United States Court of Appeals for the Federal Circuit

02-1429

RANBAXY PHARMACEUTICALS, INC.
and RANBAXY LABORATORIES LIMITED,

Plaintiffs-Appellees,

v.

APOTEX, INC.,

Defendant-Appellant.

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Appealed from: United States District Court for the District of New Jersey

Judge Mary L. Cooper

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Defendant-Appellant.

DECIDED: November 26, 2003

Before MAYER, Chief Judge, CLEVENGER and BRYSON, Circuit Judges.

MAYER, Chief Judge.

Apotex, Inc. appeals the order of the United States District Court for the District of New Jersey denying a preliminary injunction against Ranbaxy Pharmaceuticals, Inc. and Ranbaxy Laboratories Limited, (collectively "Ranbaxy"). Ranbaxy Pharms. v. Apotex, Inc., No. 02-CV-848 (D. N.J. May, 8, 2002). Because the district court correctly determined that Apotex did not show a reasonable likelihood of success on the merits, we affirm.

Background

This case is one of many involving the drug cefuroxime axetil, which is a broad-spectrum antibiotic used to treat conditions such as tonsillitis, sinusitis, and skin infections, and exists in two forms: amorphous and crystalline. Ranbaxy and Apotex are generic drug manufacturers who hope to be or are marketing amorphous cefuroxime axetil. Both parties are presently defending lawsuits, separate from this case, brought by Glaxo Wellcome, the owner of United States Patent Nos. 4,562,181 and 4,267,320, both relating to cefuroxime axetil. After we vacated a preliminary injunction against Ranbaxy, Glaxo Wellcome Ltd. v. Ranbaxy Pharms., Inc., 262 F.3d 1333, 59 USPQ2d 1950 (Fed. Cir. 2001), its abbreviated new drug application was approved by the Food and Drug Administration, and it launched its cefuroxime axetil product. Less than two months from its launch date, Ranbaxy had shipped over $12,000,000 worth of cefuroxime axetil and booked an additional $27,000,000 worth of orders.

Apotex is the owner of United States Patent No. 5,847,118 ("'118 patent") directed to a process for preparing amorphous cefuroxime axetil. Ranbaxy sought a declaratory judgment that it does not infringe the claims of the '118 patent; Apotex filed a counterclaim that Ranbaxy infringes and moved for a preliminary injunction. Apotex conceded that Ranbaxy did not literally infringe the claims of the '118 patent; rather, it argued that Ranbaxy infringed under the doctrine of equivalents and should be enjoined from further marketing its cefuroxime axetil product.

Apotex's originally filed patent application contained one independent claim and nine dependent claims. These claims were:

1. Process of preparation of amorphous cefuroxime axetil which comprises the steps of:
   (a) dissolving crystalline cefuroxime axetil in a highly polar organic solvent and adding the resulting solution to water; or
   (b) dissolving crystalline cefuroxime axetil in a highly polar solvent, adding water to the resulting solution and subsequently adding the resulting aqueous-organic solution to water.

2. The process of claim 1 wherein the dissolution of crystalline cefuroxime axetil is carried out in a volume of solvent only sufficient to dissolve crystalline cefuroxime axetil.

3. The process of claim 1 or 2 wherein the highly polar solvent is a sulfoxide.

4. The process of claim 1 or 2 wherein the highly polar solvent is dimethyl sulfoxide.

5. The process of claim 1 or 2 wherein the highly polar solvent is an amide.

6. The process of claim 5 wherein the amide is selected from the consisting of dimethyl formamide, dimethyl acetamide, or hexamethyl phosporamide.

7. The process of claim 1 or 2 wherein the solvent is formic acid.

8. The process of claim 1 or 2 wherein the solvent is a homogenous mixture of dimethyl sulfoxide and the amide.

9. The process of claim 1 or 2 wherein the addition of the resulting solution to water is carried out between 0 to 40·ºC.

10. The process of claim 9 wherein the addition is carried out between 0 to 4ºC.

Ranbaxy Pharms., slip op. at 4-5 (emphases added). In a preliminary amendment, claims 3-9 were amended so as not to be dependent on claim 2.

In the first office action, the United States Patent and Trademark Office ("PTO") rejected claims 1, 8, and 10 under 35 U.S.C. § 112, second paragraph, because the phrase "highly polar organic solvent" was indefinite. Specifically, the examiner questioned where the boundary was between solvents that are highly polar and those that are less than highly polar. Claims 1, 2, 9, and 10 were rejected under 35 U.S.C. § 103(a) as obvious in view of United States Patent No. 5,013,833 ("'833 patent"). The examiner stated that the '833 patent disclosed basically the same process.

> The cefuroxime axetil is dissolved in a mixture of acetone and water. This is added to the precipitating agent, namely, water, resulting in amorphous cefuroxime axetil. Assuming that acetone is a highly polar solvent, the sole difference is that the reference dissolves the cefuroxime axetil in a mixture of acetone and water, whereas applicants dissolve the organic solvent, then add some water. But either way, an identical solution results. Moreover, one of ordinary skill in the art would understand that these are alternative methods to the same goal.

Ranbaxy Pharms., slip op. at 6-7. In its discussion of prior art, the specification of the '118 patent says that the method taught in the '833 patent has many disadvantages. Among them is that the use of acetone requires very elaborate experimental procedures. The specification goes on to state that the disclosed invention overcomes this disadvantage through the use of a highly polar solvent. This leads the examiner to note in his discussion of the obviousness rejection that "[e]ven if acetone is (somehow) not considered as a highly polar solvent, as applicants note, the reference also teaches acetonitrile." Finally, the examiner objected to claims 3-7 for being dependent upon a rejected base claim, but said they would be allowable if rewritten in independent form.

In response to this office action, Apotex canceled claims 1-10 and submitted new claims 11-16. Claim 11, the only independent claim, and the most pertinent to our discussion, reads:

> Process of preparation of amorphous cefuroxime axetil which comprises the steps of:
> (a) dissolving crystalline cefuroxime axetil in a volume of a highly polar organic solvent only sufficient to dissolve it, and adding the resulting solution to water; or
> (b) dissolving crystalline cefuroxime axetil in a volume of highly polar organic solvent, only sufficient to dissolve it, adding water to the resulting solution and subsequently adding the resulting aqueous-organic solution to water,
> wherein the highly polar organic solvent is selected from the group consisting of a sulfoxide, an amide and formic acid.

Ranbaxy Pharms., slip op. at 7-8. Claim 11 was allowed and renumbered as claim 1 of the '118 patent. See '118 patent, col. 4, l. 66 – col. 5, l. 11.

In the district court, Apotex moved for a preliminary injunction arguing that Ranbaxy's process, which uses acetic acid rather than any of the specifically claimed solvents, infringed under the doctrine of equivalents. The court denied the motion, finding that Apotex did not show a reasonable likelihood of success on the merits. It concluded that prosecution history estoppel precluded Apotex from relying on the doctrine of equivalents because either: (1) it had entered a narrowing amendment for reasons related to patentability invoking the complete bar of Festo Corp. v. Shokestu Kinsoku Kogyo Kabushiki Co., 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) (en banc), vacated by 535 U.S. 722, 122 S.Ct.

1831, 62 USPQ2d 1705 (2002),* or (2) it had surrendered solvents of the same polarity as acetone, which it found acetic acid was. The district court also found that Apotex had failed to establish irreparable harm, that the balance of hardships weighed against equitable relief, and that an injunction was not in the public interest.** Apotex appeals the denial of preliminary injunctive relief. We have jurisdiction under 28 U.S.C. § 1292(c)(1).

Discussion

As the moving party, Apotex was required to establish its right to a preliminary injunction in light of four factors: "(1) a reasonable likelihood of success on the merits; (2) irreparable harm if the injunction were not granted; (3) the balance of the hardships and (4) the impact of the injunction on the public interest." Purdue Pharma L.P. v. Boehringer Ingelheim GMBH, 237 F.3d 1359, 1363, 57 USPQ2d 1647, 1649 (Fed. Cir. 2001) (citing Polymer Techs. v. Bridwell, 103 F.3d 970, 973, 41 USPQ2d 1185, 1188

(Fed. Cir. 1996)). If Apotex as the moving party "clearly establishe[s] the first factor (by making a 'clear showing' of both validity and infringement), it [is] entitled to a rebuttable presumption" of irreparable harm. Id.

The decision to grant a preliminary injunction is within the sound discretion of the district court. See 35 U.S.C. § 283 (2000); Polymer Techs., 103 F.3d at 973, 41 USPQ2d at 1188. We review the denial of a preliminary injunction for an abuse of discretion, which may be shown if the district court made a clear error of judgment, or based its decision on an erroneous legal conclusion or clearly erroneous factual findings. Purdue Pharma, 237 F.3d at 1363, (citing Canon Computer Sys. Inc. v. Nu-Kote Int'l, Inc., 134 F.3d 1085, 1087-88, 45 USPQ2d 1355, 1358 (Fed. Cir. 1998)). Because this is an early stage of the proceeding, we acknowledge that findings of fact and conclusions of law are subject to change when the court ultimately reaches the merits. See Illinois Tool Works, Inc. v. Grip-Pak, Inc., 906 F.2d 679, 681, 15 USPQ2d 1307, 1308-09 (Fed. Cir. 1990). To show a reasonable likelihood of success on the merits of the infringement claim, Apotex was required to show that "in light of the presumptions and burdens that will inhere at trial on the merits, (1) it will likely prove [infringement] and (2) its infringement claim will likely withstand [Ranbaxy's] challenges to the validity and enforceability of the . . . patent[s]." Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1364, 42 USPQ2d 1001, 1003 (Fed. Cir. 1997) (quoting New England Braiding Co. v. A.W. Chesterton Co., 970 F.2d 878, 882-83, 23 USPQ2d 1622, 1625-26 (Fed. Cir. 1992)).

An infringement analysis entails two steps. First, the meaning and scope of the asserted patent claims is determined, and then the properly construed claims are compared to the accused product or process. Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1454, 46 USPQ2d 1169, 1172 (Fed. Cir. 1998) (en banc). Claim construction is a question of law reviewed de novo. Id. at 1456, 46 USPQ2d at 1174. Infringement, both literal and under the doctrine of equivalents, is a question of fact. Insituform Techs., Inc. v. Cat Contracting, Inc., 161 F.3d 688, 692, 48 USPQ2d 1610, 1614 (Fed. Cir. 1998).

Prosecution history estoppel is a question of law that we review de novo on appeal. Cybor Corp., 138 F.3d at 1460, 46 USPQ2d at 1178. Apotex argues that the district court erred in concluding

that there had been a narrowing amendment for a substantial reason related to patentability. It contends that because the examiner in the first office action objected to dependent claims 3-7 but stated that they would be patentable if rewritten in independent form, and because claim 11 is nothing more than claims 3, 5, and 7 combined and rewritten in independent form, there was not a narrowing amendment for a substantial reason related to patentability. Apotex also argues that Bose Corp. v. JBL, Inc., 274 F.3d 1354, 61 USPQ2d 1216 (Fed. Cir. 2001), compels the outcome of this case. We disagree.

Bose Corp. is of no avail to Apotex. There, we addressed whether the addition of an inherent element to a claim was a narrowing amendment invoking the absolute bar of our en banc Festo decision and answered in the negative. We did not squarely address the effect that rewriting a dependent claim into independent form may have on prosecution history estoppel. See Brecht v. Abrahamson, 507 U.S. 619, 631 (1993) (If a decision does not "squarely address[] [an] issue," a court remains "free to address the issue on the merits" in a subsequent case.). Regardless, the Supreme Court clearly stated in Festo that such an amendment "may . . . in some cases" create an estoppel, leading us to the conclusion that the issue is best dealt with on a case-by-case basis. 535 U.S. at 736-37, 122 S.Ct. at 1840.

In Festo Corp. v. Shokestu Kinsoku Kogyo Kabushiki Co., Festo argued that "[t]he PTO might require the applicant to clarify an ambiguous term, to improve the translation of a foreign word, or to rewrite a dependent claim as an independent one . . . . [And] [i]n these cases . . . the applicant has no intention of surrendering subject matter and should not be estopped from challenging equivalent devices." Id. The Court responded that "[w]hile this may be true in some cases, [Festo's] argument conflates the patentee's reason for making the amendment with the impact the amendment has on the subject matter." Id. We held in Deering Precision Instruments, L.L.C. v. Vector Distribution Systems, Inc. that in deciding whether a narrowing amendment has occurred, "the correct focus is on whether [the] amendment surrendered subject matter that was originally claimed for reasons related to patentability." Nos. 02-1013, 02-1197, 2003 WL 22358859 (Fed. Cir. Oct. 17, 2003) at *9 (citing Festo Corp., 535 U.S. at 736). In this case the surrender is particularly clear. While Apotex was merely rewriting a dependent claim into independent form, the effect on the subject matter was substantial. The

dependent claims that were redrafted into independent form did more than simply add an additional limitation; they further defined and circumscribed an existing limitation for the purpose of putting the claims in condition for allowance. The additional language limited "highly polar solvent" to a defined group of solvents: sulfoxides, amides, and formic acid. In so doing, the patentee is presumed to have surrendered the equivalents that may have been encompassed by "highly polar solvent." Festo Corp., 535 U.S. at 740-41, 122 S.Ct. at 1842, remanded to 344 F.3d 1359 (Fed. Cir. 2003); Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 33 (1997).

Having concluded that the district court properly determined that there had been a narrowing amendment for a substantial reason related to patentability, we next turn to whether Apotex can overcome the presumption that it has surrendered equivalents. The Supreme Court held that the presumption can be overcome if "[t]he equivalent [was] unforeseeable at the time of the application; the rationale underlying the amendment [bears] no more than a tangential relation to the equivalent in question; or there [was] some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question." 535 U.S. at 740-41, 122 U.S. at 1842. Apotex argues that it was "not foreseeable that the acceptance of the structurally-defined subject matter could constitute surrender of a highly polar organic solvent which is the obvious structural equivalent (homolog) of one of the recited solvents." Ranbaxy responds that acetic acid is a foreseeable equivalent to formic acid that could have and should have been included in the original claim. And even if Apotex could overcome the presumption and is therefore entitled to some range of equivalents, because acetic acid and acetone are of similar polarities and because acetone was described by the '118 patent as part of the prior art, Apotex has surrendered coverage for acetic acid.

We think Ranbaxy has the better argument. First, foreseeability relates to the equivalent, not to whether an amendment may result in prosecution history estoppel. Festo Corp., 344 F.3d at 1369, enforcing 535 U.S. 722. Second, the notion that acetic acid was unforeseeable at the time of application flies in the face of the fact that Apotex stated that formic acid and acetic acid, as homologs, are readily known by chemists to exhibit similar properties and are therefore equivalent. If acetic acid was readily known by chemists to be equivalent to formic acid, it would have been foreseeable to literally include

acetic acid in the claim. Therefore, at this stage of the litigation, Apotex has not overcome the presumption that it has surrendered coverage of acetic acid.

As for Ranbaxy's argument that the '118 patent surrendered coverage of acetic acid because acetone is of the same polarity and in the prior art, there was considerable dispute among the experts over the proper criteria for determining polarity. Should Apotex be able to present sufficient evidence to rebut the presumption that it had surrendered the equivalents of "highly polar solvent," it will be necessary for the trier of fact to determine the proper criteria to gauge polarity and whether acetic acid and acetone have the same polarity.

Conclusion

Accordingly, the judgment of the United States District Court for the District of New Jersey is affirmed.

AFFIRMED

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* The district court decided this case after our en banc Festo decision, but before the Supreme Court issued its opinion.

** Because the district court correctly determined that Apotex has not shown a likelihood of success on

the merits, as we spell out below, we do not address these factors.