United States Court of Appeals for the Federal Circuit

02-1073

WARNER-LAMBERT COMPANY,

Plaintiff-Appellant,

v.

APOTEX CORP., APOTEX, INC., and TORPHARM, INC.,

Defendants-Appellees.

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Robert W. Spearman, Parker, Poe, Adams & Bernstein L.L.P., of Raleigh, North Carolina, for amicus curiae Generic Pharmaceutical Association. With him on the brief was Melanie Black Dubis.

Appealed from: United States District Court for the Northern District of Illinois

Senior Judge Paul E. Plunkett

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WARNER-LAMBERT COMPANY,

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DECIDED: January 16, 2003

Before MICHEL, Circuit Judge, PLAGER, Senior Circuit Judge, and LOURIE, Circuit Judge.

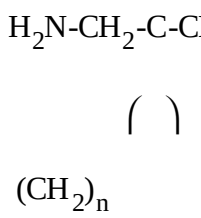
LOURIE, Circuit Judge.

Warner-Lambert Company appeals from the final order of the United States District Court for the Northern District of Illinois, granting summary judgment of noninfringement for Apotex Corp., Apotex Inc., and TorPharm, Inc. (collectively "Apotex"). Warner-Lambert Co. v. Apotex Corp., No. 98 C 4293, 2001 U.S. Dist. LEXIS 14592, 2001 WL 1104618 (N.D. Ill. Sept. 14, 2001). Because we hold that Apotex was entitled to judgment as a matter of law, we affirm.

BACKGROUND

Warner-Lambert is the assignee of U.S. Patent 5,084,479, entitled "Novel Methods for Treating Neurodegenerative Diseases." The '479 patent (the "neurodegenerative method patent") discloses and claims the use of certain cyclic amino acid compounds, as well as salts and esters derived from them, for the treatment of neurodegenerative diseases such as stroke, Alzheimer's disease, Huntington's disease,

amyotrophic lateral sclerosis ("ALS"), and Parkinson's disease. Claim 1, the only independent claim in the '479 patent, defines the invention as follows:

> 1. A method for treating neurodegenerative diseases which comprises administering a therapeutically effective amount of a compound of formula
>
> 
>
> wherein R_1 is hydrogen or a lower alkyl and n is 4, 5, or 6 or a pharmaceutically acceptable salt thereof, in unit dosage form, to a mammal in need of said treatment.

'479 patent, col. 10, ll. 8-19. One of these cyclic amino acid compounds, 1-aminomethyl-1-cyclohexane acetic acid, corresponding to the formula in claim 1 in which R_1 is hydrogen and n is 5, is commonly known as "gabapentin." Gabapentin is the subject of the present action.

Warner-Lambert is also the assignee of expired U.S. Patent 4,024,175, expired U.S. Patent 4,087,544, and U.S. Patent 4,894,476. The '175 patent (the "product patent"), entitled "Cyclic Amino Acids," disclosed and claimed the actual compounds that are used in the methods claimed in the neurodegenerative method patent; claim 2 specifically claimed 1-aminomethyl-1-cyclohexane acetic acid (i.e., gabapentin). The '544 patent (the "epilepsy method patent"), entitled "Treatment of Cranial Dysfunctions using Novel Cyclic Amino Acids," disclosed and claimed a method of treating certain forms of epilepsy, faintness attacks, hypokinesia, and cranial traumas using the cyclic amino acid compounds claimed in the product patent and used in the methods of the neurodegenerative method patent, again including gabapentin. The '476 patent (the "monohydrate patent"), entitled "Gabapentin Monohydrate and a Process for Producing the Same," claims a specific crystalline form of gabapentin monohydrate. Gabapentin monohydrate is a complex made up of gabapentin and water.

Warner-Lambert sells gabapentin under the trade name Neurontin®. In 1993, Warner-Lambert

obtained approval of a New Drug Application ("NDA") from the United States Food and Drug Administration ("FDA") to market gabapentin for use in "adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults with epilepsy," one of the several indications claimed in the now-expired epilepsy method patent. Significantly, the FDA has not approved gabapentin for any additional uses, let alone for the uses claimed in the '479 neurodegenerative method patent.

Apotex filed an Abbreviated New Drug Application ("ANDA") under the Drug Price Competition and Patent Term Restoration Act of 1984, 98 Stat. 1585 (popularly known as the Hatch-Waxman Act, hereinafter "the Act"), at the FDA on April 17, 1998, seeking approval to market a generic formulation of gabapentin upon the expiration of Warner-Lambert's epilepsy method patent on January 16, 2000. As mandated by 21 U.S.C. § 355(j)(2)(A)(i), Apotex sought approval to market gabapentin only for the same indication for which Warner-Lambert's Neurontin® was approved, i.e., for "adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults with epilepsy." Along with the bioavailability/bioequivalence test data required to be included in its ANDA, Apotex filed a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (a "paragraph IV certification"), declaring that its proposed manufacture, use, and sale of gabapentin would not infringe either the monohydrate patent or the neurodegenerative method patent. According to Apotex, its formulation would be anhydrous (i.e., would not contain water), and would accordingly be outside the scope of the monohydrate patent. Moreover, Apotex declared that its "pharmaceutical product's labeling does not include any indication for use in the treatment of either neurodegenerative or neurogenerative diseases." Because all of the claims of the neurodegenerative method patent "are directed to a use of gabapentin in the treatment of neurodegenerative diseases," Apotex argued, the manufacture, use, or sale of its gabapentin products would not infringe the neurodegenerative method patent.

Under 21 U.S.C. § 355(j)(2)(B)(i), an ANDA applicant who files a paragraph IV certification is required to include in its application a statement that it will give notice of that filing to the owner of the patent to which the certification pertains, § 355(j)(2)(B)(i)(I), and to the holder of the approved NDA for

that drug, § 355(j)(2)(B)(i)(II). Pursuant to those provisions, Apotex notified Warner-Lambert that it had filed the ANDA and paragraph IV certification. Also, as required by 21 U.S.C. § 355(j)(2)(B)(ii), Apotex provided in its notice letter a detailed statement of the factual and legal basis for its opinion of noninfringement of the neurodegenerative method patent. It explained that its "indicated use for its pharmaceutical product is partial seizure. The '479 neurodegenerative method patent does not claim a method of using gabapentin and its derivatives for partial seizure." Because the claims of the neurodegenerative method patent were limited to "a method of using gabapentin and its derivatives in the treatment of neurodegenerative diseases," and "partial seizure is not a neurodegenerative disease," Apotex argued that its gabapentin would "not fall within the scope of any of the claims of . . . the '479 patent."

Warner-Lambert commenced the present patent infringement action on July 14, 1998, alleging that Apotex's submission of its ANDA was an act of infringement of the neurodegenerative method patent under 35 U.S.C. § 271(e)(2)(A).[1] Although the FDA had not approved the use of gabapentin for any of the indications claimed in the neurodegenerative method patent, and 21 C.F.R. § 202.1(e)(4) forbids the promotion of unapproved uses by NDA or ANDA holders, Warner-Lambert argued that "patients will use the Apotex Defendants' gabapentin for all purposes for which Warner-Lambert's Neurontin® product has been and customarily is used, and doctors will prescribe the Apotex Defendants' gabapentin product for such uses, including the treatment of neurodegenerative diseases."

Apotex moved for summary judgment. Warner-Lambert opposed Apotex's motion, arguing that: (1) the FDA does not regulate the uses for which doctors prescribe drugs once they are approved, (2) "more than three-quarters of the prescriptions written by doctors for Warner-Lambert's Neurontin® are for indications other than epilepsy, including the treatment of neurodegenerative diseases," and (3) "doctors, managed care organizations, and other institutions commonly and routinely substitute generic drugs for all indications for which the brand name drug is used." Warner-Lambert's "Memorandum in Opposition to Apotex's Motion for Summary Judgment" at 20 (Dec. 10, 1998). Warner-Lambert further argued that "Apotex knows and expects that its generic gabapentin will be prescribed by doctors for all the same reasons they prescribe Neurontin," including "the treatment of . . .

neurodegenerative diseases." Id. at 21. The district court denied Apotex's motion. Warner-Lambert Co. v. Apotex Corp., No. 98 C 4293, 1999 U.S. Dist. LEXIS 6208, 1999 WL 259946 (N.D. Ill. Apr. 8, 1999). At the close of discovery, however, Apotex again moved for summary judgment, and the district court granted that second motion. Warner-Lambert Co. v. Apotex Corp., No. 98 C 4293, 2001 U.S. Dist. LEXIS 14592, 2001 WL 1104618 (N.D. Ill. Sept. 14, 2001).[2]

Warner-Lambert now appeals. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

"We review a district court's grant of summary judgment de novo, reapplying the standard used by the district court." Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp., 149 F.3d 1309, 1315, 47 USPQ2d 1272, 1275 (Fed. Cir. 1998). Summary judgment is appropriate "if the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." Fed. R. Civ. P. 56(c). "The evidence of the nonmovant is to be believed, and all justifiable inferences are to be drawn in his favor." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 255 (1986).

A. Infringement under 35 U.S.C. § 271(e)(2)

The principal statute at issue in the present case provides as follows:

> It shall be an act of infringement to submit – (A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act [codified at 21 U.S.C. § 355(j); i.e., 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 under such Act [i.e., Title 21 of the United States Code] 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.

35 U.S.C. § 271(e)(2) (2000).

The district court's opinion took for granted that our decision in Bayer AG v. Elan Pharmaceutical Research Corp., 212 F.3d 1241, 1248-49, 54 USPQ2d 1710, 1715-16 (Fed. Cir. 2000), foreclosed

Warner-Lambert's claim of infringement under 35 U.S.C § 271(e)(2)(A). Warner-Lambert, 2001 U.S. Dist. LEXIS 14592, at *6 n.3. The court then discussed whether or not Apotex would, alternatively, induce infringement of the neurodegenerative method patent under 35 U.S.C. § 271(b). Although we agree with the district court that Warner-Lambert has no cause of action under 35 U.S.C. § 271(e)(2)(A), we will also address the question whether Warner-Lambert has presented a genuine issue of material fact with respect to the elements of an inducement claim under § 271(b).

The central issue in the present case is whether it is an act of infringement under 35 U.S.C. § 271(e)(2)(A) to submit an ANDA seeking approval to make, use, or sell a drug for an approved use if any other use of the drug is claimed in a patent, or if it is only an act of infringement to submit an ANDA seeking approval to make, use, or sell a drug if the drug or the use for which FDA approval is sought is claimed in a patent. That issue presents a matter of first impression for this court. Although we have previously construed portions of 35 U.S.C. § 271(e)(2) in Glaxo, Inc. v. Novopharm, Ltd., 110 F.3d 1562, 42 USPQ2d 1257 (Fed. Cir. 1997), and in Bayer, we have not yet had occasion to parse the specific statutory language at issue here. For the reasons stated below, we conclude that it is not an act of infringement to submit an ANDA for approval to market a drug for a use when neither the drug nor that use is covered by an existing patent, and the patent at issue is for a use not approved under the NDA.

Because statutory interpretation is a legal issue, we review the district court's interpretation without deference. Waymark Corp. v. Porta Sys. Corp., 245 F.3d 1364, 1366, 58 USPQ2d 1456, 1458 (Fed. Cir. 2001). "The starting point of every case involving construction of a statute is the language itself." Blue Chip Stamps v. Manor Drug Stores, 421 U.S. 723, 756 (1975). Moreover, we "give effect, if possible, to every clause and word of [the] statute." United States v. Menasche, 348 U.S. 528, 538-39 (1955) (citation omitted). When a statute does not define a given word or phrase, we presume that Congress intended the word or phrase to have its ordinary meaning. Asgrow Seed Co. v. Winterboer, 513 U.S. 179, 187 (1995). However, "[i]n expounding a statute, we must not be guided by a single sentence or member of a sentence, but look to the provisions of the whole law, and to its object and policy." U.S. Nat'l Bank of Or. v. Indep. Ins. Agents of Am., Inc., 508 U.S. 439, 455 (1993) (internal quotation marks omitted). "When interpreting a statute, the court will not look merely to a particular clause in which general words may be used, but will take in connection with it the whole statute (or statutes on the same subject) and the objects and policy of the law, as indicated by its various provisions, and give it such a construction as will carry into execution the will of the Legislature." Kokoszka v. Belford, 417 U.S. 642, 650 (1974) (internal quotation marks omitted).

Warner-Lambert argues that the district court erred in interpreting § 271(e)(2). It asserts that, under that provision, a patent claiming a use of a drug is infringed by the filing of an ANDA irrespective of whether approval is sought to market the drug for the patented use. We disagree. Warner-Lambert quotes the "pertinent part" of 35 U.S.C. § 271(e)(2)(A) as follows:

> It shall be an act of infringement to submit . . . an application under [the ANDA provisions of the Hatch-Waxman] Act for a drug . . . the use of which is claimed in a patent before the expiration of such patent.

Warner-Lambert's abridged quotation suggests that the mere filing of an ANDA for a drug having a use claimed in a patent is an infringing act per se. Based on that reading, Warner-Lambert argues that Apotex's ANDA infringes the neurodegenerative method patent:

> Apotex submitted an ANDA seeking FDA approval "for a drug" (gabapentin) "the use of which is claimed in" the '479 patent in suit. Section 271(e)(2)(A) explicitly defines the filing of an ANDA in the face of such a patent as an act of infringement.

Warner-Lambert's interpretation is incorrect. It has eviscerated an important part of the statutory provision by conflating the first and second clauses of § 271(e)(2)(A) in its quotation; the phrase "before the expiration of such patent" cannot be read apart from the phrase "if the purpose of such submission is to obtain approval under such Act." Whether or not other portions of the statute may be unclear, cf. Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661, 679 (1990) ("No interpretation we have been able to imagine can transform § 271(e)(1) into an elegant piece of statutory draftsmanship."), it is abundantly clear that the statute does not make the filing of an ANDA prior to patent expiration an act of infringement unless the ANDA seeks approval to manufacture, use, or sell the drug prior to expiration of a patent that would otherwise be infringed by such manufacture, use, or sale, apart from the provisions of § 271(e)(2). Accordingly, to prevail in this case, where the relevant patents covering the drug and the indication for which approval is sought have both expired, the plaintiff must prove that the defendant's manufacture, use, or sale of the drug would nonetheless infringe the neurodegenerative method patent under a traditional infringement analysis. At the very least, to succeed in this appeal of the district court's grant of summary judgment, Warner-Lambert would have needed to demonstrate the existence

of a genuine issue of material fact to support a traditional infringement claim, i.e., that Apotex induced or will induce infringement of the neurodegenerative method patent.

As Apotex notes, 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. The statute recites "a drug . . . the use of which is claimed" (emphasis added), not "a drug . . . a use of which is claimed," or "a drug . . . any use of which is claimed," or "a drug having a use which is claimed." The FDA does not grant across-the-board approval to market a drug. Rather, it grants approval to make, use, and sell a drug for a specific purpose for which that drug has been demonstrated to be safe and efficacious. Read in the context of the Act, of which the provision now codified at 35 U.S.C. § 271(e) was just a part, it is clear that the phrase "the use" in § 271(e)(2)(A) refers to the use for which the FDA has granted an NDA. That is, as we indicated above, the only use for which an ANDA applicant can seek approval. While a physician may prescribe an approved drug for any use consistent with acceptable medical practice, an NDA, and hence an ANDA, only approves a use for which safety and efficacy have been proven.

It is also significant that Congress used the word "a" before "drug" and the word "the" before "use." The words "the use" require antecedent basis; thus, "the use" refers to a specific "use" rather than a previously undefined "use." See, e.g., Freytag v. Comm'r, 501 U.S. 868, 902 (Scalia, J., concurring) (analyzing the definite article "the" as narrowing a class to specific "envisioned" members of the class); Work v. United States, 262 U.S. 200, 208 (1923); Am. Bus Ass'n v. Slater, 231 F.3d 1, 4-5 (D.C. Cir. 2000) ("[I]t is a rule of law well established that the definite article 'the' particularizes the subject which it precedes. It is a word of limitation as opposed to the indefinite or generalizing force of 'a' or 'an.'" (citations omitted)). Thus, the statutory language "the use" is most reasonably interpreted to mean "the use listed in the ANDA." Congress could have been expected to use quite different language if it wanted to reach the opposite result.

The history of the Hatch-Waxman Act is well known, see, e.g., Eli Lilly, 496 U.S. at 665-78, and we will not attempt to provide an exhaustive treatment of it here. Nonetheless, a brief review of that

history will shed some light on the proper interpretation of §271(e)(2)(A). Under federal law at the time the Act was negotiated and signed into law, a patent "granted to the patentee, his heirs, or assigns, for the term of seventeen years . . . the right to exclude others from making, using, or selling the invention throughout the United States." 35 U.S.C. § 154. "Except as otherwise provided . . . , whoever without authority makes, uses, or sells any patented invention, within the United States during the term of the patent therefor, infringes the patent." Id. § 271(a).[3]

As the Supreme Court wrote in Eli Lilly, the Act was designed to respond to two problems that the patent and pharmaceutical regulatory statutes were perceived to have led to by the 1980s. 496 U.S. at 669. One of those problems arose from the fact that an inventor ordinarily applies for patent protection for newly discovered drugs, or for methods for the use of new or existing drugs, well before securing regulatory approval, even though it generally cannot legally market such products or promote their use until it obtains that approval. Since the FDA generally took much longer to approve an NDA than the United States Patent and Trademark Office took to grant a patent, a manufacturer's patent term was substantially eroded by the time the patentee was able to derive any profit from the invention. Id. [4]

The second problem inhered in the need for a generic manufacturer to obtain its own NDA if it wanted to market a product.[5] A new NDA required the generic company to provide its own safety and efficacy data, which it was argued was a waste of resources. This need was complicated by the assumption, confirmed by this court's holding in Roche Products, Inc. v. Bolar Pharmaceutical Co., 733 F.2d 858, 221 USPQ 937 (Fed. Cir. 1984), that the plain language of § 271(a) made the manufacture and testing (a use) of a patented product prior to the expiration of the patent an act of infringement, even if that manufacture or use was solely for the purpose of conducting tests and developing the necessary information to apply for regulatory approval later on. Eli Lilly, 496 U.S. at 670. Because it took a substantial amount of time for a second or subsequent manufacturer to obtain data and secure regulatory approval, requiring those manufacturers to wait until after the expiration of the patent to begin testing and other pre-approval activities resulted in a de facto extension of the patent term. The Hatch-Waxman Act intended to deal with both of these issues, i.e., to restore to innovators patent time lost during testing

and regulatory approval, but to enable generic manufacturers to be ready to enter the market once patents expired. The latter no longer would have to prove the safety and efficacy of a drug that was already the object of an NDA; they would just have to prove bioequivalence.

Section 201 of the Act, codified at 35 U.S.C. § 156, accordingly provided for patent term extension for products "subject to a regulatory review period before its commercial marketing or use," if "the permission for the commercial marketing or use of the product after such regulatory review period [was] the first permitted commercial marketing or use of the product." Id. at 676 (quoting 35 U.S.C. § 156(a)).

Section 202 of the Hatch-Waxman Act added to 35 U.S.C. § 271 a new subsection, (e)(1), on the other hand, that provided that "it shall not be an act of infringement to make, use, or sell a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs." Id. Section 271(e)(1) thus partially eliminated the second problem, i.e., the de facto unintended extension of the patent term, and enabled generic manufacturers to test and seek approval to market during the patent term. To further the overall goals of the Act, § 101 also amended § 505 of the Federal Food, Drug, and Cosmetic Act ("FDCA"), codified at 21 U.S.C. § 355, to authorize the filing and approval of ANDAs. Id. Included in the ANDA provisions was a mechanism to facilitate the adjudication of claims of infringement of patents relating to the innovator's drugs. That mechanism included, inter alia, provision for patentees and NDA holders to list patents that claim the approved drug or the approved use of the drug, 21 U.S.C. §355(b)(1); and provision for ANDA applicants to "certify": (I) that no such patent information is listed, or, if such information is listed, then, for each listed patent, (II) that it has expired, (III) that it will expire prior to the ANDA applicant's marketing of the drug, or (IV) that it is invalid or will not be infringed by the manufacture, use, or sale of the drug by the ANDA applicant, 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV). Eli Lilly, 496 U.S. at 676-77. The ANDA provisions now codified at 35 U.S.C. § 271(e)(2)(A) also created an artificial act of infringement that consists of submitting an ANDA containing a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) that a listed patent is invalid or that the manufacture, sale, or use of the proposed product would not infringe that patent. Eli Lilly, 496 U.S. at 678.

The Hatch-Waxman Act was accordingly a compromise between two competing sets of interests: those of innovative drug manufacturers, who had seen their effective patent terms shortened by the testing and regulatory processes; and those of generic drug manufacturers, whose entry into the market upon expiration of the innovator's

patents had been delayed by similar regulatory requirements. The legislative history of the Act stated its ultimate purposes:

> The purpose of Title I of the Bill is to make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962. . . .
>
> The purpose of Title II of the Bill is to create a new incentive for increased expenditures for research and development of certain products which are subject to premarket government approval. The incentive is the restoration of some of the time lost on patent life while the product is awaiting pre-market approval.

H.R. Rep. No. 98-857(I), at 14-15 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2647-48. In light of this history, as well as the legislative language itself, we cannot agree with Warner-Lambert that Congress intended it to be 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 and the applicant sought approval of its ANDA prior to the expiration of that patent.

Warner-Lambert's proposed interpretation is inconsistent with both of the stated purposes of the Hatch-Waxman Act, and would confer substantial additional rights on pioneer drug patent owners that Congress quite clearly did not intend to confer. If Warner-Lambert's interpretation were correct, for example, an NDA holder would be able to maintain its exclusivity merely by regularly filing a new patent application claiming a narrow method of use not covered by its NDA. It would then be able to use § 271(e)(2)(A) as a sword against any competitor's ANDA seeking approval to market an off-patent drug for an approved use not covered by the patent. Generic manufacturers would effectively be barred altogether from entering the market. That would certainly not advance the purpose of making available "more low cost generic drugs," and was not what Congress intended. Moreover, although Warner-Lambert argues that our affirming the district court's decision would be a disincentive for research and development by innovators, Congress explicitly stated that the incentive created by the Act was patent term restoration. There is no evidence that Congress intended to enable an innovator to extend its exclusivity merely by asserting patents on unapproved uses. Moreover, if an innovator has not made the investment to test and obtain approval of the new use, what investment is to be protected by creating an added incentive?

Other relevant portions of the legislative history support our interpretation. For example, House Report No. 98-857(I) states, in part:

> . . . [A]n ANDA must include a certification by the applicant regarding the status of certain patents applicable to the listed drug if the patent information has been submitted under section 505(b) or (c). With respect to all product patents which claim the listed drug and all use patents which claim an indication for the drug for which the applicant is seeking approval (hereafter described as a controlling use patent), the applicant must certify, in his opinion and to the best of his knowledge, as to one of four circumstances.
>
> . . .
>
> If appropriate, the applicant may certify that one or more of the product or controlling use patents provided have expired. . . . [A]n applicant may certify if applicable that one or more of the product or controlling use patents are invalid or will not be infringed.
>
> The committee recognizes that in some instances an applicant will have to make multiple certifications with respect to product or controlling use patents. For example, if the product patent has expired and a valid controlling use patent will not expire for three years, then the applicant must certify that one patent has expired and the other will expire in three years. The committee intends that the applicant make the appropriate certification for each product and controlling use patent.
>
> . . . [I]f there are indications which are claimed by any use patent and for which the applicant is not seeking approval, then an ANDA must state that the applicant is not seeking approval for those indications which are claimed by such use patent. For example, the listed drug may be approved for two indications. If the applicant is seeking approval only for Indication No. 1, and not Indication No. 2 because it is protected by a use patent, then the applicant must make the appropriate certification and a statement explaining that it is not seeking approval for Indication No. 2.

H.R. Rep. No. 98-857(I), at 22, 1984 U.S.C.C.A.N. at 2655 (emphasis added).

The quoted portion of the House Report demonstrates that Congress recognized that a single drug could have more than one indication and yet that the ANDA applicant could seek approval for less than all of those indications. Congress clearly contemplated that the FDA could grant approval of an NDA, and hence eventually an ANDA, seeking to market a drug for a single indication even when other indications were known or even approved. Moreover, and perhaps more importantly, Congress made it clear that the ANDA applicant need not certify with respect to every "use" patent that claims an indication for the drug. Rather, the applicant needs only to certify with respect to use patents that claim an indication for which the applicant is seeking approval to market the drug. Id.; see also H.R. Rep. No. 98-857(II), at 13 (1984), reprinted in 1984 U.S.C.C.A.N. 2686, 2697 ("With respect to . . . all use patents which claim an indication for the drug for which the applicant is seeking approval, i.e., a controlling use patent, the applicant must certify . . . ."). And an ANDA applicant can only seek approval for a use approved in the underlying NDA.

The last example in the above-quoted portion of H.R. Rep. 98-857(I) describes a scenario very similar to the one at issue in the present case. Here, Apotex is seeking approval only for the indication of treating epilepsy, which corresponds to "Indication No. 1." It is not seeking approval for "Indication No. 2," i.e., treatment of neurodegenerative diseases. Although Congress did not explicitly provide an

example in which only Indication No. 1 is FDA-approved while only Indication No. 2 is still patented, the same conclusion applies a fortiori to that situation as to the provided example in which both indications are approved. The applicant here is not only stating that it is not seeking approval for Indication No. 2, it is positively forbidden from obtaining such approval, unless it files its own NDA with full safety and efficacy data. Thus, according to H.R. Rep. 98-857(I), Apotex only needed to provide a statement explaining that it was not seeking approval for Indication No. 2. That it did. Although formally labeled as a "paragraph IV certification," we note that Apotex's statement with respect to the neurodegenerative method patent was effectively a statement of non-applicable use pursuant to 21 U.S.C. § 355(j)(2)(A)(viii).

Warner-Lambert argues that Apotex was required to certify under one of the subparagraphs of 21 U.S.C. § 355(j)(2)(A)(vii) with respect to the neurodegenerative method patent, because that patent was listed in the FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" publication (the "Orange Book"). That is incorrect. That provision and 21 U.S.C. § 355(j)(2)(A)(viii), which follows it, provide in pertinent part that:

> [An abbreviated application for a new drug shall contain --]
>
> (vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) . . . and
>
> -
>
> (viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) for a method of use patent which does not claim a use for which the applicant is seeking

approval under this subsection, a statement that the method of use patent does not claim such a use.

21 U.S.C. § 355(j)(2)(A)(vii)-(viii) (emphasis added). Thus, a certification need not be provided for a patent claiming a use for which the ANDA applicant is not seeking approval, i.e., a use not covered by the NDA.

Warner-Lambert has not produced any authority that information regarding the neurodegenerative method patent was "required to be filed under subsection (b) or (c)"; indeed, the evidence of record suggests that it need not have been. The listing provision, 21 U.S.C. § 355(b), simply allows the innovator to give warning of all of its relevant patents, by requiring that it file with its application "the patent number and expiration date of any patent which claims the drug . . . or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted." 21 U.S.C. § 355(b)(1) (emphasis added).[6] Of course, the mere listing of even a properly listed patent would not in itself entitle the patent owner to a judgment that that patent would be infringed by sale of the drug for an approved use. It simply provides the basis for a lawsuit that may be won or lost based on the general infringement provisions of the patent laws.

As noted above, the House Reports indicate that Congress intended to draw a distinction in the Act between those indications for which an ANDA applicant is seeking approval and those for which it is not when determining if certification is necessary. The applicant needs to certify only with respect to (a) product patents that claim the listed drug for which approval is sought, and (b) "controlling use patents," defined as patents that claim "an indication for the drug for which the applicant is seeking approval." Even when a listed drug is approved for more than one indication, Congress contemplated the possibility that there could be indications that are claimed by a use patent but for which the applicant is not seeking approval. There is no suggestion whatsoever in the statute or the legislative history that Congress intended that approval of a drug for a particular indication should be denied or even delayed by the existence of a patent that claims some other, unapproved indication of the drug. Although the issue is irrelevant to this case, we note that Apotex was likely required to, and did, certify under paragraph IV with respect to the monohydrate patent. We see no reason why the fact that Apotex also certified under paragraph IV with respect to the neurodegenerative method patent, perhaps in an overabundance of caution, should subject them to the Draconian penalty that Warner-Lambert seeks under 35 U.S.C. § 271 (e)(4)(A) of having approval of their ANDA delayed until the expiration of the neurodegenerative method patent in the year 2010.

Warner-Lambert attempts in its reply brief to find significance in the fact that subsections (vii) and (viii) of 21 U.S.C. § 355(j)(2)(A) are connected with "the conjunctive 'and' rather than the disjunctive 'or,'" arguing that an ANDA applicant is required to file both a certification under subsection (vii) and a statement of inapplicable use under subsection (viii). That fact is irrelevant to our conclusion. As our analysis of the legislative history, supra, indicates, Congress contemplated the possibility that there could be more than one approved indication for a given drug, and that an ANDA applicant can seek approval to label and market the drug for fewer than all of those indications. In that situation, it would be necessary to certify under subsection (vii) with respect to a patent claiming an indication for which approval is sought, and to file a statement of inapplicable use under subsection (viii) with respect to the other indications. In a situation such as the one at issue in the present case, however, where the applicant is not seeking approval to market a drug for a use claimed in a patent, there is no need to file any certification at all under subsection (vii).

Warner-Lambert further argues that "[a] comparison of the language in subparts (vii) and (viii)

confirms that the antecedent for the phrase 'for which the applicant is seeking approval' in subpart (vii) is 'drug' rather than 'use'. In contrast . . . subpart (viii) . . . does use the phrase 'a use for which the applicant is seeking approval,' and the phrase 'for which the applicant is seeking approval' obviously modifies 'use'." That argument is unconvincing. As we noted above, one does not obtain across-the-board approval to market a drug. Instead, one obtains approval to market a drug for a specific use for which the drug has been demonstrated to be safe and effective. Thus, the antecedent for the phrase "for which the applicant is seeking approval" in subpart (vii) is neither "drug" nor "use," but "use for such listed drug."

In summary, Warner-Lambert does not have a cause of action under § 271(e)(2)(A). Congress clearly intended to limit actions for infringement of method-of-use patents under § 271(e)(2)(A) to "controlling use patents," or patents that claim an approved use of a drug. An ANDA applicant, who necessarily "piggybacks" on the approved NDA of the innovator, can only apply to sell the approved drug, which, in this case, is no longer under patent, and to market it for the use for which the FDA has indicated that the drug is safe and efficacious, for which use the patent here has also expired. Apotex has neither submitted an application to sell a drug claimed in an extant patent, nor submitted an application to sell a drug the use of which is claimed in an extant patent. Both gabapentin and its only FDA-approved use are now off-patent.

Because Apotex is not submitting an application to sell a drug for treatment of neurodegenerative diseases, which is the only use covered by the patent involved in this case, we conclude that Apotex is entitled to summary judgment of noninfringement.

B. Infringement under 35 U.S.C. § 271(b)

Having concluded that 35 U.S.C. § 271(e)(2)(A) is inapplicable to the present case and that Warner-Lambert accordingly does not have a cause of action against Apotex under that statute, we might close this opinion here. However, since the issue has been decided by the district court and argued here, and since it may arise if Apotex's ANDA is approved, we will address the question whether Warner-Lambert has demonstrated the existence of a genuine issue of material fact with respect to inducement under 35 U.S.C. § 271(b).

As an initial matter, we note that there is no evidence in the record that Apotex has directly practiced or will ever practice any of the methods claimed in the neurodegenerative method patent, all of which are directed to a method for treating neurodegenerative diseases by administering gabapentin or another cyclic amino acid compound to a mammal.[7] Accordingly, Warner-Lambert has not established that there is any genuine issue of material fact with regard to direct infringement by Apotex, and Warner-Lambert therefore has no cause of action for direct infringement under 35 U.S.C. § 271(a).

Warner-Lambert has asserted inducement of infringement under 35 U.S.C. § 271(b). Under § 271(b), "whoever actively induces infringement of a patent shall be liable as an infringer." To succeed on this theory, a plaintiff must prove that the defendants' "actions induced infringing acts and that [they] knew or should have known [their] actions would induce actual infringement." Manville Sales Corp. v. Paramount Sys., Inc., 917 F.2d 544, 553, 16 USPQ2d 1587, 1594 (Fed. Cir. 1990). However, that defendants have "knowledge of the acts alleged to constitute infringement" is not enough. Id. "[P]roof of actual intent to cause the acts which constitute the infringement is a necessary prerequisite to finding active inducement." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1529 (Fed. Cir. 1990). "Inducement requires proof that the accused infringer knowingly aided and abetted another's direct infringement of the patent." Rodime PLC v. Seagate Tech., Inc., 174 F.3d 1294, 1306, 50 USPQ2d 1429, 1437 (Fed. Cir. 1999). "While proof of intent is necessary, direct evidence is not required; rather, circumstantial evidence may suffice." Water Techs. Corp. v. Calco, Ltd., 850 F.2d 660, 668, 7 USPQ2d 1097, 1103 (Fed. Cir. 1988).

Warner-Lambert argues that the district court erred in requiring that, to be liable for inducement, Apotex had to have "known" that physicians were prescribing gabapentin for treatment of neurodegeneration. Warner-Lambert contends that the district court ignored the "should have known" standard. According to Warner-Lambert, by 1998, only about 22% of gabapentin sales were for treatment of epilepsy, the remaining 78% being prescribed for off-label uses, including the infringing use of treating neurodegenerative diseases. By October 1999, the percentage of uses other than for epilepsy treatment had risen to "more than 89%." In addition, Warner-Lambert argues that: (1) it is common knowledge to many in and out of the pharmaceutical field that physicians routinely prescribe approved drugs for purposes other than those listed on the drugs' labels; indeed, such off-label use is supported by both the FDA and the American Medical Association, (2) information regarding both on- and off-label prescriptions is readily available to the public from publications and databases to which most pharmaceutical companies subscribe, (3) "pharmacists and other drug dispensing organizations . . . commonly substitute generic drugs for name brand drugs wherever possible -- unless specifically instructed otherwise by the physician writing the prescription," and, "in many states, substitution is

mandatory," (4) Apotex expects to get an "A-B rating" for its gabapentin, which would allow physicians and pharmacists to substitute generic gabapentin for Neurontin® regardless of the indication for which it is to be used, and (5) Apotex should be assumed to have considered the market size and growth potential of gabapentin when it made the strategic decision to file an ANDA and enter the gabapentin market.

Whether or not these statements are true, and for the purposes of deciding whether or not summary judgment was proper we must assume they are, we have already observed that precedent holds that mere knowledge of possible infringement by others does not amount to inducement; specific intent and action to induce infringement must be proven. Manville Sales, 817 F.2d at 554, 16 USPQ2d at 1594. Thus, if a physician, without inducement by Apotex, prescribes a use of gabapentin in an infringing manner, Apotex's knowledge is legally irrelevant. In the absence of any evidence that Apotex has or will promote or encourage doctors to infringe the neurodegenerative method patent, there has been raised no genuine issue of material fact.

Warner-Lambert also argues that the court ignored its own earlier ruling that intent and knowledge must be assessed as of the date of hypothetical FDA approval, rather than at the time the decision was made to file the ANDA. According to that ruling, the relevant question would be whether Apotex would actively induce infringement when its ANDA is approved and it introduces generic gabapentin to the market, rather than whether Apotex had the intent to induce infringement at the time it filed its ANDA. Even if Warner-Lambert is correct, however, and if we assume that Apotex did not have knowledge of the potential for infringing use at the time it filed its ANDA, but that it does now as a result of this lawsuit, we have already held that mere knowledge alone of possible infringement by others is insufficient to prove inducement. In any event, the ANDA must be judged on its face for what an accused infringer seeks the FDA's approval to do. Section 271(e)(2) does not encompass "speculative" claims of infringement. The statute explicitly defines the act of infringement as the filing of the ANDA. The infringement case is therefore limited to an analysis of whether what the generic drug maker is requesting authorization for in the ANDA would be an act of infringement if performed. Here, the 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. That a generic maker may someday induce someone to infringe can only be determined when that act occurs, and § 271(e)(2) was not designed to cover such future acts.

Moreover, according to Warner-Lambert's own data, only about 2.1% of the prescriptions written for gabapentin from August 1999 to July 2000 were for neurodegenerative diseases. Even viewing the evidence in the light most favorable to Warner-Lambert, and assuming that Apotex is "counting on" sales for off-label uses, it defies common sense to expect that Apotex will actively promote the sale of its approved gabapentin, in contravention of FDA regulations, for a use that (a) might infringe Warner-Lambert's patent and (b) constitutes such a small fraction of total sales.

Even if Warner-Lambert's estimate that 2.1% represents $50 million is correct,[8] it is an inescapable fact that the remaining 97.9% still represents more than 46 times that amount. Especially where a product has substantial noninfringing uses, intent to induce infringement cannot be inferred even when the defendant has actual knowledge that some users of its product may be infringing the patent. Where there are many uses for a product, as the record reflects to be true of gabapentin, and fewer than 1 in 46 sales of that product are for infringing uses, we are not in a position to infer or not infer intent on the part of Apotex without any direct evidence.

Warner-Lambert raises two other rather curious arguments in its briefs. First, it argues that the district court erred by applying principles regarding the law of inducement under 35 U.S.C. § 271(b) to actions brought under 35 U.S.C. § 271(e)(2)(A). Warner-Lambert asserts that "Section 271(e)(2)(A) states that the filing of an ANDA for a drug 'the use of which is claimed in a patent' is an act of infringement and mentions neither inducement nor any of the judicially developed intent factors that give rise to inducement." Therefore, Warner-Lambert argues, once it is established that prescriptions are being written for a patented use, the ANDA filing itself represents an act of infringement.

Warner-Lambert is mistaken. As we explained in Glaxo, 35 U.S.C. § 271(e)(2)(A) simply provides an "artificial" act of infringement that creates case-or-controversy jurisdiction to enable the

resolution of an infringement dispute before the ANDA applicant has actually made or marketed the proposed product. 110 F.3d at 1569, 42 USPQ2d at 1263. Once jurisdiction is established, however, the substantive determination whether actual infringement or inducement will take place is determined by traditional patent infringement analysis, just the same as it is in other infringement suits, including those in a non-ANDA context, the only difference being that the inquiries now are hypothetical because the allegedly infringing product has not yet been marketed. Id. (holding that the patentee still carries the burden to prove that the product a generic drug maker ultimately will put on the market would likely infringe the patent). "The plain language of [35 U.S.C. § 271(e)(2)(A)] does not alter a patentee's burden of proving infringement." Id. at 1567, 42 USPQ2d at 1262. The proper inquiry under § 271(e)(2)(A) is "whether, if a particular drug were put on the market, it would infringe the relevant patent." Bristol-Myers Squibb Co. v. Royce Labs., Inc., 69 F.3d 1130, 1135, 36 USPQ2d 1641, 1646 (Fed. Cir. 1995). In Glaxo, we also rejected the argument that an action brought under § 271(e)(2)(A) requires a unique type of infringement analysis in which the burden is shifted to the accused infringer to disprove infringement where the ANDA would permit sale of a composition that may include an infringing product. 110 F.3d at 1568, 42 USPQ2d at 1262. We held in that case that "a patentee seeking relief under § 271(e)(2) must prove by a preponderance of the evidence that what is to be sold will infringe. That burden is not shifted under § 271(e)(2)." Id.

Secondly, Warner-Lambert argues that the district court transplanted into § 271(e)(2)(A) principles "developed in a wholly inapposite non-ANDA context," and extrapolated from both § 271(b) and the holding in Manville Sales to formulate a more stringent standard and to impose a higher burden of proof than would have been encountered in an infringement suit brought directly under § 271(b) rather than under § 271(e)(2)(A). Again, Warner-Lambert is mistaken. The district court did not transplant any alien principles into § 271(e)(2)(A); rather, the court concluded that Warner-Lambert's claim under § 271(e)(2)(A) was foreclosed, and then proceeded to address the question whether or not a genuine issue of material fact existed with regard to an inducement claim. Warner-Lambert, 2001 U.S. Dist. LEXIS 14592, at *6.

We have considered Warner-Lambert's other arguments, including its argument that the court resolved several genuinely disputed issues of material fact adversely to Warner-Lambert, and find them

unpersuasive.

CONCLUSION

The district court did not err in granting summary judgment of noninfringement in favor of Apotex. The court's decision to award judgment to Apotex is therefore

AFFIRMED.

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[1] Warner-Lambert also included a claim under the monohydrate patent. The district court granted summary judgment of noninfringement with respect to that patent on March 2, 2001. Warner-Lambert Co. v. Apotex Corp., No. 98 C 4293, Doc. No. 67 (N.D. Ill. Mar. 2, 2001). The propriety of summary judgment with respect to that patent is not an issue raised by Warner-Lambert in this appeal.

[2] The second opinion mistakenly stated that "Plaintiff does not contend that defendants have violated 35 U.S.C. § 271(e)(2)(A)." Warner-Lambert, 2001 U.S. Dist. LEXIS 14592, at *6 n.3. Not only did Warner-Lambert assert a claim under § 271(e)(2)(A) in its complaint, but the applicability of that statutory provision is also one of the central issues in this appeal.

[3] Pub. L. No. 103-465, Dec. 8, 1994, expanded the definition of infringement in § 271(a) to include offers to sell patented inventions and importation into the United States.

[4] Pub. L. No. 103-465 also revised § 154 such that, except as otherwise provided, for patents granted on applications filed on or after June 8, 1995, "such grant shall be for a term beginning on the date on which the patent issues and ending 20 years from the date on which the application for the patent was filed in the United States." That revision does not affect the present discussion, as it did not attenuate the potential distortions of patent term resulting from regulatory approval periods.

[5] A separate statute once existed for antibiotics (21 U.S.C. § 357).

[6] According to FDA regulations, only patents that claim an approved or pending use of a new drug can be submitted for listing in the Orange Book. The FDA promulgated 21 C.F.R. § 314.53 for submission of patent information by an NDA applicant for the Orange Book listing. For patents that claim a method of use, the FDA regulations state that "the applicant shall submit information only on those patents that claim indications or other conditions of use of a pending or approved application." 21 C.F.R. § 314.53(b). Further, the FDA regulations expressly exclude from the certification requirements patents that claim no uses for which the applicant is seeking approval. 21 C.F.R. § 314.52(a)(3). The neurodegenerative method patent does not claim an indication in Warner-Lambert's currently approved NDA at issue in this case, and we have no information whether that patent claims a use in a pending application.

[7] That is hardly surprising -- pharmaceutical 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. Pharmaceutical companies also occasionally give samples of drugs to doctors and hospitals. In none of these cases, however, does the company itself treat the disease. There can of course be exceptions to this rule, such as in-house testing to establish bioequivalence and bioavailability (which would in any event be noninfringing according to 35 U.S.C. § 271(e)(1)), but they are not relevant here.

[8] It is not entirely clear what the basis is for Warner-Lambert's $50 million figure; 2.1% of Warner-Lambert's own $1.1 billion in Neurontin® sales in 2000 is only about $23 million, and there is no evidence of record to controvert Apotex's assertion that that market will shrink as a result of studies showing that gabapentin is ineffective for treatment of ALS and spinal muscular atrophy.