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DESCRIBING DRUGS: A RESPONSE TO PROFESSORS ALLISON AND OUELLETTE

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INTRODUCTION

In their article, *How Courts Adjudicate Patent Definiteness and Disclosure*, John R. Allison and Lisa Larrimore Ouellette present a comprehensive study—thirty years' worth of cases—of federal courts' application of patent law's written-description, definiteness, and enablement requirements.[1] Using their own hand-coded dataset, Allison and Ouellette measure a number of interesting disparities in courts' application of the two doctrines across various industries and technologies. But one of their results is simply shocking: the massive disparity in how courts apply patent law's written-description requirement in pharmaceutical cases.[2] In Allison and Ouellette's study, pharmaceutical patents litigated as part of generic drug manufacturers' Abbreviated New Drug Applications (ANDAs) before the U.S. Food and Drug Administration (FDA) fare no worse on courts' written-description analyses than a control, industrial/business goods and services patents.[3] But pharmaceutical

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1. John R. Allison & Lisa Larrimore Ouellette, *How Courts Adjudicate Patent Definiteness and Disclosure*, 65 DUKE L.J. 609 (2016); *see also* 35 U.S.C. § 112(a) (2012) (requiring that patents "contain a written description of the invention" and "enable any person skilled in the art to which it pertains . . . to make and use the same").

2. *See* Allison & Ouellette, *supra* note 1, at 639 (defining pharmaceutical cases as "patents on drugs for treating diseases or other abnormal conditions in humans or animals, as well as processes for producing or using such drugs").

3. *See id.* at 666 tbl.7.

patents litigated outside of the ANDA context fare *substantially* worse on courts' written-description analyses—they are, by far, *the worst* performers on written description of any industry.[4] Indeed, non-ANDA pharmaceutical patents' poor written-description score is the third most statistically significant result of any of the article's sixty-one comparisons across different definiteness and disclosure requirements, industries, jurisdiction, and procedural postures.[5]

From the outset, there does not seem to be any ready explanation for this disparity. Pharmaceutical patents in both the ANDA and non-ANDA contexts are, obviously, part of the same technology class (pharmaceutical patents);[6] they are typically owned by the same type of litigant, that is, brand pharmaceutical manufacturers;[7] and they are typically litigated in the same jurisdictions.[8] And yet, given the total sample size of pharmaceutical patents in Allison and Ouellette's dataset—only sixty-five unique opinions[9]—it is unclear whether the differences that exist between courts' written-description opinions of ANDA and non-ANDA patents can be teased apart by more robust statistical analysis. To that end, this brief response provides a qualitative analysis of Allison and Ouellette's quantitative one. It briefly reviews ANDA versus non-ANDA patent litigation in Part I. It engages in several hypotheses about differences between ANDA and non-ANDA pharmaceutical patent cases in Part II. Next, in Part III, it reviews the most significant ANDA and non-ANDA written-description cases from Allison and

4. *See id.*

5. *See id.* To be clear, statistical significance alone is no guarantee that a reported result is the result of nonrandom effects, and differences in *p*-value across multivariable comparisons may not amount to much. *See generally* STEPHEN T. ZILIAK & DEIRDRE N. MCCLOSKEY, THE CULT OF STATISTICAL SIGNIFICANCE (2008) (describing the myriad problems of overreliance on significance). Factors such as study design, small sample size, and the number of variables measured often produced statistically significant measurements that are, in fact, meaningless. *See* Regina Nuzzo, *Scientific Method: Statistical Errors*, NATURE (Feb. 12, 2014), http://www.nature.com/news/scientific-method-statistical-errors-1.14700 [https://perma.cc/BHD4-8PFZ] (discussing problems with *p* values). Nonetheless, the huge disparity between ANDA and non-ANDA cases presented by Allison and Ouellette suggests something is worth investigating.

6. Allison & Ouellette, *supra* note 1, at 639–40.

7. *See* FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY 17–19 (2002), https://www.ftc.gov/sites/default/files/documents/reports/generic-drug-entry-prior-patent-expiration-ftc-study/genericdrugstudy_0.pdf [https://perma.cc/WYV5-C9VQ].

8. BRIAN C. HOWARD & JASON MAPLES, LEX MACHINA: HATCH-WAXMAN / ANDA LITIGATION REPORT (2014) (on file with author).

9. *See infra* Appendix.

Ouellette's dataset. In particular, it shows that different types of technologies at issue in some non-ANDA cases, such as biologics rather than small molecule drugs, play a role in courts' written-description assessments. Finally, Part IV provides several suggestions for areas of future research and litigation.

I. ANDA VERSUS NON-ANDA PATENT LITIGATION

Before examining several hypotheses for Allison and Ouellette's ANDA versus non-ANDA written-description disparity, it may be helpful to briefly recount how patent litigation differs procedurally in both contexts. As part of any New Drug Application with the FDA, a drug manufacturer must inform the agency which patents cover its drug.[10] The FDA then dutifully lists the "corresponding patent numbers and expiration dates, in a fat, brightly hued volume called the Orange Book (less colorfully but more officially denominated Approved Drug Products with Therapeutic Equivalence Evaluations)."[11] Drug companies wishing to manufacture a generic version of the original (brand) drug must then submit an Abbreviated New Drug Application, an ANDA, to the FDA certifying that its proposed generic product will not infringe the Orange Book-listed patents or that those patents are invalid. This certification is, by statute, an artificial act of patent infringement, and typically begins ANDA patent litigation.[12]

By contrast, non-ANDA patent litigation can take several forms. Like ANDA patent litigation, it can be between a generic and brand drug manufacturer on patents not included in the Orange Book, both before and after the generic product has been approved by the FDA.[13] Non-ANDA patent litigation can also exist between two brand manufacturers with two separately approved drug products.[14] And in

10. Jacob S. Sherkow, *Administrating Patent Litigation*, 90 WASH. L. REV. 205, 214–15 (2015).

11. Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S, 132 S. Ct. 1670, 1676 (2012).

12. *See* Sherkow, *supra* note 10, at 214–15.

13. *See, e.g.*, AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc., 759 F.3d 1285 (Fed. Cir. 2014) (demonstrating a non-ANDA patent-infringement action after approval); Eli Lilly & Co. v. Teva Pharm. USA, Inc., 619 F.3d 1329 (Fed. Cir. 2010) (demonstrating a non-ANDA injunctive action prior to approval).

14. *See, e.g.*, Complaint for Declaratory Relief (Patent Infringement), Medicis Pharm. Corp. v. Stiefel Labs., Inc., No. 5:10-CV-00621 (W.D. Tex. July 28, 2010).

rare circumstances, non-ANDA patent litigation can be fought between two rival generic manufacturers.[15]

Despite these differences, ANDA and non-ANDA patent litigation is mostly alike. Both generally concern the same technological class of patents, that is, pharmaceutical patents. Both are almost always between business competitors of one sort or another—drug manufacturers seeking to sell similar, if not identical, products. Both employ the same procedures found in federal district court for all patent cases. And both groups of cases tend to be filed in the same districts.[16] At a high level of abstraction, there is little reason that courts should apply differing written-description standards to these two groups of pharmaceutical cases—let alone ones that are subject to the dramatic differences reported by Allison and Ouellette.

II. HYPOTHESES ON THE ANDA VERSUS NON-ANDA WRITTEN-DESCRIPTION DISPARITY

In their article, Allison and Ouellette provide a few hypotheses for the ANDA versus non-ANDA written-description disparity. The first concerns differences in types of claims in ANDA versus non-ANDA patents. Allison and Ouellette describe their reported discrepancy between the two types of cases on "written-description and definiteness grounds, likely because [non-ANDA] patents mostly relate to various methods rather than FDA-approved drug compositions."[17] The implication here is that claims on methods of using approved drugs are more likely to fall afoul of patent law's definiteness requirement than claims on the drug compositions themselves. The belief that non-ANDA patent litigation tends to focus on "follow on patents," rather than patents covering original drug compositions, is widespread.[18]

15. *See, e.g.*, Teva Pharm. USA, Inc. v. Sandoz, Inc., 723 F.3d 1363 (Fed. Cir. 2013).

16. *See generally* HOWARD & MAPLES, *supra* note 8.

17. Allison & Ouellette, *supra* note 1, at 614.

18. *See* Janet Freilich, *The Paradox of Legal Equivalents and Scientific Equivalence: Reconciling Patent Law's Doctrine of Equivalents with the FDA's Bioequivalence Requirement*, 66 SMU L. REV. 59, 61–62 (2013); *see also* Yaniv Heled, *Patents vs. Statutory Exclusivities in Biological Pharmaceuticals—Do We Really Need Both?*, 18 MICH. TELECOMM. & TECH. L. REV. 419, 468 n.218 (2012) (defining "follow on" or "secondary" patents as "patents claiming (1) particular ways of formulating the product, (2) additional methods of manufacturing the [active pharmaceutical ingredient] or any of the intermediate compounds involved in making it and (3) additional methods of using the product or [active pharmaceutical ingredient] for treating additional medical conditions").

Yet patents in both groups of Allison and Ouellette's analysis—ANDA and non-ANDA patents—contain both composition and method claims. Of the seven unique opinions that blocked written-description challenges to ANDA patents, *six* concerned patents that covered method claims.[19] And of these six cases, four concerned patents that claimed only methods of administration, rather than compositions.[20] Empirically, at least, the ANDA–non-ANDA written-description disparity cannot be explained by differences in the types of claims presented in the two types of cases.

At a more theoretical level, Allison and Ouellette's hypothesis puts to test a long-standing belief that patent claims covering drug compositions and methods of use differ in their judicial treatment. Even though claims covering drug compositions are for tangible things—and thus, perhaps, more easily described than abstract methods—composition claims can, and do, fail the written-description requirement. Claims for drug compositions often allow some variability in the drug's chemical structure, usually in an effort to claim analogs to the principal drug. Drug composition claims may allow so much variability, however, as to make the written-description requirement virtually impossible. In *Boston Scientific Corp. v. Johnson & Johnson*,[21] for example, the U.S. Court of Appeals for the Federal Circuit famously upheld the invalidation of a patent claiming a rapamycin-eluting heart stent because the claims contemplated tens of thousands of rapamycin analogs, only a miniscule fraction of which were described.[22] In other instances "a single generic [drug composition] claim can easily encompass millions, billions, or novemdecillions of compounds."[23] Aside from the strength or weakness of pharmaceutical composition patents, it is

19. Bone Care Int'l, LLC v. Pentech Pharm., Inc., 862 F. Supp. 2d 790 (N.D. Ill. 2012); Pfizer Inc. v. Teva Pharm. U.S.A. Inc., 882 F. Supp. 2d 643 (D. Del. 2012); Acorda Therapeutics Inc. v. Apotex Inc., No. 07-CV-4973, 2011 WL 4074116 (D.N.J. Sept. 6, 2011); Research Found. of State Univ. of N.Y. v. Mylan Pharm. Inc. (*SUNY*), 809 F. Supp. 2d 296 (D. Del. 2011); Alza Corp. v. Mylan Labs., Inc., 388 F. Supp. 2d 717 (N.D. W. Va. 2005); Astra Aktiebolag v. Andrx Pharm., Inc., 222 F. Supp. 2d 423 (S.D.N.Y. 2002).

20. *Bone Care*, 862 F. Supp. 2d at 793 (concerning U.S. Patent No. 5,602,116); *Acorda Therapeutics Inc.*, 2011 WL 4074116 at *1 (concerning U.S. Patent No. 6,455,557); *SUNY*, 809 F. Supp. 2d at 298 (concerning U.S. Patent Nos. 7,211,267; 7,232,572); *Astra*, 222 F. Supp. 2d at 591 (concerning U.S. Patent No. 5,093,342).

21. Boston Sci. Corp. v. Johnson & Johnson, 647 F.3d 1353 (Fed. Cir. 2011).

22. *Id.* at 1365.

23. Sean B. Seymore, *Heightened Enablement in the Unpredictable Arts*, 56 UCLA L. REV. 127, 146 (2008) (footnotes omitted).

unclear that pharmaceutical method-of-use patents are, by their nature, *relatively* weaker than composition claims. Many pharmaceutical method-of-use claims, despite their perception as being weak, have easily vaulted over the written-description requirement.[24]

Allison and Ouellette also suggest that ANDA patents may outperform their non-ANDA counterparts on various validity scores because they "are likely to have far more private economic value to their owners than many other kinds of patents, meaning that patentees will invest much more in fighting to preserve their validity."[25] It is indeed true that Orange Book-listed patents—or, at least, the market exclusivity that comes with them—are worth tremendous amounts of money.[26] But here, too, the hypothesis does not seem to account for the *relative* performance of ANDA to non-ANDA pharmaceutical patents. Non-ANDA patents protect a pharmaceutical product, too—one that, like an Orange Book-listed patent, quells competition in a lucrative arena. In *Medicis Pharmaceutical Corp. v. Stiefel Laboratories, Inc.*[27]—a non-ANDA patent dispute between two brand competitors[28]—Medicis's patents protected a franchise worth roughly $400 million per year.[29] It is unclear in situations like these whether the economic value of the patents, or the attorneys' incentives to preserve those patents' validity, shifts with such patents being listed (or not) in the Orange Book. It is also unclear why the written-description requirement, of all of patent law's several substantive requirements, appears to greatly disfavor those patents not listed in the Orange Book.

At PatCon V in 2015, at the University of Kansas, another patent scholar, David Schwartz, discussed yet another hypothesis for the ANDA–non-ANDA disparity described by Allison and Ouellette's

24. *See, e.g.*, Allergan Inc. v. Watson Labs. Inc., 869 F. Supp. 2d 456, 469 (D. Del. 2012) (concerning U.S. Patent No. 7,759,359, covering methods of treating bladder dysfunction by using trospium).

25. Allison & Ouellette, *supra* note 1, at 662.

26. C. Scott Hemphill, *Paying for Delay: Pharmaceutical Patent Settlement as a Regulatory Design Problem*, 81 N.Y.U. L. REV. 1553, 1568–69 (2005).

27. Complaint for Declaratory Relief (Patent Infringement), Medicis Pharm. Corp. v. Stiefel Labs., Inc., No. 5:10-CV-00621 (W.D. Tex. July 28, 2010) (N.B.: the author represented Medicis in this dispute).

28. *Id.* at 3–4.

29. Medicis Pharm. Corp., Annual Report, (Form 10-K) 71 (Dec. 31, 2012). The case was later dismissed by stipulation in 2013. Amended Stipulation and Order of Dismissal, Medicis Pharm. Corp. v. Stiefel Labs., Inc., No. 5:10-CV-00621 (W.D. Tex. June 26, 2013).

results. All things being equal, ANDA cases are more likely to settle than their non-ANDA counterparts because the stakes involved are often much higher. By and large, ANDA cases operate in the context of monopoly: at the time the infringement suit is filed, only the brand pharmaceutical product has been approved by the FDA.[30] That monopoly is often worth billions of dollars to the patent holder. The uncertainty of litigation, therefore, frequently counsels brand manufacturers to settle with their generic rivals—often for large sums of money—to preserve their patents' validity.[31] Non-ANDA cases, however, often operate in the context of competition: at the time the infringement suit is filed, both rivals' products have been approved by the FDA.[32] To that end, the incentives for settling—and the importance of maintaining patent validity—are relatively low as compared to their ANDA counterparts. ANDA patent cases are therefore, according to Schwartz, likely to center on stronger patents—patents that brand drug manufacturers believe will survive generics' challenges.

Whether ANDA cases do settle more frequently than non-ANDA cases remains to be seen. But, again, Schwartz's hypothesis does not seem to explain why non-ANDA cases' written-description scores fare more poorly than their enablement or indefiniteness scores. It seems odd to suggest, all things being equal, that ANDA holders' incentives to maintain drug monopolies are only more sensitive to invalidity claims predicated on written-description, but not invalidity claims predicated on enablement or indefiniteness. Furthermore, if the stakes are high enough, a settlement-incentive theory that *is* uniquely sensitive to written-description-invalidity claims should work equally well in the non-ANDA context. Preventing competitors from entering a $400-million marketplace, as in *Medicis*, should provide an equal incentive to patent holders in the ANDA and non-ANDA contexts.

None of the strongest hypotheses seem to provide satisfying answers to the chasm in written-description treatment between ANDA and non-ANDA cases. And yet, Allison and Ouellette's evidence clearly demonstrates the existence of such a disparity. The answers, if clear ones exist, likely lie in the cases themselves.

30. *See* 21 U.S.C. § 355(j) (2010).

31. Hemphill, *supra* note 26, at 1557.

32. *See supra* notes 13–15 and accompanying text.

III. ANDA VERSUS NON-ANDA WRITTEN-DESCRIPTION DECISIONS

Allison and Ouellette's dataset concerning § 112 decisions in pharmaceutical patent cases consists of sixty-five unique opinions: thirty-six ANDA opinions and twenty-nine non-ANDA opinions. Of the ANDA opinions, ten had a written-description score of at least one on either Allison and Ouellette's five-level scale or three-level scale.[33] Of the non-ANDA opinions, nine had a written-description score of at least one. Thus, it would appear that the written-description requirement was at issue in roughly equal proportions: 27.7 percent (10/36) of ANDA cases and 31.0 percent (9/29) of non-ANDA cases.[34]

Interestingly, Allison and Ouellette's written-description disparity arises in how the courts dispose of these issues. Of the ten ANDA opinions where written-description was at issue, seven declared valid *all* of the claims of the asserted patents under the written-description requirement; one declared at least some of the claims invalid for lacking a proper written description; and two concluded that factual issues prevented a resolution of the defendants' written-description arguments. But of the nine non-ANDA cases discussing the written-description requirement, five declared at least one claim of the asserted patent invalid for failing the written-description requirement; three concluded that factual issues prevented a disposition of the defendants' written-description arguments; and only one affirmatively rebuffed the defendant's written-description challenges.[35]

To put these numbers in this context, Allison and Ouellette's dataset shows that out of thirty-six ANDA opinions, only a single one—*Alcon Research Ltd. v. Barr Laboratories Inc.*[36]—invalidated a

33. Allison and Ouellette describe their two scales as follows. First, the five-level scale

> record[s] the relative strength of each decision on the following . . . (1) invalid as a matter of law; (2) fact issue followed by a ruling of invalidity; (3) fact issue remaining; (4) fact issue followed by a ruling of validity; or (5) valid as a matter of law. . . . We also created a coarser one-to-three scale by collapsing "as a matter of law" and "fact issue followed by a validity or invalidity ruling" to produce "total valid" and "total invalid" outcomes on each of the three issues.

Allison & Ouellette, *supra* note 1, at 631.

34. *See infra* Appendix.

35. *See id.*

36. Alcon Research Ltd. v. Barr Labs. Inc., 837 F. Supp. 2d 364 (D. Del. 2011), *aff'd in part, rev'd in part*, 745 F.3d 1180 (Fed. Cir. 2014).

patent's claims on lack-of-written-description grounds.[37] By contrast, out of twenty-nine non-ANDA opinions, only a single one—*Allergan, Inc. v. Watson Laboratories, Inc.*[38]—rejected the defendants' written-description arguments,[39] while five others invalidated the claims at issue for lacking a proper written description. In short, the disparity uncovered by Allison and Ouellette seems to show that, while both ANDA and non-ANDA litigants raise written-description issues in relatively equal proportions, courts in the ANDA context rarely, if ever, invalidate those patents on written-description grounds.

This comparative examination shows one surprising facet: courts' differing levels of engagement with the merits of the written-description arguments. The single opinion to invalidate an ANDA patent on written-description grounds, *Alcon*, appears to have done so reluctantly and with little analysis. Alcon's patents covered Travatan, a medication indicated for treating glaucoma and ocular hypertension that used castor oil to stabilize the formulation's components.[40] Alcon's patent's claims, however, did not specify the precise quantities of castor oil for either effective preparation or treatment.[41] To that end, the district court concluded that the patents were too broad to be enabling.[42] But the court's opinion came on the heels of *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*,[43] a seminal case from the U.S. Court of Appeals for the Federal Circuit that separated enablement and written-description as free-standing doctrines.[44] Perhaps confused by the application of these two doctrines—or cuing up the case for a single appeal—the *Alcon* court concluded that the breadth of the patent's claims merited invalidation under *both* theories:

> [W]e believe that the Section 112, first paragraph, analysis in this case proceeds more cleanly through the enablement framework than through a written description-type inquiry. Nonetheless, given the current state of written description jurisprudence, we find that the castor oil patent claims also fail the written description requirement

37. *Id.* at 392.

38. Allergan, Inc. v. Watson Labs., Inc., 869 F. Supp. 2d 456 (D. Del. 2012).

39. *Id.* at 469. And even there, the court ultimately invalidated the asserted patents for obviousness. *Id.* at 519.

40. *Alcon Research Ltd.*, 837 F. Supp. 2d at 367.

41. *Id.* at 381.

42. *Id.*

43. Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336 (Fed. Cir. 2010).

44. *Id.* at 1351.

> for essentially the same reasons that they fail the enablement requirement: the art in question is highly unpredictable and the claims are extremely broad, but the written description is relatively limited.[45]

By contrast, the only non-ANDA opinion to uphold the asserted patents on written-description grounds—*Allergan*—did so after a lengthy analysis of the written-description requirement and expert testimony as to the substance of the claims.[46] In contrast to the claims at issue in *Alcon*, the claim discussed in *Allergan* was narrow: it required that the maximum concentration of the drug, trospium, in patients' blood fell below a much larger range than disclosed in the patent's specification.[47] The court examined testimony from three experts on this aspect of the invention alone, comparing their testimony to four formulations of the same invention disclosed in the patent.[48] Ultimately, after finding one expert's testimony to be the most persuasive, the court concluded that the patent "provided guidance to those skilled in the art that the low [maximum blood concentration] range limitation is an aspect of the invention and the applicants were in possession of it."[49]

Apart from the level of engagement, the non-ANDA and ANDA opinions in Allison and Ouellette's dataset appear to concern differing technologies. For example, by statutory design, the ANDA opinions exclusively cover "small molecule" drugs, which are relatively simple to describe in writing. Biologics—the focus of several non-ANDA cases in Allison and Ouellette's dataset—however, are larger, complex molecules that are much more difficult to describe in writing. Indeed, in many instances, patentees of biologics can only describe them in functional terms: what they bind to or from where they are derived, rather than their precise chemical structure.[50] For that reason, at the margins at least, non-ANDA patents may be more susceptible to written-description attacks than their ANDA counterparts.

45. *Alcon Research Ltd.*, 837 F. Supp. 2d at 384 (footnote omitted).

46. Allergan, Inc. v. Watson Labs., Inc., 869 F. Supp. 2d 456, 497–99 (D. Del. 2012).

47. *Id.* at 498–99.

48. *Id.*

49. *Id.* at 499.

50. *See generally* Jason Kanter & Robin Feldman, *Understanding and Incentivizing Biosimilars*, 64 HASTINGS L.J. 57 (2012) (discussing the differences in patents claiming biologics relative to small molecule therapies).

Indeed, of the five non-ANDA opinions finding the asserted patents invalid for lacking a sufficient written description, three appear to have concerned non-traditional pharmaceutical technologies. Both *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*[51] and *Centocor Ortho Biotech, Inc. v. Abbott Laboratories*,[52] for example, concerned antibodies—large, complex biologics famously difficult to describe.[53] And in both cases, the Federal Circuit faulted the patentee for claiming, but failing to fully describe, a broad "genus" of antibodies. In *AbbVie*, the Federal Circuit affirmed a jury's finding that the asserted patents did not "adequately describe representative antibodies to reflect the structural diversity of the claimed genus," a problem that is prevalent "in technology fields that are highly unpredictable, where it is difficult to establish a correlation between structure and function for the whole genus or to predict what would be covered by the functionally claimed genus."[54] In *Centocor*, the Federal Circuit was incredulous that "the patent broadly claim[ed] a class of antibodies that contain[ed] human variable regions, [even though] the specification d[id] not describe a single antibody that satisfie[d] the claim limitations."[55] Similarly, in *University of Rochester v. G.D. Searle & Co.*,[56] the court was tasked with determining the sufficiency of the patent's description of methods of genetically inhibiting PGHS-2, a protein involved in inflammation.[57] Because the patent described the invention in functional rather than tangible terms, the Federal Circuit upheld the invalidation of the patent, noting that "[e]ven with the three-dimensional structures of [related] enzymes . . . in hand, it may even now not be within the ordinary skill in the art to predict what compounds might bind to and inhibit them . . . ."[58]

Competing problems of broad claiming and technological uncertainty are simply unlikely to occur in small-molecule ANDA

51. AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc., 759 F.3d 1285 (Fed. Cir. 2014).

52. Centocor Ortho Biotech, Inc. v. Abbott Labs., 636 F.3d 1341 (Fed. Cir. 2011).

53. Douglas G. Metcalf, *Therapeutic Antibody Patent Infringement Litigation: Untested and Uncertain Litigation Strategies Underpin Patents Protecting Multibillion-Dollar Pharmaceuticals*, 19 B.U. J. SCI. & TECH. L. 194, 203–04 (2013).

54. *AbbVie Deutschland GmbH & Co.*, 759 F.3d at 1301.

55. *Centocor*, 636 F.3d at 1350–51.

56. Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916 (Fed. Cir. 2004).

57. *Id.* at 917–18.

58. *Id.* at 925.

cases—something borne out by the seven ANDA opinions finding the asserted claims valid despite written-description objections. In those cases, the courts confronted traditional pharmaceutical claims directed toward a chemically precise compound, formulations, or methods of using a previously known drug. The patent at issue in *GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*,[59] for example, concerned composition claims—that is, claims covering a specific chemical compound dutasteride.[60] There, the court simply concluded that "under each side's construction and reading of the specification, the description matches the claim, and regardless of which side is right, the description remains entirely based on structure of the compound and its process of creation. . . . We have no precedent . . . [that this] would be insufficient."[61] Similarly, in *Acorda Therapeutics Inc. v. Apotex Inc.*,[62] the asserted claims covered a method of treating a spastic patient with tizanidine, a well-known drug, as well as a way of manufacturing the treatment.[63] The court's written-description analysis in *Acorda* consisted of a single, short paragraph finding "no lack of description in the specification for the claim scope," especially because "the claim term's inclusion of [the contested term] came directly from its express definition in the specification."[64] And in *Pfizer Inc. v. Teva Pharmaceuticals U.S.A. Inc.*,[65] the district court sided with the patent holder's expert to find that the patent's description of the drug and its variants proved that "chemists would understand what the disclosure meant" and would be "more than sufficient to convey to those of skill in the art the subject matter of the claimed invention and that the inventors were in 'possession of it.'"[66]

From a broader perspective, the substance of these decisions suggests that technology class plays a crucial role in courts' written-description determinations of pharmaceutical patents. The more basic the pharmaceutical technology—simple compounds, traditional formulations, or typical methods of use—the less likely it is that

59. GlaxoSmithKline LLC v. Banner Pharmacaps, Inc., 744 F.3d 725 (2014).

60. *Id.* at 726–27.

61. *Id.* at 730.

62. Acorda Therapeutics Inc. v. Apotex Inc., No. 07-CV-4973, 2011 WL 4074116 (D.N.J. Sept. 6, 2011).

63. *Id.* at *2.

64. *Id.* at *25.

65. Pfizer Inc. v. Teva Pharm. U.S.A. Inc., 882 F. Supp. 2d 643 (D. Del 2012).

66. *Id.* at 702.

challengers will be able to prove, by clear and convincing evidence, that the asserted patents lack a sufficient written description. But the more complex the technology—derivative compounds with numerous radical groups, new formulations or dosage forms, or atypical methods of use—the more likely it is that challengers will be able to prove a lack of written description. Put another way, the more complex or unpredictable the technology, the easier it will be to prove that the claims are not sufficiently described. As a consequence, ANDA patents will seem to survive written-description challenges more frequently than their non-ANDA cousins because ANDA patents—by their nature—focus only on traditional, small-molecule pharmaceuticals. Furthermore, where this analysis fails, it seems to fail only at the extremes. Where courts have given either short shrift or Talmudic thoroughness to their written-description analyses, results, like those in *Alcon* and *Allergan*, seem more likely to occur. In all, a more detailed examination of the cases scoring at least Level One on Allison and Ouellette's written-description scales suggests that the ANDA/non-ANDA disparity is perhaps best explained not by "litigation metrics"—the value in dispute or the likelihood of settlement, for example—but by the underlying technology itself.

VI. FUTURE RESEARCH

Allison and Ouellette note that their "results on how § 112 has been applied in practice will be helpful in evaluating current proposals for reform, and our rich dataset—which we are making publicly available—will enable more systematic [future] studies of these critical doctrines."[67] This is undoubtedly true for their written-description results in the pharmaceutical context. To that end, Allison and Ouellette's study—and the analysis here—suggests several avenues for further research, both quantitative and, perhaps more importantly, qualitative.

First, Allison and Ouellette's dataset runs through 2012. As a result, the dataset does not include two major patent decisions that may significantly affect how courts apply the written-description doctrine to pharmaceutical technologies going forward. The first of these is the Federal Circuit's en banc decision of the *Ariad* case, discussed earlier.[68] Although that case was decided in 2011, and is

67. Allison & Ouellette, *supra* note 1, at 612.

68. *See supra* note 44 and accompanying text.

captured in Allison and Ouellette's dataset, the implications of *Ariad* are likely to be recognized in the future—to the detriment of patentees in both the ANDA and non-ANDA contexts. *Ariad*'s conclusion, that the written-description doctrine exists separately from either definiteness or enablement, may become additional fodder for patent challengers. The second case is the Supreme Court's recent decision in *FTC v. Actavis, Inc.*[69] That decision barred many types of settlements between brand pharmaceuticals and generic challengers in ANDA cases.[70] With these "reverse payment" settlements now off the table, it appears that more ANDA cases will be litigated to judgment—thus, potentially producing more invalidating-written-description opinions than exist currently. Because these shifts in doctrine portend a greater number of ANDA patents failing under the written-description requirement, a post-*Ariad* and *Actavis* follow-up study to Allison and Ouellette's article would be informative.

A second avenue for further research concerns the rise of biologic drugs or, simply, "biologics." An increasing number of top-selling therapeutics are biologics.[71] Current law mandates that biologics patents are litigated outside of the ANDA context.[72] But with the 2009 Biologics Price Competition and Innovation Act (BPCIA)—and with a recent decision by the Federal Circuit clarifying the BPCIA—there may be an increasing amount of ANDA-style patent-litigation.[73] The BPCIA, nonetheless, has thus far proven famously fruitless, with only a single generic biologic—termed a biosimilar—approved to date.[74] Should the FDA approve an increasing number of biosimilars—an act likely to generate an increasing amount of non-ANDA patent litigation—commentators interested in the written-description requirement may want to revisit Allison and Ouellette's study with fresh data.

Lastly, a more thorough analysis of Allison and Ouellette's dataset would also review pharmaceutical cases where the written-

69. FTC v. Actavis, Inc., 133 S. Ct. 2223 (2013).

70. *Id.* at 2237–38.

71. Jeanne Yang, Note, *A Pathway to Follow-On Biologics*, 3 HASTINGS SCI. & TECH. L.J. 217, 217 (2011).

72. *See* Kanter & Feldman, *supra* note 50, at 59.

73. *See, e.g.*, Amgen Inc. v. Sandoz Inc., 794 F.3d 1347 (Fed. Cir. 2015).

74. *See* Lindsay Kelly, *Biologics in the Practice of Law*, 39 HARV. J.L. & PUB. POL'Y 21, 23 (2016) ("[O]nly a few biosimilar applications have been filed with the Food and Drug Administration (FDA), and just one biosimilar has been approved to date.").

description requirement was *not* litigated. A review of the related patents and their specifications may prove informative as to why parties did not litigate such issues to judgment. Such an investigation may uncover some of the technology-specific effects addressed here—that, for example, traditional technologies in both the ANDA and non-ANDA contexts did not give rise to written-description issues. Here, as in other instances, the "curious incident" worthy of study lies in the dog that did not bark.[75]

More generally, Allison and Ouellette's study provides insight into the future of empirical versus doctrinal patent scholarship. The authors' methodology appears to be helpful for collecting and analyzing, at a high level, a large number of otherwise complex and doctrinally diverse cases. Simply determining—and counting—what constitutes a "written-description opinion," and what to do where multiple patents are at issue, is difficult. This is especially the case when done in bulk. But, more than anything, Allison and Ouellette's study demonstrates that it is possible to define a closed universe of cases for a given doctrine or technology area, and to weigh their outcomes and the levels of their analyses.

Their study also demonstrates, however, the limits of larger empirical assessments for narrower doctrines or technology classes. In some data slices—such as non-ANDA pharmaceutical cases that upheld the validity of a patent subject to written-description challenges—we have an *N* of 1.[76] This means that the power of their specific results for any given case is open to further *qualitative* analysis—and possible contradiction. As demonstrated by the *Alcon* decision, some questions will simply turn on idiosyncrasies that empirical analyses cannot capture. Allison and Ouellette's article, therefore, shows the importance of close doctrinal analyses of cases.[77] Their study, and others like it, provide excellent jumping-off points for further research—both quantitative and quantitative.

75. *Cf.* Dan L. Burk, *The Curious Incident of the Supreme Court in* Myriad Genetics, 90 NOTRE DAME L. REV. 505, 505–06 (2014) (comparing the Supreme Court's silence on *Mayo Collaborative Services v. Prometheus Laboratories, Inc.* in the later-decided *Association for Molecular Pathology v. Myriad Genetics, Inc.* to be like the "curious incident" of the dog that did not bark in the Sherlock Holmes tale, *Silver Blaze*).

76. *See, e.g.*, Allergan, Inc. v. Watson Labs., Inc., 869 F. Supp. 2d 456, 459 (D. Del. 2012) (invalidating a patent, but not for written-description issues).

77. *See supra* notes 40–65 and accompanying text.

CONCLUSION

Allison and Ouellette's article concerning patent law's written-description requirement provides a shocking disparity between pharmaceutical cases in the ANDA versus non-ANDA contexts. Scholars, including Allison and Ouellette, have provided several high-level hypotheses as to these results, but none appear to provide satisfactory answers. A further examination of the underlying cases in Allison and Ouellette's dataset provides two insights: One, the written-description requirement is at issue in roughly equal numbers in ANDA versus non-ANDA cases. But, two, for the decisions that do discuss the written-description requirement, almost every ANDA case survives the courts' written-description analyses, while a large number of non-ANDA cases fail them. A closer examination of these cases reveals that this disparity is likely due to particular idiosyncrasies in each case, rather than a high-level of assessment of whether they arose in the ANDA or non-ANDA contexts. Allison and Ouellette's article, in turn, demonstrates the power and limits of empirical patent scholarship when addressing narrow doctrinal or technological inquiries.

APPENDIX
UNIQUE PHARMACEUTICAL PATENT OPINIONS IN ALLISON & OUELLETTE (2016)

Legend: 1 = Written Description Valid as a Matter of Law; 2 = Written Description Fact Issue—Valid; 3 = Written Description Invalid as a Matter of Law; 4 = Written Description Fact Issue—Invalid; 5 = Written Description Fact Issue—Remaining

						Written Description	
ANDA Opinions	**1**	**2**	**3**	**4**	**5**	**3-level**	**5-level**
Acorda Therapeutics Inc. v. Apotex Inc., No. 07-CV-4973, 2011 WL 4074116 (D.N.J. Sept. 6, 2011)		1				3	4
Alza Corp. v. Mylan Labs., Inc., 388 F. Supp. 2d 717 (N.D. W. Va. 2005)		1				3	4
Astra Aktiebolag v. Andrx Pharm., Inc., 222 F. Supp. 2d 423 (S.D.N.Y. 2002)		1				3	4
Bone Care Int'l, LLC v. Pentech Pharm., Inc., 862 F. Supp. 2d 790 (N.D. Ill. 2012)		1				3	4
GlaxoSmithKline LLC v. Banner Pharmacaps, Inc., 744 F.3d 725 (Fed. Cir. 2014)		1				3	4
Pfizer Inc. v. Teva Pharm. U.S.A. Inc., 882 F. Supp. 2d 643 (D. Del. 2012)		1				3	4
Research Found. of State Univ. of N.Y. v. Mylan Pharm. Inc., 809 F. Supp. 2d 296 (D. Del. 2011)		1				3	4
Abbott Labs. v. Andrx Pharm., Inc., 473 F.3d 1196 (Fed. Cir. 2007)					1	2	3
Glaxo Wellcome Inc. v. Eon Labs Mfg. Inc., No. 00-CV-9089, 2003 WL 22004874 (S.D.N.Y. Aug. 22, 2003)					1	2	3
Alcon Research Ltd v. Barr Labs., 837 F. Supp. 2d 364 (D. Del. 2011)				1		1	2
Abbott Labs. v. TorPharm Inc., 300 F.3d 1367 (Fed. Cir. 2002)						0	0
Alza Corp. v. Mylan Labs., Inc., 349 F. Supp. 2d 1002 (N.D. W. Va. 2004)						0	0

Legend: 1 = Written Description Valid as a Matter of Law; 2 = Written Description Fact Issue—Valid; 3 = Written Description Invalid as a Matter of Law; 4 = Written Description Fact Issue—Invalid; 5 = Written Description Fact Issue—Remaining

						Written Description	
ANDA Opinions	**1**	**2**	**3**	**4**	**5**	**3-level**	**5-level**
Aventis Pharma Deutschland GmbH v. Lupin Ltd., No. 2:05-CV-421, 2006 WL 2008962 (S.D.N.Y. July 17, 2006)						0	0
Bristol-Myers Squibb Co. v. Andrx Pharm., Inc., 343 F. Supp. 2d 1124 (S.D. Fla. 2004)						0	0
Cephalon, Inc. v. Watson Pharm., Inc., 707 F.3d 1330 (Fed. Cir. 2013)						0	0
Eli Lilly & Co. v. Actavis Elizabeth LLC, 435 F. App'x 917 (Fed. Cir. 2011)						0	0
Eli Lilly & Co. v. Sicor Pharm. Inc., 705 F. Supp. 2d 971 (S.D. Ind. 2010)						0	0
Eli Lilly & Co. v. Teva Parenteral Medicines, No. 1:10-CV-1376, 2012 WL 2358102 (S.D. Ind. June 20, 2012)						0	0
Glaxo Grp. Ltd v. Teva Pharm. USA Inc., No. 02-CV-219, 2004 WL 1875017 (D. Del. Aug. 20, 2004)						0	0
Glaxo Grp. Ltd. V. Apotex Inc., 376 F.3d 1339 (Fed. Cir. 2004)						0	0
Glaxo Wellcome Inc. v. EON Labs Mfg. Inc., No. 00-CV-9089, 2002 WL 1874830 (S.D.N.Y. Aug. 13, 2002)						0	0
Glaxo Wellcome Inc. v. Eon Labs Mfg. Inc., No. 00-CV-9089, 2003 WL 22004871 (S.D.N.Y. Aug. 22, 2003)						0	0
Imperial Chemical Indus. PLC v. Barr Labs., 795 F. Supp. 619 (S.D.N.Y. 1992)						0	0
Imperial Chemical Indus. PLC v. Danbury Pharmacal Inc., 777 F. Supp. 330 (D. Del. 1991)						0	0
Medicis Pharmaceutical Corp. v. Actavis Mid Atl. LLC, No. 11-409-LPS-CJB, 2012 WL 2126873 (D. Del. June 12, 2012)						0	0

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						Written Description	
ANDA Opinions	**1**	**2**	**3**	**4**	**5**	**3-level**	**5-level**
Momenta Pharm., Inc. v. Amphastar Pharm., Inc., 887 F. Supp. 2d 303 (D. Mass. 2012)						0	0
Ortho-McNeil Pharm. Inc. v. Kali Labs., 482 F. Supp. 2d 478 (D.N.J. 2007)						0	0
Ortho-McNeil Pharm. Inc. v. Mylan Labs., Inc., No. 04-CV-1689, 2006 WL 2865469 (D.N.J. Oct. 5, 2006)						0	0
Ortho-McNeil-Janssen Pharm. Inc. v. Watson Labs. Inc., No. 08-5103(SRC), 2011 WL 254313 (D.N.J. Oct. 5, 2006)						0	0
Ranbaxy Labs. Ltd v. Abbott Labs., No. 04-CV-8078, 2005 WL 3050608 (N.D. Ill. Nov. 10, 2005)						0	0
Schering Corp. v. Mylan Pharm. Inc., No. 09-CV-6383, 2011 WL 3736503 (D.N.J. Aug. 22, 2011)						0	0
Senju Pharm. Co. Ltd v. Apotex Inc., 717 F. Supp. 2d 404 (D. Del. 2010)						0	0
SmithKline Beecham Corp. v. Apotex Corp., 286 F. Supp. 2d 925 (N.D. Ill. 2001)						0	0
SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331 (Fed. Cir. 2005)						0	0
Takeda Pharm. Co, Ltd v. Handa Pharm., LLC, No. 11-CV-840, 2012 WL 1243109 (N.D. Cal. Apr. 11, 2012)						0	0
Wyeth v. Mylan Pharm. Inc., No. 07-CV-91, 2009 WL 3335062 (N.D. W. Va. Oct. 14, 2009)						0	0

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						Written Description	
Non-ANDA Opinions	**1**	**2**	**3**	**4**	**5**	**3-level**	**5-level**
Allergan Inc. v. Watson Labs. Inc., 869 F. Supp. 2d 456 (D. Del. 2012)		1				3	4
Emory Univ. v. Glaxo Wellcome Inc., 96-CV-1868, 1997 WL 817342 (N.D. Ga. July 14, 1997)					1	2	3
O'Hara Mfg. Ltd v. Eli Lilly & Co., No. 85-cv-3979, 1986 WL 8391 (N.D. Ill. July 21, 1986)					1	2	3
Oakwood Labs. v. Tap Pharm. Prods. Inc., No. 01-CV-7631, 2003 WL 22400759 (N.D. Ill. 2003)					1	2	3
AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc., 759 F.3d 1285 (Fed. Cir. 2014)				1		1	2
Eli Lilly & Co. v. Teva Pharm. USA Inc., 619 F.3d 1329 (Fed. Cir. 2010)				1		1	2
Purdue Pharma LP v. Faulding Inc., 230 F.3d 1320 (Fed. Cir. 2000)				1		1	2
Centocor Ortho Biotech Inc. v. Abbott Labs., 636 F.3d 1341 (Fed. Cir. 2011)			1			1	1
Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916 (Fed. Cir. 2004)			1			1	1
Abbott GMBH & Co., KG v. Centocor Ortho Biotech, Inc., 870 F. Supp. 2d 206 (D. Mass. 2012)						0	0
Abbott Labs. v. Teva Pharm. USA Inc., No. 02-CV-1512, 2005 WL 6225546 (D. Del. May 6, 2005)						0	0
ALZA Corp. v. Andrx Pharm., LLC, 603 F.3d 935 (Fed. Cir. 2010)						0	0
Amgen Inc v. Chugai Pharm. Co. Ltd., 927 F.2d 1200 (Fed. Cir. 1991)						0	0
Amgen Inc. v. F. Hoffman-LA Roche Ltd., 580 F.3d 1340 (Fed. Cir.2009)						0	0

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						Written Description	
Non-ANDA Opinions	**1**	**2**	**3**	**4**	**5**	**3-level**	**5-level**
Apotex, Inc. v. UCB, Inc., 970 F. Supp. 2d 1297 (S.D. Fla. 2013)						0	0
Aventis Pharma S.A. v. Hospira Inc., 743 F. Supp. 2d 305 (D. Del. 2010)						0	0
Glaxo Group Ltd v. Kali Labs. Inc., 03-CV-399, 2005 WL 1793728 (D.N.J. July 27, 2005)						0	0
Graceway Pharm. LLC v. Perrigo, No. 10-CV-937, 2011 WL 3206481 (D.N.J. July 27, 2011)						0	0
Hoffman-La Roche Inc. v. Lemmon Co., No. 84-CV-4303, 1989 WL 89241 (E.D. Pa. Aug. 7, 1989).						0	0
Liposome Co. Inc. v. Vestar Inc., No. 92-CV-332, 1994 WL 738952 (D. Del. Dec. 20, 1994)						0	0
McNeil-PPC Inc. v. Perrigo Co., No. 05-CV-1321, 2007 WL 81918 (S.D.N.Y. Jan. 12, 2007)						0	0
Medicis Pharm. Corp. v. Acella Pharm. Inc., No. 10-CV-1780, 2011 WL 810044 (D. Ariz. Mar. 2, 2011)						0	0
N. Am. Vaccine Inc. v. Am. Cyanamid Co., 7 F.3d 1571 (Fed. Cir. 1993)						0	0
Pharm. Res. Inc. v. Roxane Labs. Inc., 253 Fed. App'x 26 (Fed. Cir. 2007)						0	0
Teva Pharm. USA, Inc. v. Sandoz, Inc., 723 F.3d 1363 (Fed. Cir. 2013)						0	0
Tristrata Tech. Inc. v. ICN Pharm. Inc., 313 F. Supp. 2d 405 (D. Del. 2004)						0	0
UCB Inc. v. KV Pharm. Co., 08-CV-223, 2009 WL 2524519 (D. Del. Aug. 18, 2009)						0	0
Unigene Labs. Inc. v. Apotex Inc., No. 06-CV-5571, 2010 WL 2730471 (S.D.N.Y. July 7, 2010)						0	0
Warner Lambert Co. v. Teva Pharm. USA Inc., No. 99-CV-922, 2007 WL 4233015 (D.N.J. Nov. 29, 2007)						0	0