

Generics Beware: Pre-Marketing Infringement Suits On Use Patents

Can a generic company be sued pre-approval for infringement of a method of treatment patent in view of potentially infringing acts of others when its ANDA product is commercialized, even if the generic company has not sought approval for that method of treatment and has engaged in no actual activity to promote the sale of its product for that treatment?

In the typical scenario involving the development and filing of an ANDA, the generic company considers Orange Book patents listed by the NDA holder and develops a strategy concerning the same, for example, filing a paragraph IV challenge to the Orange Book patent(s) taking the position that such patent(s) is invalid, not infringed, or both. Of course, the prudent generic company also has considered non-Orange Book listed patents by the NDA holder and third parties in developing its proposed generic product. However, those patents are generally further out on the radar screen and not considered a threat for pre-marketing litigation.

Under the FDA rules, patents which may be listed in the Orange Book include those patents directed to the “drug substance” (active ingredient); “drug product” (formulation and composition); and the approved method(s) of use. It is not uncommon for NDA holders to have multiple method of use patents (directed to the different approved methods of use) listed in the Orange Book. It is also not uncommon for a generic company to seek FDA approval only for one approved use (perhaps a use that is off-patent), and to not seek approval for one or more other uses that are covered by Orange Book listed patents. This is accomplished by the generic company filing a “little section VIII”, a Statement under filed under *21 U.S.C. § 355(j)(2)(A)(viii)* stating that the method of use patent does not claim a use for which the applicant is seeking approval.

There are two different statutes under which a patent holder (e.g., an NDA holder) might have an opportunity to bring an infringement action.

Most cases brought prior to commercialization of a generic product are brought under *35 U.S.C. §271(e)(2)(A)*. This statute deems the act of filing an ANDA (or a 505(b)(2) application) to be an act of infringement, enabling the patent holder (e.g., brand name drug manufacturer) to bring a lawsuit prior to FDA approval, if the purpose of such ANDA is to obtain FDA approval prior to the expiration of a patent which claims the use of the drug.

In *Warner-Lambert Company v. Apotex Corp.*, 316 F. 3d 1348 (Fed. Cir. 2003), Warner-Lambert obtained FDA approval through a NDA to market gabapentin for epilepsy, which was covered by a use patent. Warner-Lambert also had a second method of use patent directed to the treatment of neurodegenerative diseases with gabapentin (this is an off-label use). Apotex filed an ANDA seeking approval to market a generic formulation of gabapentin upon the expiration of Warner-Lambert’s epilepsy method

patent.¹ The District Court held that Warner-Lambert was entitled to proceed on an induced infringement theory under *35 U.S.C. § 271(e)(2)(A)* with respect to the patent directed to the treatment of neurodegenerative disease and that it was irrelevant whether the asserted method of use patent claimed the use that Apotex sought for marketing approval in its ANDA. On appeal, the Court of Appeals for the Federal Circuit (CAFC) reversed the District Court's decision and held that it is not an act of infringement under *35 U.S.C. §271(e)(2)(A)* 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*. Significantly, the Court stated that "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 I the ANDA would be an act of infringement if performed."²

Warner-Lambert had also sued Apotex for induced infringement under *35 U.S.C. 271(b)*, and this cause of action was addressed both at the district court level and by the CAFC. Under *35 U.S.C. 271(b)*, "whoever actively induces infringement of a patent shall be liable as an infringer."³ It has been long been held by the courts that to succeed on this theory, a plaintiff must prove that the defendant's actions induced infringement and that the defendant knew or should have known that its actions would induce actual infringement.⁴ Proof of actual intent to cause the acts of actual infringement (e.g., use of gabapentin for neurodegenerative disease) is a necessary prerequisite to a court finding active inducement of infringement.⁵ Upon considering Warner-Lambert's cause of action under *35 U.S.C. 271(b)*, the CAFC concluded that "[i]n 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"⁶ and therefore upheld the District Court's decision to dismiss the suit.

Shortly following the *Warner-Lambert* decision, the CAFC was again faced with similar issues in *Allergan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322 (Fed. Cir. 2003). In that case, Alcon and B&L filed ANDAs seeking approval from FDA to produce and sell

¹ Both patents were listed in the Orange Book. Through the course of the litigation, it became clear that the neurodegenerative disease patent should not have been listed because it did not cover an approved indication, and that Apotex should have filed a statement of non-applicable use pursuant to *21 U.S.C. § 355(j)(2)(A)(viii)* with respect to the indication for neurodegenerative diseases rather than filing a Paragraph IV Certification. The new recently enacted rules further clarify this point.

² *Id.* at 1364.

³ This situation is somewhat unusual in that the generic product was not on the market, and therefore actual infringement was prospective and the inducement issue pertained to direct acts of infringement which would only (possibly) take place sometime in the future. The basis for such prospective actions is *Lang v. Pacific Marine and Supply Co. Ltd.*, 895 F.2d 761 (Fed. Cir. 1990), where the CAFC held that a Declaratory Judgment action could be brought by a patentee against a third party for its prospective future acts.

⁴ *Warner-Lambert, supra*, citing *Manville Sales Corp. v. Paramount Sys., Inc.*, 917 F.2d 544,553 (Fed. Cir. 1990).

⁵ *Warner-Lambert, supra*, citing *Hewlett-Packard Co. v. Bausch & Lomb Inc.*, 909 F.2d 1464, 1469 (Fed. Cir. 1990).

⁶ *Id.* at 1364.

a generic version of brimonidine for use in lowering IOP in patients with open-angle glaucoma or ocular hypertension, but neither company sought FDA approval for the prevention of neurodegeneration, which was covered in Allergan's Orange Book listed patents. On Appeal, the CAFC held that §271(e)(2) may support an action for induced infringement, and mentioned in particular the situation where a patent holder asserts infringement of a FDA-approved method of use for *which an ANDA seeks approval*. The CAFC stated that “[s]ummary judgment of non-infringement under section 271(e)(2), therefore, is inappropriate where the plaintiff can demonstrate the existence of a genuine issue of material fact with respect to the claim that the ANDA filer will induce infringement of its patent upon approval of the ANDA.” 324 F.3d at 1332; citing *Warner-Lambert*, 316 F.3d at 1356.⁷ However, the CAFC affirmed the District Court's grant of summary judgment in favor of Alcon and B&L and held that the decision in *Warner-Lambert* controlled this case and that, under *Warner-Lambert*, Allergan may not sue Alcon and Bausch & Lomb under section 271(e)(2) for inducing infringement of the '415 and '741 patents, because both parties were not seeking FDA approval for the uses claimed in the patents and because the uses claimed in the patents were not FDA-approved. However, concurring opinions in this case made it clear that all of the judges were not pleased with the ruling in *Warner-Lambert*.

In a recent decision handed down on June 9, 2004, the U.S. District Court for the Southern District of New York held that a patentee may sue a generic firm under 35 U.S.C. §271(b) for inducing infringement based on the *filing* of an ANDA.⁸ In that case, Watson filed an ANDA for Takeda's Actos[®] (pioglitazone hydrochloride), which has been approved by FDA for use in both monotherapy and combination therapy. In addition to an Orange Book patent directed to the API, Takeda had also listed method of use patents directed to pioglitazone in combination with other active ingredients. Watson's ANDA only sought approval for monotherapy, and after initially filing its ANDA with Paragraph IV certifications directed to the combination therapy patents, Watson replaced the same with Section viii Statements (declaring that it was not seeking approval for the combination therapies covered by the Takeda patents), and revised its proposed labeling by removing the reference to combination therapy (found in the Actos labeling). Takeda brought a Declaratory Judgment action against Watson, arguing that Watson's sale of pioglitazone will induce infringement of Takeda's combination use patents in violation of 35 U.S.C. § 271 (b), because Watson was aware or should have been aware of the widespread use of the drug in combination therapy and therefore knew or should have known that health care providers will use its product in combination therapy; concluding that Watson therefore knowingly and actively intended to induce its customers to use the drug in combination therapy.

⁷ Allergan had presented evidence that third-party doctors and patients will likely infringe its two method of use patents and that Alcon and B&L may knowingly induce this infringement through their actions.

⁸ *Takeda Chemical Industries, Ltd and Takeda Pharmaceuticals, North America, Inc. v. Watson Pharmaceuticals, Inc., Watson Pharma, Inc. and Danbury Pharmacal, Inc., S.D.N.Y., No. 03 Civ. 8254(DLC)*, 6/9/04.

The district court held that inducement actions brought under 35 U.S.C. 271 (b) may anticipate future infringing conduct so long as there is a controversy of “sufficient immediacy and reality.”⁹ To meet these requirements, the patentee must demonstrate two elements: (1) the defendant must be engaged in an activity directed toward an infringement charge, or be making meaningful preparation for such activity; and (2) the defendant’s acts must indicate a refusal to change the course of its actions in the face of acts by the patentee sufficient to create a reasonable apprehension that a suite will be forthcoming.¹⁰ The Court held that at least at this preliminary stage, Takeda had adequately asserted a claim of sufficient immediacy and reality against Watson for the inducement of infringement of its combination therapy patents.

Conclusion

The District Court did not rely on any particular activities of Watson beyond the filing of its ANDA, and may have found sufficient immediacy and reality for the case to continue because the API patent was being challenged by two other generic companies, and that if either company succeeded in its challenge, Watson would be able to begin marketing its product almost immediately. By maintaining the declaratory judgment action, the *Takeda* Court provided a means for Takeda to take discovery and ascertain if Watson was in fact undertaking any activities sufficient to be found guilty of inducement of infringement.

In another recent decision, a federal court in Delaware held that a claim for inducement of infringement cannot be based solely upon allegations that a defendant aided and abetted the filing of an ANDA.¹¹ In that case, Pfizer filed suit against Ranbaxy alleging that the inducement of infringement occurred when Ranbaxy Laboratories Ltd. And Ranbaxy Pharmaceuticals Inc. filed the ANDA, because one defendant induced the other to file the ANDA.

It appears likely that the NDA holders may increasingly utilize declaratory judgment actions to attempt to pre-empt generic companies from obtaining approval for an off-patent FDA-approved indication for a drug, while “accepting” the (anticipated) benefit of sales for off-label uses.

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⁹ Citing *Lang v. Pacific Marine and Supply Co., Ltd.*, 895 F. 2d 761, 765 (Fed. Cir. 1990).

¹⁰ *Id.*, citing *Glaxo Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1571 (Fed. Cir. 1997) (citing *Lang*, 895 F.2d at 764).

¹¹ *Pfizer v. Ranbaxy Laboratories Ltd.*, D. Del., No. 03-209-JJF, June 18, 2004

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