIPs represent a small percentage of our OB patent total (2.1%), breaking them out separately would not be fruitful. Second, CIPs can raise at least some of the same notice concerns as ordinary continuations.

IV. RESULTS

As noted, 4,718 unique patents were listed on the OB during the annual editions published from 2012 to 2019. Of these 4,718 patents, 42.2% were litigated at the PTAB, in district court ("DCT"), or both, while 57.8% were not. Against the backdrop of approximately 1% of patents litigated during their lifetime, this figure indicates that OB patents are very highly litigated.

Table 2 shows the litigation venue for the 1,989 patents that were litigated at least once.[90] Table 2 reaffirms the USPTO's analysis:[91] over 90% of OB patents litigated at the PTAB (in our case, 252 of 269 patents, or 93.7%) are in litigation in district court. Going beyond the USPTO's analysis, we show that

86. Only certain parties in specific circumstances can claim priority in this way. *See id.* §§ 119, 120, 121.

87. *See id.* § 112(a). (requiring that the patent specification must "enable any person skilled in the art to which it pertains . . . to make and use" the invention). An adequately enabling disclosure must teach the person skilled in the art well enough to practice the invention "without undue experimentation." *In re* Wands, 858 F.2d 731, 736–40 (Fed. Cir. 1988).

88. *See* 35 U.S.C. § 112(a) (requiring that the patent specification must "contain a written description of the invention, and of the manner and process of making and using it"). An adequate written description must convey "to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." Ariad Pharms v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

89. *See* Lemley & Moore, *supra* note 27, at 100.

90. "0" denotes no litigation, and "1" denotes litigation.

91. Ankenbrand & Repko, *supra* note 19, at 11.

12.8% of OB patents litigated in district court are challenged at the PTAB. This is significantly[92] lower than the 20% of non-OB patents litigated in district court that were challenged at the PTAB during the same time period.[93] Meanwhile, whereas 0.8% of OB patents were challenged at the PTAB only, a significantly higher percentage (3.1%) of non-OB patents were challenged at the PTAB only.[94]

Table 2: Litigation Venue for OB Patents

	DCT		
PTAB	**0**	**1**	**Total**
0	0	1,720	1,720
1	17	252	269
Total	17	1,972	1,989

Table 3: Litigation Venue for Non-OB Patents

	DCT		
PTAB	**0**	**1**	**Total**
0	0	22,241	22,241
1	890	5,561	6,451
Total	890	27,802	28,692

Relative to PTAB challenges against non-OB patents, the structure of Hatch-Waxman makes PTAB challenges to OB patents substantially less attractive. In particular, Hatch-Waxman's 30-month automatic stay of FDA approval cannot be lifted until after the PTAB challenger succeeds on appeal and secures an entry of judgment from the district court.[95] Moreover, only those challengers that file a Paragraph IV certification, making themselves available for district court suit, can secure a 180-day marketing exclusivity.[96]

Table 4 analyzes litigation at either the PTAB or the district court by scientific category of patent. Active-ingredient patents represent a small percentage (11.5%) of all OB patents. Moreover, even within this small

92. A simple comparison of proportions yields a p-value of less than 0.00001.
93. *See infra* Table 3.
94. A simple comparison of proportions yields a p-value of less than 0.00001.
95. 21 U.S.C. § 355(j)(5)(B)(iii)(1).
96. *Id.* § 355(j)(5)(B)(iv).

percentage, they are significantly underrepresented (relative to secondary patents) in the population of litigated patents.[97]

Table 4: Number of Patents Litigated by Scientific Category

Classification	PTAB or DCT		Total
	Not Litigated	Litigated	
product	383 [14.09]	159 [8.00]	542 [11.51]
method-of-use	794 [29.20]	756 [38.03]	1,550 [32.93]
other	1,542 [56.71]	1,073 [53.97]	2,615 [55.56]
	2,719 [100.00]	1,988 [100.00]	4,707 [100.00]

Our initial-challenge data analysis thus indicates that, even after the advent of the PTAB, active-ingredient patents are perceived as less vulnerable to challenge than other types of patents.[98] When combined with analyses by other commentators showing favorable litigation outcomes for active-ingredient patents,[99] this result regarding ex ante litigation risk underscores the resiliency of these patents.

A perhaps puzzling result is the apparently high-likelihood of challenge to method-of-use patents. Method-of-use patents that claim additional molecule use have traditionally been susceptible to so-called skinny labeling by the generic drug maker. Under this approach, which is allowed under Hatch-Waxman, the generic drug maker doesn't put the subsequent use "on label" and can enter the market through a noninfringing path.[100]

97. A χ^2 analysis yields a p-value of less than 0.00001.

98. Indeed, some commentators have argued that firms are unlikely to pursue later stage research and development on molecules that cannot be the subject of strong active-ingredient patents. *See* Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503, 545–48 (2009). If that is the case, these empirical results should come as no surprise.

99. *See, e.g.*, C. Scott Hemphill & Bhaven Sampat, *Drug Patents at the Supreme Court*, 339 SCI. 1386, 1387 (2013); *see also* Prugo et al., *supra* note 54, at 2 (finding that active-ingredient patents have the lowest PTAB institution-rate).

100. *See supra* Section III.A.

That said, skinny labeling may be seen as a risky strategy that opens up the possibility of an induced infringement charge if the drug is prescribed off-label for the patented use. Method-of-use patent challenges may increase even further, on the theory that the generic is inducing physicians to prescribe for the off-label use. The Federal Circuit makes users of skinny labeling more vulnerable to charges of induced infringement.[101]

Table 5 shows the distribution of litigation between the PTAB and the district court by type of patent. The percentage of product patents litigated at the PTAB is slightly higher than in the district court (10.78% vs. 7.97%). Meanwhile the percentage of "other" patents litigated at the PTAB is slightly lower than in the district court (49.81% vs. 53.93%). However, perhaps because of the low numbers of OB patents litigated at the PTAB generally, these small differences are not statistically significant.[102]

Table 5: Venue of Litigated Patents by Scientific Category

Classification	**PTAB**	**DCT**
product	29 [10.78]	157 [7.97]
method-of-use	106 [39.41]	751 [38.10]
other	134 [49.81]	1,063 [53.93]
Total	269 [100.00]	1,971 [100.00]

Table 6 shows how these issues play out when we classify patents according to whether or not they represent a continuation. Continuations are significantly more likely to be litigated than patents than non-continuations.[103] Even though continuations do not prolong patent life, they may be vulnerable to litigation challenges for reasons of scope.

101. *See* GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 7 F.4th 1320, 1334 (Fed. Cir. 2021) (rehearing) (holding that, based on the entire trial record, there was substantial evidence to support the jury's finding that Teva induced infringement throughout the term of the patent-at-issue, including during its "skinny label" period).

102. A χ^2 goodness-of-fit analysis indicates that the distribution of PTAB challenges is not significantly different from the distribution of district court challenges (p-value of 0.14).

103. A χ^2 analysis yields a p-value of less than 0.00001.

Table 6: Comparison Between Non-Continuation and Continuation Patents

	PTAB or DCT		
Continuation Type	**Not Litigated**	**Litigated**	**Total**
	1,199	740	1,939
Non-continuations	[44.10]	[37.22]	[41.19]
Continuation or CIP	1,520	1,248	2,768
	[55.90]	[62.78]	[58.81]
Total	2,719	1,988	4,707

Table 7 shows the distribution between PTAB and district court litigation by whether the patent is a continuation. The raw numbers indicate that district court challenges appear to have a slightly greater focus on continuations than do PTAB challenges. However, this small difference is not statistically significant.[104]

Table 7: Venue of Patent by Non-Continuation or Continuation Patent

Continuation Type	**PTAB**	**DCT**
Non-continuations	112	732
	[41.6%]	[37.1%]
Continuation or CIP	157	1239
	[58.4%]	[62.9%]
Total	269	1,971
	[100.00]	[100.00]

Table 8 shows that litigation propensity differs by the scientific category of continuation patent. Not only are continuation product patents relatively smaller in number than non-continuation product patents, but they are also no more likely to be litigated than non-continuations.[105] This perhaps counterintuitive result may arise because continuations of product patents can have claims to a specific species, while the parent claimed a group of related chemicals in genus form. In that case, the species patent is narrower, and arguably stronger, than the genus claim. Meanwhile, not only are method-of-use continuations more numerous than non-continuations (a 2:1 ratio), but

104. A χ^2 goodness-of-fit analysis yields a p-value of 0.13004.
105. A χ^2 test yields a p-value of 0.678.

they are somewhat more likely to be litigated than non-continuations in that category.[106] As for continuations in the "other" category, they are significantly more likely to be litigated than non-continuations.[107]

Table 8: PTAB or DCT

Continuation Type	Not Litigated	Litigated	Total
Panel A: Product Patents			
Non-continuations	219 [57.18]	94 [59.12]	313 [57.75]
Continuation or CIP	164 [42.82]	65 [40.88]	229 [42.25]
Total	383	159	542
Panel B: Method-of-Use Patents			
Non-continuations	278 [35.01]	234 [30.95]	512 [33.03]
Continuation or CIP	516 [64.99]	522 [69.05]	1,038 [66.97]
Total	794	756	1,550
Panel C: Other types of Patents			
Non-continuations	702 [45.53]	412 [38.40]	1,114 [42.60]
Continuation or CIP	840 [54.47]	661 [61.60]	1,501 [57.40]
Total	1,542	1,073	2,615

The basic statistical analysis thus indicates that there are large differences in overall litigation propensity between OB non-OB patents, and also with respect to category of OB patent. However, the extent to which there is any difference in characteristics of patents litigated at the PTAB relative to the district court is much less clear.

To examine the latter issue further, we conducted an analysis regressing litigation at the PTAB or in district court with the patent's scientific category

106. A χ^2 test yields a p-value of 0.089.
107. A χ^2 test yields a p-value of less than 0.0003.

and continuation status. Additionally, our regression framework investigated the role that small-entity status plays in litigation.[108] This investigation is important because some commentors (including one of the Article's authors) have expressed concern that patents owned by small entities may be disproportionately subject to PTAB challenges.[109]

Table 9 shows the results of a linear regression that examines correlations between small size (relative to large size), scientific category (relative to the product category), and continuation status (relative to non-continuations). The results in columns 3 and 6, which control for both the patent examiner's art unit and the patent's issue year, are of particular interest. Controls for art unit and issue year are useful because studies show that both variables can affect the quality of the granted patent.[110]

The regression takes the form:

$$Y_i=\alpha Small_i+\beta method_i+\gamma other_i+\delta CiP\_Conti+Exam\_Art\_Uniti+Issue\_Yeari+\varepsilon_i$$

In columns 1–3, Y_i corresponds to the number of district court cases in which the patent was involved since September 16, 2011. In columns 4–6, Y_i corresponds to the number of PTAB challenges in which the patent was involved.[111]

108. The USPTO defines small entities as including the following: independent inventors; firms with fewer than 500 employees; and nonprofit institutions. 37 C.F.R. § 1.27 (2020).

109. *See, e.g.*, Saurabh Vishnubhakat, *The Mixed Case for a PTAB Off-Ramp*, 18 CHI.-KENT J. INTELL. PROP. L. 514, 517−18 (2019).

110. *See, e.g.*, Michael Frakes & Melissa Wasserman, *Do Patent Lawsuits Target Invalid Patents*, *in* SELECTION AND DECISION IN THE JUDICIAL PROCESS AROUND THE WORLD 6, 14–15 (Yun-chien Chang ed., 2019).

111. Using the number of times in which the patent was asserted (district court) or challenged (PTAB) as the dependent variable allows us to account for concerns that the PTAB might be used to harass patent owners through repetitive challenges. However, a logistic regression that uses a dichotomous dependent variable (litigation/no litigation) yields qualitatively similar results.

Table 9: Results of Regression

	(1) DCT	(2) DCT	(3) DCT	(4) PTAB	(5) PTAB	(6) PTAB
Small	-1.589***	-1.512***	-1.574***	-0.102***	-0.103***	-0.102***
	(0.107)	(0.110)	(0.123)	(0.012)	(0.012)	(0.0151)
Method-of-use	1.096***	1.123***	0.924***	0.0576*	0.0512	-0.0301
	(0.212)	(0.213)	(0.242)	(0.028)	(0.028)	(0.028)
Other	0.279	0.310	0.625**	-0.0052	-0.0130	-0.0596*
	(0.186)	(0.187)	(0.234)	(0.024)	(0.024)	(0.027)
Continuation or CIP	0.274*	0.237	0.283*	-0.0002	-0.0071	-0.0071
	(0.124)	(0.126)	(0.133)	(0.016)	(0.016)	(0.016)
Observations	4707	4707	4707	4707	4707	4707
Adjusted R^2	0.021	0.049	0.076	0.005	0.011	0.059
Examiner Art Unit	No	No	Yes	No	No	Yes
Issue Year	No	Yes	Yes	No	Yes	Yes

Robust standard errors in parentheses

* p < 0.05, ** p < 0.01, *** p < 0.001

The negative, and significant, coefficients in columns 3 and 6 indicate that patents issued to small entities are less likely to be litigated, both at the PTAB and in district court. Column 3 also shows that, relative to product patents, method-of-use and "other" patents are more likely to be litigated in district court. In contrast, at the PTAB, we see slightly lower rates of litigation relative to product patents, although the magnitude of the coefficients is small and the significance is weaker. Continuations are more likely than non-continuations to be litigated in district court. In contrast, there is no significant difference at the PTAB.[112]

In general, the weak statistical impact of patent characteristics, such as scientific category, on PTAB litigation may reflect the small number of challenges at the PTAB. But to the extent that Congress chooses to fortify the PTAB option for OB patents, the distribution of patent categories challenged

112. Note that we are using our regression model not to predict outcomes but instead to understand correlations. Because our main interest is in the sign and significance of the estimated coefficients, we view our results as useful despite the low adjusted R^2 values.

at the PTAB relative to the district court will be an important metric to monitor.

V. DISCUSSION AND CONCLUSION

This Article uses a novel dataset to provide a comprehensive quantitative analysis of an understudied question: parties' decisions to litigate OB patents relative to non-OB patents in district courts and the PTAB and to litigate different types of OB patents in these different fora.

The percentage of patents litigated solely at the PTAB is significantly lower for OB patents than for non-OB patents. Moreover, the rate of PTAB challenge for OB patents challenged in district court is significantly lower than for non-OB patents challenged in district court.

Breaking down by type of OB patent, active-ingredient patents are significantly less likely to be litigated, whether at the PTAB or in district court, than secondary patents. Additionally, whether at the PTAB or in district court, continuation patents on non-active ingredients are significantly more likely to be litigated than are non-continuations or continuations on active-ingredient patents.

The regression framework, which examines correlations between litigation frequency and scientific category, continuation status, and small-entity status, yields results that are generally consistent with the more basic statistical tests. For instance, the regression shows that method-of-use patents, secondary "other" patents, continuation patents are more likely than product patents to be challenged in district court. Notably, however, this difference does not emerge at the PTAB. Although weak statistical impact may reflect the small number of PTAB challenges, the regression does suggest a potential difference in PTAB functioning vis a vis the district courts that will be important to watch, particularly if Congress fortifies the PTAB pathway.

This Article's analysis also indicates that policymakers' concern about small entities may be misplaced: at both the PTAB and in district courts, small-entity status is correlated with a reduced likelihood of challenge. Interestingly, this result emerges even though the basic descriptive data show that small firms filed proportionally fewer product patents than large firms.[113]

Overall, the empirical findings show that the PTAB's role in adjudicating OB patents has been modest, both as an absolute matter and relative to its role for non-OB patents. That said, while district court litigation differentially targets patents that are generally considered low quality, PTAB litigation may

113. Unreported results, on file with authors.

not do so with the same force, at least based on the small amount of PTAB litigation that has occurred thus far.

In contrast with Hatch-Waxman, the BPCIA does not provide incentives to remain in district court only. Data from biologics litigation therefore provide some insight into what the PTAB's use might look like absent those incentives. According to the USPTO, during the period between September 16, 2012, and November 30, 2018, only 47% (46/98) of biologics patents challenged at the PTAB had any ongoing patent litigation.[114] This number contrasts starkly with the >90% figure for OB patents.[115] Biologics-patent owners are relatively, and notably, more likely to avail themselves of AIA proceedings irrespective of whether the patent is being challenged in district court.

The contrasting experience with biologics patents is important not only on its own terms (biologics play almost as large a role in U.S. biopharmaceutical spending as small molecules) but also because it suggests paths for restructuring small molecule patent litigation. Specifically, to expand the role of the PTAB with respect to OB patents, and perhaps particularly for secondary OB patents, Congress might reconsider multiple features unique to Hatch-Waxman. These include, for example, the 30-month stay of FDA approval granted to OB patent owners who sue in district court. The lifting of a Hatch-Waxman stay rests on a district court's entry of judgment in favor of the defendant,[116] and a district court is required to enter judgment only if the Federal Circuit affirms a PTAB invalidation.[117] Therefore, the PTAB route is unlikely to be faster than the district court route, and may even be slower.

At a minimum, Congress could amend Hatch-Waxman to allow the 30-month stay to be lifted by a PTAB decision invalidating all relevant patent claims. Even this modest change would let challengers more effectively use the PTAB's expertise, improving the status quo. Policymakers could also consider changing the mechanism by which the Hatch-Waxman awards its 180-day marketing exclusivity. This marketing exclusivity currently provides little incentive to use the PTAB. Under the Hatch-Waxman framework, the exclusivity is awarded only to entities that file a Paragraph IV certification and are thereby deemed to have committed an artificial act of infringement sufficient to create Article III standing for a branded firm's infringement suit.

114. Ankenbrand & Repko, *supra* note 19, at 22.

115. *Id.* at 11.

116. 35 U.S.C. § 355(j)(5)(B)(iii)(I).

117. *See* Fresenius USA, Inc. v. Baxter Int'l, Inc., 721 F.3d 1330 (Fed. Cir. 2013).

Symmetry between the PTAB and district courts with respect to incentive would more fully realize the AIA's substitution goals.[118]

Finally, incentivizing greater use of the PTAB might be coupled with additional ex ante efforts to improve OB patent validity. More specifically, the data indicate that OB patents come from a relatively small number of art units. For example, Art Units 1611–19 (collectively, Group 1610) all examine applications on the same subject matter: "Organic Compounds: Bio-affecting, Body Treating, Drug Delivery, Steroids, Herbicides, Pesticides, Cosmetics, and Drugs."[119] Meanwhile, Art Units 1621–29 (collectively, Group 1620) all examine applications related to "Organic Chemistry."[120] Groups 1610 and 1620 combined account for 78.0% of the OB patents in our dataset. Five other art unit groups examine 1–5% of the OB patents apiece, bringing the total up to 93.9%. Table 10 summarizes these tabulations.

Table 10: Art Unit Groups of Orange Book Patents

Group	OB Patents	Share	
1620	1,846	39.2%	
1610	1,824	38.8%	
3760	200	4.2%	
1650	196	4.2%	— 93.9%
1670	164	3.5%	
1640	104	2.2%	
3770	85	1.8%	
Other	288	6.1%	
Total	**4,707**	**100.0%**	

118. More generally, the 180-day exclusivity period likely needs reform. As currently structured, the period provides little incentive for any type of *successful* challenge. To the contrary, if the first Paragraph IV filer settles a patent infringement lawsuit, then a successful challenger must wait 180 days after it has invalidated the patent before it can enter. Some follow-on generic challengers may be using the PTAB precisely for purposes of invalidating patents on which the first Paragraph IV-filer has settled (and thereby achieving generic entry, perhaps even earlier than the settling challenger). *See* Prugo et al., *supra* note 54, at 4. We explore that issue further in a companion paper on which we are currently working. *See* Hovenkamp et al., *supra* note 20.

119. *TC 1600 Management Roster*, U.S. PAT. & TRADEMARK OFF., https://www.uspto.gov/patents/contact-patents/tc-1600-management-roster (last visited Nov. 17, 2021). The individual art units within these groups are distinct from each other as an administrative matter—e.g., each is led by its own supervisory patent examiner—but all art units within the same group focus on the same subject matter of inventions.

120. *Id.*

The data are therefore consistent with recent suggestions in the literature[121] that it may be cost-effective to target additional examination resources at patents that have a substantial likelihood of being placed on the OB. As the data show, these patents can be identified ex ante. Such resources should include lessons learned from PTAB review of OB patents. Although PTAB review is less frequent than is likely optimal, the USPTO should reuse lessons learned from its own highly expert ex post review, IPRs, in its patent examinations.

121. *See, e.g.*, Dmitry Karshtedt, *Pharmaceutical Patents and Adversarial Examination*, 91 Geo. Wash. L. Rev. (forthcoming 2023); S. Sean Tu & Mark A. Lemley, *What Litigators Can Teach the Patent Office About Pharmaceutical Patents* 43–44 (W. Va. Univ. Sch. L., Working Paper No. 2021-015, 2021); Michael D. Frakes & Melissa F. Wasserman, *Investing in Ex Ante Regulation: Evidence from Pharmaceutical Patent Examination* (Nat'l Bureau Econ. Rsch., Working Paper No. 27579, 2020).