NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

IN RE OMEPRAZOLE PATENT LITIGATION

2007-1476, -1477, -1478

ASTRAZENECA AB, AKTIEBOLAGET HASSLE,
KBI-E, INC., KBI, INC., and ASTRAZENECA LP,

Plaintiffs-Appellants,

v.

MYLAN LABORATORIES, INC., MYLAN PHARMACEUTICALS, INCORPORATED,
ESTEVE QUIMICA, S.A., and LABORATORIOS DR. ESTEVE, S.A.,

Defendants-Appellees.

Errol B. Taylor, Milbank, Tweed, Hadley & McCloy, LLP, of New York, New York, argued for plaintiffs-appellants. With him on the brief were Fredrick M. Zullow, John M. Griem, Jr., Lawrence T. Kass, Claire A. Gilmartin, and Emily J. Kunz.

James H. Wallace, Jr., Wiley Rein LLP, of Washington, DC, argued for defendants-appellees. With him on the brief was Mark A. Pacella.

Appealed from: United States District Court for the Southern District of New York

Judge Barbara S. Jones.

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Appeals from the United States District Court for the Southern District of New York in Cases No. 00-CV-6749, 03-CV-6057, and M21-81, Judge Barbara S. Jones.

DECIDED: June 10, 2008

Before LOURIE, BRYSON, and GAJARSA, Circuit Judges.

LOURIE, Circuit Judge.

Astrazeneca, AB, Aktiebolaget Hassle, KBI-E, Inc., KBI, Inc., and Astrazeneca LP (collectively "Astra") appeal from the decision of the U.S. District Court for the Southern District of New York, following a bench trial, finding noninfringement of U.S.

Patents 4,786,505 ("the '505 patent") and 4,853,230 ("the '230 patent") by Mylan Laboratories, Inc., Mylan Pharmaceuticals, Incorporated (collectively "Mylan"), Esteve Quimica, S.A., and Laboratorios Dr. Esteve, S.A. (collectively "Esteve"). Because Astra fails to identify any reversible error, we affirm.

BACKGROUND

Astra is the owner of the '505 and '230 patents, both of which relate to oral pharmaceutical preparations for omeprazole. Omeprazole is the active ingredient in Prilosec®, a widely prescribed drug marketed by Astra that can be used to treat gastric and duodenal ulcers by inhibiting the production of gastric acid. Omeprazole is difficult to formulate, however, because it is acid-labile; i.e., it is susceptible to degradation in acid-reacting and neutral media. In order to prevent degradation in the stomach, omeprazole must be protected from acidic gastric juices. In addition, omeprazole suffers from other formulation problems, including sensitivity to heat, organic solvents, moisture, and light.

Astra scientists developed an oral dosage form of omeprazole that overcomes those formulation problems. They developed an oral formulation that includes, inter alia, a core containing omeprazole and an alkaline reacting compound ("ARC"), a water soluble subcoat, and an enteric coating. Astra's formulation led to the patents in suit.

Claim 1 of the '505 patent, a representative claim, reads as follows:

> 1. An oral pharmaceutical preparation comprising
>
> (a) a core region comprising an effective amount of a material selected from the group consisting of omeprazole plus an alkaline reacting compound, an alkaline omeprazole salt plus an alkaline reacting compound and an alkaline omeprazole salt alone;

(b) an inert subcoating which is soluble or rapidly disintegrating in water disposed on said core region, said subcoating comprising one or more layers of materials selected from among tablet excipients and polymeric film-forming compounds; and

(c) an outer layer disposed on said subcoating comprising an enteric coating.

'505 patent claim 1 (emphasis added). The '230 patent claims a broader selection of active ingredients. Claim 1 of the '230 patent reads as follows:

1. A pharmaceutical preparation comprising:

(a) an alkaline reacting core comprising an acid-labile pharmaceutically active substance and an alkaline reacting compound different from said active substance, an alkaline salt of an acid labile pharmaceutically active substance, or an alkaline salt of an acid labile pharmaceutically active substance and an alkaline reacting compound different from said active substance;

(b) an inert subcoating which rapidly dissolves or disintegrates in water disposed on said core region, said subcoating comprising one or more layers comprising materials selected from the group consisting of tablet excipients, film-forming compounds and alkaline compounds; and

(c) an enteric coating layer surrounding said subcoating layer, wherein the subcoating layer isolates the alkaline reacting core from the enteric coating layer such that the stability of the preparation is enhanced.

'230 patent claim 1 (emphasis added).

Mylan filed an Abbreviated New Drug Application on May 17, 2000, seeking approval from the Food and Drug Administration ("FDA") to market its 10 mg, 20 mg, and 40 mg generic versions of Prilosec® (collectively "Mylan's products"). Astra brought suit against Mylan and Esteve (collectively "Mylan/Esteve"), along with several other generic defendants, in the United States District Court for the Southern District of New York, alleging infringement under the Hatch-Waxman Act. Those suits were

consolidated in a multi-district litigation for discovery and ultimately tried in two waves.[1] Astra's case against Mylan/Esteve was tried during the second wave litigation.

During the course of litigation, the FDA granted approval of Mylan's 10 mg and 20 mg formulations and tentative approval of the 40 mg formulation on June 2, 2003. Mylan began selling its 10 mg and 20 mg formulations in the United States in August 2003. Mylan's products consist of "(1) an inert sugar/starch sphere; (2) an active coating of omeprazole, talc, and hydroxypropyl methylcellulose ("HPMC") ("Film Coating No. 1" or "active drug layer"); (3) a subcoating of HPMC, talc, and titanium dioxide ("Film Coating No. 2"); (4) a second subcoating of HPMC and ethylcellulose ("Film Coating No. 3"); and (5) an enteric coating of methacrylic acid copolymer, triethylcitrate, and talc (the "enteric coating")." In re Omeprazole Patent Litig., 490 F. Supp. 2d 381, 425 (S.D.N.Y. 2007) (emphasis added). At issue in this appeal is the talc that is used in the active drug layer of Mylan's products.

After a forty-two day bench trial, the district court determined, inter alia, that Mylan/Esteve did not infringe either of the asserted patents. Id. In reaching its conclusion, the court held that Astra failed to show that Mylan/Esteve's omeprazole products met the limitations of paragraph (a) of claim 1 of the patents in suit. In particular, the court found that Astra failed to prove by a preponderance of the evidence that Mylan/Esteve's products contained an ARC. The court rejected Astra's assertion

[1] The district court held a trial of the first wave defendants from December 2002 through June 2003 and found the patents in suit not invalid and infringed by three of the four defendants. In 2003, we affirmed the court's decision. In re Omeprazole Patent Litigation, Nos. 03-1101 to 03-1106, 03-1131, 03-1132, to 03-1136, 03-1171, 03-1172, 03-1173, slip op. (Fed. Cir. Dec. 11, 2003) (Omeprazole I).

that carbonates in either the talc or the HPMC, or the triethylamine in the omeprazole, satisfied the ARC and "effective amount" requirements of the asserted claims.

Astra timely appealed the court's decision. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

We review "the judgment of a district court following a bench trial 'for errors of law and clearly erroneous findings of fact.'" Dow Chem. Co. v. Mee Indus., Inc., 341 F.3d 1370, 1374 (Fed. Cir. 2003) (quoting Allen Eng'g Corp. v. Bartell Indus., Inc., 299 F.3d 1336, 1343-44 (Fed. Cir. 2002)). Claim construction is an issue of law, Markman v. Westview Instruments, Inc., 52 F.3d 967, 970-71 (Fed. Cir. 1995) (en banc), that we review de novo. Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1456 (Fed. Cir. 1998) (en banc). The district court's determination of infringement, in contrast, is a question of fact that we review for clear error. Centricut, LLC v. Esab Group, Inc., 390 F.3d 1361, 1367 (Fed. Cir. 2004).

A determination of infringement requires a two-step analysis. "First, the court determines the scope and meaning of the patent claims asserted, and then the properly construed claims are compared to the allegedly infringing device." Cybor, 138 F.3d at 1454 (citations omitted). "A finding is 'clearly erroneous' when although there is evidence to support it, the reviewing court on the entire evidence is left with the definite and firm conviction that a mistake has been committed." United States v. U.S. Gypsum Co., 333 U.S. 364, 395 (1948).

The issue on appeal is whether the district court erred in concluding that Astra failed to prove the presence of an ARC in Mylan's products. Astra raises several

arguments, not all of which need to be addressed in light of the conclusions we reach. Astra primarily argues that the court erred by applying the wrong burden of proof for infringement, by misapprehending the trial evidence, and by failing to apply the proper claim construction to Mylan's products. In response, Mylan/Esteve asserts that the district court properly applied the correct legal standard, made proper findings of fact that were not clearly erroneous, and applied the correct claim construction, which we have previously affirmed on appeal.

We agree with Mylan/Esteve that it does not infringe the two patents. In order to infringe the patents in suit, the accused products must contain an ARC in the active core region. Previously, in Omeprazole I, we affirmed the district court's construction of an ARC, which was construed as:

> (1) a pharmaceutically acceptable alkaline, or basic, substance having a pH greater than 7 that (2) stabilizes the omeprazole or other acid labile compound by (3) reacting to create a micro-pH of not less than 7 around the particles of omeprazole or other acid labile compound.

Id. (quoting Astra Aktiebolag v. Andrx Pharms., Inc., 222 F. Supp. 2d 423, 453 (S.D.N.Y. 2002)).

At trial, Astra argued that the talc used in the active drug layer of Mylan's products, viz., Microace® talc, was alkaline and that the source of alkalinity was carbonates. More specifically, Astra argued that carbonates that are introduced into the active drug layer through the talc, and not the talc itself, are ARCs as that term is used in the patents in suit. Indeed, in its briefs on appeal and during oral argument, Astra repeatedly took the position that Mylan's products satisfy the ARC requirement based on the presence of carbonates that are introduced into Mylan's formulation, rather than the talc itself. See Astra Reply Br. at 4 ("The issue is not whether talc is an ARC, but

whether the carbonates that are introduced into Mylan/Esteve's formulation through Mylan/Esteve's particular talc are ARCs."); see also id. at 14 ("Again the ARC is the carbonates – not the talc itself."); id. at 27 ("[I]t is not the talc, but carbonates in Mylan/Esteve's Microace talc, that is the ARC.").

The district court considered and rejected Astra's assertion. The court primarily rested its conclusion on its finding that Astra failed to prove the presence of carbonates in Mylan's products. In doing so, the court considered the evidence proffered by both parties relating to the presence or absence of carbonates in the talc. The court first considered tests that Astra's expert, Dr. Davies, performed on Mylan's talc. Those tests, referred to as attenuated total reflectance Fourier spectroscopy ("ATR-FTIR") and energy dispersive x-ray analysis, indicated that carbonates were present in Mylan's talc and were the source of the alkalinity of the talc. The court, however, then considered evidence proffered by Mylan/Esteve, which included tests that were performed by both Esteve and Nippon, the supplier of Microace® talc, on batches of Mylan's talc for the presence of carbonates. The court found that those tests indicated that Mylan's talc contained no detectable amount of carbonates. After weighing the competing evidence, the court found that Astra failed to prove the presence of carbonates in the talc of the accused products. Omeprazole, 490 F. Supp. 2d at 430 ("Thus, the Court finds that the empirical evidence of the presence of carbonates in the talc used in Mylan/Esteve's product is inconclusive."). Such a determination is based on the district court's factfindings and cannot be overturned unless we find them to be clearly erroneous, and we do not.

Astra argues that that finding is flawed because the district court applied the wrong legal standard. According to Astra, the court misapplied the legal standard by requiring "conclusive evidence" that carbonates were present in the talc, rather than preponderant evidence. In addition, Astra asserts that the court applied an incorrect legal standard a second time during its analysis of another claim limitation by requiring Astra to dispel any "modicum of doubt" that the micro-pH in the accused omeprazole containing region is not less than seven. Id. at 441-42. Astra likens the court's purported standards to those applied in criminal matters—i.e., proof beyond a reasonable doubt.

A plain reading of the district court's decision, however, reveals that the district judge knew, understood, and applied the proper standard of proof. Indeed, the court stated:

> Plaintiffs bear the burden to prove their claims of infringement by a preponderance of the evidence. A preponderance of the evidence means such evidence which, when considered and compared with that opposed to it, produces a belief that what is sought to be proved is more likely true than not. The fact that section 271(e)(2) creates an artificial act of infringement does not lessen that burden.

Id. at 414 (emphasis added); see also id. at 422 ("Demonstration that every limitation of the claim is . . . met by the accused device [or product] must be shown by a preponderance of the evidence.") (quoting Enercon GmbH v. Int'l Trade Comm'n, 151 F.3d 1376, 1384 (Fed. Cir. 1998) (emphasis added)); see also id. at 442 ("Accordingly, Plaintiffs have failed to show by a preponderance of the evidence that Mylan/Esteve's product literally contains an ARC.") (emphasis added). Astra's focus on the isolated phrases of "inconclusive" and "modicum of doubt" is insufficient to establish reversible

error. Given the court's clear understanding and repeated recitation of the applicable burden of proof, Astra's argument is wholly inapt.

Astra argues, in the alternative, that even if the law required conclusive evidence, it met that burden. Astra asserts that the district court ignored vast amounts of evidence that showed the presence of carbonates in the talc. Astra's argument amounts to mere disagreement with the court's factual findings, which cannot serve as a basis for reversing the court. Because we find no clear error with respect to those findings, Astra's argument fails.

After concluding that Astra failed to prove the presence of carbonates in the accused products, the district court made additional findings that served as alternative grounds for concluding that the ARC limitation was not met. Shifting its focus from carbonates to the talc itself, the court analyzed whether talc could satisfy the ARC requirement of the claim. Based on the teachings of the specifications, which indicated that talc is not an ARC but rather an ordinary additive, and statements that Astra made during the prosecution of the European counterpart to the '505 patent, the court found that it could not. The court pointed out that the patent specifications, which are nearly identical in this respect, list a number of compounds that can serve as ARCs, not including talc. Omeprazole, 490 F. Supp. 2d at 430; see also '505 patent col.3 ll.47-59; '230 patent col.8 ll.43-55. In contrast, the specifications also list a number of ordinary excipients, among which is talc. Omeprazole, 490 F. Supp. 2d at 430; see e.g., '505 patent col.4 ll.54-56, col.5 ll.16-18; '230 patent col.9 ll.48-50, col.10 ll.10-12. Thus, the specifications themselves indicate that ARCs do not include talc.

In addition, during the prosecution of the European counterpart to the '505 patent, Astra's patent attorney referred to formulations 1 and 7 of Table 1 of the '505 patent—formulations that clearly include talc. The attorney argued that those formulations are "without alkaline compound in the core." Omeprazole, 490 F. Supp. 2d at 430. Once again, talc was not considered to be an ARC. Moreover, the court determined that even if talc could function as an ARC, Astra failed to prove that Mylan's products satisfied other limitations of the claim, viz., that the accused products contain an "effective amount" of talc to stabilize the omeprazole by creating a micro-pH of not less than seven.

Astra's remaining arguments raised in its briefs relate to those alternative grounds offered by the district court in support of its decision. Having determined that the district court did not clearly err in concluding that Astra failed to prove the threshold requirement that the accused products contain non-negligible amounts of carbonates, which, according to Astra, are the ARCs in Mylan's products, and thus having failed otherwise to show the presence of an ARC, we need not address Astra's remaining arguments as they relate to the court's alternative grounds for its decision.

CONCLUSION

For the foregoing reasons, we affirm the decision of the district court.

AFFIRMED