United States Court of Appeals for the Federal Circuit

00-1260

BIOVAIL CORPORATION INTERNATIONAL,

BIOVAIL LABORATORIES,INC., and GALEPHAR P.R., INC. LTD.,

Plaintiffs-Appellants,

v.

ANDRX PHARMACEUTICALS, INC.,

Defendant-Appellee.

Eric C. Cohen, Welsh & Katz, Ltd., of Chicago, Illinois, argued for plaintiffs-appellants. With him on the brief were A. Sidney Katz, Robert B. Breisblatt, Philip D. Segrest, Jr., and Charles R. Krikorian. Of counsel was Benedict P. Kuehne, Sale & Keuhne, P.A., of Miami, Florida.

James V. Costigan, Hedman, Gibson & Costigan, P.C., of New York, New York, argued for defendant-appellee. With him on the brief were Martin P. Endres, and Alan B. Clement. Of counsel on the brief was Gerald J. Houlihan, Houlihan & Partners, P.A., of Miami, Florida.

Appealed from: United States District Court for the Southern District of Florida

Judge William P. Dimitrouleas

United States Court of Appeals for the Federal Circuit

00-1260

BIOVAIL CORPORATION INTERNATIONAL,

BIOVAIL LABORATORIES, INC., and GALEPHAR P.R., INC., LTD.,

Plaintiffs-Appellants,

v.

ANDRX PHARMACEUTICALS, INC.,

Defendant-Appellee.

DECIDED: February 13, 2001

Before NEWMAN, CLEVENGER, and GAJARSA, Circuit Judges.

GAJARSA, Circuit Judge.

DECISION

Biovail Corporation International, Biovail Laboratories, Inc., and Galephar P.R., Inc., Ltd. (collectively "Biovail") appeal the decision of the United States District Court for the Southern District of Florida, Biovail Corp. Int'l v. Andrx Pharm., Inc., No. 98-CV-7096 (S.D. Fla. Mar. 6, 2000), which determined after a bench trial that Andrx Pharmaceuticals, Inc. ("Andrx") does not infringe United States Patent No. 5,529,791 ("the '791 patent") either literally or under the doctrine of equivalents. We affirm.

BACKGROUND

Biovail Corporation International and Biovail Laboratories, Inc. are the exclusive licensees of the '791 patent, which is owned by Galephar P.R., Inc., Ltd. The '791 patent is directed to a once-a-day drug used to treat hypertension and angina. Claim 1 is the only independent claim of the '791 patent and is the only claim at issue in this case. It reads:

> 1. An extended-release galenical composition of one or more pharmaceutically-acceptable salts of Diltiazem which comprises
>
> beads containing an effective amount of one or more of said Diltiazem salts as the active ingredient,
>
> each bead containing one or more of the Diltiazem salts and an effective amount

> of a wetting agent in admixture with one or more Diltiazem salts to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein,
>
> said beads being coated with a microporous membrane comprising at least a water-soluble or water-dispersible polymer or copolymer, and a water-, acid-, and base-insoluble polymer and a pharmaceutically-acceptable adjuvant, and
>
> wherein the wetting agent is selected from the group consisting of sugars, C_{12}-C_{20} fatty acid esters of sucrose or xylose, glycerides of sucrose, fatty acid esters of polyoxyethylene, esters of fatty alcohols and polyoxyethylene, esters of sorbitan, esters of polyoxyethylene sorbitan, alcohol-polyglycide esters, glyceride-polyglycides, lecithins and a combination thereof.

U.S. Patent No. 5,529,791 (issued June 25, 1996) (emphasis and paragraphing added). Biovail markets the drug described in the '791 patent under the trade name Tiazac® .

On June 22, 1998, Andrx filed an Abbreviated New Drug Application ("ANDA") with the United States Food and Drug Administration ("FDA") pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act ("FD&C Act") for a generic version of Tiazac® . See 21 U.S.C. § 355(j) (1994). Andrx also filed a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), asserting that its ANDA product does not infringe the '791 patent and that the '791 patent is invalid.

Andrx's product comprises a bead encapsulated by a microporous membrane. This bead contains both diltiazem hydrochloride (a diltiazem salt) and sugar. Unlike Biovail's product, in Andrx's beads these components are not mixed during the manufacturing process. Rather, as produced, Andrx's bead is comprised of a sugar/starch core surrounded by a mixture of diltiazem hydrochloride, ethylcellulose, and polyvinylpyrrolidone.

On October 7, 1998, Biovail filed an action in the United States District Court for the Southern District of Florida alleging patent infringement pursuant to 35 U.S.C. § 271(e)(2)(A), which provides that it is an act of infringement to submit an application under section 505(j) of the FD&C Act for a drug claimed in a patent. Andrx denied infringing the '791 patent and counterclaimed that the '791 patent is invalid. The district court denied cross-motions for summary judgment. It subsequently held a bench trial, conducting both claim construction and infringement analyses.

The court construed the term "admixture" in claim 1 of the '791 patent to describe "two or more items [that] are commingled and interdispersed to obtain a homogeneous product." Citing expert testimony, it construed the term "wetting agent" as "any of a group of surface active agents which, when added to a liquid, cause the liquid to spread more easily over, or penetrate into, a solid surface."

The court proceeded to make several findings of fact. It determined that: "Biovail has failed to prove that an admixture between the sugar and the diltiazem [in Andrx product] forms in the body." The court found Biovail's tests unreliable and further stated:

"Biovail's own tests . . . do not show that a homogeneous admixture is formed in the Andrx product."

Based on its factual findings and claim construction, the district court determined that Andrx's product did not literally infringe the '791 patent. It also found that Biovail amended its claims during prosecution to "exclude a sugar core not in admixture with the diltiazem . . . in response to a prior art rejection." Therefore, the district court concluded that "Biovail is estopped from asserting that the inert sugar core of the Andrx formulation is a 'wetting agent' within the scope of the claims of the '791 patent" and consequently held that such prosecution history estoppel "operates as a complete bar to infringement by [the] doctrine of equivalents."

DISCUSSION

A. Standard of Review

Claim construction is a matter of law that this court reviews de novo. Markman v. Westview Instruments, Inc., 52 F.3d 967, 979, 34 USPQ2d 1321, 1329 (Fed. Cir. 1995) (en banc), aff'd, 517 U.S. 370 (1996). Literal infringement is a question of fact that we review under the clearly erroneous standard. Amhil Enters. Ltd. V. Wawa, Inc., 81 F.3d 1554, 1562, 38 USPQ2d 1471, 1476 (Fed. Cir. 1996). "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." Id. at 1562, 38 USPQ2d at 1476 (quoting United States v. United States Gypsum Co., 333 U.S. 364, 395 (1948)). Prosecution history estoppel is a legal question subject to de novo review on appeal to this court. Cybor Corp. v. FAS Techs. Inc., 138 F.3d 1448, 1460, 46 USPQ2d 1169, 1178 (Fed. Cir. 1998) (en banc). Infringement under the doctrine of equivalents is a factual finding reviewed for clear error. Ryco, Inc v. Ag-Bag Corp., 857 F.2d 1418, 1426, 8 USPQ2d 1323, 1329 (Fed. Cir. 1988).

B. Claim Construction

To construe a patent claim, a court first analyzes the intrinsic evidence of record — the claims and written description of the patent itself, and, if in evidence, the prosecution history. Markman, 52 F.3d at 979, 34 USPQ2d at 1329. When intrinsic evidence unambiguously describes the scope of a patented invention, reliance on extrinsic evidence is improper. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1583, 39 USPQ2d 1573, 1577 (Fed. Cir. 1996).

"Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition is clearly stated in the patent specification or file history." Id. at 1582, 39 USPQ2d at 1576. Therefore, we review both the specification and the applicable prosecution history to determine whether the patentee defined claim terminology in a manner inconsistent with its ordinary meaning. Id. at 1582, 39 USPQ2d at 1577.

It is not necessary for this court to construe the term "wetting agent." That is, the outcome of this case does not hinge on whether the sugar used in the core of Andrx's

product meets the "wetting agent" limitation of claim 1 of the ’791 patent. This court also need not determine whether claim 1 of the ’791 patent is limited to the product in its dry state or extends to the form of the product in vivo, because the outcome of this case does not turn on that issue.

This case turns on whether the "admixture" limitation in claim 1 of the ’791 patent must be "homogeneous." As a general proposition, a limitation that does not exist in a claim should not be read into that claim. See McCarty v. Lehigh Valley R. Co., 160 U.S. 110, 116 (1895). Neither the claims nor the specification of the ’791 patent require the "admixture" to be "homogeneous." Claim language, however, must be read consistently with the totality of the patent’s applicable prosecution history. Vitronics, 90 F.3d at 1582, 39 USPQ at 1577; Elkay Mfg. Co. v. Ebco Mfg. Co., 192 F.3d 973, 978, 52 USPQ2d 1007, 1112-13. (Fed. Cir. 1999).

The ’791 patent results from a series of continuation applications stemming from Application No. 721,396 ("the ’396 application"), which was filed on June 26, 1991. After multiple amendments, certain claims of the ’396 application issued as claims in United States Patent No. 5,288,505 ("the ’505 patent") on February 22, 1994. Biovail also filed a continuation of the ’396 application on May 28, 1993 — Application No. 68,951 ("the ’951 application"). After the ’951 application was rejected for, inter alia, double patenting over the ’505 patent, Biovail abandoned the ’951 application in favor of another continuation — Application No. 311,722 ("the ’722 application"). The ’722 application eventually issued as the ’791 patent on June 25, 1996.

"When multiple patents derive from the same initial application, the prosecution history regarding a claim limitation in any patent that has issued applies with equal force to subsequently issued patents that contain the same claim limitation." Elkay, 192 F.3d at 980, 52 USPQ2d at 1114; see also Jonsson v. The Stanley Works, 903 F.2d 812, 817-18, 14 USPQ2d 1863, 1868 (Fed. Cir. 1990) (providing that when two patents issued from continuation-in-part applications derived from one original application, the prosecution history of a claim limitation in the first patent to issue was properly applied to the same limitation in the second patent to issue). The claims in the ’396 application as originally filed did not include the term "admixture." The "admixture" limitation was added to claims in the ’396 application following an amendment after final rejection, and these claims issued as claims in the ’505 patent. The ’505 and ’791 patents both derive from the initial ’396 application. The "admixture" limitation appears in a similar context in both the ’505 and ’791 patents. Therefore, any prosecution history relating to the "admixture" limitation of the ’505 patent (which includes the prosecution history of the ’396 application) applies with equal force to that limitation in claim 1 of the ’791 patent.

The initial ’396 application was first rejected, inter alia, as anticipated by United States Patent No. 4,960,596, which issued to Debregeas et al. (the "Debregeas patent"). After an amendment, the ’396 application was finally rejected, inter alia, in view of Debregeas. Subsequent to an interview with the examiner, the ’396 applicant added the "admixture" limitation to the relevant claims in an amendment after final rejection.

To distinguish Debregeas in the remarks accompanying this amendment, the applicant stated: "By contrast [to the Debregeas invention,] the extrusion-spheronization process

[of the invention in the ’396 application] leads to homogeneous type beads while the ‘building-up’ process [of the Debregeas invention], starting with a sugar core, leads to heterogeneous type beads." (emphasis in original). The applicant further argued: "Clearly, it is impossible to have a sugar central core in a homogeneous bead as in [the ’396 application]. Such a bead [with a sugar central core] is, by nature, heterogeneous." (emphasis in original). The remarks accompanying the amendment after final rejection also provided that a bead produced by the extrusion-spheronization process of the ’791 patent "is necessarily a homogeneous bead composition." (emphasis in original).

The ’396 applicant also discussed Debregeas with the examiner in an interview after the final rejection of the ’396 application, but prior to the applicant’s submission of the amendment after final rejection. The examiner summary of that interview provides: "A declaration will be submitted. . . . A showing of a homogeneous admixture of [d]iltiazem in combination with the wetting agent[] . . . would be considered for distinction over [Debregeas]." The inventor of the product described in the ’396 application subsequently submitted a declaration. In the remarks accompanying the amendment after final rejection the applicant discussed that declaration, arguing, "the [d]eclaration establishes that the ‘core’ or ‘center’ of the present composition is homogeneous with respect to diltiazem and wetting agent." Further, the experiment discussed in the declaration provides, "that the ‘center’ or ‘core’ [of the product in the ’396 application] is an inherently homogeneous or uniform composition of diltiazem of one or more salts and wetting agent. . . ." After submission of the declaration and the amendment after final rejection — which added the "admixture" limitation — the examiner allowed the relevant claims over Debregeas. These claims issued as claims 1, 6, and 11 of the ’505 patent.

The prosecution history of the ’396 application clearly indicates that at least the "bead" described in the ’396 application, in claims 1, 6, and 11 of the ’505 patent, and in claim 1 of the ’791 patent must be "homogeneous." Claim 1 of the ’791 patent provides that the "bead" contains a diltiazem salt and a wetting agent in "admixture." Therefore, the admixture of diltiazem salt and wetting agent that comprises the bead of claim 1 of the ’791 patent must be homogeneous.

C. Literal Infringement

Literal infringement requires a patentee to prove by a preponderance of the evidence that every limitation of the asserted claim is literally met by the allegedly infringing device. Enercon v. Int’l Trade Comm’n, 151 F.3d 1376, 1384, 47 USPQ2d 1725, 1731 (Fed. Cir. 1998).

Biovail does not contend that Andrx’s product is homogeneously admixed in the dry state. The district court assessed a multitude of evidence, including expert witness testimony, to determine whether a homogeneous admixture of Andrx’s product forms in vivo.

The district court stated in its factual findings that "Biovail’s tests are not reliable," listed several reasons for this determination, and concluded: "Biovail’s own tests, particularly the Electron Scanning Microscope ("ESM") slides submitted in evidence, do

not show that a homogeneous admixture is formed in the Andrx product." It also determined as a finding of fact that, "Biovail has failed to prove that an admixture between the sugar and the diltiazem [in Andrx's product] forms in the body." The district court had previously construed "admixture" as "two or more items . . . commingled and interdispersed to obtain a homogeneous product." Therefore, the district court construed "admixture" in a manner consistent with this court's construction of that limitation. Consequently, when the district court found that Biovail failed to prove Andrx's product formed an admixture in the body, it referred to a homogeneous admixture.

Appellate courts are not ideally suited to unravel the processes of scientific phenomena. Zenith Labs., Inc. v. Bristol-Myers Squibb Co., 19 F.3d 1418, 1423, 30 USPQ2d 1285, 1289 (Fed. Cir. 1994). A trial judge or jury who hears witnesses and initially assesses evidence deserves considerable latitude in making findings of fact, particularly scientific findings of fact. Id. Indeed, the Supreme Court has charged trial court judges with the responsibility of performing a gate-keeping function to ensure that all expert testimony, including scientific testimony, is not only relevant, but also reliable. See Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137, 147 (1999) (extending the basic gate-keeping obligation for "scientific" testimony established in Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 589 (1993), to all expert testimony). The district court in this case analyzed a significant amount of scientific evidence and made factual findings based on that evidence. Regardless of its construction of the limitation "wetting agent," the district court found Biovail failed to prove by a preponderance of evidence that the "sugar" in Andrx's product forms a homogeneous admixture with diltiazem in the body. Because this finding was clearly supported by the evidence, it does not leave this court with "a definite and firm conviction that a mistake has been committed." Therefore, even assuming arguendo that "admixture" is not limited to dry state compositions and that sugar as used in Andrx's product is a "wetting agent," the district court's determination that Andrx's product does not literally infringe claim 1 of the '791 patent was not clearly erroneous.

D. Prosecution History Estoppel/Doctrine of Equivalents

This case falls squarely within the reach of this court's decision in Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd., 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) (en banc). "When a claim amendment creates prosecution history estoppel with regard to a claim element, there is no range of equivalents available for the amended claim element." Id. at 569, 56 USPQ2d at 1872. That is, "[a]pplication of the doctrine of equivalents to [that] claim element is completely barred . . . ." Id. This complete bar applies "regardless of whether the amendment is explained or unexplained, if the amendment narrows the scope of the claim for a reason related to patentability . . . ." Id. at 576, 56 USPQ2d at 1878.

In this case, the '391 applicant added the term "admixture" to the pertinent claims in the amendment after final rejection of the '396 application — prosecution history that applies to the "admixture" limitation of claim 1 of the '791 patent — to distinguish Debregeas. This amendment was related to patentability. Indeed, the '505 patent issued with the "admixture" limitation shortly after it was added. Further, in the examiner's summary of an interview with the applicant prior to submission of the amendment after

final rejection of the ’396 application, the examiner stated that a declaration, which was subsequently submitted, "showing . . . a homogeneous admixture of [d]iltiazem in combination with the wetting agent . . . would be considered for distinction over [Debregeas]."

Because the "admixture" limitation was added to the pertinent claim language in the relevant prosecution history for reasons related to patentability, Biovail is completely barred from claiming that any product not containing an "admixture" as properly construed by this court infringes claim 1 of the ’791 patent under the doctrine of equivalents. Id. That is, when application of the doctrine of equivalents to a limitation is completely barred due to prosecution history estoppel, a patentee asserting infringement must show by a preponderance of the evidence that an allegedly infringing device literally reads on that limitation as properly construed.

We have determined that the "admixture" limitation in claim 1 of the ’791 patent must be homogeneous. Biovail does not contend that diltiazem salt and sugar in Andrx’s product are homogeneously admixed in the dry state. As discussed previously, the district court’s factual findings that Biovail failed to prove by a preponderance of evidence that Andrx’s product forms a homogeneous admixture in the body are not clearly erroneous. Therefore, Andrx’s product does not meet the "admixture" limitation of claim 1 of the ’791 patent either in the dry state or in vivo. Consequently, based on the complete bar raised by prosecution history estoppel, Andrx’s product does not infringe claim 1 of the ’791 patent under the doctrine of equivalents.

E. Biovail’s Motion for Vacatur and Remand

Biovail has moved for vacatur and remand on the ground that Andrx did not advise Biovail of several (eleven) amendments filed to the ANDA after the close of discovery, and which were not made known to Biovail until after trial and decision and only shortly before scheduled appellate argument. It is an abuse of the judicial role for Andrx to ask us to review on appeal what should have been made known, and adequately explored, at trial. Under 21 U.S.C. § 355(j)(2)(B), there is an obligation to disclose the filing of an ANDA, as well as its content, to the patent holder and other interested parties. See 5 C.F.R. § 314.95 (2000). The obligation to inform the parties, and the trial court, as to any material amendment to the ANDA continues throughout the litigation that is artificially provoked under Paragraph IV. Andrx's failure to disclose the amendments it filed to the ANDA after the close of discovery constitutes a violation of that obligation.

However, in the interest of bringing this case to closure, we have reviewed the texts of these amendments, which have been provided in response to the motion now before us. We conclude that the amendments do not show reversible error in the district court's decision that infringement does not lie.

F. Attorneys’ Fees

Andrx filed a motion seeking attorneys’ fees. This motion is denied.

CONCLUSION

For the reasons set forth in this opinion, we affirm the district court's judgment that Andrx's product neither literally infringes claim 1 of the '791 patent nor infringes that claim under the doctrine of equivalents.

AFFIRMED.

COSTS

Each party shall bear its own costs.