United States Court of Appeals for the Federal Circuit

H. LUNDBECK A/S, TAKEDA PHARMACEUTICAL COMPANY LIMITED, TAKEDA PHARMACEUTICALS U.S.A., INC., TAKEDA PHARMACEUTICALS INTERNATIONAL AG, TAKEDA PHARMACEUTICALS AMERICA, INC.,
Plaintiffs-Appellants

v.

LUPIN LTD., LUPIN PHARMACEUTICALS, INC., MACLEODS PHARMA USA, INC., MACLEODS PHARMACEUTICALS LTD., SANDOZ INC., SIGMAPHARM LABORATORIES, LLC, ZYDUS PHARMACEUTICALS (USA) INC., ALEMBIC GLOBAL HOLDING S.A., ALEMBIC PHARMACEUTICALS INC., ALEMBIC PHARMACEUTICALS LIMITED, CADILA HEALTHCARELTD., LEK PHARMACEUTICALS, D.D.,
Defendants-Cross-Appellants

2022-1194, 2022-1208, 2022-1246

Appeals from the United States District Court for the District of Delaware in No. 1:18-cv-00088-LPS, Judge Leonard P. Stark.

Decided: December 7, 2023

BRIANNE BHARKHDA, Covington & Burling LLP, Washington, DC, argued for plaintiffs-appellants. Also represented by GEORGE FRANK PAPPAS, EINAR STOLE; KURT CALIA, Palo Alto, CA.

DAVID BRIAN ABRAMOWITZ, Locke Lord LLP, Chicago, IL, argued for defendants-cross-appellants Alembic Global Holding S.A., Alembic Pharmaceuticals Inc., Alembic Pharmaceuticals Limited, Cadila Healthcare Ltd., Lek Pharmaceuticals, d.d., Macleods Pharma USA, Inc., Macleods Pharmaceuticals Ltd., Sandoz Inc., Sigmapharm Laboratories, LLC, Zydus Pharmaceuticals (USA) Inc. Cadila Healthcare Ltd., Zydus Pharmaceuticals (USA) Inc. also represented by HUGH S. BALSAM, CAROLYN ANNE BLESSING, MICHAEL GAERTNER, TIMOTHY FLYNN PETERSON, JONATHAN B. TURPIN; AUGUST MELCHER, Weil, Gotshal & Manges LLP, Redwood Shores, CA.

DEEPRO MUKERJEE, Katten Muchin Rosenman LLP, New York, NY, argued for defendants-cross-appellants Lupin Ltd., Lupin Pharmaceuticals, Inc. Also represented by LANCE SODERSTROM; JOSEPH JANUSZ, JITENDRA MALIK, Charlotte, NC.

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Before DYK, PROST, and HUGHES, *Circuit Judges*.

DYK, *Circuit Judge*.

H. Lundbeck A/S ("Lundbeck"), Takeda Pharmaceutical Company Ltd., Takeda Pharmaceuticals U.S.A., Inc., Takeda Pharmaceuticals International AG, and Takeda Pharmaceuticals America, Inc. (collectively "plaintiffs") appeal the final judgment of the United States District Court for the District of Delaware.

The district court held that defendants' Abbreviated New Drug Applications ("ANDAs") did not infringe two patents owned by plaintiffs, one for the use of the drug vortioxetine in patients who have previously taken certain other antidepressant medications and had to cease or reduce use due to sexually related adverse events, U.S. Patent No. 9,278,096 ("the '096 patent"), and one for using vortioxetine to treat cognitive impairment, U.S. Patent No. 9,125,910 ("the '910 patent").

Defendants Lupin Ltd., Lupin Pharmaceuticals, Inc.,[1] Macleods Pharma USA, Inc., Macleods Pharmaceuticals Ltd., Sandoz Inc.,[2] Sigmapharm Laboratories, LLC, Zydus

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[1] "Lupin" refers to Lupin Ltd. and Lupin Pharmaceuticals, Inc. collectively.

[2] "Sandoz" refers to Sandoz Inc. and Lek Pharmaceuticals d.d. collectively.

Pharmaceuticals (USA) Inc., Alembic Global Holding S.A., Alembic Pharmaceuticals Inc., Alembic Pharmaceuticals Ltd., Cadila Healthcare Ltd., and Lek Pharmaceuticals, d.d. (collectively "defendants"), conditionally cross appeal the district court judgment that the '096 and '910 patents are not invalid.

Lupin also cross appeals the district court's determination that Lupin's ANDA will infringe plaintiffs' U.S. Patent No. 9,101,626 ("the '626 patent"), covering a process for making vortioxetine, and the district court's construction of the term "reacting."

We affirm the judgment of non-infringement of the '096 and '910 patents and the determination that Lupin infringed claim 12 of the '626 patent. We do not reach the question of the validity of the '096 and '910 patents.

BACKGROUND

I

A new drug cannot be marketed for use unless the Food and Drug Administration ("FDA") has approved a New Drug Application ("NDA") for the proposed use of that drug. *See* 21 U.S.C. § 355(a)–(b). The Hatch-Waxman Act allows generic manufacturers to "piggy-back[]" on a branded drug's FDA-approved NDA by submitting an ANDA showing that the generic drug has the same active ingredients and is bioequivalent to the brand-name drug. *See Caraco Pharm. Lab'ys, Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 404–05 (2012) (discussing Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585). Under this streamlined approach, the ANDA may rely on the safety and efficacy information for an approved use of the brand-name drug. *Id.* at 405. "[T]his process is designed to speed the introduction of low-cost generic drugs to market." *Id.*

"To facilitate the approval of generic drugs as soon as patents allow, the Hatch-Waxman Amendments and FDA

regulations direct brand manufacturers to file information about their patents" in what is called the Orange Book. *Id.*; *see also* 21 U.S.C. § 355(b)(1)(A)(viii). If an ANDA applicant wishes to market a drug before the expiration of the patents listed in the Orange Book, the applicant has two options. *See Caraco*, 566 U.S. at 406.

First, if the ANDA applicant believes that a patent "is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted," the applicant may submit a "Paragraph IV" certification. 21 U.S.C. § 355(j)(2)(A)(vii)(IV). Filing a Paragraph IV certification gives the brand manufacturer a right to sue the ANDA filer for infringement. *Caraco*, 566 U.S. at 407 (citing 35 U.S.C. § 271(e)(2)(A)). Infringement can then be "determined by traditional patent infringement analysis." *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003). Under the patent statute, it is an act of direct infringement to make, use, offer to sell, or sell a patented invention without authorization. 35 U.S.C. § 271(a). The patent statute also provides for indirect infringement, which can be found in cases where the defendant "actively induces" another to infringe or in cases where a "contributory infringer" sells "a material . . . for use in practicing a patented process." 35 U.S.C. § 271(b)–(c). Sale of a material that is "suitable for substantial noninfringing use" is not contributory infringement. § 271(c).

Second, for patents that claim a method of use, the ANDA applicant may propose a label that "carves out" a patented use and submit a "section viii" statement to that effect. *Caraco*, 566 U.S. at 406 (citing 21 U.S.C. § 355(j)(2)(A)(viii)). If the FDA approves the carved-out label, the ANDA applicant may market the drug "only for a subset of approved uses—*i.e.*, those not covered by the brand's patents." *Id.* "The Hatch-Waxman Amendments authorize the FDA to approve the marketing of a generic drug for particular unpatented uses; and section viii provides the mechanism for a generic company to identify

those uses, so that a product with a label matching them can quickly come to market. The statutory scheme, in other words, contemplates that one patented use will not foreclose marketing a generic drug for other unpatented ones." *Id.* at 415.

II

Takeda U.S.A., Inc. holds the approved NDA for the branded drug Trintellix® ("Trintellix") for the treatment of major depressive disorder ("MDD") in adults. Trintellix's active ingredient is a salt of vortioxetine. Plaintiffs' patents on the drug compound and on a method of use for treating depression, U.S. Patent Nos. 7,144,884 and 8,476,279 (the "compound patents"), have expiration dates of June 17, 2026, and October 2, 2022, respectively.

Following the initial FDA approval of the use of Trintellix to treat MDD, plaintiffs secured the '096 and '910 method of use patents at issue in this case, which concern the treatment of MDD in patients who have previously taken certain other drugs but had to cease or reduce use due to sexually related adverse events and the treatment of cognitive impairment, respectively. The plaintiffs then listed the '096 and '910 patents in the FDA's Orange Book. Their expiration dates are March 21, 2032, and June 15, 2027, respectively. Defendants have submitted ANDAs seeking approval to market vortioxetine for only one indication, the treatment of MDD in adults, a method of use not covered by the '096 and '910 patents, and the ANDAs will become effective after the expiration of the compound patents.[3] Plaintiffs nonetheless contended that the '096

[3] As to the compound patents, some defendants submitted so-called "Paragraph III" certifications indicating that those defendants are not seeking approval to market vortioxetine prior to the expiration of the patents, *see* 21 U.S.C. § 355(j)(2)(A)(vii)(III), and other defendants are

and '910 patents preclude approval of defendants' ANDAs.[4] It is useful to understand the background of these two patents.

III

Some drugs for the treatment of depression are associated with high rates of sexual dysfunction. Treatment Emergent Sexual Dysfunction ("TESD") is a term used for sexual dysfunction caused by antidepressant drugs. Plaintiffs conducted clinical studies regarding the effects of Trintellix on sexual function, which concluded that it had shown less adverse effects on sexual function as compared to other antidepressants.

Using findings from some of these studies, Lundbeck and Takeda filed the application that became the '096 patent. The '096 patent concerns a method of treatment involving the use of vortioxetine by a patient who "has previously received medication or is still receiving medication for the treatment of [depression and other diseases]" who has "ceased or reduced [use of the medication] due to sexually related adverse events." '096 patent, cl. 1. The Patent and Trademark Office ("PTO") issued the '096 patent on March 8, 2016. Claim 7 of the '096 patent depends from independent claim 1 and dependent claim 6. The claims recite:

> 1. A method for the treatment of a disease selected from the group consisting of depression, anxiety, abuse and chronic pain, comprising the administration of a therapeutically effective amount of

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subject to a district court order that the ANDAs not be approved before the expiration of the compound patents, which is not an issue on appeal.

[4] Sandoz filed a Paragraph III certification as to the '910 patent and so is not a party with respect to the '910 patent issues on appeal.

> [Compound I][5] or a pharmaceutically acceptable salt thereof to a patient in need thereof,
>
> wherein said patient has previously received medication or is still receiving medication for the treatment of said disease, the medication is ceased or reduced or has to be ceased or reduced due to sexually related adverse events, and the medication is selected from the group consisting of selective serotonin reuptake inhibitors, selective noradrenaline reuptake inhibitors, noradrenaline/serotonin reuptake inhibitors, and tri-cyclics.
>
> 6. The method according to claim 1, wherein Compound I or a pharmaceutically acceptable salt thereof is administered to the patient in unit doses of about 1–50 mg.
>
> 7. The method according to claim 6, wherein the patient is administered between about 1 and 20 mg per day of the hydrobromic acid salt of Compound I orally.

The second patent at issue is the '910 patent concerning treatment of cognitive impairment. Cognitive impairment is very common in MDD patients. The PTO issued the '910 patent on September 8, 2015. Claim 6 of the '910 patent depends from independent claim 1 and dependent claim 3. The claims recite in relevant part:

> 1. A method of treating cognitive impairment involving decline in speed of processing, executive function, attention, or verbal learning and memory in a patient diagnosed with depression, the method

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[5] The patents at issue define 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine, also known as vortioxetine, and pharmaceutically acceptable salts thereof as Compound I.

> comprising administering a therapeutically effective amount of Compound I or a pharmaceutically acceptable salt thereof to the patient, wherein . . . the method alleviates a symptom or complication of the cognitive impairment or delays the progression of the cognitive impairment.
>
> 3. The method of claim 1, wherein the depression is major depressive disorder.
>
> 6. The method of claim 3, wherein the method comprises administering a hydrobromide salt of Compound I to the patient.

IV

Plaintiffs sued seeking to enjoin defendants from marketing a generic version of Trintellix until after the expiration of the '096 and '910 patents, alleging induced and contributory infringement of the '096 patent and contributory infringement of the '910 patent. Following a bench trial, the district court determined that the defendants' ANDAs neither induced infringement of nor contributorily infringed the '096 and '910 patents. Plaintiffs timely appealed. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

V

A third patent at issue in this case is the '626 patent concerning a process for manufacturing vortioxetine. Claim 12 of the '626 patent depends from independent claim 1 and dependent claim 11. Claim 1 recites in relevant part:

> 1. A process for the preparation of [compound I] or a pharmaceutically salt thereof, the process comprising reacting compound II . . ., with a compound of formula III . . ., and a compound [IV] . . ., in the presence of a solvent, a base and a palladium catalyst consisting of a palladium source and a

> phosphine ligand at a temperature between 60° C. and 130° C.

Lupin filed an ANDA seeking approval to market vortioxetine prepared by a process that plaintiffs contend will infringe claim 12 of the '626 patent. Plaintiffs sued Lupin for infringement and to bar Lupin from using the process before the expiration of the '626 patent. The parties disputed the construction of the term "reacting." After a bench trial, the district court agreed with plaintiffs' construction and found that Lupin infringes under that construction. Lupin timely cross appealed. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

"This court reviews a district court's judgment following a bench trial for errors of law and clearly erroneous findings of fact." *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1343–44 (Fed. Cir. 2002).

I

A

Typically, under the Hatch-Waxman Act, plaintiffs sue ANDA filers for direct, induced, and/or contributory infringement. *See, e.g.*, *Allergan, Inc. v. Alcon Lab'ys, Inc.*, 324 F.3d 1322, 1331 (Fed. Cir. 2003) ("The only difference in the analysis of a traditional infringement claim and a claim of infringement under section 271(e)(2) is the timeframe under which the elements of infringement are considered."). Plaintiffs argue that the district court erred in not finding infringement of the '096 and '910 patents because section 271(e)(2)(A) creates a separate cause of action that does not require a showing of direct, induced, or contributory infringement by the ANDA filer. Section 271(e)(2)(A) provides:

> It shall be an act of infringement to submit an application under [the Hatch-Waxman Act] for a drug

> . . . the use of which is claimed in a patent . . . if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug . . . the use of which is claimed in a patent before the expiration of such patent.

Thus, plaintiffs argue, defendants infringe under the plain text of section 271(e)(2)(A) because they filed ANDAs seeking approval to market vortioxetine; some uses of vortioxetine—for the treatment of patients that have previously taken other drugs but had to cease or reduce use due to sexually related adverse events and for the treatment of cognitive impairment—are covered by the '096 and '910 patents; and the labels do not prohibit prescribing vortioxetine for those uses, even though the defendants do not propose to market the drug for those patented uses. In other words, according to plaintiffs it makes no difference that the drug is proposed to be sold for a use not covered by the '096 and '910 patents because the drug could be prescribed for those patented uses. We disagree. Our cases establish that "the use . . . claimed in a patent" under section 271(e)(2)(A) must be the use for which an applicant is seeking marketing approval.

As an initial matter, we note that plaintiffs did not make this statutory interpretation argument before the district court, and defendants argue that plaintiffs forfeited the argument by not raising it below. Because the construction of a statute is a pure question of law, we nonetheless elect to address plaintiffs' arguments. *See Singleton v. Wulff*, 428 U.S. 106, 121 (1976) ("The matter of what questions may be taken up and resolved for the first time on appeal is one left primarily to the discretion of the courts of appeals, to be exercised on the facts of individual cases."); *Columbia Sportswear N. Am., Inc. v. Seirus Innovative Accessories, Inc.*, 80 F.4th 1363, 1374 (Fed. Cir. 2023) ("[W]hether to excuse a forfeiture is generally within our discretion."); *Cemex, S.A. v. United States*, 133 F.3d

897, 902 (Fed. Cir. 1998) (addressing an argument not raised below "because an issue of statutory interpretation is involved").

In *Warner-Lambert* and its progeny, we considered and rejected plaintiffs' interpretation of section 271(e)(2)(A). 316 F.3d at 1354–62. The plaintiff in *Warner-Lambert*, which owned a patent on methods of treatment for neurodegenerative disease that was listed in the Orange Book, sued to block a generic company from securing approval of an ANDA that would allow the marketing of the drug for another use not covered by the patent. *Id.* at 1352. The plaintiff argued that, because the generic company sought FDA approval "for a drug," "the use of which is claimed in" a patent, the company infringed "irrespective of whether approval is sought to market the drug for the patented use." *Id.* at 1355. We disagreed, holding that such an interpretation "eviscerated an important part of the statutory provision" by severing the phrase beginning "if the purpose . . ." from the rest of the statute. *Id.*

We explained that "'the use' in § 271(e)(2)(A) refers to the use for which the FDA has granted an NDA" and for which the ANDA was submitted. *Id.* at 1356. Thus, it is not "an act of infringement under 35 U.S.C. § 271(e)(2)(A) to submit an ANDA for a drug if just *any* use of that drug were claimed in a patent." *Id.* at 1358–59. If it were, a brand could "maintain its exclusivity merely by regularly filing a new patent application claiming a narrow method of use not covered by its NDA," which "would confer substantial additional rights on pioneer drug patent owners that Congress quite clearly did not intend to confer." *Id.* at 1359. Rather, actions for infringement of method of use patents under section 271(e)(2)(A) are limited to patents that claim an indication of the drug for which indication the applicant is seeking approval. *Id.* at 1361.

Plaintiffs argue that the *Warner-Lambert* line of cases are distinguishable, at least as to the '096 patent, because

the use covered by the '096 patent still involves the treatment of MDD and will not be an off-label use. Our other section 271(e)(2)(A) cases confirm that *Warner-Lambert* is not limited to cases in which the "patent at issue is for a use not approved under the NDA." *Id.* at 1355; *see, e.g.*, *AstraZeneca Pharms. LP v. Apotex Corp.*, 669 F.3d 1370, 1379 (Fed. Cir. 2012) ("Although [plaintiff] is correct that the patent at issue in *Warner-Lambert* claimed an off-label use for a drug, that distinction is irrelevant for purposes of § 271(e)(2).").

Here, the district court found that defendants are not seeking approval for an indication claimed by the '096 and '910 patents. Defendants solely seek approval to market the drug for the treatment of MDD pursuant to the methods of expiring patents—that is the "purpose" of the ANDA submissions. Thus, the patented uses are not those for which ANDA approval is sought. Plaintiffs have failed to establish that section 271(e)(2)(A) provides an independent basis of infringement.

B

Plaintiffs next argue that the district court erred in finding no induced infringement of claim 7 of the '096 patent. Under the law of induced infringement, "[w]hoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). "The accused infringer must have 'knowingly aided and abetted' direct infringement" and taken active steps to encourage, recommend, or promote infringement. *Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 630–31 (Fed. Cir. 2015) (quoting *Warner-Lambert*, 316 F.3d at 1363). Examples of active steps include "advertising an infringing use or instructing how to engage in an infringing use." *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 936 (2005). In order to support inducement liability, instructions may not merely describe an infringing mode; they must "evidence 'intent to encourage infringement.'"

Takeda, 785 F.3d at 631 (emphasis omitted) (quoting *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1329 (Fed. Cir. 2009)).

Here, plaintiffs' inducement case relied solely on defendants' proposed ANDA labels as the inducing conduct. Because plaintiffs did not identify any advertising or promotional materials that encouraged infringement, this case is unlike *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.*, 7 F.4th 1320, 1333 (Fed. Cir. 2021), and other cases where we have found infringement based on communications outside the ANDA label. Here the district court found the label in question is not a label that induces infringement of the '096 patent. It is the label FDA required for the sale of the drug to treat MDD—a label that the patentee itself proposed for that purpose in connection with its NDA for treating MDD and that preexisted the issuance of the '096 patent.

Nonetheless, plaintiffs contend that because the '096 patent exists and clinicians will prescribe the ANDA products for the uses claimed in the '096 patent, defendants have induced infringement and cannot obtain approval for their ANDAs. However, it cannot be, as plaintiffs suggest, that a patentee can bar the sale of a drug for a use covered only by patents that will have expired simply by securing a new patent for an additional, narrower use, as we recognized in *Warner-Lambert*. 316 F.3d at 1359. Such an approach to indirect infringement would be inconsistent with a stated purpose of the Hatch-Waxman Act—"to enable generic manufacturers to be ready to enter the market once patents expired." *Id.* at 1357. A patentee may not use Hatch-Waxman to "maintain its exclusivity merely by regularly filing a new patent application claiming a narrow method of use not covered by its NDA." *Id.* at 1359. Accordingly, we do not see how, in the normal course, a label required to market the drug for a use covered by expired patents could demonstrate the required specific intent to encourage infringement of new patents covering different

uses. This is particularly so here since plaintiffs' infringement theory depends entirely on the "Adverse Reactions" section of the defendants' ANDA labels, which was essential to FDA approval to market the drug for the treatment of MDD and has been present in the Trintellix label since FDA first approved the drug for the treatment of MDD on September 30, 2013[6]—years before the PTO issued the '096 patent in 2016.[7]

To be sure, there may be situations where the owner of an expired compound patent or expired method of use patent makes a new discovery that requires a new method of use to ensure patient safety. If FDA requires, in order to protect patient safety, that the new method of use must be included in the label, the ANDA label may induce infringement of the new safety patents. Our cases have considered instances where the ANDA label includes necessary safety instructions, for example instructions to titrate to a lower dose, *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060–61 (Fed. Cir. 2010), to request a lab test and adjust the dose in response, *Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1131 (Fed. Cir. 2018), or to take a critical supplement along with the drug to reduce potentially life-threatening toxicities, *Eli Lilly & Co. v. Teva Parenteral Medicines, Inc.*, 845 F.3d 1357, 1365, 1368–69 (Fed. Cir. 2017). This is not such a case. Here, there is no new discovery requiring instructing how to safely take the drug, or identifying a class of patients who should not take the drug at all.

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[6] The original brand named of Trintellix was Brintellix®.

[7] This case is thus unlike *GlaxoSmithKline*, where the portion of the label relied on to support a finding of induced infringement, the post-MI LVD indication, did not describe or relate to a use claimed in an expired patent. 7 F.4th at 1327–29.

This is also not a situation in which there is an "express[] direct[ion]" in the label to review data about "the class of patients for whom the drug is indicated to achieve the stated objective" of a new patent. *Sanofi v. Watson Lab'ys Inc.*, 875 F.3d 636, 645 (Fed. Cir. 2017). With FDA approval, defendants have "carved out" the portions of the NDA labels relating to the '096 patent and identifying those individuals who would particularly benefit from taking the drug (because of the low incidence of TESD).[8]

Under section 355(j)(4), which is part of the Hatch-Waxman Act, the FDA is instructed "to approve an ANDA filed with a section viii statement when it proposes to market a drug for only unpatented methods of use" in order to facilitate the approval of noninfringing generic drugs. *See Caraco*, 566 U.S. at 419. FDA regulations permit an ANDA filer to omit "an indication or other aspect of labeling protected by patent" as an exception to the general rule that an ANDA label must be the same as the branded drug's. 21 C.F.R. § 314.94(a)(8)(iv). Here, defendants' ANDA labels "carved out" the superiority data in the clinical studies portion of the label and the cross-reference to that data. The label itself does not even reference the patient class

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[8] The '096 patent and the corresponding portions of the label followed after the plaintiffs conducted two superiority studies, which were successful in demonstrating clinically meaningful improvement in sexual functioning when patients switched to Trintellix as compared to other drugs. Based on these further studies, at plaintiffs' request, on October 19, 2018, FDA approved additions to the Trintellix label in a section entitled "Clinical Studies," to present data from the two superiority studies. FDA also approved adding a new sentence at the beginning of the section describing the adverse reactions of sexual dysfunction that cross-references the superiority studies presented elsewhere in the new label.

recited in claim 7 of the '096 patent and instructs physicians not to compare rates of adverse reactions of sexual dysfunction between vortioxetine and other drugs. The district court correctly determined that, under these circumstances and consistent with our cases,[9] the proposed ANDA labels "will not encourage, recommend, or promote an infringing use." J.A. 227.

It remains only to consider two additional arguments offered by plaintiffs. First, they contend that an ANDA label induces infringement if physicians will prescribe the drug for uses claimed by the '096 patent based on their background knowledge together with information in the carved-out label. In the Hatch-Waxman context, we have

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[9] *See, e.g.*, *Grunenthal GmbH v. Alkem Lab'ys Ltd.*, 919 F.3d 1333, 1339–40 (Fed. Cir. 2019) (affirming that a generic label can avoid inducing infringement by carving out the inducing material from the label); *HZNP Meds. LLC v. Actavis Lab'ys UT, Inc.*, 940 F.3d 680, 702 (Fed. Cir. 2019) (affirming that a label did not induce infringement when it did not instruct carrying out all of the claimed method's steps); *Takeda*, 785 F.3d at 632 ("[V]ague label language cannot be combined with speculation about how physicians may act to find inducement."); *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1324 (Fed. Cir. 2012) (affirming that a label did not induce infringement when, despite presenting data suggesting that a claimed combination of effects could occur, the label as a whole did not "recommend or suggest to a physician that [the drug] is safe and effective for inducing the claimed combination of effects in patients in need thereof"); *AstraZeneca*, 669 F.3d at 1380 (affirming no infringement when, despite "market realities" that doctors will substitute the generic for all indications, "[s]ection viii statements and corresponding proposed labeling explicitly and undisputedly carve out all patented indications").

held that "mere knowledge of possible infringement by others does not amount to inducement; specific intent and action to induce infringement must be proven." *Warner-Lambert*, 316 F.3d at 1364. This is so because a central purpose of the Hatch-Waxman Act is to allow, through the section viii carve out process, the sale of drugs for unpatented uses even though those sales result in some infringing uses. *Takeda*, 785 F.3d at 631–32. So too, the fact that some individuals may have been influenced by one piece of information from a label required to sell the drug for other purposes does not amount to inducement. Plaintiffs' argument is nothing more than an attempt to impose contributory infringement liability on the sale of a product knowing it will be put to infringing uses without recognition of the additional requirement that there be no substantial noninfringing use.

Second, plaintiffs argue that the district court's induced infringement analysis "ignored [the] 5 mg, 10 mg, and 15 mg doses" and "failed to cite any record evidence" for them. Appellants' Brief at 53. We disagree. The district court relied on multiple sources of evidence that applied equally to all dosage forms, including the label's instruction against comparing TESD rates between vortioxetine and other drugs and a survey of clinicians regarding how they understand the label. The district court explicitly noted that clinicians would not be encouraged to prescribe vortioxetine to the implicated patient class "particularly for the recommended 20 mg dose." J.A. 146 (emphasis added). There is no error in relying on evidence about the recommended dose in addition to evidence that applies equally to all approved doses. Notably, plaintiffs argued in their post-trial brief on validity that "a POSA would have understood all therapeutic doses to have similarly low levels of [sexually related adverse events]." J.A. 236 (quoting D.I. 1059 at 28). Plaintiffs cannot now fault the district court for crediting their own argument.

The district court did not err in finding that plaintiffs failed to establish induced infringement under 35 U.S.C. § 271(b).

C

Plaintiffs next argue that the district court erred by concluding that the plaintiffs had not established contributory infringement of the '096 and '910 patents. The plaintiffs' theory is that defendants will contributorily infringe by selling their ANDA products because physicians will prescribe them in accordance with the methods claimed in the '096 and '910 patents. Under 35 U.S.C. § 271(c), there is no liability for contributory infringement for selling an article that is "suitable for substantial noninfringing use."

The district court concluded that there was no contributory infringement because there are substantial noninfringing uses of vortioxetine. With respect to the '096 patent, the district court found that there will be substantial noninfringing uses including prescribing vortioxetine to patients with no prior treatment, patients with prior treatment other than with the drugs referenced in the '096 patent, and in cases where the prior antidepressant was ceased or reduced for reasons other than sexually related adverse events (for example, due to poor efficacy). Similarly, with respect to the '910 patent, there will be substantial noninfringing uses including prescription for treating MDD, prescription to patients without cognitive impairment, and prescription for purposes unrelated to cognition.

Plaintiffs contend nonetheless that the district court erred as a matter of law in finding substantial noninfringing uses when those uses purportedly infringe other patents owned by Lundbeck, specifically patents on the drug compound. However, substantial noninfringing use in section 271(c) refers to uses that do not infringe the patent in question, not other patents. The text is clear: to support liability, the accused infringer must sell a material part of an invention or an article for use in practicing a patented

process "knowing the same to be especially made or especially adapted for use in an infringement of such patent." 35 U.S.C. § 271(c) (emphasis added). "Such patent" is in the singular and refers to a specific patent—the asserted patent. In *Sony v. Universal City Studios*, describing the scope of the patent laws, the Supreme Court noted that "[t]here is no suggestion in the statute [section 271(c)] that one patentee may object to the sale of a product that might be used in connection with other patents" and stated that "the Court has always recognized the critical importance of not allowing the patentee to extend his monopoly beyond the limits of his specific grant." 464 U.S. 417, 440–41 (1984). To consider patents other than those asserted against a defendant, as urged by plaintiffs, would impermissibly expand the exclusive grant Congress provided.

Plaintiffs also argue that the district court legally erred in its factual finding that "Plaintiffs have not shown that Defendants possess the intent required to prove contributory infringement" because intent is not an element of contributory infringement. J.A. 151. While section 271(c) does not use the word "intent," the statute still imposes a scienter requirement—that the accused infringer sells articles "knowing the same to be especially made or especially adapted for use in an infringement of such patent." The Supreme Court has characterized this as "§ 271(c)'s intent requirement." *Global-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754, 765 (2011); *see also Grokster*, 545 U.S. at 932 ("The [contributory infringement] doctrine was devised to identify instances in which it may be presumed from distribution of an article in commerce that the distributor intended the article to be used to infringe another's patent . . . ."). The district court using similar language was not error. In any event, the district court did not cite a lack of intent in its legal analysis of contributory infringement. Rather, the district court relied on the existence of substantial noninfringing uses to find no contributory infringement. We see no error in this analysis.

The district court did not err finding that plaintiffs failed to establish contributory infringement under 35 U.S.C. § 271(c).

II

Lupin on its cross appeal argues that the district court erred in construing "reacting" in the '626 patent to mean "the changing of a reactant(s) to product(s)" and in finding infringement under that construction. We see no error.

"Claim construction is a matter of law and is reviewed de novo." *Allen Eng'g Corp.*, 299 F.3d at 1344. "[T]he words of a claim are generally given their ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art" determined "in the context of the entire patent." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc) (citations and internal quotation marks omitted).

Claim 12 depends from claim 1, which recites "a process for the preparation of [compound I] . . . the process comprising reacting compound II . . ., with a compound of formula III . . ., and a compound [IV] . . ." (emphasis added). The parties disagree on the construction of "reacting" in claim 1. Plaintiffs argued for the purported plain and ordinary meaning, "the changing of a reactant(s) to product(s)." J.A. 222. Lupin contended that "reacting" means "the specified chemicals are added to the reaction vessel at the beginning of the process as starting material." *Id.* The district court adopted plaintiffs' construction. Lupin, on cross appeal, contends the district court erred in that construction and in finding infringement because Lupin's process does not use compound II as a starting material. While it is true that the specification only refers to using compound II as a starting material, nothing in the claims, specification, or file history requires Lupin's narrower reading.

The '626 patent's specification does not define the word "reacting." The 2004 Fifth Edition of the Oxford Dictionary of Chemistry defines "chemical reaction" as "[a] change in which one or more chemical elements or compounds (the *reactants*) form new compounds (the *products*)." J.A. 124. Plaintiffs' expert agreed with this definition, as did defendants' invalidity expert. The district court noted that the "claims of the '626 Patent do not expressly recite 'added,' 'reaction vessel,' 'beginning of the process,' or 'starting material,' and they do not otherwise limit Claim 12 to a process in which 'the specified chemicals are added to the reaction vessel at the beginning of the process as starting material.'" J.A. 223.

Lupin primarily argues on appeal that the district court erred by discounting evidence from the prosecution history. In the referenced office action, the examiner used the phrase "starting compound" to refer to the materials that are reacted together. The examiner here appears to have used "starting compound" to distinguish between claimed reactants and the claimed products. *See* J.A. 18671 ("The level of skill and knowledge in the art would not allow the Examiner to predict the use of a [particular] starting compound in the production of the product of the instant claims."). But the examiner said nothing about the scope of "reacting," and the examiner's use of the word "starting compound" in isolation does not suggest that he defined reacting as referring only to starting materials. In any event, there are no statements by the patentee during prosecution that limited the scope of "reacting," and "the examiner's unilateral remarks alone do not affect the scope of the claim." *Salazar v. Procter & Gamble Co.*, 414 F.3d 1342, 1347 (Fed. Cir. 2005).

Lupin also argues that the claims must be read to restrict the construction of "reacting" because claim 2, which depends from claim 1, involves a two-reaction sequence that first reacts compounds II and III and then reacts the product of that reaction with compound IV in a subsequent

reaction. Lupin failed to explain how claim 2 is inconsistent with the district court's construction, which requires only the changing of reactants to products. Moreover, Lupin's construction is in tension with dependent claim 3, which recites "[t]he process according to claim 1, wherein compound II, compound III and compound IV are mixed together at the start of the process." Lupin's construction requires that the compounds be added "at the beginning of the process as starting material," rendering claim 3 superfluous.

The district court did not err in its construction of "reacting" or in its determination of infringement.

CONCLUSION

We conclude that the district court did not err in finding no infringement of the '096 or '910 patents. Lupin's cross appeal challenging the district court's determination that Lupin infringed the '626 patent is similarly without merit. We do not reach the conditional cross appeal as to invalidity.

AFFIRMED

COSTS

Costs in the 22-1194 appeal to defendants Lupin Ltd., Lupin Pharmaceuticals, Inc., Macleods Pharma USA, Inc., Macleods Pharmaceuticals Ltd., Sandoz Inc., Sigmapharm Laboratories, LLC, Zydus Pharmaceuticals (USA) Inc., Alembic Global Holding S.A., Alembic Pharmaceuticals Inc., Alembic Pharmaceuticals Ltd., Cadila Healthcare Ltd., and Lek Pharmaceuticals, d.d.

No costs in the 22-1246 cross appeal. Costs in the 22-1208 cross appeal to plaintiffs H. Lundbeck A/S, Takeda Pharmaceutical Company Ltd., Takeda Pharmaceuticals U.S.A., Inc., Takeda Pharmaceuticals International AG, and Takeda Pharmaceuticals America, Inc., and against defendants Lupin Ltd. and Lupin Pharmaceuticals, Inc.