# United States Court of Appeals for the Federal Circuit

01-1151

GLAXO GROUP LIMITED and GLAXO WELLCOME, INC.,

Plaintiffs-Appellees,

v.

RANBAXY PHARMACEUTICALS, INC.,

Defendant-Appellant.

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Appealed from: U.S. District Court for the District of New Jersey

Judge Mary L. Cooper

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DECIDED: August 20, 2001

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Before MAYER, Chief Judge, NEWMAN, and RADER, Circuit Judges.

RADER, Circuit Judge.

The United States District Court for the District of New Jersey entered a preliminary injunction against Ranbaxy Pharmaceuticals, Inc. The order enjoined Ranbaxy from offering for sale or selling in the United States any cefuroxime axetil product under its Abbreviated New Drug Application (ANDA). Because Glaxo Group Limited and Glaxo Wellcome, Inc., (collectively "Glaxo") would not likely succeed in proving that Ranbaxy's proposed cefuroxime axetil product infringes U.S. Patent No. 4,562,181 (the '181 patent), this court vacates the preliminary injunction and remands.

I.

On May 12, 1981, Glaxo obtained United States Patent No. 4,267,320 (the '320 patent) on a family of cephalosporin antibiotics, including esters of the antibiotic cefuroxime. Cefuroxime—a broad spectrum antibiotic—treats many conditions, including tonsillitis, sinusitis, and skin infections. The esters of cefuroxime deliver the active drug,

also referred to as the active moiety, to the patient. The '320 patent discloses that one specific ester of cefuroxime, cefuroxime axetil, is "particularly preferred" and expressly claims this compound in claim 4. Glaxo obtained a two-year term extension for the '320 patent under 35 U.S.C. § 156. The '320 patent expired on May 12, 2000.

Cefuroxime axetil has two physical forms: (1) amorphous (without molecules in an ordered arrangement); and (2) crystalline (with molecules in an ordered arrangement). On December 31, 1985, Glaxo obtained the '181 patent which discloses that the amorphous form of cefuroxime axetil provides various advantages over the crystalline form. Claim 1 of the '181 patent recites: "Cefuroxime axetil in amorphous form essentially free from crystalline material, and having a purity of at least 95% aside from residual solvents." (Emphasis added). The '181 patent will expire on June 29, 2003.

Glaxo obtained approval from the Food and Drug Adminsitration (FDA) on its New Drug Application for cefuroxime axetil. In 1988, Glaxo began marketing Ceftin®, the commercial embodiment of the '320 and '181 patents.

On April 19, 1999, Ranbaxy filed an ANDA with the FDA seeking approval to market a generic tablet form of cefuroxime axetil in anticipation of the '320 patent's expiration. Ranbaxy's proposed cefuroxime axetil product contains about 10 to 15% crystalline cefuroxime axetil, with the balance of the content amorphous. Glaxo opposed Ranbaxy's ANDA by filing a citizen's petition in the FDA and by filing suit against Ranbaxy in the district court under 35 U.S.C. § 271(e)(2).

The district court interpreted the limitation "essentially free from crystalline material" of claim 1 of the '181 patentas "excluding from the claimed invention any item having sufficient crystalline cefuroxime axetil that materially affects the basic characteristics of the invention." Glaxo Group Ltd. v. Ranbaxy Pharm., Inc., No. 00-5172, slip op. at 26-27 (D. N.J. Dec. 21, 2000). The district court determined that claim 1's scope encompassed

cefuroxime axetil with a 10 to 15% crystalline content. Based on this claim construction, the district court found that Glaxo was likely to succeed on the merits in proving that Ranbaxy's proposed product infringes the '181 patent. The district court also found that Glaxo stood to lose more money in sales of Ceftin® before the '181 patent expired than Ranbaxy's total net worth. Balancing the hardships in Glaxo's favor and finding a public interest in preventing the launch of Ranbaxy's product, the district court entered a preliminary injunction, precluding Ranbaxy from marketing any cefuroxime axetil product under its ANDA.

Ranbaxy appeals the district court's grant of the preliminary injunction. This court has jurisdiction to hear this interlocutory appeal under 28 U.S.C. § 1292(c)(1).

II

This court sustains the grant of a preliminary injunction unless the district court abused its discretion, or based its decision on an erroneous legal standard or clearly erroneous findings of fact. Mentor Graphics Corp. v. Quickturn Design Sys., Inc., 150 F.3d 1374, 1377, 47 USPQ2d 1683, 1685 (Fed. Cir. 1998). This court reviews claim construction without deference. Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1454, 46 USPQ2d 1169, 1172 (Fed. Cir. 1998) (en banc). Applying the claim construction to the accused device to determine infringement is a question of fact, which receives substantial deference on review. Embrex, Inc. v. Serv. Eng'g Corp., 216 F.3d 1343, 1348-49, 55 USPQ2d 1161, 1164 (Fed. Cir. 2000).

To obtain an injunction, a party must prove four factors: (1) its reasonable likelihood of success on the merits; (2) irreparable harm to its interests; (3) the balance of hardships tipping in its favor; and (4) public interest in favor of the injunction. Chrysler Motors Corp. v. Auto Body Panels, Inc., 908 F.2d 951, 952, 15 USPQ2d 1469, 1410 (Fed. Cir. 1990).

This court turns first to Glaxo's likelihood of success in showing that Ranbaxy's proposed cefuroxime axetil product would infringe the '181 patent.

In review of Glaxo's likelihood of success, this court examines the construction of claim 1 and its application to Ranbaxy's proposed product. Bell & Howell Document Mgmt. Prods. Co. v. Altek Sys., 132 F.3d 701, 704, 45 USPQ2d 1033, 1036 (Fed. Cir. 1997). Claim language defines claim scope. York Prods., Inc. v. Cent. Tractor Farm & Family Ctr., 99 F.3d 1568, 1572, 40 USPQ2d 1619, 1622 (Fed. Cir. 1996). To determine the meaning of disputed claim terms, however, a construing court may consider the patent specification and the administrative record leading to patent issuance. Whittaker Corp. v. UNR Indus., Inc., 911 F.2d 709, 711, 15 USPQ2d 1742, 1744 (Fed. Cir. 1990).

As found by the district court, "essentially" means "fundamentally." Webster's Third New Int'l Dictionary 777 (1986). "Free from" means "without." Thus, in other words, "essentially free from crystalline material" means "fundamentally without crystalline material." See In re Marosi, 710 F.2d 799, 803, 218 USPQ 289, 291-292 (Fed. Cir. 1983) (interpreting "essentially free" to mean that a material is present only as an unavoidable impurity). The claims do not further enlighten the amount of crystalline material permitted within the scope of claim 1.

The written description of the '181 patent discloses in several places that cefuroxime axetil should be "substantially amorphous." E.g., Col. 2, ll. 24-25. The written description further discloses: "The cefuroxime axetil ester in accordance with the invention is preferably essentially free from crystalline material." Col. 2, ll. 38-40. The examples in the written description also shed little further quantitative light on the meaning of "essentially free from crystalline material."

According to Example 1, an analysis of the prepared product by the Debye-Scherrer x-ray method "gave a plain halo (absence of crystals, confirming the amorphous

nature of the product)." Col. 8, ll. 8-9. The same analysis of the Example 18 product "showed a few faint lines which may suggest the presence of a few crystals." Example 21 states: "Microscopic examination suggested <1% crystalline material." Col. 10, ll. 4-5. Tests of several other examples by x-ray crystallography, microscopic examination, and infrared analyses showed a "substantially amorphous" product. No example specifically quantifies "substantially amorphous" or "essentially free from crystalline material."

The prosecution history of the '181 patent, however, is more illuminating. As originally filed on June 29, 1983, claims 1 and 4 of the application which led to the '181 patent recited:

> 1. Cefuroxime axetil in highly pure, substantially amorphous form.
> . . . .
> 4. The product of claim 1 essentially free from crystalline material.

Dependent claims are generally narrower in scope than the claims from which they depend. Lampi Corp. v. Am. Power Prods., Inc., 228 F.3d 1365, 1376, 56 USPQ2d 1445, 1453 (Fed. Cir. 2000). Accordingly, "essentially free from crystalline material," as recited in original dependent claim 4, would apparently carry a narrower meaning than "substantially amorphous." Example 22 of the written description states: "X-ray crystallography revealed the product was substantially amorphous with a small content of crystalline material." Col. 10, ll. 26-28. Thus, cefuroxime axetil that is "essentially free from crystalline material" must have less than "a small content of crystalline material."

During the prosecution of Glaxo's United States Patents Nos. 4,994,567 and 5,013,833, both related to the '181 patent and containing the same Example 22, Glaxo explained: "Example 22 of the specification has shown that the product contains approximately 10% crystalline material." Further, during trial, Glaxo conceded that Example 22 does indeed contain 10% crystalline material. As noted above, the written description characterizes Example 22 as "substantially amorphous." In the original

application, the independent claim 4 used the term "substantially amorphous," while a dependent claim used the narrower term "essentially free from crystalline material." This chain of reasoning suggests that "essentially free from crystalline material" means a maximum crystalline cefuroxime axetil content of less than 10%.

Other prosecution history bolsters this reading of "essentially free from crystalline material." The '181 patent claims priority to United Kingdom Patent Application No. 8222019. During prosecution of the '181 patent, Glaxo submitted a copy of the UK application to show its claim of priority. The UK application states:

> The cefuroxime 1-acetoxyethyl ester in accordance with the invention is preferably essentially free from crystalline material, by which we mean that any amount of crystalline material which may be present is low as to be undetectable by X-ray crystallography, i.e., that an X-ray photograph of a sample of the compound shows no rings. The crystalline content of such a sample may be assumed to be zero for all practical purposes.

Col. 3, ll. 25-33 (emphasis added).

To explain this language during trial, Glaxo submitted a 1983 internal Glaxo report of methods for detecting low levels of crystalline material in amorphous cefuroxime ester. Glaxo further submitted the declaration of its expert, Dr. Lancaster, explaining the 1983 report. In his declaration, Dr. Lancaster opined that "it is difficult to distinguish between 5%, 10%, and 15% mixtures" of crystalline material. He further opined: "the detection level is about 10 to 15% crystalline material." Based on this declaration and reference to various x-ray photographs, the district court determined that "a level between 10% to 15% is, 'for all practical purposes,' essentially free of crystalline material." Glaxo Group Ltd., slip op. at 33.

The 1983 report itself, however, explains more fully the value of x-ray photographs. In the presence of cefuroxime axetil with a crystalline content over 10%, X-ray photographs, according to the 1983 report, identify the particular isomers and polymorphs of the

crystalline material—not the presence of crystalline material in the first place. The report specifically explains that "Isomer A (I) did not show up in the 5% mixture but was visible in the 10 and 15% mixtures. Isomer A (II) was visible at the 5% level." A summary table in the report concludes that an appropriate X-ray photograph detection limit for crystalline material is 10%. In other words, a crystalline content above 10% would show up as rings in X-ray photographs. Therefore, because the UK priority application says that the X-ray photograph should show no rings, "essentially free from crystalline material" means a maximum crystalline content of less than 10%.

The inquiry under 35 U.S.C. § 271(e)(2) is a standard infringement test. "The only difference . . . is that the allegedly infringing drug has not yet been marketed and therefore the question of infringement must focus on what the ANDA applicant will likely market if its application is approved." Glaxo, Inc. v. Novopharm, Ltd., 110 F.3d 1562, 1569, 42 USPQ2d 1257, 1263 (Fed. Cir. 1997). Thus, to determine whether Ranbaxy's proposed product literally infringes the '181 patent, this court compares Ranbaxy's ANDA described product to claim 1 as construed. In order to infringe, Ranbaxy's proposed product must contain all the limitations recited in Glaxo's asserted claim either literally or under the doctrine of equivalents. Zelinski v. Brunswick Corp., 185 F.3d 1311, 1316, 51 USPQ2d 1590, 1593 (Fed. Cir. 1999). Because the product for which Ranbaxy seeks FDA approval contains a higher content of crystalline cefuroxime axetil than permitted by claim 1, Glaxo is unlikely to succeed in showing that Ranbaxy's product literally infringes the '181 patent.

Ranbaxy argues that infringement under the doctrine of equivalents in the present case is precluded by prosecution history estoppel. The district court did not specifically address infringement under the doctrine of equivalents. Rather, in a footnote, the district

court stated: "The [c]ourt also does not have to consider whether Ranbaxy's likely product infringes the '181 patent under the doctrine of equivalents. If it needed to do so, it most likely would have concluded that it would infringe the '181 patent under this doctrine as well." Glaxo Group Ltd., slip op. at 42, n.17. In another footnote, the district court stated: "The [c]ourt also notes that it does not appear that Glaxo's amendment satisfies the requirements for a 'narrowing amendment,' which the Festo Corp. court held precludes the application of the doctrine of equivalents." Id. at 38, n.15.

Glaxo's application which led to the '181 patent contained nine claims as originally filed in the United Stated Patent & Trademark Office (USPTO), including originally files claims 1 and 4 as described above. In the first USPTO Office Action, the examiner rejected all of the filed claims as being indefinite under 35 U.S.C. § 112, ¶ 2. The examiner stated: "It is not definite what is particularly included or excluded by the term 'highly pure, substantially amorphous form.' . . . It is also not clear how much crystalline material is permitted." In response, Glaxo cancelled claims 1 and 4 and added new claim 10, explaining: "Claims 1, 2 and 4 have been cancelled and Claim 10 added to the application . . . . Claim 10 is a combination of Claim 1, 2 and 4." Claim 10 of the application became claim 1 of the '181 patent. Thus, Glaxo narrowed the scope of issued claim 1 by adding the narrowing limitation of "essentially free from crystalline material" from originally filed claim 4.

Under this court's current law, "a narrowing amendment made for any reason related to the statutory requirements for a patent will give rise to prosecution history estoppel with respect to the amended claim element." Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 234 F.3d 558, 567, 56 USPQ2d 1865, 1870 (Fed. Cir. 2000) (en banc) (cert. granted). The definiteness requirement of § 112, ¶ 2 is such a statutory requirement. Id. "When a claim amendment creates prosecution history estoppel with regard to a claim

element, there is no range of equivalents for the amended claim element." Id. at 569. Thus, Glaxo cannot assert any scope of equivalents to the "essentially free from crystalline material" limitation of claim 1. Glaxo would not, therefore, likely succeed in showing that Ranbaxy's proposed product infringes claim 1 under the doctrine of equivalents.

Because this court's interpretation of the claims makes it unlikely that Glaxo will succeed in its infringement showing, this court need not address the other factors for a preliminary injunction. Reebok Int'l Ltd. v. J. Baker, Inc., 32 F.3d 1552, 1556, 31 USPQ2d 1781, 1783-84 (Fed. Cir. 1994). This court notes, however, that the district court determined that Ranbaxy would not be able to compensate Glaxo in the event of infringement. The record support for this assessment considers Glaxo's anticipated lost sales if its Ceftin® product faced any generic competition. Glaxo Group Ltd., slip op. at 44. The purpose of compensatory damages is not to punish the infringer, but to make the patentee whole. Aro Mfg. Co. v. Convertible Top Replacement Co., 377 U.S. 476, 507, 141 USPQ 681, 694 (1964) ("The question to be asked is 'Had the infringer not infringed, what would the patent holder . . . have made?'"). Thus, patent damages are not paid for a total amount of lost sales. Rather, if Ranbaxy were somehow found liable for infringement of the '181 patent, it would owe Glaxo either a reasonable royalty or lost profits on Glaxo's lost sales. Glaxo, however, made no showing of its anticipated lost profits. The record, therefore, does not show that Ranbaxy would be unable to compensate Glaxo for any potential infringement of the '181 patent.

Furthermore, under this court's claim construction, Glaxo is unlikely to prove that Ranbaxy's proposed cefuroxime axetil product infringes the '181 patent. Thus, the record does not support a showing that sale of Ranbaxy's product would irreparably harm Glaxo.

In its claim interpretation, the district court found "that Glaxo demonstrates that the balance of hardships tips, perhaps just slightly, in its favor." Glaxo Group Ltd., slip op. at 48. Stated otherwise, the district court acknowledged that this case presented a close call even under its claim interpretation. Under this court's conclusions, the likelihood of success and irreparable harm factors now fall in Ranbaxy's favor. Therefore, under this court's claim interpretation, the record no longer supports a preliminary injunction. This thus court vacates the district court's order entering a preliminary injunction against Ranbaxy and remands this case for further proceedings.

## CONCLUSION

The district court made an error of law in its claim construction and thereby abused its discretion in granting a preliminary injunction enjoining Ranbaxy from offering for sale or selling cefuroxime axetil products under Ranbaxy's ANDA.

## COSTS

Each party shall bear its own costs.

VACATED and REMANDED