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ARTICLE

Infringement by Drug Label

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Abstract. In pharmaceutical patent cases, the drug label is often the primary piece of evidence regarding whether generic drug companies induce doctors to infringe brand drug companies' patents. But a series of recent decisions from the U.S. Court of Appeals for the Federal Circuit has taken this focus on the label too far. Rather than assessing what doctors actually did (or would do) based on a drug label, the Federal Circuit has treated drug labels as if they were patent claims, assessing whether their text merely "contains" a patented method of use. This has yielded a new, problematic doctrinal turn—what we call "infringement by label"—that threatens generics' ability to enter the market, even when their products would not actually cause doctors to practice any of the brands' patents. Infringement by label spotlights the Federal Circuit's misunderstanding of drug labeling at the U.S. Food and Drug Administration (FDA) and a lack of clarity in the court's case law about the nature of induced patent infringement, the theory of infringement most common in label-focused drug patent litigation. By identifying these deficiencies, this Article aims to return drug patent litigation to its factual and doctrinal moorings. At the same time, we show how the Federal Circuit's infringement-by-label theory underscores several broader, unresolved questions in patent law—namely, whether the interpretation of drug labels is an issue of law or fact; whether the objects of induced infringement are statements made by the defendant or how such statements are perceived by a direct infringer; and how to construct a hypothetical direct infringer to prove inducement. Answering these questions would

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improve pharmaceutical patent litigation and clarify how generics can enter the market while being faithful to the FDA's drug labeling regime.

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Introduction

In pharmaceutical patent cases, the drug label is king and the king is a lie. Under the Hatch-Waxman Act, whether generic drugs can be lawfully sold often depends on whether their labels would induce physicians to prescribe a patent-infringing use.[1] But that principle is predicated on the fiction that doctors read drug labels and do what they say.[2] In cases where no generic version is yet on the market, this inquiry devolves into asking how a hypothetical doctor would read a hypothetical label to treat a hypothetical patient[3]—none of which may *actually* happen once the generic is sold. Legal fiction heaped upon fiction produces odd results in litigation, faulted, in roughly equal measure, by courts' myopic view of drug labels and the U.S. Court of Appeals for the Federal Circuit's standards of appellate review.[4] Decisions in the area muddle patent infringement doctrine and theory.[5] More practically, they retreat from the Hatch-Waxman Act's "Grand Bargain": "balancing early generic entry with new incentives for sustainable . . . innovation."[6]

Though this discussion of drugs, labels, doctors, and patents might seem arcane, the stakes are enormous: Label-centric infringement disputes regularly involve hundreds of millions of dollars in potential damages, and they are fast becoming the most important contest at the intersection of patent law and drug

1. 21 U.S.C. § 355(c)(3)(C); *see, e.g.*, Grunenthal GMBH v. Alkem Lab'ys Ltd., 919 F.3d 1333, 1339 (Fed. Cir. 2019) ("[W]e ask whether the Hikma and Actavis labels instruct users to treat polyneuropathic pain with tapentadol hydrochloride."); Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp., 785 F.3d 625, 631 (Fed. Cir. 2015) ("The principles that can be distilled from these cases are . . . [whether] the drug label induces infringement by physicians. The label must encourage, recommend, or promote infringement."); AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1060 (Fed. Cir. 2010) ("The pertinent question is whether the proposed label instructs users to perform the patented method.").

2. *See, e.g.*, GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 7 F.4th 1320, 1328 (Fed. Cir. 2021) (per curiam) (reviewing expert evidence of how physicians would have read a drug label); *see also id.* at 1342 (Prost, J., dissenting) (noting that "every expert cardiologist at trial said he *didn't even read* the label to make prescribing decisions").

3. *See, e.g.*, Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1365 (Fed. Cir. 2003) (noting that an infringement analysis, in this context, is "hypothetical because the allegedly infringing product has not yet been marketed").

4. *See infra* Part II.D.

5. *See infra* Part III.

6. Susan K. Finston, Neil S. Davey, Ananda M. Chakrabarty & Raj S. Davé, *The Biopharmaceutical Social Contract and U.S. Patent Social Contract: Historical Antecedents and Recent Developments*, *in* INTELLECTUAL PROPERTY ISSUES IN MICROBIOLOGY 308 (Harikesh Bahadur Singh, Chetan Keswani & Surya Pratap Singh eds., 2019). For a critique of the "Grand Bargain" framing, see John R. Thomas, *Hatch-Waxman's Renegades*, 2023 U. ILL. L. REV. 831, 876-77.

policy.[7] Indeed, as of this writing, Congress is considering legislation that would purport to immunize generic companies from infringement suits when they attempt to remove patented methods of use from their labels.[8]

All new drugs sold in the United States come with "labeling": "all labels and other written, printed, or graphic matter" accompanying the drugs' packaging.[9] One labeling document in particular—what practitioners before the U.S. Food and Drug Administration (FDA) call the "package insert" (which is often equated by courts to a drug's "label"[10])—is the product of carefully crafted negotiations between the FDA and the drug's regulatory sponsor.[11] The FDA takes a keen interest in the package insert, and drug labeling more generally, because drugs' *labeling* is the primary object of the agency's regulatory oversight.[12] The FDA's power lies in policing "misbranded" drugs.[13] And a drug is "misbranded"—and therefore violates FDA law—if it uses labeling that is "false or misleading in any particular."[14]

Usually, generic drugs must have package inserts identical to their branded counterparts.[15] This identity requirement is the trigger for pharmaceutical patent litigation under the Hatch-Waxman Act.[16] If the branded drug is protected by a patent on the drug product itself, a generic company can't lawfully sell that drug unless it proves that the patent is invalid or that its generic product won't infringe.[17] Similarly, if a brand company's patents cover all of its drug's FDA-approved uses, a generic's package insert must, by law,

7. *See* Matthew Lane, *Federal Circuit Should Restore Generics 'Skinny Label' Process*, BLOOMBERG L. (Jan. 12, 2021, 1:01 AM PST), https://perma.cc/34BQ-WE2K ("Teva has been subjected to a $234 million judgment . . . [yet] made only $74 million in sales during the relevant period . . . . [T]he Teva case will further erode the Hatch-Waxman Act, destroy the balance that was reached by Congress after months of deliberation, and cause higher drug prices for patients.").

8. Skinny Labels, Big Savings Act, S. 5573, 118th Cong. (2024).

9. 21 U.S.C. § 321(m).

10. For more on this terminological distinction and how it is employed in this Article, see Part I.A below.

11. 21 C.F.R. § 201.57 (2024); *see also* NAITEE TING, DING-GENG CHEN, SHUYEN HO & JOSEPH C. CAPPELLERI, PHASE II CLINICAL DEVELOPMENT OF NEW DRUGS 18 (2017) (describing these negotiations). Other aspects of labeling, for example, branding graphics, are not necessarily preapproved by the FDA.

12. *See* DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA 73-117 (2010) (describing the FDA's authority under the Federal Food, Drug, and Cosmetics Act of 1938); Nathan Cortez, *The Statutory Case Against Off-Label Promotion*, 83 U. CHI. L. REV. ONLINE 124, 128-33 (2017) (explaining the FDA's authority over drugs through labeling).

13. *E.g.*, 21 U.S.C. § 331(a)-(c).

14. *Id.* § 352(a)(1).

15. *Id.* § 355(j)(2)(A)(v).

16. 35 U.S.C. § 271(e)(2)(A).

17. *Id.* § 282(b).

recite the same, patented uses.[18] The package insert, therefore, can establish that the generic will *induce* doctors to practice a patented use, an act of indirect infringement under the patent statute.[19]

Yet the Hatch-Waxman Act provides an exception to generics' package-insert identity requirement. If at least one FDA-approved use of the branded drug is unpatented, a generic can avoid patent infringement—and obtain FDA approval—by "carving out" the patented uses from its package insert, leaving only the unpatented use.[20] Congress made a policy choice to permit these carveouts to expedite the approval of generic drugs: If the drug product itself is not covered by a patent, and if there is at least one unpatented use for it, a brand company shouldn't be able to leverage its method-of-use patents to block generic entry altogether.[21] Congress's choice to permit carveouts also implicitly recognizes that, without a patent covering the drug product or every FDA-approved use, a generic drug would not necessarily infringe a brand's patents. Carveouts are emblematic of the broader purpose of the Hatch-Waxman Act: "to get generic drugs into the hands of patients at reasonable prices—fast."[22]

Recent decisions from the Federal Circuit, however, have undermined Congress's policy choice—and made a mess of patent infringement theory and doctrine in the process.[23] In *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.*, the Federal Circuit reinstated a $236 million jury verdict in favor of the patent holder even though the generic had carved the only patented indication out of its package insert.[24] The Federal Circuit decision—which prompted an unusual rehearing at the Circuit, made national news, and spurred the Solicitor General to urge the Supreme Court to grant certiorari—stood largely on procedural grounds: judicial deference to jury factfinding, even though the only evidence of inducement was the generic's package insert and statements it made

18. 21 U.S.C. § 355(j)(2)(A)(i).

19. 35 U.S.C. § 271(b); *see also* cases cited *supra* note 1 (asking whether a generic label instructs or induces infringement). In this circumstance, the doctors are what patent lawyers call "direct infringers"—they are the ones actually *using* the brand's patented method to treat their patients. *See* 35 U.S.C. § 271(a). But suing individual doctors isn't a great look for a drug company, and it would be economically infeasible to boot. Better to sue the generic company that is selling the product *inducing* direct infringement.

20. 21 U.S.C. § 355(j)(2)(A)(viii).

21. Caraco Pharm. Lab'ys, Ltd. v. Novo Nordisk A/S, 566 U.S. 399, 415 (2012) ("The statutory scheme . . . contemplates that one patented use will not foreclose marketing a generic drug for other unpatented ones.").

22. *In re* Barr Lab'ys, Inc., 930 F.2d 72, 76 (D.C. Cir. 1991).

23. The Federal Circuit has exclusive jurisdiction over all appeals in patent cases nationwide. 28 U.S.C. § 1295(a)(1).

24. 7 F.4th 1320, 1323, 1348 (Fed. Cir. 2021) (per curiam).

about the FDA's standards for approval.[25] In holding the generic liable for inducement, the Federal Circuit conjured the spirit of an infringement theory it had seemingly buried twenty years earlier: infringement by label.[26]

Since *GlaxoSmithKline*, the Federal Circuit has decided a string of cases shaping the contours of this newly recognized infringement-by-label theory—most notably, *United Therapeutics Corp. v. Liquidia Technologies, Inc.*, upholding a finding of inducement from a single, FDA-required "instruct[ion]" on the generic's package insert,[27] and *Amarin Pharma, Inc. v. Hikma Pharmaceuticals USA Inc.*, reversing a dismissal where the allegedly inducing conduct consisted of an FDA-mandated warning on the package insert along with public statements about generic equivalence.[28] As of this writing, the Federal Circuit is currently considering yet another infringement-by-label case, *Corcept Therapeutics, Inc. v. Teva Pharmaceuticals USA, Inc.*,[29] in which the district court granted summary judgment *against* the patent holder because the package insert warned *against* the allegedly infringing use.[30]

Some of the confusion surrounding infringement by label, which this Article is the first to comprehensively document, stems from the Federal Circuit's misunderstanding of drug labeling and how package inserts come to be.[31] Some confusion stems from how the Federal Circuit has applied its own standards of review.[32] And still more confusion flows from yet-unanswered questions—more than forty years after the enactment of the Hatch-Waxman Act—about the contours of inducement in cases about drug patents.[33] The bottom line is that the Federal Circuit's recent decisions—and *GlaxoSmithKline*,

25. Namely, that the generic was "therapeutically equivalent" to its branded counterpart. *Id.* at 1326, 1335-39; Brief for the United States as Amicus Curiae at 1, Teva Pharms. USA, Inc. v. GlaxoSmithKline LLC, 143 S. Ct. 2483 (2023) (No. 22-37), 2023 WL 2717391; *see* Jonathan Stempel, *U.S. Appeals Court Revives Glaxo $235.5 Million Verdict Against Teva*, REUTERS (Oct. 2, 2020), https://perma.cc/U79Q-2QK8.

26. *See* Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1364-65 (Fed. Cir. 2003) ("[T]he request to make and sell a drug labeled with a permissible (non-infringing) use cannot reasonably be interpreted as an act of infringement (induced or otherwise) with respect to a patent on an unapproved use, as the ANDA does not induce anyone to perform the unapproved acts required to infringe.").

27. 74 F.4th 1360, 1371-72 (Fed. Cir. 2023).

28. 104 F.4th 1370, 1379, 1381 (Fed. Cir. 2024); *see also* Janssen Pharms., Inc. v. Mylan Lab'ys Ltd., No. 23-2042, 2025 WL 946390, at *3 (Fed. Cir. Mar. 28, 2025) (affirming a ruling of induced infringement because the generic label recited a reinitiation regimen covered by a patent).

29. Docket, Corcept Therapeutics, Inc. v. Teva Pharms. USA, Inc., No. 24-1346 (Fed. Cir. filed Jan. 11, 2024).

30. 709 F. Supp. 3d 138, 164 (D.N.J. 2023).

31. *See infra* Part I.A.

32. *See infra* Part II.D.

33. *See infra* Part III.

in particular—complicate generics' path to market and may discourage some generic entry altogether.[34] This is important: For drugs with both patented and unpatented uses, the first generic tries to carve out a patented use nearly half the time.[35]

Giving the Hatch-Waxman Act's carve-out provisions full effect will require the Federal Circuit to resolve bigger issues at the edge of patent infringement theory and doctrine. The first regards how to treat evidence of inducement—especially the package insert—along the law-fact spectrum. While inducement, like other forms of patent infringement, is an issue of fact, the Federal Circuit's infringement-by-label theory threatens to turn inducement into an interpretive exercise—a quasi-issue of law—inappropriate for the deference the appellate court has given district court decisions on infringement.[36] The second concerns identifying the object of inducement in cases where labeling is at issue: What specific aspects of a package insert (and its accompanying marketing copy) can be said to induce a physician into performing an infringing activity?[37] The third relates to the hypothetical nature of infringement in generic prelaunch inducement cases: Whether the hypothetical direct infringer—often, a doctor—should be informed by actual physician practice or, instead, should be a further fictional construct, such as a reasonably informed prescriber?[38] Beyond all this, the Federal Circuit would do well to simply recognize that drugs' package inserts are not coequal with their labeling—a recognition that would come with a host of practical virtues for litigators and litigants alike.[39]

The remainder of this Article proceeds as follows. Part I explains the nature of novel drugs, their labeling, and how those concepts fold into pharmaceutical patent litigation. Part II lays the foundation of patent infringement law before discussing the Federal Circuit's infringement-by-label cases, both before and after *GlaxoSmithKline*. Part III considers what these cases tell us about patent doctrine and theory more generally, exploring the law-fact distinction, the object of inducement, and the hypothetical nature of prescriber information for a not-yet-launched drug. Part IV provides suggestions for aligning pharmaceutical patent litigation with drug labeling realities.

34. *See* Dani Kass, *GSK Redo Doesn't Cure Generics' 'Skinny Label' Uncertainty*, LAW360 (Aug. 9, 2021), https://perma.cc/AY9Q-Q2EW.

35. Bryan S. Walsh, Ameet Sarpatwari, Benjamin N. Rome & Aaron S. Kesselheim, *Frequency of First Generic Drug Approvals with "Skinny Labels" in the United States*, 181 JAMA INTERNAL MED. 995, 995 (2021).

36. *See infra* Part III.A.

37. *See infra* Part III.B.

38. *See infra* Part III.C.

39. *See infra* Part IV.

I. Drugs, Their Labeling, and the Hatch-Waxman Act

A. Labeling Versus Labels

In the United States, all pharmaceutical products, or, more colloquially, "drugs" (although that word is a specialized term of art in FDA law), come with "labeling."[40] Labeling includes something akin to a consumer product *label*, designed to catch the eye, indicate what's inside, and encourage a purchase.[41] But it also includes two documents: "Full Prescribing Information" and "Highlights of Prescribing Information," the latter of which is a single-page summary of the former; together, the two documents constitute the "package insert."[42] By law, the package insert provides "a summary of the essential scientific information needed for the safe and effective use of the drug,"[43] detailing information about the drug and its uses: the drug's active pharmaceutical ingredient, how the drug has been prepared, directions for using the drug safely, the indications for which the drug has been demonstrated to be effective, possible "adverse reactions" (i.e., side-effects), and so on.[44]

FDA regulations specify the format of package inserts, dividing the document into seventeen numerical sections, such as "Dosage and Administration" and "Warnings and Precautions."[45] Two sections, in particular, describe the illness the drug is meant to treat: "Indications and Usage" (Section 1), including "[a] concise statement of each of the product's indications"[46]; and "Clinical Studies" (Section 14), including "those clinical studies that facilitate an understanding of how to use the drug safely and effectively" and "the studies that support effectiveness for the labeled indication(s)."[47] Taken together, these two sections identify the specific disease the drug is approved to treat, the patient population meant to be treated and under what circumstances, and the evidence supporting those determinations.[48] Other sections of the package insert identify negative effects from taking the drug (say, the amount of the drug that constitutes an overdose), contraindications (if any), and the potential for abuse or dependency.[49]

40. 21 U.S.C. § 321(m); *see also id.* § 321(g)(1) (defining "drug").

41. *See id.* § 321(k); *see also* Frank I. Schechter, *The Rational Basis of Trademark Protection*, 40 HARV. L. REV. 813, 819 (1927) (describing trademark as a consumer efficiency law).

42. 21 C.F.R. § 201.56(d).

43. *Id.* § 201.56(a)(1).

44. *Id.* § 201.57(a)-(c); *see, e.g.*, FDA, COREG® (carvedilol) Tablets (2010), https://perma.cc/RLC5-NHA5.

45. 21 C.F.R. § 201.56(d)(1) (2024).

46. *Id.* § 201.57(a)(6).

47. *Id.* § 201.57(a)(15).

48. *See id.* § 201.57(a)(6), (a)(15).

49. *Id.* § 201.57(c)(5), (c)(10)-(11).

As technical as this may seem, the package insert is not unilaterally prepared by some FDA bureaucrat or drug company scientist. Rather, the package insert results from negotiations between the FDA and the drug sponsor—the company shepherding the new drug through the regulatory approval process.[50] Sponsors want their package inserts to be as expansive as possible with few warnings to maximize the potential patient and physician market.[51] The FDA, by contrast, wants the package insert to be exacting—only as broad as the safety and efficacy data allow.[52] An FDA consultant described these negotiations as, essentially, a letter writing campaign on the road to approval:

> The FDA reviews the proposed PI [package insert], makes edits, and returns the PI to the company. The process may go back and forth several times before [the company] and FDA concur on the contents of the PI. The FDA will send the final, approved version of the PI with the approval letter. The duration of the labeling negotiations depends upon the nature and volume of edits required.[53]

For those unfamiliar with FDA law, the FDA's collaboration with drug sponsors to wordsmith package inserts may seem odd. But this is one of the FDA's core functions: The Agency's power to police misbranded drugs centers on regulating *labeling*.[54] Understanding why is an exercise in statutory logic.[55] Section 301(a) of the Food, Drug, and Cosmetics Act (FDCA) prohibits introducing "misbranded" drugs into interstate commerce.[56] Section 502(a) of the Act considers a drug to be misbranded "[i]f its labeling is false or misleading in any particular."[57] For prescription drugs, this includes an absence of "adequate information" for safe use by practitioners.[58] Circuitously, an applicant can satisfy that criteria by exemption if the labeling includes a complete and

50. TING ET AL., *supra* note 11, at 18-19.

51. *Id.* Of course, this risks the sponsor being sued under a "failure to warn" theory. *See, e.g.*, Wyeth v. Levine, 555 U.S. 555, 558-60 (2009) (allowing a failure-to-warn suit for a harm not explicitly warned against on the drug's package insert).

52. *See* TING ET AL., *supra* note 11, at 18-19.

53. FDA, DRUG APPROVAL—BRINGING A NEW DRUG TO THE MARKET 19 (June 2022), https://perma.cc/M8SD-HZKB.

54. *See* CARPENTER, *supra* note 12, at 73-117 (detailing the history of the FDA's authority over labels); Cortez, *supra* note 12, at 128-33 (explaining how the FDA regulates drugs through labeling).

55. *See* Cortez, *supra* note 12, at 130-31 (similarly walking through this logic).

56. Federal Food, Drug, and Cosmetic Act § 301(a), ch. 675, 52 Stat. 1040, 1042 (1938) (codified as amended at 21 U.S.C. § 331). The Section prohibits numerous other acts related to drugs as well. *Id.*

57. *Id.* § 502(a) (codified at 21 U.S.C. § 352(a)).

58. That is, a new drug's labeling is misbranded or misleading if it "fails to reveal facts material in the light of [the labeling's] representations . . . under the conditions of use prescribed in the labeling or advertising thereof." Drug Amendments of 1962, Pub. L. No. 87-781 sec. 131(a), § 301(n), 76 Stat. 780, 791-92, (codified as amended at 21 U.S.C. § 331(n)). An absence of "[a]dequate information" for practitioners to "use the drug safely" is one such failure. 21 C.F.R. § 201.100(d)(1).

accurate statement of "indications, effects, dosages, routes, methods, and frequency and duration of administration," i.e., the package insert.[59] It is the FDA that determines whether this information satisfies the exemption, granting the agency significant power over whether a drug does or does not run afoul of the Food, Drug, and Cosmetics Act.[60] Practically, this means drug sponsors cannot include in their labeling any use—or for that matter, any information—that has not been sanctioned by the FDA.[61] This is why drug sponsors and the FDA negotiate over the precise wording of package inserts, down to the errant comma.[62]

Even then, package inserts are not set in stone. Drug sponsors often amend them—with the FDA's permission, of course—to supplement clinical trial summaries, add novel indications, amend warnings, and so on.[63] In 2023, the FDA reviewed more package-insert amendments about clinical efficacy specifically than new package inserts.[64] The FDA allows this fluidity to fulfill labeling's overarching purpose: documenting a drug's safety and efficacy.[65]

The text of the package insert, however, is not the end of the story. The FDA has long taken an expansive view of what constitutes a drug's labeling, far beyond the package insert.[66] Labeling, under FDA law, includes a variety of information sources, including:

> expressions, the design or composition of the [drug product,] . . . circumstances surrounding the distribution of the [drug product,] . . . advertising matter[,] . . . oral or written statements[,] . . . [or] circumstances in which the [drug product] is . . . offered or used for a purpose for which it is neither labeled nor advertised.[67]

As these regulations make clear, adequate labeling turns on a drug's "intended uses"—not just the words of the package insert but the overall "*objective*

59. 21 C.F.R. § 201.100(d) (2022); *see also* Cortez, *supra* note 12, at 130-33 (explaining the exemption framework).

60. Cortez, *supra* note 12, at 130-33.

61. *See* 21 C.F.R. § 201.56 (2022) (establishing the labeling requirements).

62. *See, e.g.*, Center for Drug Evaluation and Research, Approval Package for Application Number NDA 20-3214/S002, at 183 (Nov. 18, 2013), https://perma.cc/35XR-LPGN (requesting that the sponsor remove certain commas from drug description); *cf.* Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 347 (2007) (reconceptualizing the FDA's role as an *information-generating* agency).

63. *See* 21 C.F.R. § 314.70 (2022).

64. FDA, PERFORMANCE REPORT TO CONGRESS: PRESCRIPTION DRUG USER FEE ACT 12-13 (2023), https://perma.cc/PDQ6-9KNZ (reviewing 235 supplements about clinical efficacy and 156 new package inserts). Other types of amendments include those pertaining to safety and manufacturing information. *Id.* at 99-102.

65. *See* 21 C.F.R. § 314.70(b)(1) (2022) (requiring amendments if there have been changes "to the safety or effectiveness of the drug product").

66. Kordel v. United States, 335 U.S. 345, 349-50 (1948); *see also* Cortez, *supra* note 12, at 131.

67. 21 C.F.R. § 201.128 (2022).

intent of the persons legally responsible for the labeling" of the product.[68] A sponsor cannot avoid the practical effects of negotiating a narrow package insert with the FDA and then market the same drug to physicians more broadly; this would be "misbranding" under the FDCA.[69]

To be clear, pharmacists, physicians, and patent lawyers routinely refer to the package insert as a drug's "label," even though that is technically incorrect. For example, a well-respected pharmacists' trade journal advised its members to make use of "[o]ne important information source that pharmacists as well as other practitioners have access to, but sometimes overlook, . . . the drug's label, also known as the prescribing information or the package insert."[70] Medical journals routinely conflate the two, perhaps because prescribing drugs for uses not stated on the package insert is "off-label."[71] And patent cases, as we detail later, almost exclusively denominate the package insert as a drug's label.[72] This is exacerbated by the FDA itself which, in its online database of package inserts, Drugs@FDA, refers to package inserts under both "Labels" *and* "Labeling" headings.[73] Rather than being pedants, we generally adopt courts' vernacular in the remainder of this Article, especially in our discussion of patent cases that refer to the package insert as a "drug label." But this slippage in terminology belies an important point: Instructions to safely and effectively administer drugs go beyond just the statutory definition of "label."

All of this, then—a drug's broader labeling, including the package insert—would seem to be critically important for physicians. In theory, were a prescribing physician to sit down and actually read, say, the Full Prescribing Information document, they would be able to give the underlying drug to their patients in a safe and effective manner.[74] That may be true, although evidence

68. *Id.* (emphasis added).

69. *See* 21 U.S.C. § 321(n) (defining misbranding as, among other things, having misleading labeling).

70. Joseph P. Nathan & Etty Vider, *The Package Insert*, 40 U.S. PHARMACIST 8, 8 (2015).

71. *E.g.*, Jill Jin, *Safety of Medications Used During Pregnancy*, 328 JAMA 486, 486 (2022). ("[I]nformation from the FDA about the safety of a medication used during pregnancy can be found on the drug label (also known as the package insert).").

72. *See infra* Parts II.B-.D.

73. *Contrast* COREG, *supra* note 44 (stating, at the head of the package insert, "This label may not be the latest approved by FDA. For current labeling information, please visit."), *with* FDA, *COREG (carvedilol)*, DRUGS@FDA, https://perma.cc/9M77-H2R3 (archived Nov. 16, 2025) (listing the package insert under "Labeling-Package Insert," linking to the package insert under "Label (PDF)").

74. *See* TING ET AL., *supra* note 11, at 18; Helen W. Sullivan et al., *Physicians' Use of and Preferences for FDA-Approved Prescribing Information*, 18 RES. SOC. & ADMIN. PHARMACY 3027, 3027 (2022).

of doctors' use of drug labels is mixed.[75] The reality may be that most doctors—especially for medications they are otherwise familiar with—simply do not read drug labels.[76] And sometimes physicians' neglect of drug labels goes beyond indifference; it can be downright purposeful. Despite the FDA's sovereignty over the package insert, doctors are not legally required to prescribe medications according to their labels; they are free to prescribe drugs "off label"—for indications or patient populations not included on the package insert, for example, or at dosages different from what is recommended.[77] Carbatrol (carbamazepine), for example, is indicated for epilepsy and certain forms of neuralgia, or nerve pain.[78] But physicians have long used carbamazepine to treat bipolar disorder, even though no such indication is on the drug's label.[79] Off-label prescribing is common: "An estimated one in five prescriptions written are for an off-label use."[80] In extreme instances, an off-label use is the medical standard of care, effectively obliging doctors to use a drug beyond what is detailed in the package insert.[81]

Off-label prescribing does not violate any tenet of FDA law. What the FDA regulates is *labeling*—which drug products, package inserts included, can be sold in interstate commerce. The FDA does not generally regulate the practice of medicine—what doctors choose to *do* with drug products.[82] For all the attention heaped on drug labeling, many physicians treat drugs' package inserts as, essentially, wrapping paper.

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75. *See* Sullivan et al., *supra* note 74, at 3035 (finding that physicians do not consider the package insert to be a primary source of drug information); Michael B. Shea et al., *Outdated Prescription Drug Labeling: How FDA-Approved Prescribing Information Lags Behind Real-World Clinical Practice*, THERAPEUTIC INNOVATION & REGUL. SCI. 771, 771 (2018) (finding a high-level of off-label use among oncologists); H. W. Sullivan, A. C. O'Donoghue & K. J. Aikin, *Primary Care Physicians' Use of FDA-Approved Prescription Drug Labels*, 5 J. AM. BD. FAM. MED. 694, 697 (2014) (finding that roughly 25% of physicians, even when presented with a drug label, do not read past the content section); *Do Doctors Read Drug Warning Labels?*, CBS NEWS (May 16, 2000), https://perma.cc/8FQ8-WKKN (quoting former FDA Commissioner Robert Califf as saying, "Less than 1% of physicians have seen a [drug] label in the last year").

76. Sullivan et al., *supra* note 74, at 3035; Shea et al., *supra* note 75, at 771.

77. Russel G. Thornton, *Package Inserts and the Standard of Care*, 16 BAYLOR UNIV. MED. CTR. PROC. 502, 503 (2003); Patricia J. Zettler, *The Indirect Consequences of Expanded Off-Label Promotion*, 78 OHIO ST. L.J. 1053, 1061 (2017).

78. FDA, CARBATROL® (carbamazepine) Extended-Release Capsules, at 2, https://perma.cc/U9TP-6QX4 (archived July 26, 2024).

79. Steven C. Stoner et al., *Historical Review of Carbamazepine for the Treatment of Bipolar Disorder*, 27 PHARMACOTHERAPY 68, 68 (2007).

80. ELIZABETH RICHARDSON, *Off-Label Drug Promotion*, HEALTH AFFS.: HEALTH POL'Y BRIEF 1 (June 30, 2016), https://perma.cc/7DVA-ST5J.

81. *See* Thornton, *supra* note 77, at 503.

82. *See* Patricia J. Zettler, *Toward Coherent Federal Oversight of Medicine*, 52 S.D. L. REV. 427, 434-46 (2015).

B. The Hatch-Waxman Act and Pharmaceutical Patent Infringement

To ensure novel drugs are both safe and effective—and labeled as such—drug developers sponsor clinical trials, experiments measuring drugs' safety profiles at different doses and effectiveness in treating given conditions.[83] Assuming the trials are successful—though they frequently are not—the drug sponsor can file an application for approval with the FDA: a New Drug Application, or NDA.[84]

An NDA contains a raft of information about the drug product: a proposed package insert, of course, but also chemistry and manufacturing information, an ingredient list, information about any facilities used to produce the drug product, data generated by clinical trials, information about "nonclinical" toxicology, and so on.[85] An NDA must also contain information about any patents protecting: (1) the active ingredient, (2) the drug's formulation or composition, or (3) "a method of using such drug."[86] If the NDA is approved, the FDA lists the patent information in the *Approved Drug Products with Therapeutic Equivalence Evaluations* database, better known as the Orange Book—a duty the agency has described as "purely ministerial"[87] because it does not assess whether the patents actually cover the drug or a method of using it.[88] The novel drug with its approved labeling can then be sold in interstate commerce. And it often has a brand name, to contrast the drug product from the generic name of its active ingredient.[89] Tylenol, for example, is simply Johnson & Johnson's brand name for a drug product that includes acetaminophen—the active ingredient.[90]

Not every drug company wants to sell a branded version of a drug product; store-brand acetaminophen cures a headache as well as Tylenol. But imparting the same regulatory requirements to generics where the FDA has already approved the branded version might seem wasteful—especially requiring a generic company to rerun clinical trials to demonstrate the product's safety and

83. *See* 21 U.S.C. § 355(d) (requiring a new drug applicant to demonstrate "substantial evidence" of the drug product's safety and effectiveness and defining "substantial evidence" to include "adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience").

84. *Id.* § 355(b)(1)(A); *see also* Asher Mullard, *Parsing Clinical Success Rates*, 15 NATURE REV. DRUG DISCOVERY 441, 447 (2016) (reviewing evidence on clinical trial failure rates).

85. 21 U.S.C. § 355(b)(1)(A).

86. *Id.* § 355(b)(1)(A)(viii).

87. aaiPharma Inc. v. Thompson, 296 F.3d 227, 230, 237 (4th Cir. 2002).

88. *See* 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, 260 (2015).

89. *See* U.S. DEP'T OF HEALTH & HUM. SERVS., BEST PRACTICES IN DEVELOPING PROPRIETARY NAMES FOR HUMAN PRESCRIPTION DRUG PRODUCTS 7 (Dec. 2020), https://perma.cc/PEA7-3X7D (describing best practices for choosing drug brand names).

90. FDA, *Tylenol (acetaminophen)*, DRUGS@FDA, https://perma.cc/7VG8-A9E8 (archived July 26, 2024).

efficacy. Moreover, if the branded product were protected by patents, the generic could not, without fear of infringement, even begin those clinical trials until the brand's patents expired.[91] Nonetheless, prior to 1984, generic drug companies needed to do just that—an expenditure and delay many policymakers viewed as an impediment to lower drug prices.[92]

In 1984, after years of failed legislative, administrative, and judicial efforts in the area, Congress passed the Drug Price Competition and Patent Term Restoration Act—also known as the Hatch-Waxman Act—establishing the modern relationship among drug labels, generic drugs, and patents.[93] At its core, the Hatch-Waxman Act sought to protect brand sponsors' drug franchises and patents, encourage the development of new drugs, and lower the costs and administrative burden of generic entry.[94]

Under the Hatch-Waxman Act, a generic sponsor can obtain FDA approval by filing an *Abbreviated* New Drug Application—an ANDA—rather than a traditional NDA.[95] An ANDA must show that the generic product has the same "route of administration, . . . dosage form, and . . . strength" as the reference product and is similarly metabolized by the body, often referred to as "bioequivalence."[96] An ANDA need not otherwise provide safety and effectiveness data; the generic can piggyback on the clinical trial information submitted by the NDA holder.[97] Crucially, though, an ANDA must generally use the same label—a virtually identical package insert—as the branded reference drug.[98] In this way, the Hatch-Waxman Act sought to speed the FDA's review of generic drugs by requiring them to be as similar as possible to already approved brand drugs, label included.

As simple as the Hatch-Waxman Act made filing an ANDA, it also established a complex process for how a generic sponsor was to contend with a brand company's patents. This process—arguably the most heatedly negotiated aspect of the Act's creation—links the FDA's approval of a generic's ANDA to

91. Erika Lietzan, *The History and Political Economy of the Hatch-Waxman Amendments*, 49 SETON HALL L. REV. 53, 96-98 (2018).

92. The pre-1984 requirements for generic entry and the realities of generic competition are much more complex than this simplistic account. For a history of those, and their basis for the eventual passage of what became the Hatch-Waxman Act, see *id.* at 91-98.

93. Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act), Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of the U.S. Code).

94. *See* Finston et al., *supra* note 6, at 308 (describing this in terms of innovation as the "Grand Bargain"); Lietzan, *supra* note 91, at 59 (describing the genesis of the Hatch-Waxman Act in similar terms).

95. 21 U.S.C. § 355(j)(1).

96. *Id.* § 355(j)(2)(A)(iii)-(iv).

97. *Id.* § 355(j)(2)(A)(i).

98. *Id.* § 355(j)(2)(A)(v).

whether the generic drug product would infringe one of the brand company's patents listed in the Orange Book.[99] In short, the FDA is prohibited from approving an ANDA that would infringe an Orange Book patent until the threat of infringement dissipates through expiration, license, settlement, or a court order that the patent is invalid or will not be infringed.[100] Linking generic entry to patent infringement was key to the Hatch-Waxman Act's "Grand Bargain."[101]

To obtain approval, a generic sponsor must submit, as part of its ANDA, one of four certifications for each patent the brand sponsor has listed in the Orange Book.[102] The first two, paragraph I and paragraph II certifications—denominated for their subsectional home in the statute—arise, respectively, when there are no patents listed in the Orange Book for the branded drug or when a listed patent has already expired.[103] The third, a paragraph III certification, comes into play when an ANDA applicant does not seek FDA approval until the given patent will expire.[104] A generic's paragraph IV certification asks the FDA to grant approval *now*, even against an unexpired patent, because the generic applicant contends the patent is invalid or its product will not infringe.[105] This paragraph IV certification is, by statute, an act of patent infringement—giving rise to an almost inevitable lawsuit between the patent-holding brand company and the defendant generic company.[106]

That patent infringement suit, in turn, prevents the FDA from approving the generic product for thirty months—roughly the time it takes to litigate a patent dispute through trial.[107] Assuming the generic sponsor's ANDA is otherwise in condition for approval, the FDA can approve the generic application at the end of the thirty-month period, even if the patent suit has not been resolved.[108] If the court finds that the brand's patent would be infringed,

99. *Id.* § 355(j)(5)(B); *see also* Lietzan, *supra* note 91, at 106 ("The patent litigation provisions were similarly the subject of intense negotiation until the very end.").

100. 21 U.S.C. § 355(j)(5)(B).

101. *See* Thomas, *supra* note 6, at 865-66, 871.

102. 21 U.S.C. § 355(j)(2)(A)(vii).

103. *Id.* § 355(j)(2)(A)(vii)(I)-(II).

104. *Id.* § 355(j)(2)(A)(vii)(III).

105. *Id.* § 355(j)(2)(A)(vii)(IV).

106. 35 U.S.C. § 271(e)(2). There are yet further complexities here, including limits on how long a brand has to file a lawsuit against the ANDA filer, the availability of declaratory judgments and injunctions, and generic exclusivity and forfeiture. *E.g.*, 21 U.S.C. § 355(c)(3)(C)-(D). But none of these are important for our discussion below.

107. 21 U.S.C. § 355(c)(3)(C). This is often referred to as the "thirty-month stay." Thomas, *supra* note 6, at 842; *see also* Emily Deer, *Open to Close: An Empirical Study of Patent Case Termination Times*, BAKER BOTTS THOUGHT LEADERSHIP BLOG (May 1, 2020), https://perma.cc/5UU6-VS4X (documenting patent cases' roughly thirty-month time-to-trial metrics).

108. *See* Thomas, *supra* note 6, at 843. A generic that launches before a final decision in the patent suit, however, risks being liable for damages if it ultimately loses. *Id.*

the FDA cannot typically approve the ANDA until the expiration of the latest infringed patent.[109]

When the disputed patent—or patents, as is usually the case—covers the drug product itself, the litigation is relatively straightforward. Either the brand wins—because the patent is infringed and not invalid—and continues its exclusivity until the patent expires, or the ANDA applicant wins—because it does not infringe or the patent is invalid—and is allowed to sell its product.[110] Ditto for patents on a drug product's formulation or composition. Things get complicated, however, when the asserted patent covers methods of *using* a drug, and more complicated still where the branded drug is FDA-approved for more than one indication, not all of which are covered by the brand's method-of-use patents.[111]

This situation—a relatively common one—raises several policy tensions. Allowing brand companies to patent new uses of previously approved drugs encourages research into new indications for old drugs, a major public health policy objective.[112] But brands can also leverage method-of-use patents to extend their products' exclusivity beyond the protection of the product's original, unpatented use.[113] Separate patents on different uses can also lead to numerous amendments of Orange Book listings, undercutting the Hatch-Waxman Act's goal of efficiently circumscribing patent disputes.[114] Most relevant to this Article, the process raises questions about whether a generic's package insert *should* mimic the brand's package insert in every way[115]—particularly when there are methods of using the drug that are not patented.

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109. 21 U.S.C. § 355(c)(3)(C)(ii).

110. *Id.* § 355(c)(3)(C). As an incentive to challenge the NDA holder's patents, the first ANDA applicant to successfully maintain a paragraph IV certification receives 180 days of generic market exclusivity, preventing the approval of *another* generic during that time. *Id.* § 355(j)(5)(B)(iv).

111. For a description of method-of-use patents, see Timothy R. Holbrook, *Method Patent Exceptionalism*, 102 IOWA L. REV. 1001, 1005 (2017).

112. *See Addendum to FDA Memorandum, Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products (January 2017)—Additional and Updated Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products*, FDA, 9 (Jan. 2025), https://perma.cc/YDE6-LDHF; Karel H. van der Pol et al., *Drug Repurposing of Generic Drugs: Challenges and the Potential Role for Government*, 21 APPLIED HEALTH ECON. & HEALTH POL'Y 831, 832 (2023).

113. Michael A. Carrier & S. Sean Tu, *Why Pharmaceutical Patent Thickets Are Unique*, 32 TEX. INTELL. PROP. L.J. 79, 82-83 (2024).

114. *See* Julie Dohm, *Expanding the Scope of the Hatch-Waxman Act's Patent Carve-Out Exception to the Identical Drug Labeling Requirement: Closing the Patent Litigation Loophole*, 156 U. PA. L. REV. 151, 162 (2007).

115. *See* Benjamin Baek, GSK v. Teva*: The End of Generic Skinny Labels?*, 56 U.C. DAVIS L. REV. ONLINE 29, 35 (2022).

Enter the Hatch-Waxman Act's provision on Section viii carveouts—named, again, for its place in the statute.[116] If a branded drug is approved for at least one unpatented use, the Hatch-Waxman Act allows the generic applicant, as an alternative to one of the four patent-related certifications listed above, to submit to the FDA a statement asserting that it will market its generic product only for those unpatented uses.[117] If the ANDA applicant follows the Section viii route, it must, like a branded company, negotiate a label with the FDA for its generic drug that "carves out" the still-patented uses that appear on the brand's label.[118] In an exception to the usual rule that a generic must bear the same label as the brand, the FDA may, in turn, approve the generic's so-called "skinny label."[119] FDA approval of the skinny label allows the generic company to demonstrate that its drug—really, its label—is safe and effective, albeit only for a subset of uses, namely, those not covered by the brand's patents.[120] Lastly, while a paragraph IV certification temporarily blocks the FDA from approving an ANDA, a skinny label allows the FDA to immediately approve an ANDA because it operates as an act of *noninfringement*.[121]

An eagle-eyed reader may have noticed a slippage in terminology: Drug labels contain a section describing *"[i]ndications and usage"*—not *"uses."*[122] But Section viii centers on carving out patented "method[s] of *use*" from the generic label.[123] Labeled indications and patented methods of use are often not the same. The FDA has squared this circle by requiring NDA applicants, as part of the patent information submitted for the Orange Book, to craft "use codes"—250-character length summaries of the primary method of use claimed in a patent.[124]

116. 21 U.S.C. § 355(j)(2)(A)(viii). For a cogent description of the Section viii carve-out option, see Caraco Pharm. Lab'ys, Ltd. v. Novo Nordisk A/S, 566 U.S. 399, 406-07 (2012).

117. 21 U.S.C. § 355(j)(2)(A)(viii).

118. 21 C.F.R. § 314.94(a)(8)(iv) (2024).

119. 21 U.S.C. § 355(j)(2)(A)(v), 355(j)(4)(G); *see also* GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 7 F.4th 1320, 1328 (Fed. Cir. 2021) (per curiam) (using the phrase "skinny label").

120. *Caraco*, 566 U.S. at 406.

121. For a method-of-use patent listed in the Orange Book, the generic must choose *either* to make a paragraph IV certification *or* to pursue a Section viii carveout. If an ANDA applicant chooses the paragraph IV route and loses the infringement suit, it can't later attempt to carve out the relevant method of use under Section viii to get around the paragraph IV judgment against it, unless it files an entirely new ANDA—something that, of course, takes time. Rather, the approval of the litigated ANDA will be stayed until the relevant patent expires. *See* Salix Pharms. Ltd. v. Norwich Pharms. Inc., 98 F.4th 1056, 1069 (Fed. Cir. 2024) (rejecting an attempt to reopen a judgement of infringement under Federal Rule of Civil Procedure 60(b) after the generic company amended its ANDA to include a Section viii carveout).

122. 21 C.F.R. § 201.57(a)(6) (2024).

123. 21 U.S.C. § 355(j)(2)(A)(viii) (emphasis added).

124. *Caraco*, 566 U.S. at 428-29; John R. Thomas, *Towards FDA-USPTO Cooperation*, 66 ARIZ. L. REV. 1021, 1050-51 (2024) (discussing the FDA's role in use codes and specifying the 250-character length).

Like the listed patents themselves, the FDA does not police the accuracy of use codes.[125] It is information touching on these use codes that generic carve-out applicants must excise from their labels.[126] That often entails carving one of several FDA-approved indications out of the "Indications and Usage" section of the package insert. But as we describe in the cases below, Section viii carveouts can also implicate clinical studies described in the label, warnings, and more. All of this has a fox-guarding-the-henhouse quality, encouraging brand applicants to submit broad use codes, stretching the boundaries of their patents.[127] Doing so hampers a generic's ability to carve out *only* the patented use, raising the possibility that the proposed carveout will be rejected by the FDA as unsafe. A carveout that removes important safety information from a generic's label, for instance, would risk mislabeling the generic product, effectively requiring the FDA to reject the generic sponsor's ANDA.[128]

To be clear, these disputes over patents and labels under the Hatch-Waxman Act all occur prior to FDA approval, establishing the entry conditions for a generic product. Once a generic product has been fully approved by the FDA and launched into the market, the specialized provisions of the Hatch-Waxman Act no longer apply. While post-launch patent disputes are not technically Hatch-Waxman Act cases, they have a similar cadence, tone, and intensity. Patent litigators often distinguish the two types of cases by the provision of the Patent Act that creates the claim for infringement: Section 271(e)(2) for pre-FDA-approval Hatch-Waxman Act disputes, and Section 271(a) and (b) for their post-approval siblings.[129]

This overall structure has been described as a "delicate 'balance,'" both "careful and fragile."[130] There is good reason to doubt this view of the Hatch-Waxman Act as being so wispy.[131] For all of its careful crafting, the Act "has been subject to continuous legislative revisiting and revision" in its forty-year life.[132] But, delicate or not, such a careful structure should not belie how hotly pharmaceutical patent cases are litigated—often to the statute's breaking point.

125. Jacob S. Sherkow, *Administrating Patent Litigation*, 90 WASH. L. REV. 205, 215-16 (2015).

126. Thomas, *supra* note 124, at 1051-52.

127. *Id.* at 1053-54.

128. *See* CENTER FOR DRUG EVALUATION AND RESEARCH, FDA, ANDA SUBMISSIONS—REFUSE-TO-RECEIVE STANDARDS REVISION 2, 13 (Dec. 2016), https://perma.cc/FU5S-MHGR (noting poor use code carveouts as being one basis for refusing ANDA applications).

129. *See, e.g.*, Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1354 (Fed. Cir. 2003) (distinguishing the two types of claims).

130. Lietzan, *supra* note 91, at 105 (quoting Alan D. Lourie, *Patent Term Restoration*, 66 J. PAT. OFF. SOC'Y 526, 546 (1984)); *id.* at 126.

131. *See* Thomas, *supra* note 6, at 876.

132. *Id.*

II. Pharmaceutical Patent Infringement

Pharmaceutical patent litigation often turns on the nature of patent infringement—that is, what is and is not an infringing act.[133] Patent infringement comes in two basic flavors: direct infringement—making, using, or selling (among other activities) something covered by a patent's claims[134]—and indirect infringement, one species of which is inducement, i.e., "actively induc[ing]" another to directly infringe.[135] In pharmaceutical cases, brand sponsors typically litigate drug substance and product patents on theories of direct infringement, alleging that the generic sponsor will infringe by making and selling the patented composition.[136] But method-of-use patents present a different story; "pharmaceutical companies do not generally treat diseases" and generic sponsors, as corporate entities, do not use the drug themselves.[137] Method-of-use patents, therefore, must be asserted on a theory of indirect infringement: that a generic sponsor will induce a physician (or a patient) to commit an act of direct infringement.[138] Whether—and how—the drug label factors into allegations of inducement is at the heart of many cases.[139] Here, we provide some essential background on patent infringement doctrine and then critically assess the Federal Circuit's infringement-by-label case law.

A. Direct Infringement

Section 271(a) of the Patent Act imposes liability on anyone who, without the patentee's permission, "makes, uses, offers to sell . . . sells . . . or imports" the patented invention.[140] In the parlance of patent lawyers, these are acts of *direct*

133. In a patent infringement suit, the defendant typically raises two main defenses: (1) that it does not infringe the patent and (2) that the patent is invalid because it does not meet the statutory requirements of novelty, nonobviousness, sufficient disclosure, and so on. *See* 35 U.S.C. §§ 102, 103, 112. *See generally id.* § 282(b) (listing the defenses to a claim of patent infringement). As the title of our Article suggests, we focus on how courts have treated the noninfringement defense, though defendants often litigate both noninfringement and invalidity because a win on either issue will avoid liability. For a discussion of the strategic tradeoffs and policy implications of the two defenses, see Roger Allan Ford, *Patent Invalidity Versus Noninfringement*, 99 CORN. L. REV. 71, 76 (2013).

134. The "claims" are the stylized sentences at the end of the patent document that define the patent holder's exclusive rights. *See generally* Greg Reilly, *Patent "Trolls" and Claim Construction*, 91 NOTRE DAME L. REV. 1045, 1045 (2016) (discussing the importance of claim construction to patent litigation).

135. 35 U.S.C. § 271(a)-(b).

136. *See* Christopher M. Holman, GlaxoSmithKline v. Teva*: Holding a Generic Liable for an Artificial Act of Inducement*, 39 BIOTECH. L. REP. 425, 426 (2020) (describing this dynamic).

137. Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1363 n.7 (Fed. Cir. 2003).

138. *See, e.g.*, *id.* at 1354.

139. Holman, *supra* note 136, at 426-30.

140. 35 U.S.C. § 271(a).

infringement. Direct infringement is akin to a "strict liability tort,"[141] and perhaps even a form of ultra-hazardous liability[142]: The infringer need not have any particular mental state and is liable even if they are wholly ignorant of the infringed patent.[143]

The strict-liability nature of direct infringement makes litigation over patents on drug substances and products straightforward: The brand company claims that the generic sponsor will make or sell the patented drug substance (i.e., the active ingredient) or the patented drug product (i.e., the larger pharmaceutical composition).[144] If the patent is valid and its claims cover the proposed generic formulation, the generic sponsor will directly infringe.[145]

Things aren't so simple for patents covering *methods of using* pharmaceutical products, such as patents for treating particular medical conditions or covering dosage practices. Under the direct infringement statute, the generic sponsor is not, itself, *using* these methods to treat patients. Rather, a medical professional or—depending on the wording of the claim, the patient—is using the patented method.[146] If there is a direct infringer for a pharmaceutical method-of-use patent, it is the medical professional or patient.[147]

B. Indirect Infringement

That brings us to the other flavor of patent infringement: indirect infringement. The goal of indirect infringement (sometimes called secondary liability) is to give patentees legal protection when "the actual infringer either is

141. Arctic Cat Inc. v. Bombardier Recreational Prod. Inc., 876 F.3d 1350, 1366 (Fed. Cir. 2017).

142. *See* Saurabh Vishnubhakat, *An Intentional Tort Theory of Patents*, 68 FLA. L. REV. 571, 588 (2017).

143. Glob.-Tech Appliances, Inc. v. SEB S.A., 563 U.S. 754, 761 n.2 (2011) ("Direct infringement has long been understood to require no more than the unauthorized use of a patented invention.") (citing Aro Mfg. Co. v. Convertible Top Replacement Co., 377 U.S. 476, 484 (1964)).

144. 21 C.F.R. § 314.53(b)(1).

145. Though an ANDA must, generally, possess the same "route of administration, the [same] dosage form, and the [same] strength" as the reference listed drug, and be "bioequivalent" to it, 21 U.S.C. § 355(j)(2)(A)(iii)-(iv), one should not unhesitatingly equate generic equivalency, for the FDA's purposes, to being captured by patent claims. *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, 60 (2013).

146. *See* Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1363 n.7 (Fed. Cir. 2003) ("[P]harmaceutical companies do not generally treat diseases; rather, they sell drugs to wholesalers or pharmacists, who in turn sell the drugs to patients possessing prescriptions from physicians.").

147. *Id.*

not the truly responsible party or is impractical to sue."[148] Indirect infringement itself comes in two varieties: inducement, under Section 271(b) of the Patent Act, and contributory infringement, under Section 271(c).[149] Contributory infringement imposes liability on anyone who sells, offers to sell, or imports a component of a patented invention that has no "substantial noninfringing use."[150]

For infringement-by-label cases, contributory infringement is rarely an issue because the cases almost always involve drugs that can treat multiple conditions, only one of which is patented.[151] The existence of other, noninfringing methods of use means the drug product itself has "substantial noninfringing use[s]" and so the generic defendant would not contributorily infringe under Section 271(c) by merely selling that product.[152]

More relevant to infringement-by-label cases is the other variety of indirect infringement: inducement under Section 271(b). That subsection of the patent statute could hardly be less illuminating about what conduct, exactly, imposes liability. It states, in its entirety: "Whoever actively induces infringement of a patent shall be liable as an infringer."[153] This short phrase's meaning has been hashed out in scores of Supreme Court and Federal Circuit decisions.[154] At its simplest, a patentee must show that the alleged inducer actually knew of or was "willfully blind[]" to the existence of the patent[155] and that the defendant acted with the specific intent to encourage another to perform acts the inducer knew

148. Mark A. Lemley, *Inducing Patent Infringement*, 39 U.C. DAVIS L. REV. 225, 228 (2005); *see also* Michael P. Goodyear, *Infringing Information Architectures*, 58 U.C. DAVIS L. REV. 1959, 1971 (2025) ("Secondary liability punishes defendants for the direct infringement of others.").

149. 35 U.S.C. § 271(b)-(c).

150. *Id.* § 271(c).

151. *See infra* Part II.C.

152. *See, e.g.*, *Warner-Lambert*, 316 F.3d at 1365 (rejecting indirect infringement claim where "fewer than 1 in 46 sales of [the] product are for infringing uses"); *cf.* Bone Care Int'l, L.L.C. v. Roxane Lab'ys, Inc., No. 09-cv-285, 2012 WL 2126896, at *33 (D. Del. June 11, 2012) ("[U]nlike Anchen and Roxane's proposed products, which can be used for the treatment of Stage 3 and Stage 4 chronic kidney disease, Sandoz's proposed products can only be used for the treatment covered in claim 7. Consequently, because Sandoz's products have no substantial noninfringing use . . . the court concludes that Sandoz contributorily infringes claim 7 of the patent-in-suit."). That said, we question whether an FDA-approved drug can be a "staple article or commodity of commerce" under the statute. *See* 35 U.S.C. § 271(c).

153. 35 U.S.C. § 271(b).

154. *See generally* Timothy R. Holbrook, *The Supreme Court's Quiet Revolution in Induced Patent Infringement*, 91 NOTRE DAME L. REV. 1007, 1008 (2016) ("Given [the] general, unenlightening language [of Section 271(b)], the courts have been left to determine the contours of this provision . . . .").

155. Glob.-Tech Appliances, Inc. v. SEB S.A., 563 U.S. 754, 771 (2011).

would constitute direct infringement.[156] For a defendant to be liable for indirect patent infringement, there must be an underlying act of direct infringement somewhere.[157] That is, the indirect infringer must induce *someone else* to make, use, sell, offer to sell, or import the patented invention.

In pharmaceutical patent litigation, brand companies typically assert method-of-use patents against generics on an inducement theory, accusing the generic defendant of "actively induc[ing]" others to perform the claimed method of treatment or use the claimed dosage regimen.[158] That theory meets the basic contours of inducement liability: Physicians (or patients) are the putative direct infringers,[159] the generic sponsor clearly *knows* of the existence of the brand's patents because it needed to certify against them when filing its ANDA,[160] and the generic's sales activities (including, as we'll soon see, its package insert) allegedly demonstrate the company's intent that physicians (or patients) practice the patent claims.[161]

Before an ANDA is approved, however, this inquiry is entirely hypothetical. No patient could have taken the generic drug, and no doctor could have prescribed it, because it has yet to be sold. Relatedly, the yet-to-be-sold generic drug doesn't have an actual drug label to use as evidence that physicians would or would not be induced to prescribe the drug in an infringing matter. Nonetheless, courts have allowed brand companies to allege induced infringement in a pre-generic-launch suit under Section 271(e)(2) of the Hatch-Waxman Act.[162] As the Federal Circuit has ruled, Section 271(e)(2) creates a *mechanism* for asserting a pre-launch infringement claim; "the substantive determination whether . . . inducement will take place is determined by traditional patent infringement analysis, just the same as it is in other infringement suits."[163] The only difference between a "traditional" inducement analysis under Section 271(b) and an inducement analysis under Section 271(e)(2) of the Hatch-Waxman Act is that "the inquiries [under Section 271(e)(2)] are hypothetical because the allegedly infringing product has not yet been marketed."[164]

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156. DSU Med. Corp. v. JMS Co., 471 F.3d 1293, 1305 (Fed. Cir. 2006) (en banc in relevant part); *accord Glob.-Tech.*, 563 U.S. at 766.

157. Aro Mfg. Co. v. Convertible Top Replacement Co., 365 U.S. 336, 341 (1961).

158. *See, e.g.*, Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1363 (Fed. Cir. 2003) (quoting 35 U.S.C. § 271(b)).

159. *See id.*

160. *See* 21 U.S.C. § 355(j)(2)(A)(vii).

161. *See* AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1060 (Fed. Cir. 2010) (walking through this analysis).

162. 35 U.S.C. § 271(e)(2).

163. *Warner-Lambert*, 316 F.3d at 1365.

164. *Id.*

C. Infringement by Label

The question, of course, is what such marketing entails. For approved generic products, many pharmaceutical method-of-use cases hinge on the generic's sales activity. For generic products that have yet to enter the market, there are scant—sometimes no—marketing materials; there's just the proposed generic drug label. In that circumstance, the Federal Circuit has noted, a "proposed label may provide evidence of [a generic's] affirmative intent to induce infringement."[165] "May" is doing significant work here; the law is clear that a label's mere mention of a patented use does not, by itself, rise to the level of "actively inducing" another to infringe.[166] Rather, "[t]he label must encourage, recommend, or promote infringement."[167]

That is all well and good when the branded reference drug has a single indication and no substantial off-label use. If the proposed generic label contains the drug's only indication—an indication wholly covered by a brand's patent—an inducement finding should be simple.[168] But where there are multiple uses for the same drug, not all of which are patented, and some of which may not be FDA approved, whether a proposed generic label would truly induce physicians (or patients) to practice one specific, patented use—and was intended by the generic to do so—is far from clear. That's particularly so when a generic has tried to carve the patented use *out* of its label under Section viii.

For drugs that have multiple uses, only some of which are patented, "skinny labels"—generic labels with Section viii carveouts—present an uncomfortable truth: Despite the brand's patented methods of use being omitted from the generic's label, everyone knows the generic drug will be used in ways that infringe those method patents. As the Federal Circuit has recognized, "the Hatch-Waxman Act . . . was designed to enable the sale of drugs for non-patented uses even though this would result in some off-label infringing uses."[169] Those off-label infringing uses occur in part because many states have laws on generic substitution: If a generic version of a prescribed drug is available, those laws strongly encourage—and in some instances require—pharmacists to dispense the

165. *AstraZeneca*, 633 F.3d at 1060.

166. *See, e.g.*, Bayer Schering Pharma AG v. Lupin, Ltd., 676 F.3d 1316, 1322 (Fed. Cir. 2012) ("[W]hile the label mentions potential anti-mineralocorticoid and anti-androgenic activity [covered by the asserted method-of-use patent], it does not do so in any way that recommends or suggests to physicians that the drug is safe and effective for administration to patients for the purposes of inducing these effects.").

167. Sanofi v. Watson Lab'ys Inc., 875 F.3d 636, 644 (Fed. Cir. 2017) (alteration in original) (quoting Takeda Pharms. USA, Inc. v. W.-Ward Pharm. Corp., 785 F.3d 625, 631 (Fed. Cir. 2015)).

168. Presuming, of course, physicians' primary use of the drug is the labeled indication rather than an off-label use. *See Sanofi*, 875 F.3d at 646.

169. *Takeda*, 785 F.3d at 631.

generic unless the prescribing doctor specifically requests the brand.[170] Equating brand and generic drugs is also a core function of the Orange Book; it's formally titled *Approved Drug Products with Therapeutic Equivalence Evaluations* because it shows which generic drug products are therapeutically equivalent to branded ones.[171]

The uncomfortable truth of off-label prescribing for carved-out generics has confounded courts in numerous circumstances, including in true "skinny label" situations, where the generic has indisputably carved the patented method of use out of its label. But it has also caused confusion in more factually nuanced circumstances: cases where the patented method of use was never actually *on* the brand's label and cases where there is a dispute over what, exactly, the label teaches. Central to the infringement analysis in all these situations, however, is the content of the drug label—that is, the package insert—itself.

Examining the Federal Circuit's jurisprudence in this area, we categorize these labeling cases in three groups: (1) noninfringement-by-label cases, where the absence of an infringing method on the package insert leads to a ruling of noninfringement; (2) infringement *from* labels, where the package insert's explicit language is used as evidence of induced infringement; and (3) ambiguous label cases, where the package insert might or might not be understood to include a patented method of use. We then discuss the Federal Circuit's landmark 2021 decision in *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.*, which, we argue, has made it much easier for brands to pursue label-based claims of induced infringement.

1. Noninfringement by label

In some cases involving theories of infringement by label—particularly some of the earliest cases—the Federal Circuit's analysis focused tightly on the drug label's precise wording, regardless of any realities of off-label infringement. When the generic label said nothing about the patented use, the court affirmed findings of noninfringement.

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170. *See* Chana A. Sacks, Victor L. Van de Wiele, Lisa A. Fulchino, Lajja Patel, Aaron S. Kesselheim & Ameet Sarpatwari, *Assessment of Variation in State Regulation of Generic Drug and Interchangeable Biologic Substitutions*, 181 JAMA INTERNAL MED. 16, 19 (2021). It's worth noting that generic substitution laws are neither universal nor uniform; they are patchwork across the United States and vary widely. *Id.* at 17. Nonetheless, it's often said that "[a]ll fifty states have enacted laws that either allow or mandate generic substitution." Anna B. Laakmann, *The Hatch-Waxman Act's Side Effects: Precautions for Biosimilars*, 47 LOY. L.A. L. REV. 917, 921 (2014).

171. *See* FDA, EVALUATION OF THERAPEUTIC EQUIVALENCE: GUIDANCE FOR INDUSTRY (2022), https://perma.cc/Z94V-9TZM ("FDA's therapeutic equivalence evaluations are listed for multisource prescription drug products approved under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. § 355) in the active section of the *Approved Drug Products With Therapeutic Equivalence Evaluations* (commonly known as the Orange Book).").

For instance, in its 2003 decision in *Warner-Lambert Co. v. Apotex Corp.*, which, as far as we can tell, is the first Federal Circuit decision discussing induced infringement in the ANDA context, the court ruled there was no induced infringement, despite evidence of off-label infringing use, because the patented use was not described on the drug label.[172] In that case, the brand company, Warner-Lambert, had received FDA approval to market the drug, gabapentin, for only one indication: "treatment of partial seizures."[173] Warner-Lambert, however, held a patent on the use of gabapentin to treat "neurodegenerative diseases."[174] Evidence suggested that 80-90% of gabapentin prescriptions were for off-label uses—that is, for uses other than the FDA-approved indication of treating partial seizures, including to treat neurogenerative diseases.[175] The generic company, Apotex, filed an ANDA seeking approval with a label that was, as the Hatch-Waxman Act requires, identical to Warner-Lambert's—reciting only the unpatented partial-seizure indication.[176] As to Warner-Lambert's in-force patent on using gabapentin to treat neurodegenerative diseases, Apotex made a paragraph IV certification, arguing that its generic product could not infringe because it would be indicated only to treat seizures, not neurodegenerative diseases.[177]

The district court granted summary judgment of noninfringement to Apotex and the Federal Circuit affirmed, rejecting two theories of infringement advanced by Warner-Lambert. First, the Federal Circuit held that it is not an act of infringement under Section 271(e)(2) of the Hatch-Waxman Act for a generic company to submit an ANDA when the only patent at issue is for a use not approved under the NDA.[178] The court noted that, though Apotex had styled its statement that its product wouldn't infringe the neurodegenerative-disease patent as a paragraph IV certification, it was, effectively, more like a "statement of non-applicable use" under the Section viii carve-out provision because, as an ANDA applicant, it was "positively *forbidden*" to seek approval for the *unapproved* neurodegenerative disease indication.[179]

Second, the Federal Circuit rejected Warner-Lambert's argument that, upon FDA approval of Apotex's ANDA, Apotex's generic product would induce

172. 316 F.3d 1348, 1364-65 (Fed. Cir. 2003).

173. *Id.* at 1352.

174. *Id.* at 1351-52.

175. *Id.* at 1352, 1363-64.

176. *Id.* at 1352.

177. *See id.*

178. *Id.* at 1354-55; *see also* 35 U.S.C. § 271(e)(2) ("It shall be an act of infringement to submit [an ANDA] for a drug claimed in a patent or the use of which is claimed in a patent . . . if the purpose of such submission is to obtain approval . . . to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.").

179. *Warner-Lambert*, 316 F.3d at 1360.

infringement of the neurodegenerative disease patent under Section 271(b). Warner-Lambert contended that, because most gabapentin prescriptions were for off-label uses (including its patented neurogenerative-disease use), Apotex must know that prescribing doctors will commit direct infringement.[180] The Federal Circuit, however, held that any knowledge Apotex had about physician practices was irrelevant "[i]n the absence of any evidence that Apotex has or will promote or encourage doctors to infringe the neurodegenerative method patent"[181]—something its label clearly did not do.

At first glance, the Federal Circuit's decision in *Warner-Lambert* appears fact-specific: Because Apotex's label did not (and, as a matter of FDA regulation, could not) recite the patented method, and because Apotex did not otherwise "promote or encourage" doctors to infringe Warner-Lambert's patent, there was no infringement, either under Section 271(e)(2), based on Apotex's ANDA, or under Section 271(b), based on what might happen after FDA approval of that ANDA.[182] In that specific situation—where the only evidence of inducement was a proposed package insert that did not even mention the patented method—there could be no finding of infringement.

The Federal Circuit, however, quickly turned *Warner-Lambert*'s fact-specific holding into something approaching a rule of law. In *Allergan, Inc. v. Alcon Laboratories, Inc.*, decided just two months after *Warner-Lambert*, the Federal Circuit again upheld a district court decision granting summary judgment of noninfringement on the basis of the generic's label, even though there was evidence that the generic knew about and, unlike in *Warner-Lambert*, *promoted* infringing uses.[183]

In *Allergan*, the NDA holder, Allergan, owned two patents on using the (unpatented) drug brimonidine, one for protecting the optic nerve and another for "neural protection."[184] Importantly, the FDA had not approved brimonidine for either of those uses.[185] But brimonidine was effective for those uses.[186] And, according to the Federal Circuit, "Allergan presented evidence that third-party doctors and patients will likely infringe its two method of use patents and that Alcon and B&L [the ANDA applicants] may knowingly induce this

180. *Id.* at 1363-64.

181. *Id.* at 1364.

182. *Cf.* Gary N. Frischling & Miriam Bitton, *Grokking* Grokster*: Has the Supreme Court Changed Inducement Under Patent Law?*, 34 AIPLA Q.J. 265, 281-84 (2006) (quoting *Warner-Lambert*, 316 F.3d at 1364-65) (suggesting that the "commercially significant" infringing, off-label uses in *Warner-Lambert* could have been sufficient for liability under the Supreme Court's landmark indirect *copyright* infringement decision, *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 933 (2005)).

183. 324 F.3d 1322, 1332, 1334 (Fed. Cir. 2003) (per curiam).

184. *Id.* at 1324.

185. *Id.*

186. *Id.*

infringement through their actions,"[187] that is, by marketing their proposed generic product to physicians who would use Allergan's product for the patented, off-label use.[188]

Nevertheless, the Federal Circuit affirmed the district court's grant of summary judgment on Allergan's induced infringement claim under Section 271(e)(2) of the Hatch-Waxman Act. Treating *Warner-Lambert* as having established the pertinent rule of law, the court wrote:

> This issue was decided in *Warner-Lambert*. *Warner-Lambert* held that, pursuant to section 271(e)(2), a method-of-use patent holder may not sue an ANDA applicant for induced infringement of its patent, if the ANDA applicant is not seeking FDA approval for the use claimed in the patent and if the use claimed in the patent is not FDA-approved. *Warner-Lambert* reasoned that "because an ANDA may not seek approval for an unapproved or off-label use of a drug under 21 U.S.C. § 355(j)(2)(A)(i), it necessarily follows that 35 U.S.C. § 271(e)(2)(A) does not apply to a use patent claiming only such a use."[189]

Two of the three judges on the Federal Circuit panel, however—Judges Schall and Clevenger—joined a concurrence in the judgment arguing that *Warner-Lambert* was wrongly decided.[190] Importantly, Judges Schall and Clevenger contended that, though an NDA holder's label is necessarily silent on any patented-but-not-FDA-approved use, an NDA holder should be able to establish an inducement claim under Section 271(e)(2) *by pointing to evidence outside the package insert*.[191] The concurring judges also pointed out a potentially harmful consequence of *Warner-Lambert*: "In the absence of the section 271(e)(2) mechanism"—which allows infringement to be litigated before ANDA approval based on a paragraph IV certification—"the owner of a method of use patent claiming an off-label use will bring a section 271(b) induced infringement action, after the ANDA has been approved by the FDA, to enjoin infringement of its patent."[192] Contra the purpose of the Hatch-Waxman Act, such a Section 271(b) suit would threaten any certainty that once a generic received FDA approval and launched it would stay on the market. Because a Section 271(b) suit would

187. *Id.* at 1332; *see also id.* at 1336 (Schall, J., concurring in the judgment) ("[Allergan] alleges that, with knowledge of the . . . patents, *Alcon and B&L have taken steps to promote brimonidine for neuroprotection.*" (emphasis added)).

188. *See* Allergan, Inc. v. Alcon Lab'ys, Inc., 200 F. Supp. 2d 1219, 1230 (C.D. Cal. 2002).

189. *Allergan*, 324 F.3d at 1332-33 (citation omitted) (quoting Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1356 (Fed. Cir. 2003)).

190. *Id.* at 1334 (Schall, J., concurring in the judgment).

191. *Id.* at 1336 ("Under my reading of the statute, Allergan has stated a cause of action for induced infringement under section 271(e)(2) and would have been able to use evidence outside the ANDA itself to show infringement of its patents.").

192. *Id.* at 1337.

occur after launch, it could also expose the generic to large amounts of damages.[193]

Despite Judge Schall's critique of *Warner-Lambert*,[194] the rule of law that induced infringement claims won't lie for patented uses not approved by the FDA is now so clear that it can be resolved at the pleading stage, whether through a motion to dismiss or for judgment on the pleadings. In *Bayer Schering Pharma AG v. Lupin, Ltd.*, for instance, Bayer, the NDA holder, owned a patent that claimed a method of using the drug drospirenone (sold by Bayer under the brand name Yasmin) to achieve three effects simultaneously: a contraceptive effect, an anti-androgenic effect (e.g., to reduce acne), and an anti-aldosterone effect (to reduce water retention).[195] But Yasmin was FDA-approved only for one indication: oral contraception.[196] And so, when Bayer sued ANDA applicants under Hatch-Waxman for infringing its method patent, the district court dismissed Bayer's claim, citing *Warner-Lambert*'s rule that an infringement claim exists under Section 271(e)(2) only if the FDA has approved the use claimed in the patent.[197]

The Federal Circuit affirmed, noting that Yasmin was not FDA-approved for the anti-androgenic and anti-aldosterone effects claimed in Bayer's patent.[198] Though there were references to those effects in Bayer's FDA-approved label, the Federal Circuit emphasized that "the label, taken in its entirety, fails to recommend or suggest to a physician that Yasmin is safe and effective for inducing the claimed combination of effects."[199]

2. Infringement from labels

At the other extreme, if the label specifically teaches clinicians to practice a patented method of use for an FDA-approved indication, the Federal Circuit has

193. A Section 271(e)(2) suit takes place before the generic has made any sales, so no damages are at stake—only injunctive relief.

194. The third judge on the Federal Circuit panel in *Allergan*, Judge Linn, also wrote an opinion concurring in the judgment, arguing that the court in *Warner-Lambert* improperly "ventured beyond our interpretative role and . . . allowed its policy choices and its evaluation of the legislative history . . . to override the terms of the statute." *Allergan*, 324 F.3d at 1345 (Linn, J., concurring in the judgment). The panel's voting lineup raises a philosophical question: if all three judges concurred only in the *judgment*, how could they have issued an *opinion*? We think the answer here is that the judges did not actually concur only in the judgment—they all three agreed that *Warner-Lambert* (even if wrongly decided, in their view) controlled the outcome in *Allergan*, which was the premise of the court's per curiam opinion.

195. 676 F.3d 1316, 1320 (Fed. Cir. 2012).

196. *Id.* at 1319.

197. *Id.* at 1320.

198. *Id.* at 1322.

199. *Id.* at 1324.

upheld findings of inducement. In *Sanofi v. Watson Laboratories*, for example, the relevant patent claimed a method of using the drug dronedarone for reducing the risk of hospitalization from a heart attack in patients with one or more specified risk factors (such as being older than seventy-five, having hypertension or diabetes, and so on).[200] Sanofi's NDA product, Multaq, was approved for a single indication—a bit labyrinthine, but important to reproduce in full: "Multaq® is indicated to reduce the risk of hospitalization for atrial fibrillation in patients in sinus rhythm with a history of paroxysmal or persistent atrial fibrillation (AF) *[see Clinical Studies (14)]*."[201]

One of those referenced clinical studies, called ATHENA, reported "positive results, relating to reduced hospitalization, for patients having the risk factors written into [Sanofi's] patent."[202] The ANDA filers, Watson and Sandoz, proposed using the exact same label as Sanofi, including the reference to the ATHENA study.[203] They filed a paragraph IV certification regarding Sanofi's patent,[204] apparently on the thinking that, because the risk factors recited in the patent were not stated in the FDA-approved indication, they would not induce infringement.[205]

After a bench trial, the district court rejected that argument and, on appeal, the Federal Circuit upheld the finding of inducement.[206] The Federal Circuit emphasized that the label's reference to "Clinical Studies . . . expressly directs the reader to that section for elaboration of the class of patients for whom the drug is indicated to achieve the stated objective, i.e., reduced hospitalization."[207] And the ATHENA study in that section listed the exact risk factors recited in Sanofi's patent.[208] In other words, "[t]he label . . . directs medical providers to information identifying the desired benefit for only patients with the patent-claimed risk factors."[209] And the court noted that "[t]here was considerable testimony that this label encourages—and would be known by [the defendants] to encourage—

200. 875 F.3d 636, 642 (Fed. Cir. 2017).

201. *Id.* at 642-43 (alteration in original) (quoting the Multaq label).

202. *Id.* at 645.

203. *Id.* at 643.

204. Sanofi v. Glenmark Pharms. Inc., USA, 204 F. Supp. 3d 665, 671 (D. Del. 2016).

205. *See id.* at 676 ("Defendants argue that their proposed labels do not evidence the specific intent to instruct or encourage administration of dronedarone only to patients with risk factors. Defendants cite the original Multaq® label, which included in its indications and usage section an express reference to the risk factors of the ATHENA population, as evidence that the modified Multaq® label, which Defendants' [sic] copied, fails to comparably highlight the risk factors.").

206. *Sanofi*, 875 F.3d at 639, 646.

207. *Id.* at 645.

208. *See id.*

209. *Id.*

administration of the drug to . . . patients [with the risk factors listed in the patent], thereby causing infringement."[210]

The Federal Circuit has also upheld findings of inducement where the generic has unsuccessfully tried to carve the patented method of use out of its label. In *AstraZeneca LP v. Apotex, Inc.*, the NDA holder, AstraZeneca, owned a patent on a method of treating respiratory ailments such as asthma by using its budesonide product (sold under the brand name Pulmicort) "not more than once per day."[211] Because of safety concerns, AstraZeneca's label repeatedly warned that patients should "'titrate down' to the lowest effective dose"—a warning the FDA required be included.[212] In an attempt to avoid infringement, Apotex filed an ANDA seeking to sell a generic version of budesonide for twice-daily use—a use not claimed in AstraZeneca's patent.[213] Apotex filed a Section viii statement and carved out all mentions of the once-daily administration covered by AstraZeneca's patents.[214] But Apotex's label retained the FDA-mandated downward-titration language from AstraZeneca's label.[215]

The day after the FDA approved Apotex's ANDA, AstraZeneca sued for infringement and sought a preliminary injunction.[216] The district court granted the injunction, finding that the downward-titration warnings in Apotex's label would induce consumers to use the drug once daily because, in some cases, once-a-day would be the lowest effective dose.[217]

The Federal Circuit, applying an abuse of discretion standard of review, affirmed.[218] The Federal Circuit noted that, as acts of direct infringement, the downward-titration language would "inevitably" lead some patients to use Apotex's generic product once a day.[219] The court noted that Apotex's product would be available in only two doses, 0.25 and 0.5 milligrams; that many patients would start with 0.25 milligram doses twice daily; and that, for those patients, the only downward-titration option would be 0.25 milligrams once daily.[220] As evidence of specific intent to encourage infringement, the Federal Circuit leaned heavily on the downward-titration warning in Apotex's label.[221] The court also noted that, based on communications with AstraZeneca, Apotex was aware of

210. *Id.*

211. 633 F.3d 1042, 1046 (Fed. Cir. 2010).

212. *Id.* at 1047.

213. *Id.*

214. *Id.*

215. *Id.*

216. *Id.*

217. *Id.* at 1049.

218. *Id.* at 1065.

219. *See id.* at 1060.

220. *Id.* at 1057.

221. *See id.* at 1059-60.

the infringement risk and "had other options at its disposal," such as submitting a paragraph III certification and waiting for AstraZeneca's patents to expire, appealing an FDA decision refusing to let Apotex make further amendments to its label, or seeking approval for smaller dosages that would make once-daily use less likely.[222] Apotex's label, in other words, contained instructions about "actions directed to promoting infringement."[223]

Cases like *AstraZeneca* and *Sanofi* demonstrate that the Federal Circuit is willing to hinge its infringement analysis largely on its interpretation of generic drug labels, read in light of the indications approved by the FDA. That approach has the virtue of clarity—sometimes.[224] When, as in *AstraZeneca* and *Sanofi*, the generic label recites a patented, FDA-approved indication, there is infringement by inducement. But when the patented method does not cover the sole generic indication (*Warner-Lambert*), or an indication approved by the FDA (*Bayer*), or both (*Allergan*), there is no inducement.

These cases operate as a bit of formalism: What is on the package insert induces and what is absent from the package insert cannot induce. This approach meshes with conventional wisdoms about the semi-specialized Federal Circuit as an institution: The court prefers rules over standards;[225] thinks that words possess single, objective meanings;[226] and tends to turn fact-intensive, case-specific inquiries into points of law.[227] But this label-focused inducement rule—this theory of infringement *by* label—is subject to the same critiques as the Circuit's other formalistic proclivities.[228] And it provides a clear outcome only when the facts fit the court's rule hand in glove.[229]

In practice, not all cases are so clear. As we discussed above, in *Allergan*, the court upheld a finding of no inducement because the patented-but-not-FDA-approved method of use did not appear on the label—even though there was

222. *Id.* at 1058-59, 1061.

223. *Id.* at 1059-60 (quoting Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd., 545 U.S. 913, 935 (2005)).

224. *See infra* Part II.C.3.

225. *See, e.g.*, John R. Thomas, *Formalism at the Federal Circuit*, 52 AM. U. L. REV. 771, 773-74 (2003).

226. *See, e.g.*, Mark A. Lemley, *Chief Justice Webster*, 106 IOWA L. REV. 299, 312 (2020).

227. *See, e.g.*, Arti K. Rai, *Engaging Facts and Policy: A Multi-Institutional Approach to Patent System Reform*, 103 COLUM. L. REV. 1035, 1047-48 (2003).

228. *See* Craig Allen Nard & John F. Duffy, *Rethinking Patent Law's Uniformity Principle*, 101 NW. U. L. REV. 1619, 1644 (2007) (suggesting that "the Federal Circuit has fallen out of rhythm with some of the technological communities its decisions affect because the court has retreated into its own legal formalisms at the expense of gaining a good understanding of industrial and technological needs").

229. *See* Duncan Kennedy, *Form and Substance in Private Law Adjudication*, 89 HARV. L. REV. 1685, 1690 (1976) ("[F]ormal realizability eliminates the sub rosa lawmaking that is possible under a regime of standards. It will be clear what the rule is, and everyone will know whether the judge is applying it.").

outside-the-label evidence that the generics would promote infringing uses.[230] Conversely, in *AstraZeneca*, the generic unequivocally carved the patented once-a-day indication out of its label.[231] Yet the Federal Circuit upheld a finding of inducement based on FDA-mandated warning language that remained.[232]

As we discuss next, in some cases, the Federal Circuit has been forced to acknowledge that it is genuinely unclear whether the patented method, in fact, appears on the package insert, presenting a host of complications for both patent law and civil procedure.

3. Ambiguous labels

In cases with truly ambiguous labels, the Federal Circuit has turned to established principles of patent law to help resolve the infringement-by-label problem. One key principle is that merely *knowing about* direct infringement is not enough to hold a defendant liable for inducement. Rather, the defendant must *encourage, recommend, or promote* the infringing use.[233] When that inquiry requires looking beyond the package insert, the results haven't always been consistent—or, in our view, correct.

Take, for example, *HZNP Medicines LLC v. Actavis Laboratories, Inc.*, which upheld a ruling of no inducement even though a patient who obeyed a warning on the generic's label would, indisputably, infringe the brand's method-of-use patent.[234] In *HZNP*, the brand company, Horizon, held patents on a method of using the topical pain reliever, diclofenac (sold under the brand name Pennsaid), to treat joint pain.[235] The claimed method consisted of three steps: applying diclofenac, waiting for the treated area to dry, and then applying another substance such as sunscreen or insect repellant.[236] The proposed label of the ANDA applicant, Apotex, was, in relevant respects, identical to Horizon's.[237] Most importantly, the label contained a warning that a user should "wait until the treated area is dry" before putting on clothing or applying other topical medications.[238] This paralleled Horizon's patents, which required users to "wait[] for the treated area to dry; [and then] subsequently apply[] a sunscreen, or

230. Allergan, Inc. v. Alcon Lab'ys, Inc., 324 F.3d 1322, 1324 (Fed. Cir. 2003); *id.* at 1336 (Schall, J., concurring in the judgment).

231. AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1047 (Fed. Cir. 2010).

232. *Id.* at 1060. Indeed, the FDA, in requiring generics to include the warning language about downward titration, had specifically said that the warning did not "'teach' once-daily dosing." *Id.* at 1058 (quoting Letter from the FDA to AstraZeneca 18 (Nov. 18, 2008)).

233. *See* H. Lundbeck A/S v. Lupin Ltd., 87 F.4th 1361, 1370 (Fed. Cir. 2023).

234. 940 F.3d 680, 702 (Fed. Cir. 2019).

235. *Id.* at 683.

236. *Id.*

237. *Id.* at 700.

238. *Id.*

an insect repellant to said treated area."[239] Upon receiving a paragraph IV certification from Apotex, Horizon sued for induced infringement under Section 271(e)(2)(A).[240]

Horizon's primary argument was that the label warning to "wait until the treated area is dry" would "lead to an infringing use" of Apotex's generic product by encouraging users to perform the three steps recited in Horizon's patents: apply diclofenac, wait for it to dry, and then apply sunscreen, bug spray, etc.[241] But the district court found no inducement at summary judgment, and the Federal Circuit affirmed.[242] The Federal Circuit noted that, as a matter of inducement law, "[m]erely *describing* the infringing use" isn't enough: "[S]pecific intent and action to induce infringement must be shown."[243] The Federal Circuit read the diclofenac label to operate in an "if/then" manner: "*if* the user wants to . . . apply another substance . . . *then* the patient should wait until the area is dry."[244] Even though the evidence was clear that some users would practice the infringing method, the court emphasized that the label did not *instruct* them to do so; it "merely provided guidance to patients about what to do *if* the [patient] desired to have anything come into contact with the [skin] after application of the medication."[245]

The ambiguity in *HZNP* laid in whether the labeled instruction to "wait . . . before applying" was the same as the patents' command to "wait . . . [and *then*] subsequently apply[]."[246] Though the Federal Circuit said it was not, it seems equally plausible to say that the claimed method was literally in the generic label's warning: "[a]pply diclofenac," "wait until the treated area is dry," "apply[]" other substances.[247] Anyone who followed the label's instructions, just like anyone who downward-titrated in *AstraZeneca*, would infringe.[248] Nonetheless,

239. U.S. Patent No. 8,546,450 cols. 73-74.

240. *HZNP*, 940 F.3d at 684-85.

241. *Id.* at 700-01.

242. *Id.* at 702.

243. *Id.* at 702 (emphasis added) (citing Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp., 785 F.3d 625, 631 (Fed. Cir. 2015)).

244. *Id.*

245. *Id.* (emphasis added).

246. *See id.* at 700.

247. *See id.* at 699-700.

248. *See* AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1058 (Fed. Cir. 2010) (discussing the district court's finding that the defendant's "affirmative intent that consumers use the generic drug in an infringing manner" could be found in the defendant's "inclusion of the downward-titration language in the proposed label"); *see also id.* at 1060 ("Even if [the defendant] were correct that the downward-titration language may be applied to other dosing regimens . . . [it] would inevitably lead some consumers to practice the claimed method.").

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Horizon's instructions were not sufficient, in the Federal Circuit's view, to raise a factual dispute about inducement.

Takeda Pharmaceuticals U.S.A., Inc. v. West-Ward Pharmaceutical Corp. similarly rejected a claim of inducement when following the generic label's instructions would have sometimes led to direct infringement.[249] There, the brand company, Takeda, held several patents on methods of using the drug colchicine (sold under the brand name Colcrys) to treat acute gout flares.[250] When Hikma launched its own, FDA-approved version of colchicine for *preventing* gout flares, Takeda sued for induced infringement under Section 271(b).[251] Takeda's inducement argument hinged on Hikma's package insert, which stated, "[i]f you have a gout flare while taking" Hikma's product, Mitigare, "tell your healthcare provider."[252] This statement induced infringement, Takeda contended, because the health care provider would likely then tell the patient to take the Mitigare on hand to treat the flare, infringing Takeda's patents.[253] Moreover, Hikma appeared to *know* that Mitigare would be put to off-label infringing uses: Both the FDA and the American College of Rheumatology recommended that Colcrys—Takeda's chemically identical drug product—be used to treat acute gout flares.[254]

The district court denied Takeda's request for a preliminary injunction, and the Federal Circuit affirmed.[255] The Federal Circuit again emphasized that, to support a finding of inducement, "[t]he label must encourage, recommend, or promote infringement,"[256] not merely be "combined with speculation about

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As a matter of common sense, one might be uneasy about basing a finding of active inducement of patent infringement on FDA-mandated safety warnings in a drug label. After all, those warnings are there for good reasons that have nothing to do with patent law. As the pertinent FDA regulations explain, warnings should include "information that would affect decisions about whether to prescribe a drug, recommendations for patient monitoring that are critical to safe use of the drug, and measures that can be taken to prevent or mitigate harm." 21 C.F.R. § 201.57(a)(10) (2024). But the Federal Circuit did not mention this issue of FDA law in rejecting the infringement claim in *HZNP*—let alone in upholding the infringement claims in *AztraZeneca* and *Sanofi*. Rather, the Federal Circuit seemed more comfortable analogizing to secondary infringement in copyright law. *See, e.g.*, Sanofi v. Watson Lab'ys Inc., 875 F.3d 636, 644 (Fed. Cir. 2017) ("[I]nducement is present where 'active steps . . . taken to encourage direct infringement,' such as advertising an infringing use or instructing how to engage in an infringing use, show an affirmative intent that the product be used to infringe." (quoting Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd., 545 U.S. 913, 936 (2005))).

249. 785 F.3d 625, 630, 633 (Fed. Cir. 2015).

250. *Id.* at 627-28.

251. *Id.* at 628.

252. *Id.* at 630 (alteration in original).

253. *Id.*

254. *Id.* at 632.

255. *Id.* at 627.

256. *Id.* at 631.

how physicians may act to find inducement."[257] The label's suggestion to "tell your healthcare provider" was, on the court's reading, "vague label language"—not "active encouragement."[258] For a suggestive statement to trigger inducement liability, direct infringement, the court indicated, needs to be "inevitabl[e]."[259] And though Hikma knew about infringing off-label uses of its product, the court repeated the admonition that "mere knowledge of infringing uses . . . does not establish inducement."[260]

The Federal Circuit also demanded evidence of active inducement beyond label language nodding toward a patented use in its 2019 decision, *Grunenthal GmbH v. Alkem Laboratories Ltd.*,[261] which rejected an argument for induced infringement because the label didn't "specifically encourage" use of the drug in an infringing manner.[262] The patent in that case claimed a method of using the drug tapentadol (sold by Grunenthal under the brand name Nucynta) to treat "polyneuropathic pain," that is, pain caused by damage to multiple nerves (as compared to "mononeuropathic pain" from damage to one nerve).[263] Grunenthal's product was FDA-approved for two indications, to treat "severe chronic pain" and to treat "neuropathic pain associated with diabetic peripheral neuropathy (DPN)," which is a species of the polyneuropathic pain recited in Grunenthal's patent.[264] Under Section viii, the ANDA applicants, Hikma and Actavis, carved the DPN indication out of their proposed labels, leaving only the severe chronic pain indication.[265] Grunenthal nevertheless sued them for inducing infringement.[266]

Grunenthal's main argument was one of logic: Because "severe chronic pain," even with DPN carved out, necessarily includes *some* polyneuropathic pain, Hikma's and Actavis's labels would induce infringement by at least some users.[267] Yet, after a bench trial, the district court found no inducement, and the

257. *Id.* at 632; *see also id.* at 631 ("Merely describing an infringing mode is not the same as recommending, encouraging, or promoting an infringing use, or suggesting that an infringing use should be performed." (citation modified)).

258. *Id.* at 632.

259. *Id.* at 633.

260. *Id.* at 632. Judge Newman dissented precisely on that point. *Id.* at 636 (Newman, J., dissenting) ("I dissent from the court's ruling that the provider of a known drug product, with knowledge that it is likely to be used in direct infringement, can never be liable for induced infringement. These are fact-specific circumstances, and are not amenable to final disposition at a preliminary injunction hearing.").

261. 919 F.3d 1333 (Fed. Cir. 2019).

262. *Id.* at 1339.

263. *Id.* at 1336.

264. *Id.* at 1338.

265. *Id.* at 1340.

266. *See id.* at 1337-38.

267. *Id.* at 1339.

Federal Circuit affirmed,[268] emphasizing trial evidence that "severe chronic pain" *could be* polyneuropathic (making the use of tapentadol to treat it infringing) or it *could be* mononeuropathic (making the use of tapentadol to treat it noninfringing).[269] And so, in the court's view, "the proposed ANDA labels do not *specifically encourage* the use of tapentadol . . . for treatment of polyneuropathic pain."[270]

Cases like *HZNP*, *Grunenthal*, and *Takeda* (all decided from 2015 to 2019), make clear that the generic package insert alone cannot be used to demonstrate inducement unless it specifically directs patients or physicians to engage in conduct that would *necessarily* amount to direct infringement. What is required for a finding of infringement by label is something like the instruction in *AstraZeneca*, where *any* titration down, as explicitly encouraged by the generic label's warning, would directly infringe. Or like *Sanofi*, where the patented method of use, and sole FDA-approved indication, was explicitly referred to in the generic drug label in the Clinical Studies section. Or, perhaps most clearly, like *Eli Lilly & Co. v. Teva Parenteral Medicines, Inc.*, where the brand's patent claimed methods of administering the chemotherapy drug pemetrexed after pretreatment with folic acid, and the generic drug label told doctors to "*[i]nstruct* patients to initiate folic acid . . . once daily beginning 7 days before the first dose of [pemetrexed]."[271]

The rule that the label must direct readers to engage in conduct that *necessarily* infringes precluded findings of inducement (1) where the patented method appeared in the label as an *optional* step (*HZNP*); (2) where the patented method was a *species* of the broader uses recited in the label (*Grunenthal*); and (3) even where the generic sponsor *knew* that some off-label direct infringement would occur without specifically encouraging it (*Takeda*).

Left unresolved, though, was a thornier question, referenced in *Takeda*: "whether evidence as to the invariable response of physicians could ever transform a vague label"—that is, a label that does not explicitly instruct activity that would necessarily amount to direct infringement—"into active encouragement."[272] The Federal Circuit's answer to that question came soon enough, in what has become one of the most controversial patent decisions in recent memory. That decision breathed new life into the theory of infringement by label and raised numerous difficult questions about the substance of inducement law, the interplay of patent law and drug law, and the procedures

268. *Id.* at 1338.

269. *Id.* at 1339.

270. *Id.* (emphasis added).

271. 845 F.3d 1357, 1361, 1364 (Fed. Cir. 2017); *see also id.* at 1364 ("To lower your chances of side effects . . . you must also take folic acid . . . prior to and during your treatment[.]" (quoting the drug's patient information document)).

272. Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp., 785 F.3d 625, 632 (Fed. Cir. 2015).

through which pharmaceutical patent infringement claims are litigated. Identifying and attempting to resolve those questions are the primary objectives of what remains of this Article. First, though, a thorough dissection of the case itself.

4. *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.*

GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc. involved carvedilol, a heart medication, sold by GlaxoSmithKline (GSK) under the brand name Coreg.[273] The FDA had approved carvedilol for three uses: treatment of hypertension, treatment of congestive heart failure (CHF), and "to reduce cardiovascular mortality in patients suffering from left ventricular dysfunction following a myocardial infraction"—what the court called the "post-MI LVD" indication.[274] GSK owned a patent on a method of using carvedilol to treat CHF.[275] Teva, the ANDA applicant, filed a Section viii statement that its label would not include the CHF indication; so its approved drug label initially included only two indications: hypertension and post-MI LVD.[276] In 2011, four years after Teva launched its generic, the FDA instructed Teva to revise its drug label to be identical to GSK's label for Coreg.[277] Teva accordingly changed its drug label to include the previously carved-out CHF indication.[278]

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273. 7 F.4th 1320, 1323 (Fed. Cir. 2021) (per curiam).

274. *Id.*

275. *Id.* at 1324.

276. *Id.*

277. *Id.* at 1324-25.

278. *Id.* at 1325. The reasons for the FDA's demand are complicated. As briefly as possible: Teva's skinny label was predicated on one of GSK's Orange Book listed patents, U.S. Patent No. 5,760,069, which claimed a method of using carvedilol to treat CHF. *Id.* at 1323-24. After the FDA approved Teva's ANDA in 2007, the '069 Patent was reissued by the U.S. Patent and Trademark Office as U.S. Patent No. RE40,000. *Id.* at 1324. Reissue is a process by which a patentee surrenders a patent in hopes of having it reissued with narrower claims that are, presumably, less likely to be held invalid. *See* 35 U.S.C. § 251(a) (reissue statute). GSK subsequently delisted from the Orange Book the surrendered '069 Patent and added the reissued '000 Patent. *GlaxoSmithKline*, 7 F.4th at 1324.

In 2010 and 2011, the FDA approved "major changes" (an FDA term of art) to GSK's label for Coreg, mainly involving warnings about complications patients on carvedilol might encounter during surgery. *See* COREG, *supra* note 44. These changes, in turn, required Teva to amend its label; ANDA applicants have an ongoing obligation to ensure their labels conform to the reference brand's label. *See* 21 C.F.R. § 314.15(b)(10) (withdrawing approval of an ANDA if "the labeling for the drug product that is the subject of the abbreviated new drug application is no longer consistent with that for the listed drug").

In reviewing Teva's new proposed label, the FDA asked Teva in April 2011 to make several amendments concerning the now three-year old changes to GSK's Orange Book listings. *GlaxoSmithKline*, 7 F.4th at 1324-25. One was for Teva to conform its label to *include* the CHF indication now that the '069 Patent had been delisted. *See id.* at 1324-25.

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More than three years after Teva amended its label, GSK sued for inducing infringement of its CHF patent.[279] After a trial, a jury awarded GSK $236 million in damages, finding that Teva induced infringement both during the period in which Teva omitted the CHF indication from its drug label and after Teva amended its drug label to include that indication.[280] The district court, however, granted Teva's motion for judgment as a matter of law on the issue of induced infringement.[281] For the "skinny-label" period, the district court reasoned that, though there was some overlap between post-MI LVD patients (an indication in Teva's skinny label) and CHF patients (carved out of Teva's skinny label), no reasonable jury could have found that the post-MI LVD indication "caused or even encouraged" direct infringement of GSK's CHF patent.[282] Rather, in the district court's view, doctors based their prescribing decisions on sources other than Teva's label, such as their own pre-generic-launch knowledge about carvedilol, guidelines published by professional medical associations, peer-reviewed research studies, and GSK's own label and marketing efforts.[283] Likewise, for the "full label period" during which the CHF indication appeared on Teva's generic label, the district court reasoned that doctors' decisions to prescribe carvedilol were again caused by "multiple factors unrelated to Teva."[284]

The Federal Circuit, in a two-to-one decision, reversed the district court's judgment as a matter of law and reinstated the jury verdict of induced infringement and its damages award.[285] The Federal Circuit emphasized that,

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(Skinny labels are only available when predicated on an unexpired and Orange Book-listed patent.) The FDA also asked Teva to provide a patent certification on the '000 Patent now that it was listed in the Orange Book. *Id.* at 1324-25. Teva complied with the FDA's demands to fatten its skinny label but did not provide a certification to the '000 Patent on the ground that the FDA had approved its ANDA before the '000 Patent issued. *Id.* at 1325.

279. *GlaxoSmithKline*, 7 F.4th at 1324-25.

280. *Id.* at 1325, 1340.

281. GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 313 F. Supp. 3d 582, 585 (D. Del. 2018).

282. *Id.* at 592-93 n.9.

283. *Id.* at 594.

284. *Id.* at 597.

285. *GlaxoSmithKline*, 7 F.4th at 1322, 1326. As noted in the Introduction, it actually took the Federal Circuit panel two opinions to get to that outcome. The first opinion, ultimately withdrawn, was by Judge Newman. GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 976 F.3d 1347 (Fed. Cir. 2020). The second opinion, which we discuss here, was denominated per curiam. *GlaxoSmithKline*, 7 F.4th at 1323. Chief Judge Moore and Judge Newman were in the majority; Judge Prost dissented. *Id.* at 1322. Judge Newman, it's worth noting, dissented in *Takeda*, *Bayer*, and *HZNP*—all decisions that rejected inducement claims against generic manufacturers. *See* Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp., 785 F.3d 625, 635 (Fed. Cir. 2015) (Newman, J., dissenting); Bayer Schering Pharma AG v. Lupin, Ltd., 676 F.3d 1316, 1326 (Fed. Cir. 2012) (Newman, J.,

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though Teva had omitted the CHF indication from its label until 2011, "the patented use was on [Teva's] generic label at all relevant times."[286] Specifically, the Federal Circuit reasoned, Teva's "partial label" (i.e., the version of the label with the CHF indication carved out), still encouraged an infringing use "via the post-MI LVD indication" that remained on the label and through Teva's marketing materials, which, in the court's view, "encouraged prescribing carvedilol in a manner that would cause infringement" of GSK's patent.[287]

As for the drug label itself, the Federal Circuit concluded that Teva's partial label was not a true "skinny label." The court relied on expert trial testimony that the post-MI LVD indication, which remained on Teva's label, "satisfied" each element of GSK's CHF patent claim.[288] The court distinguished *HZNP* on the ground that the label there did not "require[]" two steps of the claimed use (waiting for diclofenac to dry and then applying lotion or sunscreen).[289] Teva's label, by comparison, "met each claim limitation" of GSK's patent.[290] And the court distinguished *Grunenthal* on the ground that the district court in that case had made a fact finding that the label did not instruct the claimed method of treating polyneuropathic pain, even though some "severe pain" was indisputably polyneuropathic.[291] In *GlaxoSmithKline*, by contrast, a jury had *found* inducement.[292]

As for Teva's marketing materials, the Federal Circuit noted that product catalogs released by Teva, including during the pre-2011 "partial label period," described its carvedilol product as "an AB[-]rated therapeutic equivalent to Coreg®."[293] Likewise, pre-2011 press releases issued by Teva noted that its "[Carvedilol] tablets are the AB-rated generic equivalent of GlaxoSmithKline's Coreg® Tablets, and are indicated for *treatment of heart failure* and hypertension."[294] From this evidence, the Federal Circuit reasoned, the jury reasonably concluded that "Teva was . . . encouraging the substitution of its

dissenting); HZNP Meds. LLC v. Actavis Lab'ys UT, Inc., 940 F.3d 680, 704 (Fed. Cir. 2019) (Newman, J., concurring in part and dissenting in part).

286. *GlaxoSmithKline*, 7 F.4th at 1326.

287. *Id.* at 1327.

288. *Id.* at 1328-29.

289. *Id.* at 1330.

290. *Id.*

291. *Id.* ("We found no *clear error* in the district court's finding of no inducement because the generic labels did not 'implicitly or explicitly encourage or instruct users to take action that would inevitably lead to . . . treatment of polyneuropathic pain.'" (quoting Grunenthal GMBH v. Alkem Lab'ys Ltd., 919 F.3d 1333, 1340 (Fed. Cir. 2019)).

292. *Id.*

293. *Id.* at 1335.

294. *Id.* at 1335-36 (emphasis added); *see also id.* at 1336 (discussing an additional press release stating that Teva had received approval "to market its Generic version of GlaxoSmithKline's cardiovascular agent Coreg®").

product for *all* of Coreg's® cardiovascular indications"—whether expressly on label or not.[295] For the "full label" period—the period during which the patented CHF use was indisputably described in Teva's label—the Federal Circuit also upheld the jury verdict of inducement based largely on marketing materials it sent to doctors telling them to "be familiar with the full product labeling."[296]

Lastly, the Federal Circuit confronted the question of causation: Was it "Teva's alleged inducement, as opposed to other factors, [that] actually caused physicians to directly infringe [GSK's] patent"?[297] The Federal Circuit again refused to second-guess the jury, emphasizing that "[t]he jury had sufficient circumstantial evidence, in the form of labels, marketing materials, catalogs, press releases, and expert testimony, for it to conclude that Teva succeeded in influencing doctors to prescribe carvedilol for the infringing use."[298]

Judge Prost wrote a blistering dissent, emphasizing that Congress designed the skinny-label provisions of the Hatch-Waxman Act for the precise circumstances presented by this case: where "one patented use [might] prevent public access to a generic version of a drug that also has unpatented uses."[299] By carving the Orange Book-listed CHF indication from its label, Judge Prost wrote, Teva "played by the rules, exactly as Congress intended."[300] She criticized the majority for ruling that Teva's carved-out label "intentionally encouraged" infringement even though, "by carving out everything that GSK said would infringe, [Teva] was trying to *avoid* having its label encourage infringement."[301] She also took issue with the majority's inference that doctors "as a class, *relied* on Teva's skinny label to infringe," despite trial testimony by "every expert cardiologist" that they "*didn't even read* the label to make prescribing decisions."[302] Lastly, she questioned the majority finding "culpable intent behind a generic's describing its product as the 'equivalent' of a brand drug—in a system that *requires* generic drugs to be equivalent, and in which everyone understands that generic drugs are equivalent."[303]

On the majority's point about Teva's carved-out label nevertheless containing the patented CHF indication, Judge Prost emphasized that "describing [the infringing use] is not enough" to sustain a finding of inducement—"encourag[ing], recommend[ing], or promot[ing]" the practice of

295. *Id.* at 1337 (emphasis added).

296. *Id.* at 1338.

297. *Id.* at 1339.

298. *Id.* at 1340.

299. *Id.* at 1342 (Prost, J., dissenting).

300. *Id.*

301. *Id.*

302. *Id.*

303. *Id.* at 1343.

the patented method is what's required.[304] And on whether Teva's label (or its marketing materials) *caused* doctors to infringe GSK's patent, Judge Prost emphasized that the evidence showed that doctors based their prescribing decisions "primarily on medical guidelines, experience, education, and journals"—not Teva's label.[305]

By a seven-to-three vote, the full Federal Circuit denied Teva's petition for rehearing en banc.[306] Judge Moore (one of two members of the panel majority)[307] wrote a concurring opinion, mostly emphasizing that if Teva had, in fact, relied on GSK's representations to the FDA about the scope of its patent—namely, GSK's listing of only the CHF indication in the Orange Book, which Teva then carved out—Teva could pursue an "equitable estoppel" defense on remand.[308] Judge Prost penned another dissent emphasizing the thin evidence of Teva's *intent* to induce infringement, emphasizing that "because most skinny labels contain language that . . . could be pieced together to satisfy a patent claim, essentially all of these cases will now go to trial."[309]

Teva then turned to the Supreme Court, filing for a writ of certiorari that attracted four amicus briefs in support.[310] The Court called for the views of the

304. *Id.* at 1351.

305. *Id.* at 1352. Moreover, Judge Prost noted, "[e]vidence from both sides . . . showed that pharmacies substituted generics for the brand version automatically, as all fifty states allow or even require." *Id.*

306. GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 25 F.4th 949, 950 (Fed. Cir. 2022).

307. *GlaxoSmithKline*, 7 F.4th at 1322.

308. *See GlaxoSmithKline*, 25 F.4th at 952 (Moore, C.J., concurring in denial of the petition for rehearing en banc).

309. *Id.* at 955 (Prost, J., dissenting from denial of the petition for rehearing en banc) ("When a generic plays by the skinny-label rules, the FDA-required label can't be evidence of intent. Even *if* remaining label language might be pieced together to 'meet' the elements of a patent claim, the extent to which that's true is an unreliable gauge of a generic's 'intent' in this highly regulated area . . . . Indeed, the panel majority's decision doesn't just eliminate a generic's ability to depend on the skinny-label system; it also gives brands a powerful tactic: neglect to identify language as patent-covered, then sue a generic for including that very language."). In addition, Judge Dyk dissented on the ground that the specific regulatory system adopted by the Hatch-Waxman Act—including the "FDA-required" labels used by generics like Teva—likely supplanted the more general principles of inducement law relied on by the panel majority. *Id.* at 959 (Dyk, J., dissenting from denial of the petition for rehearing en banc) ("In similar circumstances where states have sought to impose tort liability on generic drug manufacturers for using the label required under federal law, the Supreme Court has made clear that federal law preempts tort liability on the part of the manufacturers." (citations omitted)). And Judge Reyna wrote a dissent emphasizing the importance of the issues from the perspective of both drug regulation and inducement law. *See id.* at 959-60 (Reyna, J., dissenting from denial of the petition for rehearing en banc) (citing Fed. Cir. Internal Op. Proc. No. 13(2)(b)).

310. *See* Docket, Teva Pharms. USA, Inc. v. GlaxoSmithKline LLC, No. 22-37 (U.S. filed July 11, 2022).

Solicitor General[311]—an action that makes a grant of certiorari significantly more likely than in the average case.[312] And the Solicitor General recommended granting review[313]—a recommendation the Court almost always follows, particularly in patent cases.[314] Nonetheless, and over the dissent of Justice Kavanaugh, the Court denied the petition.[315]

GlaxoSmithKline turned two decades of Federal Circuit jurisprudence on drug labels and inducement on its head, solidifying a new theory of induced infringement based not on a label's express instructions to engage in activity that necessarily infringes, but on the mere existence of package insert language that was interpreted by an expert witness to simply *mention* a patented use—even though the generic had attempted to carve that patented use out of the label and had followed the brand's Orange Book listing in doing so. Although the court in *GlaxoSmithKline* tried to distinguish *HZNP* and *Grunenthal*, where the Federal Circuit had previously upheld findings of no inducement, *GlaxoSmithKline* cast significant doubt on those cases, which required labels to do more than merely suggest an infringing use, but to "specifically encourage" it.[316] The court's decision in *GlaxoSmithKline* also suggests that "vague label language," discounted in *Takeda*,[317] can in some cases be enough to induce physicians to practice otherwise absent indications—particularly when coupled with marketing materials noting that the generic is "equivalent" to the branded drug.[318] *GlaxoSmithKline* also, perhaps surprisingly, weakens the Federal Circuit's formalistic bent in cases like *Sanofi* and *AstraZeneca*, by substituting textual analyses of labels for expert testimony on what doctors think about them. *GlaxoSmithKline*, in short, offers not a theory of *how* labels can be used in infringement analyses so much as a theory of infringement *by* label.

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311. Teva Pharms. USA, Inc. v. Glaxo-SmithKline LLC, 143 S. Ct. 80 (2022).

312. *See* Paul R. Gugliuzza, *The Supreme Court Bar at the Bar of Patents*, 95 NOTRE DAME L. REV. 1233, 1253 (2020).

313. Brief for the United States as Amicus Curiae, *supra* note 25, at 1.

314. Paul R. Gugliuzza & Pyry P. Koivula, *Stepping Out of the Solicitor General's Shadow: The Federal Circuit and the Supreme Court in a New Era of Patent Law*, 64 B.C. L. REV. 459, 491 (2023) (finding that, from 2002 through 2019, the Supreme Court followed the Solicitor General's certiorari recommendation in 92.5% of patent cases, as compared to 78.8% overall).

315. Teva Pharms. USA, Inc. v. Glaxo-SmithKline LLC, 143 S. Ct. 2483 (2023).

316. Grunenthal GmbH v. Alkem Lab'ys Ltd., 919 F.3d 1333, 1339 (Fed. Cir. 2019); HZNP Meds. LLC v. Actavis Lab'ys UT, Inc., 940 F.3d 680, 701-02 (Fed. Cir. 2019) ("[W]e examine whether the proposed label 'encourage[s], recommend[s], or promote[s] infringement.'" (quoting Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp., 785 F.3d 625, 631 (Fed. Cir. 2015))).

317. *Takeda*, 785 F.3d at 632.

318. GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 7 F.4th 1320, 1335-36 (Fed. Cir. 2021) (per curiam).

D. *GlaxoSmithKline*'s Progeny and Standards of Review

GlaxoSmithKline's infringement-by-label theory departs not just from the Federal Circuit's jurisprudence in pharmaceutical patent cases but from the law of inducement writ large. Inducement, more generally, focuses on what is communicated by the defendant—what the accused indirect infringer "encourage[s], recommend[s], or promote[s]."[319] By contrast, infringement by label, as articulated in *GlaxoSmithKline*, turns on whether physicians would *think* the label *includes* a patented use, even if they would not follow it and even if the generic has tried to avoid including—much less encouraging the practice of—that patented use. That is, the law of inducement generally focuses on what was *spoken*, but an infringement-by-label theory focuses on what could plausibly be *heard*. This thins the line between active encouragement of infringement and happenstance infringement.

Part of the problem is one of procedural posture: In few of the cases involving infringement-by-label was the Federal Circuit reviewing a district court decision de novo. The majority in *GlaxoSmithKline* leaned heavily on the fact that it was reviewing a jury finding of inducement only for clear error.[320] Likewise, in *AstraZeneca*, cited by Judge Prost in *GlaxoSmithKline* as the only (other) case in which the court had previously "upheld an inducement finding involving a putative skinny label,"[321] the district court had granted a preliminary injunction—a decision that's reviewed only for abuse of discretion.[322]

Though it didn't involve an attempted skinny label, another example of the Federal Circuit upholding an infringement-by-label claim under a deferential standard of review is *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals International Ltd.*[323] In that case, the NDA holder, Vanda, owned a patent on a method of treating a patient with schizophrenia by (1) determining, through a genotyping assay, whether the patient is or is not a "poor metabolizer" of the drug, iloperidone; and (2) if the patient is a poor metabolizer, treating them with twelve milligrams or less of iloperidone per day, or, if the patient is not a poor metabolizer, treating them with between twelve and twenty-four milligrams per day.[324] The label of both Vanda's brand product and West-Ward's proposed

319. *Takeda*, 785 F.3d at 631.

320. *E.g.*, *GlaxoSmithKline*, 7 F.4th at 1340 ("Teva asks us to supplant the role of the jury and reweigh evidence in its favor. But it was for the jury to decide—not us, the district court, or the dissent—whether Teva's efforts actually induced infringement.").

321. *Id.* at 1350 (Prost, J., dissenting).

322. AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1065 (Fed. Cir. 2010); *see also id.* at 1056 (noting that the district court's factfinding about inducement is reviewed only for clear error).

323. 887 F.3d 1117, 1123 (Fed. Cir. 2018).

324. *Id.* at 1121.

generic contained admonitions that iloperidone doses "should be reduced" for poor metabolizers and stated that "[l]aboratory tests are available to identify [poor metabolizers]."[325] The district court, after a bench trial, found that this language "recommends" that a physician perform the method recited in Vanda's patent and that the ANDA label would "inevitably" lead to infringement.[326] The Federal Circuit affirmed, noting that the district court did not "clearly err" in its interpretation of the label.[327]

More recently, in its 2023 decision in *United Therapeutics Corp. v. Liquidia Technologies, Inc.*, the Federal Circuit upheld, again under a clear error standard of review, a finding of infringement where the only apparent evidence of inducement was an "instruction[]" in the label to perform the claimed method.[328] In that case, United owned a patent on methods of using "a therapeutically effective single event dose" of the drug treprostinil (sold by United under the brand name Tyvaso) to treat pulmonary hypertension.[329] The district court found that a single administration of treprostinil would be therapeutically effective (making its use a direct infringement).[330] Accordingly, the label's instructions to administer the drug—even in the absence of information about what it meant for a dose to be "therapeutically effective"—would, in the district court's view, "inevitably lead to the administration of a therapeutically effective single event dose," so the defendant, Liquidia, was liable for inducement.[331] With little analysis, the Federal Circuit affirmed. In the single paragraph discussing Liquidia's active inducement, the court noted that "Liquidia's product does not need to provide [data about therapeutic effectiveness] to constitute inducement of infringement; it merely needs to instruct doctors and patients to administer a therapeutically effective single event dose, which it does."[332]

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325. *Id.* at 1122, 1131.

326. *Id.* at 1130.

327. *Id.* at 1131.

328. 74 F.4th 1360, 1365, 1367 (Fed. Cir. 2023).

329. *Id.* at 1363-64.

330. *Id.* at 1365.

331. *Id.*

332. *Id.* at 1372. The *United Therapeutics* case contained an additional procedural wrinkle: At the time the Federal Circuit decided the appeal, United's patent had been held invalid by the Patent Office in an inter partes review proceeding, and an appeal of the Patent Office's decision was pending at the Federal Circuit. *Id.* at 1364. Liquidia argued that invalidity ruling negated any intent to induce, but the Federal Circuit rejected that argument, emphasizing (1) its prior holding that inter partes review decisions don't have collateral estoppel effect until any appeal concludes, *id.* at 1372 (citing XY, LLC v. Trans Ova Genetics, L.C., 890 F.3d 1282, 1294 (Fed. Cir. 2018)), and (2) that patent claims aren't actually canceled until the Patent Office issues a certificate confirming unpatentability, which doesn't happen until after the appeal process concludes, *id.* (citing 35 U.S.C. § 318(b)). Interestingly, less than five months after its decision upholding the inducement

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Vanda and *United Therapeutics* are, on our reading, a lot like *HZNP* ("wait until dry") and *Grunenthal* (where the patented use was a species of the "severe chronic pain" indication), cases in which no infringement was found even though the label could plausibly be interpreted to contain the infringing method. Yet in *Vanda* and *United Therapeutics*, the Federal Circuit deferred to district court interpretations equating the infringement analysis to package insert language merely *reciting* a claimed method as *one* treatment option, not *demanding* the infringing treatment.

At first glance, it may seem that these differing outcomes turn on how the cases were presented to the Federal Circuit. *Grunenthal*, *Vanda*, and *United Therapeutics* were all decided after bench trials, and the Federal Circuit deferred to the district court's findings about inducement. But that oddly suggests that interpreting drug labels—that is, construing the words of a regulatory document—is an issue of fact. And treating claims of infringement by label as turning on questions of fact is inconsistent with *Warner-Lambert*, which suggested that no facts outside the label could make up for the absence of an infringing use in it.[333]

None of this is clarified by the Federal Circuit's most recent precedential opinion in an infringement-by-label case, *Amarin Pharma, Inc. v. Hikma Pharmaceuticals USA Inc.*—even though it was decided under a de novo standard of review following a granted motion to dismiss.[334] In that case, the NDA holder, Amarin, sold the drug icosapent ethyl (under the brand name Vascepa) for two FDA-approved indications: treating severe hypertriglyceridemia and reducing cardiovascular risk.[335] Only the cardiovascular risk indication was covered by a method-of-use patent, so the ANDA applicant, Hikma, carved that indication out of its proposed label.[336]

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ruling, the Federal Circuit affirmed the Patent Office's invalidation of United's patent in an opinion by Judge Lourie—the same judge who wrote the opinion on inducement. *See* United Therapeutics Corp. v. Liquidia Techs., Inc., No. 2023-1805, 2023 WL 8794633, at *1 (Fed. Cir. Dec. 20, 2023). After the Federal Circuit's ruling on invalidity, the district court vacated its order enjoining final approval of Liquidia's FDA application until the patent expired. *See* United Therapeutics Corp. v. Liquidia Techs., Inc., No. 20-755, 2024 WL 1328902, at *1 (D. Del. Mar. 28, 2024).

333. *See* Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1364-65 (Fed. Cir. 2003). A more recent decision similar to *Warner-Lambert* is *H. Lundbeck A/S v. Lupin Ltd.*, 87 F.4th 1361, 1370-71 (Fed. Cir. 2023), in which the Federal Circuit upheld a district court's ruling, after a bench trial, that generic ANDA applicants did not induce infringement of a brand's method patent because, the district court found, the sole FDA-approved indication was not covered by the patent-in-suit and because the generics carved out of their labels data reporting the clinical studies that led to the patent-in-suit.

334. 104 F.4th 1370, 1376 (Fed. Cir. 2024).

335. Amarin Pharma, Inc. v. Hikma Pharms. USA Inc., 578 F. Supp. 3d 642, 643-44 (D. Del. 2022).

336. *Id.* at 644.

Amarin sued Hikma, arguing that inducement could be found in (1) warnings about side effects among patients who have cardiovascular risk that remained in the label and (2) Hikma's marketing its product as a "generic equivalent to Vascepa."[337] On Hikma's motion to dismiss, the district court rejected these arguments, ruling that (1) a warning is not an instruction to infringe and (2) the "generic equivalent" advertisements were not specifically encouraging infringement because of icosapent ethyl's noninfringing uses.[338]

The Federal Circuit, however, reversed. It emphasized the early stage at which the district court had dismissed, noting that all Amarin had to do was "plausibly" plead inducement.[339] And the court held that Amarin had done so. As for the label, the court ruled that intent to induce could be found in the allegations (1) that patient populations for severe hypertriglyceridemia (the lone indication in Hikma's generic label) and cardiovascular risk (carved out of Hikma's label) overlap, (2) that Hikma had removed a "limitation of use" for cardiovascular risk from its label, and (3) that Hikma's label retained a warning about side effects for patients with cardiovascular disease.[340]

The Federal Circuit conceded that Hikma's label alone might not, as a matter of law, constitute active inducement.[341] But the court also emphasized that Hikma promoted its product as AB-rated (i.e., therapeutically equivalent) for hypertriglyceridemia, which, as noted, overlaps with the cardiovascular-risk population covered by the patent; that Hikma marketed its product as the "generic equivalent to Vascepa"; and that most sales of Vascepa were for the patented cardiovascular-risk use.[342]

The upshot is that after *GlaxoSmithKline* and *Amarin*, all that's required to move forward with an inducement claim is (1) label language that could be read to recite or reference a patented method of use and (2) marketing copy touting generic equivalence. It's not surprising, then, that infringement-by-label cases continue to bubble up. Pending at the Federal Circuit as of this writing is *Corcept Therapeutics, Inc. v. Teva Pharmaceuticals USA, Inc.*, which involves Corcept's patent on a method of administering mifepristone with a "strong CYP3A inhibitor" to treat Cushing's syndrome.[343] (Cushing's syndrome is a rare but debilitating endocrine disorder characterized by an excess of cortisol; CYP3A inhibitors block cortisol synthesis.[344]) After a bench trial, the district judge found that no physician had ever actually practiced the asserted claims and that

337. *Id.* at 646.

338. *Id.* at 646-47.

339. *Amarin*, 104 F.4th at 1377.

340. *Id.* at 1378.

341. *Id.* at 1379.

342. *Id.*

343. 709 F. Supp. 3d 138, 146-47 (D.N.J. 2023).

344. *Id.* at 144-45.

the label didn't *encourage* the coadministration of mifepristone along with a strong CYP3A inhibitor—it actually cautioned *against it*.[345] Given the procedural posture and the deferential standard of review that applies, it would seem that an affirmance is likely. Still, in *GlaxoSmithKline*, Teva was trying to *avoid* infringement through its carveout—much like how Teva's label in *Corcept* provided warnings about the alleged infringing use—and yet the court upheld an inducement finding. Time will tell.[346]

III. The Puzzles of Inducement by Label

The infringement-by-label theory is not going away. To the contrary, recent litigation suggests the theory may be extended to additional defendants in the drug supply chain beyond generic companies themselves, such as health insurers and pharmacy benefit managers.[347] And some case studies have warned of a read-through effect on biologic drugs, even though they are governed by a different statutory scheme than the Hatch-Waxman Act.[348]

The Federal Circuit's infringement-by-label jurisprudence obscures several questions about the relationship between drug labels and inducement. Where does label language fit amid the law-fact distinction? What aspects of a drug label can be said to induce a physician to infringe? And how to reconcile the hypothetical nature of induced infringement in pre-launch cases with the realities of medical practice? Solving these puzzles, or at least calling attention to them, will help bring coherence to infringement-by-label litigation.

A. Labels Between the Law-Fact Divide

Like other forms of patent infringement, inducement is a question of fact.[349] The Federal Circuit has repeated this mantra again and again in infringement-by-label cases. In *GlaxoSmithKline*, the court characterized "whether Teva effected a section viii carveout of GSK's patented methods of use" as "a

345. *See id.* at 155, 159.

346. For some speculation based on oral argument, see Paul R. Gugliuzza & Jacob S. Sherkow, Corcept v. Teva *Oral Argument: Infringement by Drug Label, Again*, PATENTLYO (July 8, 2025), https://perma.cc/ABA9-5BE2.

347. *See, e.g.*, Amarin Pharma, Inc. v. Hikma Pharms. USA Inc., 578 F. Supp. 3d 642, 648-49 (D. Del. 2022) (denying motion to dismiss inducement claim against insurance company).

348. *See generally* PATIENT ACCESS & AFFORDABILITY PROJECT, SPECIAL REPORT: THE BIOSIMILARS MARKET IN 2023, https://perma.cc/V3NR-FYRB (discussing *GlaxoSmithKline*'s potential effect on both generic drugs and "biosimilars"—the quasi-generic versions of large-molecule biologic drugs, such as Humira (rheumatoid arthritis), Rituxan (cancer), and Enbreal (also arthritis)).

349. Barry v. Medtronic, Inc., 914 F.3d 1310, 1334 (Fed. Cir. 2019).

quintessential fact question."[350] And in *Amarin*, the court noted "what Hikma's label and public statements would communicate to physicians and the marketplace . . . . is a question of fact—not law."[351]

But the evidence proffered in infringement-by-label cases makes it seem like inducement, via package inserts, is more like a question of *law*. The Federal Circuit has construed drugs' package inserts as if they were patent claims, parsing their words to see if they contained the patented method of use,[352] rather than asking what physicians did (or would have done) with the information. The "quintessential fact question" in *GlaxoSmithKline* was whether Teva's "partial label" "satisfied" the patent's claim limitations, including whether the label's notation that the drug was effective in patients with "a left ventricular ejection fraction of ≤40% (with or without symptomatic heart failure)" meant they had "congestive heart failure," as required by the patent.[353] In *Amarin*, the Federal Circuit assessed whether "the patient population for the [patented] SH indication (i.e., triglyceride levels ≥500 mg/dL) overlaps with that for the [labeled] CV indication (i.e., triglyceride levels ≥150 mg/dL)."[354] That label analysis was then supplemented with reference to marketing materials stating the generic product's equivalence to the brand product—an unremarkable statement given that the law *requires* bioequivalence.[355] The Federal Circuit's close reading of label language, comparison of the label to the patent's claims, and review of marketing documents, all shaded by expert testimony, make the inducement analysis look a lot like patent claim construction—a legal question that can be based on underlying factfinding and which the Supreme Court has held is ultimately to be decided by the judge.[356]

Treating infringement-by-label as ultimately a legal question that can be based on factfinding, akin to claim construction, would provide better notice to generic drug sponsors and litigants about what the law prohibits and permits. Dissenting in *GlaxoSmithKline*, Judge Prost wryly observed that "inferring

350. GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 7 F.4th 1320, 1328 (Fed. Cir. 2021) (per curiam).

351. Amarin Pharma, Inc. v. Hikma Pharms. USA Inc., 104 F.4th 1370, 1379 (Fed. Cir. 2024).

352. *See, e.g.*, HZNP Meds. LLC v. Actavis Lab'ys UT, Inc., 940 F.3d 680, 701-02 (Fed. Cir. 2019) (assessing the label's "wait for the area to dry" instructions).

353. *GlaxoSmithKline*, 7 F.4th at 1328.

354. *Amarin*, 104 F.4th at 1378.

355. 21 U.S.C. § 355(j)(2)(A)(iv); *see also* Brief for the United States as Amicus Curiae, *supra* note 25, at 17 n.5 ("S]tatements describing petitioner's carvedilol as the 'AB-rated generic equivalent of' Coreg simply reflect the truism that a generic drug is required to be therapeutically equivalent to its brand-name reference drug." (citation omitted)).

356. Markman v. Westview Instruments, Inc., 517 U.S. 370, 390 (1996); *see also* Garrett T. Potter, Note, *Beefing Up Skinny Labels: Induced Infringement as a Question of Law*, 97 NOTRE DAME L. REV. 1707, 1732-33 (2022) (arguing that "the question of whether a party intended to induce infringement of a patent should be determined by a judge" as "a question of law").

intentional encouragement to infringe a method—from a label that has intentionally omitted everything that the brand said covers that method—is a lot to ask of a reasonable factfinder."[357] Such an inference does not center on a "quintessential fact question"[358]—did the drug label *actually* induce anyone to practice the patented method—so much as it "*manufactures* a factual dispute"—did the label contain *enough* instruction to uphold an infringement finding?[359] If the Federal Circuit in *GlaxoSmithKline* had been conducting de novo review, it might not have been able to justify that inference of intentional encouragement. As it stands, however, anyone who reads the Federal Circuit's inducement-by-label opinions with an eye toward the standard of review[360] is left in the dark about what is or is not infringement in disputes over pharmaceutical method-of-use patents.

B. Identifying the Object of Inducement

Despite the focus on label language, the Federal Circuit's opinions are unclear about *how* drug labels affect doctors' behavior. Instead, the Federal Circuit seems to make *all* of a drug label's information potentially inducing, suggesting that physicians read every part of the label and comply with all of it. This is, of course, simply not true, to the point where designing labels to increase physician compliance is its own area of study.[361] The Federal Circuit's error lies in a conflation of the *evidence* used to prove inducement—the package insert—with the ultimate *object* of the inducement inquiry—whether the package insert would compel a prescriber or patient to *act* in an infringing manner.

Take, for example, *Sanofi v. Glenmark Pharmaceuticals, Inc.*[362] In *Sanofi*, the Indications and Usage section referenced a clinical trial, the summary statistics of which were listed elsewhere in the label (the Clinical Trials section).[363] The mere presence of this information led the Federal Circuit to uphold a finding of inducement.[364] On one hand, the claimed method of use was literally "in" the

357. *GlaxoSmithKline*, 7 F.4th at 1350 (Prost, J., dissenting).

358. *Id.* at 1328.

359. *Id.* at 1350-51 (Prost, J., dissenting) (emphasis added).

360. *See* Jonathan S. Masur & Lisa Larrimore Ouellette, *Deference Mistakes*, 82 U. CHI. L. REV. 643, 645 (2015) (arguing that a "deference mistake" occurs when a court "relie[s] on precedent without fully accounting for the legal and factual deference regime under which that precedent was decided"—for instance, one appellate panel not recognizing that the pertinent precedent was not reviewing a question de novo, but with the scales tipped toward affirmance).

361. *See, e.g.*, Sullivan et al., *supra* note 74, at 694 (linking label design to physician use).

362. 875 F.3d 636 (Fed. Cir. 2017).

363. *Id.* at 642-43.

364. *Id. at* 645.

label.[365] On the other, though, the court did not assess whether physicians would have examined the Indications and Usage section, turned to the Clinical Trials section, cross-referenced the studies presented in the Clinical Trials section with their complete reports, and then acted accordingly.

Indeed, physicians prescribe for off-label indications all the time, even where there are not comparable clinical trials—suggesting that, in some instances, the Indications and Usage section is more akin to non-inducing background information than inducing encouragement.[366] And even when a physician is prescribing a drug for a listed indication, there are often limits or caveats they ignore. Provigil (modafinil), for example, "is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder."[367] But a 2013 survey of physicians concluded that "89% of patients prescribed modafinil did not have an on-label diagnosis."[368] Furthermore, Provigil is far from the only medication indicated to treat excessive sleepiness; its competitors include Xyrem (sodium oxybate), Xywav (sodium oxybate), Lumryz (sodium oxybate), Wakix (pitolisant), Celexa (citalopram), Prozac (fluoxetine), Paxil (paroxetine), Zoloft (sertraline), and Ritalin (methylphenidate).[369] Provigil's Indications and Usage section does nothing more than inform a physician what the drug has been approved for. But it can hardly be said to *cause* physicians to prescribe Provigil *for* excessive sleepiness, or to prescribe it *at all* when treating a patient suffering from excessive sleepiness.

This isn't to say that physicians don't take a drug's indications or clinical studies reported in the label seriously—they do.[370] But the label isn't the mechanism that *causes* physicians to take them seriously. If anything, physicians tend to distrust the summary statistics of clinical trials presented on labels and marketing materials.[371] Perhaps physicians pay more attention to sections pertaining to drug-drug interactions, dosage, counterindications, and black box

365. *Id.*

366. *See* David A. Simon, *Off-Label Inducement*, 111 IOWA L. REV. (forthcoming 2026) (manuscript at 9) (describing where physicians typically get information from concerning off-label uses).

367. FDA, PROVIGIL® (modafinil) Tablets (Aug. 17, 2007), https://perma.cc/MCH9-BPJQ.

368. Renée A. Peñaloza, Urmimala Sarkar, David A. Claman & Theodore A. Omachi, *Trends in On-Label and Off-Label Modafinil Use in a Nationally Representative Sample*, 173 JAMA INTERNAL MED. 704, 704 (2013).

369. *See generally* Julie M. Hereford, *Clinical Pharmacology of Sleep*, *in* SLEEP AND REHABILITATION 181-88 (2013) (assessing these drugs).

370. Caitlin K. Moynihan, Panne A. Burke, Sarah A. Evans, Amie C. O'Donoghue & Helen W. Sullivan, *Physicians' Understanding of Clinical Trial Data in Professional Prescription Drug Promotion*, 31 J. AM. BD. FAM. MED. 645, 649 (2018).

371. *Id.*

warnings, those most serious of labeled safety concerns. But even there the evidence is mixed.[372] In any event, the infringement-by-label jurisprudence does not separate those portions of drug labels—as informative as they are, and as much as they *may* compel a physician in an individual case—from the rest.

Flattening drug labels in this manner also ignores the realities of how package inserts are made. Practically, the FDA grants the NDA applicant considerable leeway for some aspects of the label, e.g., how to word the Indications and Usage section and the Clinical Studies section.[373] But dose titration curves? Not so much.[374] Because a generic sponsor is required by law to use the brand's label, it seems inequitable to hold the label's precise wording against the generic where a physician's behavior isn't actually affected by that language. That's especially true when the wording was at least a partial effort by the brand to capture infringement.[375]

Finding infringement based on a generic's label is even weirder for carveouts, where evidence of *nonintent*—the purposeful avoidance of inducement—is, in a post-*GlaxoSmithKline* landscape, turned into circumstantial evidence of *intent to induce*. This upends the distinction between mere knowledge of infringement and its active encouragement.[376] And it seems to diminish the purpose of carveouts: "to enable the sale of drugs for non-patented uses even though this would result in some off-label infringing uses."[377]

The weak causal link between drug labels (and generics' marketing copy) and actual physician practice points to another flaw in the Federal Circuit's infringement-by-label case law: the massive damages liability generics face in cases brought after ANDA approval. In *GlaxoSmithKline*, for instance, Teva was liable for GSK's—the brand's—lost profits: roughly $234 million. But Teva made only $74.5 million in *gross revenue* on its sales of generic carvedilol.[378] The

372. *See* Craig Geoffrey Smollin, Jonathan Fu & Ross Levin, *Recognition and Knowledge of Medications with Black Box Warnings Among Pediatricians and Emergency Physicians*, 12 J. MED. TOXICOL. 180, 180, 183 (2016).

373. *See* TING ET AL., *supra* note 11, at 18-19 (discussing crafting these sections); *see also* 21 C.F.R. § 201.57(c)(2), (c)(15) (describing optional information to be included for these sections).

374. *See* 21 C.F.R. § 201.57(c)(3) (describing a host of necessary information about dose "based on clinical pharmacologic data").

375. *Cf.* TING ET AL., *supra* note 11, at 18-19 (noting that one purpose of label design is competitive).

376. *See* GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 7 F.4th 1320, 1342, 1356-57 (Fed. Cir. 2021) (Prost, J., dissenting) (noting that the majority "never meaningfully engages with the legal distinction between encouraging, recommending, or promoting an infringing use and describing it").

377. Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp., 785 F.3d 625, 631 (Fed. Cir. 2015).

378. As of 2008, GSK's Coreg sold for $2.33 per pill; Teva's generic sold for $0.02 per pill. Petition for a Writ of Certiorari at 11, Teva Pharms. USA, Inc. v. GlaxoSmithKline LLC,

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chilling effects for generics of even the threat of an infringement-by-label suit are clear from those numbers.[379] Moreover, even allowing that a patent holder is entitled to lost profits damages under black-letter patent law, those profits should be traceable to the acts of direct infringement induced by the generic.[380] In *GlaxoSmithKline*, the evidence suggested that only 17% of carvedilol prescriptions were for the patented CHF indication.[381] Yet the Federal Circuit appeared to allow GSK to recover the profits it had lost on *all* of Teva's sales.[382]

C. The Nature of Artificial Inducement

Pre-generic-launch Hatch-Waxman Act inducement cases under section 271(e)(2) present a further puzzle: just how far to take the hypothetical nature of the infringement inquiry. As the Federal Circuit noted in *Warner-Lambert*, infringement under Hatch-Waxman is "hypothetical because the allegedly infringing product has not yet been marketed," so the inquiry becomes "whether, if a particular drug *were* put on the market, it *would* infringe the relevant patent."[383] For drug substance and drug product patents, this is an easily translated command. But for method-of-use patents that turn on inducement, this adds an obfuscating layer of inquiry. Is the question how an *actual* doctor would, hypothetically, prescribe the generic product if it were put on the market? Or is it how a *hypothetical doctor*—say, a reasonably informed prescriber—would prescribe the generic product if it were put on the market?

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143 S. Ct. 2483 (2023) (No. 22-37), 2022 WL 2757522; *see also id.* at 12 (reporting that Teva realized a net loss of $13 million on carvedilol).

379. *Id.* at 3 ("Generic versions of no-longer-patented drugs with patented uses launch with a skinny label almost half the time, saving patients and the federal government billions . . . . Generic manufacturers . . . make pennies per pill . . . ." (emphasis omitted)).

380. Grain Processing Corp. v. Am. Maize-Prod. Co., 185 F.3d 1341, 1349 (Fed. Cir. 1999); *see also* Dmitry Karshtedt, *Damages for Indirect Patent Infringement*, 91 WASH. U. L. REV. 911, 920 (2014) ("[T]he plaintiff should recover from the indirect infringer the sum total of the damages that it would have recovered from all *direct* infringers, had they all been sued instead of the indirect infringer." (emphasis added)).

381. *GlaxoSmithKline*, 7 F.4th at 1340.

382. *Id.* at 1352 (Prost, J., dissenting) ("[A]s both sides acknowledge, the damages award in this case was *not* confined to just the appropriate subset of infringing prescriptions to post-MI LVD patients who also had CHF—it encompassed CHF patients more broadly. GSK's damages testimony was not predicated on, nor did it quantify, the subset of uses that would infringe under the majority's skinny-label-based inducement theory." (citations omitted)). The majority, for its part, noted tersely that "GSK's expert's analysis accounted for Teva's sales for the infringing use, amounting to 17.1% of Teva's total carvedilol sales." *Id.* at 1341 (majority opinion). For a persuasive argument that the Federal Circuit improperly assumed that "100% of the infringing sales were induced by Teva," see Maya Lorey, Note, *Insurance Coverage and Induced Infringement: A Threat to Hatch-Waxman's Skinny Labeling Pathway?*, 90 U. CHI. L. REV. 1517, 1538 (2023).

383. Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1365-66 (Fed. Cir. 2003) (citation omitted).

In practice, these two approaches to the hypothetical inducement inquiry are different, and each has problems. The first—assessing how a flesh-and-blood physician would prescribe a hypothetical product—requires some testimony from a real doctor. But there is no guarantee that such a physician would be representative—or even broadly characteristic—of physicians as a whole. Indeed, it seems like little more than a form of expert shopping in the guise of doing so through what is purportedly a fact witness. Such testimony would also, by necessity, be absent a patient; with only a hypothetical drug product to prescribe, the physician must also conjure up a hypothetical patient. As the above discussion of Provigil illustrates, prescribing decisions are far more granular than automatically treating a patient suffering from the labeled indication by prescribing them the listed drug product. Indeed, were it otherwise, counterindications, drug-drug interactions, patient history and preferences—all the things that make up physicians' bedside practice—would be meaningless. The real doctor presented by the patentee would also have to testify that the doctor would do one thing if the label said so and another if it did not. Yet this greatly contrasts with how drug labels are read in the medical profession writ large.[384] And to anyone with a modicum of common sense, such testimony seems solely to be an artifact of litigation.

The second approach to the hypothetical inducement inquiry—assessing how a fictional *reasonable* physician would prescribe a generic product—would require the court to craft a legal construct of a hypothetical doctor, informed—presumably—by expert testimony. This sounds awkward: a hypothetical doctor, prescribing a hypothetical drug, to a hypothetical patient, from a hypothetical label. But it is perhaps no less weird than the courts' animation of a "reasonable person" in tort law or, for that matter, a "person having ordinary skill in the art," that fictional mechanic that patent courts are already familiar with.[385] This reasonably informed prescriber standard—like a "reasonable person" or a "person having ordinary skill in the art"—would, like its real-world counterpart, be a factual inquiry. But it may quickly depart from reality depending on whether the court is willing to assume that generic labels affect prescribing practices. That is, if a court adopts the reasonably informed prescriber standard, it must also smuggle in some untruths about labels being the vehicle for inducing that physician's behavior.

The Federal Circuit's pre-*GlaxoSmithKline* cases, unfortunately, provide little clarity about the hypothetical infringement analysis. In *AstraZeneca LP v. Apotex, Inc.* (the case about titrating down), the court seemed to adopt the reasonably informed prescriber approach because—and without any expert testimony in this regard—a reading of the generic label suggested that "at least

384. Sullivan et al., *supra* note 75, at 3031.

385. *Cf.* 35 U.S.C. § 103 (assessing whether an invention would be obvious to a "person having ordinary skill in the art to which the claimed invention pertains").

some users" would prescribe the generic product in an infringing manner.[386] But *Grunenthal* (the case in which the infringing, polyneuropathic use was a species of the broader, severe-pain indication in the label) tacked against this approach, affirming a finding of *no* inducement even where there *was* evidence that a reasonably informed prescriber would have practiced the asserted claims.[387] In *Vanda*, the brand sponsor attempted to show that the generic label would induce a physician to practice the patented method by "identify[ing] a doctor, Dr. Alva, who practiced the steps of the asserted claims with [the brand drug]"[388]—the flesh-and-blood physician approach. In affirming the district court decision of infringement, though, the Federal Circuit noted "that a patentee does not need to prove an actual past instance of direct infringement by a physician to establish infringement under 35 U.S.C. § 271(e)(2)(A)"[389]—giving credence to the hypothetical physician approach, or something like it.

This becomes even more complicated where the direct infringer is the patient, not a prescriber, as with *HZNP* ("wait until dry"). Finding a hypothetical patient who would directly infringe the asserted claims suffers from similar issues as finding similarly situated physicians. And, as for, say, a "reasonably informed patient" approach, that seems downright laughable given that the average patient is *not* reasonably informed by their drugs' labels. Furthermore, the package insert—the Full Prescribing Information document—is not written with patients in mind. Rather, the FDA uses a different labeling document—the *patient* package insert—which, with some exceptions, is not even mandatory.[390] No cases, it seems, make any legal distinction between doctors as direct infringers and patients as direct infringers.

Query, too, whether whatever choices made regarding the nature of the infringing doctor (or patient) in the Hatch-Waxman Act context need to (or should) align with post-approval cases. Post-approval cases do seem to consider actual physician testimony, even if—as in *GlaxoSmithKline*—it was discounted in favor of exegetically reading the label as if it were a patent claim.[391] Notably, treating the infringing physician in the pre-approval context as a reasonably informed prescriber would have the oddity of making assumptions about labels and physicians that—immediately following approval—would no longer be true. For example: a reasonably informed physician analysis finding that the prescriber would *not* be induced by the generic label—only to have physicians

386. 633 F.3d 1042, 1060 (Fed. Cir. 2010).

387. Grunenthal GmbH v. Alkem Lab'ys Ltd., 919 F.3d 1333, 1339-40 (Fed. Cir. 2019).

388. Vanda Pharms. Inc. v. W.-Ward Pharms. Int'l Ltd., 887 F.3d 1117, 1129 (Fed. Cir. 2018).

389. *Id.* at 1129.

390. *See Patient Labeling Resources*, FDA, https://perma.cc/PR3Q-6VU5 (last updated Aug. 19, 2024).

391. *See* GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 7 F.4th 1320, 1327-28 (Fed. Cir. 2021) (per curiam) (reviewing the testimony of a cardiology expert).

follow it *after* approval. In that circumstance, the generic sponsor would be liable for damages for what it thought, in the pre-approval context, was a go-to-launch signal—not wholly different from the damages assessed against Teva in *GlaxoSmithKline*.[392] Or, the opposite reading: a finding that a reasonably informed physician *would* have been induced by the generic label, only to demonstrate—once the generic is finally sold—that no one bothered to read it. In that circumstance, the generic could have—and should have—launched earlier, thus accomplishing one of the core goals of the Hatch-Waxman Act.

IV. Improving Pharmaceutical Patent Litigation—and Drug Labels

The Federal Circuit's infringement-by-label turn yields too many complexities for a simple solution. Though it's great that Congress has recognized the chilling effect decisions like *GlaxoSmithKline* and *Amarin* may have on generic entry,[393] its first cut at legislation probably wouldn't fix much. The bill simply declares that labels with Section viii carveouts can't be the basis for an inducement claim.[394] But, as we've seen, successful label-based claims against generics inevitably involve (1) patented methods of use that, the court determined, were not actually carved out of the label[395] or (2) inducement evidence beyond the label, such as advertising statements.[396]

Likewise, it is doubtful that any one Federal Circuit case would be a good vehicle to resolve the many doctrinal puzzles we've identified in this Article. Nonetheless, in future cases, the Federal Circuit could make a few changes to its understanding and assessment of drug labels and their role in inducement to better align patent doctrine with the FDA and medical practice.

To start, the Federal Circuit should recognize—in both word and deed—that there is a functional difference between what it refers to as a drug *label*, i.e., the package insert and related documents, and *labeling*, the sum of a drug sponsor's statements about the drug accompanying it, the latter of which seems especially significant in the post-approval context. Indeed, because the package insert is part of a drug's *labeling*, it makes sense—and, from an FDA law perspective, seems no large step—to include other evidence that comes within the broader regulatory definition.

This would improve current cases, both under the Hatch-Waxman Act and outside of it, that narrowly focus on the package insert and blind themselves to the nuances of how and which parts of the package insert get crafted by the

392. *See id.* at 1323.

393. Skinny Labels, Big Savings Act, S. 5573, 118th Cong. (2024).

394. *Id.* § 2(a)(2).

395. *E.g.*, *GlaxoSmithKline*, 7 F.4th at 1327.

396. *E.g.*, Amarin Pharma, Inc. v. Hikma Pharms. USA Inc., 104 F.4th 1370, 1379 (Fed. Cir. 2024).

brand sponsor. Doing so, as we've discussed, is both near- and farsighted: It presumes that where package inserts are "on point," they generally induce physicians to follow their commands; and it assumes that even where there is contrary evidence for or against inducement, labels are still the primary vehicle to determine liability. Demanding that brand sponsors provide *better* evidence of how and under what circumstances their labels were crafted—including permitting discovery into the label negotiation process with the FDA and making more use of *non*-package insert evidence—would better align pharmaceutical patent litigation with FDA practice and the competitive realities of the drug market.

Relatedly, the Federal Circuit should explicitly come to grips with the empirical reality that *most* doctors do not typically read *most* package inserts—and as a consequence, hew to its earlier decisions in *Warner-Lambert* and *Apotex* that the package insert, standing alone, cannot be sufficient evidence of inducement. At a minimum, brand sponsors should be required to demonstrate a link between what the label says and how physicians behave. Contra to *GlaxoSmithKline*, this evidence should be something other than a generic's statements that it *is* "a generic" or that it has received a therapeutic equivalency rating from the FDA. This means that evidence of off-label use, absent evidence of *promoting* that use, should not be enough to prove inducement—even if the off-label use is known, widely prescribed, and is the *purpose* of entering the generic market.[397] The court should also acknowledge, as Judge Prost urged in *GlaxoSmithKline*, that a Section viii carve-out is an attempt at *non*inducement. These changes would not necessarily benefit only generics. If there is, in fact, evidence of promoting an off-label, infringing use, there is no reason why that could not demonstrate induced infringement. If inducement is about what uses generics "encourage, recommend, or promote,"[398] this should extend to circumstances beyond just the package insert.

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397. Some may say this runs counter to the spirit of *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913 (2005), in which the Supreme Court held a peer-to-peer file sharing network liable for "indirect copyright infringement" because an overwhelming number of downloads by users were infringing and where the software's "purpose [was] to cause infringing use [as] shown by evidence independent of design and distribution of the product." *Id.* at 934; *see also* AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1059 (Fed. Cir. 2010) (analogizing inducement to indirect liability under *Grokster*); Frischling & Bitton, *supra* note 182, at 284 (same). But we don't think that's how *Grokster* should apply in the drug patent context. First, the Court in *Grokster* emphasized that inducement, unlike other forms of indirect infringement, "premises liability on purposeful, culpable expression and conduct." *Grokster*, 545 U.S. at 937. And second, the facts in *Grokster* are readily distinguishable from the cases we present here: Generics do not engage in carveouts for the *purpose* of causing infringing uses—as was the very point of the software in *Grokster*—so much as to *prevent* them from committing infringing uses.

398. Sanofi v. Watson Lab'ys Inc., 875 F.3d 636, 644 (Fed. Cir. 2017) (alteration in original) (quoting Takeda Pharms. USA, Inc. v. W.-Ward Pharm. Corp., 785 F.3d 625, 631 (Fed. Cir. 2015)).

Apart from getting the law right, these changes would provide a host of benefits to drug sponsors and litigants alike. First, these changes would better provide drug companies—both brands and generics—information about how to plan their labels and marketing. They would sensibly absolve generics of liability when their labels comply with what the FDA requires. Carving out the uses the brand puts in the Orange Book and saying nothing more than the drug is a "generic equivalent" would help solve the problem articulated in *GlaxoSmithKline*: a lack of clarity about "what Teva even did wrong—or, put another way, what another generic in its shoes should do differently."[399]

Second, these changes would cabin the incentive to game the label negotiation process to capture infringement. Generic package inserts—mandated, as they are, to mirror brands' package inserts—cannot and should not be used as the sole basis for an inducement finding. On the flip side, though, generics' marketing statements about patented indications, such as "Dear Doctor" letters, should be considered as evidence of inducement, even *if* those indications are not in the generic package insert. To put it another way, if evidence existed that Teva had, in fact, marketed its carved-out generic product to physicians for treating CHF—the patented indication—the skinny label should not have stood in GSK's way. After all, the FDA considers communications to doctors to be part of a drug's *labeling*; the Federal Circuit should, too.

Third, a better understanding of labeling and inducement dispenses with the need for generics to carve out information in their labels beyond the use codes placed in the Orange Book by the brand. This change would remove—or at least diminish—issues concerning patent infringement from the FDA's purview, a legal area in which the agency has long disclaimed expertise.[400] One could even say it fulfills the FDA's mission by making labels *safer*, insofar as safety means *more* rather than *less* information on the label. To be clear, this would not be a safe-harbor for infringement—a generic should still be liable for inducement if it markets for a patented use even with an approved carve-out. But at least the precise wording of the carved-out label itself would not swing the sword of Damocles over generic sponsors' heads.

Fourth and finally, a better understanding of package inserts and labeling would, we hope, largely resolve the procedural quandary in the recent infringement-by-label cases. Were the Federal Circuit to focus primarily on the real-world activity of the generic sponsor in promoting its product, this would make these facts, well, *facts*, truly deserving of the deference the Federal Circuit has given them. And it avoids the artifice of construing labels as if they were patent claims and then treating those interpretations as issues of fact. Counterintuitively, this would make summary judgment motions, and maybe

399. *GlaxoSmithKline*, 7 F.4th at 1360 (Prost, J., dissenting).

400. *See* Sherkow, *supra* note 125, at 215-16 (discussing FDA's reluctance in this area).

even pleading-stage motions, easier to resolve; where there is an *absence* of real-world activity regarding inducement apart from the drug label, there would not be a *genuine issue of material fact* about inducement. On that view, Teva's bench-trial win in its case against Corcept could have been obtained much sooner—and more cheaply. Similarly, where there is contested evidence of inducement beyond the mere wording of a drug label—thus preventing the grant or denial of summary judgment—brands and generics alike would have their day in court.

Conclusion

In pharmaceutical patent cases, the Federal Circuit has effectively equated drug labels to patent claims for the purpose of demonstrating induced infringement. This theory of infringement—infringement *by* label—is both doctrinally and factually wrong. It ignores the realities that should be at the heart of the inducement analysis, such as what actual doctors would or would not take away from a drug's label. It threatens to upend large swaths of the Hatch-Waxman Act, especially Section viii carve-outs. It is unfaithful to longstanding principles of patent law doctrine. And it is plagued by procedural quirks that obscure what the law regarding inducement really demands. The Federal Circuit could address many of these ills by simply recognizing nuances of drug labeling that its recent decisions ignore.

From a broader vantage point, infringement by label also serves as a lesson about "delicately balanced" laws, a characteristic used to describe not just the Hatch-Waxman Act, but laws pertaining to international relations,[401] workers' compensation,[402] federal criminal law,[403] bankruptcy,[404] and the Eleventh Amendment to the Constitution,[405] among others. Even forty years out, infringement by label shows there are still major gaps in the Hatch-Waxman Act as applied, even if not intended or foreseen by its drafters. This was, perhaps, inevitable: There is so much pressure on the Act's statutory machinery—and there is so much money involved—that smart and well-paid advocates will

401. Rubin v. Islamic Republic of Iran, 583 U.S. 202, 215 (2018) (describing the Foreign Sovereign Immunities Act as evincing a "delicate balance").

402. Decoteau v. Cozzini, Inc., No. CIV-08-401, 2009 WL 10693595, at *1 (E.D. Okla. Apr. 20, 2009) ("This potentially upsets the delicate balance of mutual compromise represented by the Workers' Compensation Act.").

403. United States v. Ferber, 966 F. Supp. 90, 102-03 (D. Mass. 1997) ("[T]he Travel Act must not be read so expansively as to upset the delicate balance between the powers of the federal and state sovereigns.").

404. Midland Funding, LLC v. Johnson, 581 U.S. 224, 234 (2017) ("To find the Fair Debt Collection Practices Act applicable here would upset that 'delicate balance.'").

405. Karns v. Shanahan, 879 F.3d 504, 512 (3d Cir. 2018) ("Immunity from suit in federal court under the Eleventh Amendment is designed to preserve the delicate and 'proper balance between the supremacy of federal law and the separate sovereignty of the States.'" (quoting Alden v. Maine, 527 U.S. 706, 757 (1999))).

endlessly come up with ways to game it. This suggests, in the words of Jay Thomas, that the Act "is not one of a singular 'Grand Bargain[]' . . . [but] instead a deal that has been subject to continuous legislative revisiting and revision."[406] With that in mind, Congress may wish to clarify the contours of inducement under the Hatch-Waxman Act to give the statute the full measure of its aims, without worrying that it will sink some historically intractable compromise. In the meantime, the Federal Circuit should not blindly use drug labels as a heuristic for complex questions of intent and real-world behavior by doctors.

406. Thomas, *supra* note 6, at 876.