AstraZeneca Pharmaceuticals LP v. Apotex Corp. (Fed. Cir. 2012)

By Andrew Williams -- February 09, 2012

On Thursday, the Federal Circuit affirmed the dismissal of a § 271(e)(2) patent infringement action based on method-of-use claims because the ANDA filer was only seeking FDA approval for non-patented uses. In *AstraZeneca Pharms. LP v. Apotex Corp.*, the Court held that alleging infringement under 35 U.S.C. § 271(e)(2) was sufficient to confer subject-matter jurisdiction on a federal district court regardless of the merits of the claim, and therefore dismissal under Rule 12(b)(1) is inappropriate in such circumstances. However, to survive a motion to dismiss for failure to state a claim upon which relief can be granted, pursuant to Rule 12(b)(6), a holder of method-of-use patents must allege that an ANDA filer is seeking approval to market its generic drug for a claimed use. If, instead, the ANDA filer is seeking approval for only non-patented indications, even if the reference listed drug is additionally approved for a claimed use, the patent holder cannot support an infringement claim pursuant to 35 U.S.C. § 271(e)(2).

The brand-name drug at issue in this case was CRESTOR®, which has as its active ingredient the cholesterol-lowering statin rosuvastatin calcium. Statins work by competitively inhibiting 3-hydroxy-3-methylglutaryl-CoA ("HMG-CoA") reductase, a key enzyme for cholesterol biosynthesis, thereby reducing circulating cholesterol. The patents-at-issue all claimed methods of using rosuvastatin calcium: U.S. Patent 6,858,618 ("the '618 patent") for the treatment of heterozygous familial hypercholesterolemia, "a genetic condition characterized by impaired cholesterol metabolism and clinically elevated blood cholesterol," and U.S. Patent 7,030,152 ("the '152 patent") with claims to using rosuvastatin calcium to lower the risk of cardiovascular disease in individuals with normal cholesterol levels but with elevated levels of circulating C-reactive protein. CRESTOR® is also approved for the unpatented treatment of homozygous familial hypercholesterolemia and hypertriglyceridemia. In order to skirt AstraZeneca's method-of-use patents, the ANDA filers in this case "carved out" the patented indications from their proposed label, only seeking approval to market the generic version for treating homozygous familial hypercholesterolemia and hypertriglyceridemia. After the conclusion of a separate ANDA litigation involving composition-of-matter patents (which expire in 2016), AstraZeneca sued the ANDA filers pursuant to 35 U.S.C. § 271(e)(2), claiming infringement of the claims of the '618 and '152 patents. The U.S. District Court for the District of Delaware dismissed the action for lack of subject matter jurisdiction and because AstraZeneca's claims were not ripe, even if the FDA may require the ANDA filers to amend their proposed label to include the patented indications at some future date.

Subject Matter Jurisdiction

On appeal, the Federal Circuit agreed with AstraZeneca that alleging that the ANDA filers infringed its method-of-use patents pursuant to § 271(e)(2) was sufficient to confer subject matter jurisdiction on the district court. Consistent with the holding in *Allergan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322 (Fed. Cir. 2003), the Court concluded that, in order to establish subject matter jurisdiction pursuant to § 1338(a), nothing more than alleging infringement by the filing of an ANDA was required. This is true even if it is clear that the plaintiffs cannot succeed on their infringement claims, because the "threshold jurisdictional determination does not depend on the ultimate merits of the claims."

Failure to State a Claim

Nevertheless, the Federal Circuit affirmed the lower court's dismissal of the action based on Rule 12(b)(6) because AstraZeneca failed to state a claim on which it could ultimately succeed. The decision hinged on the language of the statute:

(e) It shall be an act of infringement to submit - (A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act 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 to engage in the commercial manufacture, use, or sale of a drug or veterinary biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

(emphasis added). AstraZeneca appeared to read the "or" out of the highlighted portion, resulting in following language: "It shall be an act of infringement to submit [an ANDA] for a drug . . . the use of which is claimed in a patent." The Court noted that such parsing of the statute "'eviscerated an important part of the statutory provision by conflating the first and second clauses of § 271(e)(2)(A),'" citing *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348 (Fed. Cir. 2003)). Therefore, quite simply, an ANDA applicant seeking to market a drug for a non-patented indication cannot infringe under § 271(e)(2)(A).

This holding is virtually identical to the *Warner-Lambert* decision. AstraZeneca attempted to exploit the main difference between the two cases, namely that the NDA holder in *Warner-Lambert* had not obtained approval for its patented methods, and therefore in that case it was not possible for an ANDA filer to obtain approval that would infringe the claims. Here, instead, the ANDA filers chose to carve out the patented methods, although, of course, they could have sought such approval. Nevertheless, the Court found that the action of the ANDA filers did nothing to change the text of the statute, and therefore § 271(e)(2)(A) still does not apply.

This outcome does raise some real-world complications for AstraZeneca, or for that matter any other NDA holder with approved drugs indicated for non-patented uses. Regardless of what the label says, the ANDA filers in this case are seeking approval of a drug that is bioequivalent to CRESTOR®. After the generic is approved, it is very possible that doctors will prescribe the generic over the branded drug regardless of how the label reads. If that happens, the patent holder will be forced to bring suit against the ANDA filer pursuant to § 271(b) for inducement of infringement of its patents. In such a suit, however, the patent holder will have the added complication of establishing that doctors are prescribing the generic for off-label use. As a result of this outcome, generic challengers can skirt Orange Book listed method-of-use patents by carving out the patent-protected methods, provided there exists a non-patented approved indication. However, as one of the panel members noted during the oral hearing, even if the Court were sympathetic to the policy concerns expressed by AstraZeneca, there is little that it could do. Instead, as was suggested, the outcome that AstraZeneca wanted would have to be effectuated on Capitol Hill, not in the courts.

Ripeness

AstraZeneca also suggested that the FDA will require the ANDA filers to amend their label to include information related to the claimed uses. However, because this alleged amendment will occur at some unspecified point in the future, the lower court dismissed the claims as insufficiently ripe for adjudication. The Federal Circuit noted that it could not conclude that the FDA would require the ANDA filers to amend their applications in the future, in part because the Hatch-Waxman Act provides for the affirmative carving out of patented indications. Therefore, the Court also affirmed the dismissal on these grounds.

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Panel: Chief Judge Rader and Circuit Judges Lourie and Moore
Opinion by Circuit Judge Lourie