United States Court of Appeals for the Federal Circuit

06-1179

PFIZER INC., PFIZER IRELAND PHARMACEUTICALS,
WARNER-LAMBERT COMPANY, WARNER-LAMBERT COMPANY, LLC
and WARNER-LAMBERT EXPORT, LTD.,

Plaintiffs-Appellees,

v.

RANBAXY LABORATORIES LIMITED
and RANBAXY PHARMACEUTICALS INCORPORATED,

Defendants-Appellants.

Rudolf E. Hutz, Connolly Bove Lodge & Hutz LLP, of Wilmington, Delaware, argued for plaintiffs-appellees. With him on the brief were Jeffrey B. Bove, Collins J. Seitz, Jr., Mary W. Bourke, and William E. McShane.

William R. Zimmerman, Knobbe, Martens, Olson & Bear, LLP, of Irvine, California, argued for defendants-appellants. With him on the brief were Darrell L. Olson, John P. Giezentanner, Douglas G. Muehlhauser, and Payson LeMeilleur, of Irvine, California; and Joseph M. Reisman and Darryl H. Steensma, of San Diego, California. Of counsel on the brief were Jay R. Deshmukh and George E. Heibel, Ranbaxy, Inc., of Princeton, New Jersey.

Appealed from: United States District Court for the District of Delaware

Judge Joseph J. Farnan, Jr.

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RANBAXY LABORATORIES LIMITED
and RANBAXY PHARMACEUTICALS, INCORPORATED,

Defendants-Appellants.

DECIDED: August 2, 2006

Before MICHEL, Chief Judge, SCHALL and DYK, Circuit Judges.

MICHEL, Chief Judge.

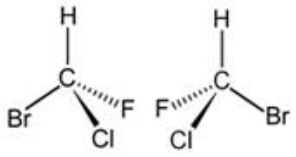
In this patent case concerning the prescription drug Lipitor®, which is used to reduce low-density lipoprotein (LDL) cholesterol levels, defendants-appellants Ranbaxy Laboratories Limited and Ranbaxy Pharmaceuticals, Inc. (collectively "Ranbaxy") appeal from a final judgment of the United States District Court for the District of Delaware. Plaintiffs-appellees Pfizer Inc., Pfizer Ireland Pharmaceuticals, Warner-Lambert Co., Warner-Lambert Co. LLC, and Warner-Lambert Export, Ltd. (collectively "Pfizer") filed four complaints, later consolidated into a single action,

alleging that the product described in Ranbaxy's Abbreviated New Drug Application ("ANDA") No. 76-477 infringed United States Patent Nos. 4,681,893 and 5,273,995 under 35 U.S.C. § 271(e)(2). Ranbaxy appeals the following rulings by the district court: (1) that claim 1 of the '893 patent was infringed; (2) that the '893 patent term extension was not proven invalid; (3) that claim 6 of the '995 patent was infringed; (4) that claim 6 was not proven invalid for failure to comply with § 112, ¶ 4; as anticipated or obvious; or for non-statutory double patenting; and (5) that the '995 patent was not proven unenforceable due to inequitable conduct.

Because we agree with the district court's claim construction of claim 1 of the '893 patent, we affirm the finding of infringement. We also affirm the ruling that the '893 patent term extension was not invalid. With respect to the '995 patent, however, we reverse on the question of invalidity under § 112, ¶ 4 and find the other issues moot.

I. BACKGROUND

Stereochemistry is the study of the three-dimensional structure of molecules. Stereoisomers have the same molecular formula or atomic composition, but different spatial arrangements. Enantiomers are a pair of stereoisomers that are non-superimposable mirror images of each other and often have distinct physical properties.[1] In organic chemistry, enantiomeric pairs include compounds that have one or more chiral centers, i.e., carbon atoms with four non-identical substituent atoms or groups of atoms. For example, the enantiomers of bromochlorofluoromethane are displayed here. A solid wedge is



[1] Thalidomide is a well-known example: one enantiomer is effective against morning sickness while the other causes birth defects.

used to indicate that the chlorine atom is projecting out of the page, while a hashed line indicates that the fluorine atom is behind the page.

To distinguish between different enantiomers of the same compound, chemists use various naming conventions. Enantiomers are sometimes called optical isomers because a pure enantiomer rotates plane-polarized light in a particular direction. If the light rotates clockwise, then that enantiomer is labeled "(+)" or "d" for dextrorotatory; its counterpart will rotate the light counterclockwise and is labeled "(-)" or "l" for levorotatory. A racemate (or racemic mixture) is an equal mixture of two enantiomers. A racemate is labeled "(±)" because it is not optically active (i.e., will not rotate plane-polarized light in either direction since its constituent enantiomers cancel each other out). Another system labels biochemical molecules "D" or "L" (unrelated to the labels "d" and "l", described above) by reference to the isomers of glyceraldehyde. Yet another nomenclature system labels each chiral center "R" or "S" according to Cahn-Ingold-Prelog priority rules.[2] Racemates are designated "RS" because they are comprised of both R-enantiomers and S-enantiomers.

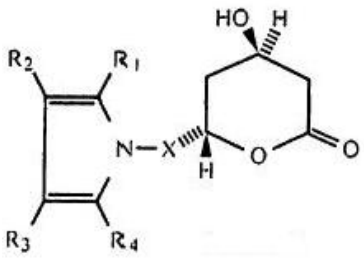
The terms "cis" and "trans" refer to the relative spatial arrangement of two particular substituents: "cis" means they are on the same side of a plane, while "trans" means they are on opposite sides. In organic compounds, the "plane" is typically a

[2] These rules are briefly summarized as follows. Each substituent is assigned a "priority" based on the molecular weight of the atom closest to the chiral center. If more than one substituent starts with the same type of atom, then the molecular weight of the next closest atom is used as a tiebreaker, so an ethyl group ($-C_2H_5$) has a higher priority than a methyl group ($-CH_3$). If there are multiple bonds, the atoms are counted once for each bond so a vinyl group ($-CH=CH_2$) has a higher priority than an ethyl group ($-C_2H_5$). The lowest priority (i.e., lowest molecular weight) substituent is then pointed away from the viewer. If the remaining three substituents are arranged from highest priority to lowest priority in a clockwise direction, then the molecule is labeled "R." If counterclockwise, then it is labeled "S."

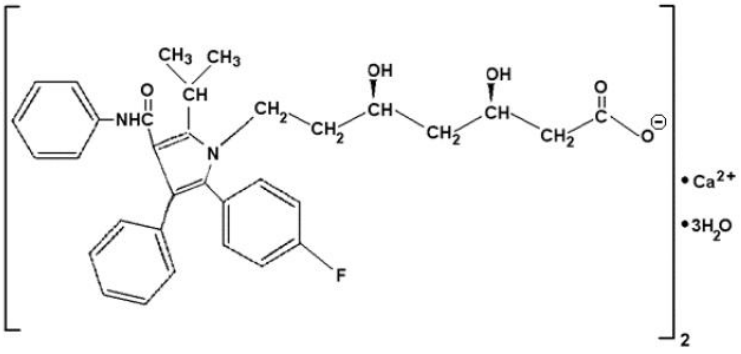
central ring structure. If there are two chiral centers on the aromatic ring, then there are four possible isomers: R-trans, S-trans, R-cis and S-cis. An equal mixture of R-trans and S-trans enantiomers is called the trans-racemate. An equal mixture of R-cis and S-cis enantiomers is called the cis-racemate.

* * *

Pfizer asserted claims 1-4, 8, and 9 of the '893 patent. Claim 1 is the only independent claim. It recites a compound having structural formula I (as shown), where there is a pyrrole ring on the left with four substituent groups (labeled R_1, R_2, R_3, and R_4), a pyran (or lactone) ring on the right and an alkyl chain (labeled X) joining the two rings. Claim 1 expressly defines the possible substituent groups represented by X, R_1, R_2, R_3, and R_4. Claim 1 also covers "a hydroxyl acid or pharmaceutically acceptable salts thereof, corresponding to the opened lactone ring of the compounds of structural formula I above."



Originally, the '893 patent was to expire on May 30, 2006, but Pfizer filed for a patent term extension pursuant to 35 U.S.C. § 156. Pfizer presented evidence that the active ingredient in Lipitor® is atorvastatin calcium or [R-(R*,R*)]-2-(4-fluorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate. Its structural formula is:



On July 15, 1998, the United States Patent and Trademark Office ("PTO") agreed that this compound was within the scope of the '893 patent and extended the patent term to September 24, 2009.

As for the '995 patent, Pfizer only asserted dependent claim 6.[3] The relevant claims are:

> 1. [R-(R *,R*)]-2-(4-fluorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)-carbonyl]-1H-pyrrole-1-heptanoic acid[4] or (2R-trans)-5-(4-fluorophenyl)-2-(1-methylethyl)-N,4-diphenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3-carboxamide;[5] or pharmaceutically acceptable salts thereof.
>
> 2. A compound of claim 1 which is [R-(R*R*)]-2-(4-fluorophenyl)-β-δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid.
>
> 6. The hemicalcium salt of the compound of claim 2.

A bench trial commenced on November 30, 2004. The district court issued its findings of fact and conclusions of law on December 16, 2005, concluding that both patents were infringed, not invalid and not unenforceable. Pfizer Inc. v. Ranbaxy Labs., 405 F. Supp. 2d 495 (D. Del. 2005). Judgment was entered on January 4, 2006. The next day, Ranbaxy filed its notice of appeal. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

II. DISCUSSION

Following a bench trial, a district court's conclusions of law are reviewed de novo while its findings of fact are reviewed for clear error. Allen Eng'g Corp. v. Bartell Indus.,

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[3] At oral argument, counsel for Ranbaxy revealed that Pfizer had entered into a covenant not to sue under independent claim 1 of the '995 patent. The parties also stipulated that claim 6 was a dependent claim.

[4] This compound is also known as atorvastatin acid.

[5] This compound is also known as atorvastatin lactone.

Inc., 299 F.3d 1336, 1343-44 (Fed. Cir. 2002). A factual finding is clearly erroneous if, despite some supporting evidence, "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).

A. '893 Patent.

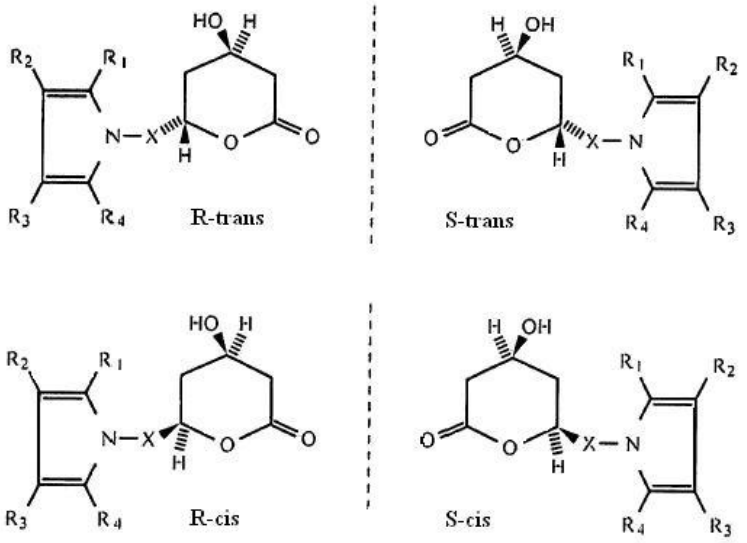
1. Correct Claim Construction.

Claim construction is a question of law reviewed de novo. Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1454-56 (Fed. Cir. 1998) (en banc). We determine the ordinary and customary meaning of claim terms as understood by a person of ordinary skill in the art, using the methodology first set forth in Vitronics Corp v. Conceptronics, Inc., 90 F.3d 1576, 1582-83 (Fed. Cir. 1996), and reaffirmed in Phillips v. AWH Corp., 415 F.3d 1303, 1312-19 (Fed. Cir. 2005) (en banc). The subsequent infringement analysis is reviewed "for clear error if performed by the court and for substantial evidence if performed by a jury." Young Dental Mfg. Co. v. Q3 Special Prods., 112 F.3d 1137, 1141 (Fed. Cir. 1997).

The parties agree that under the district court's claim construction, Ranbaxy's ANDA product infringes claim 1. On appeal, Ranbaxy argues that the district court erred in construing structural formula I "to embrace all trans-form isomers, including enantiomeric atorvastatin calcium" in lieu of accepting its proffered construction limiting claim 1 to racemates. Pfizer, 405 F. Supp. 2d at 507. Instead, Ranbaxy contends that structural formula I is limited to racemates, because (1) one skilled in the art would represent a racemate by depicting one of its constituent enantiomers; (2) the specification only discloses reaction sequences that produce racemates; (3) during

prosecution of foreign counterparts to the '893 patent, the patentee represented that its references to "trans" should be read as "trans-(±);" and (4) during prosecution of the '995 patent, the patentee argued that the '893 patent was limited to mixtures of enantiomers rather than the R-isomer. Thus, Ranbaxy argues, its ANDA product does not infringe claim 1 of the '893 patent because it is the R-enantiomer of atorvastatin calcium. We disagree.

It is undisputed that the drawing in claim 1 depicts an R-trans enantiomer. All four isomers of structural formula I are shown here.



These compounds are labeled "R" and "S" based on the stereochemistry of the chiral center at the top (i.e., 4-hydroxy position) of the pyran-2-one ring. The "cis" and "trans" designations refer to the spatial relationship between the hydroxyl group (-OH) and the alkylpyrrole group relative to the plane of the pyran-2-one ring.

The district court correctly observed that the '893 patent consistently describes the invention as a class of "trans" compounds. The specification of the '893 patent explains at col. 3, ll. 45-54:

> The compounds of structural formula I above possess two asymmetric carbon centers . . . [which] gives rise to four possible isomers, two of which are the R-cis- and S-cis-isomers and the other two of which are the R-trans- and S-trans-isomers. This invention contemplates only the trans-form of the compounds of formula I above.

We read this language to mean that the invention would otherwise encompass all four isomers of the compounds of structural formula I, but for the patentee's express disclaimer of the R-cis- and S-cis-isomers. There is no further disavowal of claim scope that would limit the '893 patent to trans-racemates. Indeed, as noted by the district court, the terms "racemate" or "racemic mixture" do not appear in the '893 patent; nor is claim 1, unlike claim 5, limited by a "trans-(±)" designation. In sum, the district court correctly found that no intrinsic evidence limits claim 1 of the '893 patent to trans-racemates, as opposed to an R-trans enantiomer, an S-trans enantiomer or any (equal or unequal) mixtures thereof.

We are not persuaded by Ranbaxy's arguments to the contrary. First, even accepting Ranbaxy's contention that a racemate is commonly represented by depicting one of its constituent enantiomers, it does not follow that the depiction of an R-enantiomer always represents only a racemate. Here, only an R-trans enantiomer is depicted in the '893 patent, yet the specification expressly indicates that there are four possible isomers of the compounds of structural formula I and limits the invention to the trans- form. If one skilled in the art would have understood the drawing of structural formula I to limit the scope of claim 1 to trans-racemates, then an express disclaimer of the cis- form would not have been necessary.

Second, while the examples do describe reaction sequences that produce racemates, restricting claim 1 on this basis would improperly import limitations from the

specification into the claims, which should be avoided unless the patentee clearly "intends for the claims and the embodiments in the specification to be strictly coextensive." Phillips, 415 F.3d at 1323. But here, the specification, at col. 10, ll. 36-38, states that "[t]hese examples are illustrative and are not to be read as limiting the scope of the invention as it is defined by the appended claims."

Third, we agree with the district court's conclusion that the statements made during prosecution of foreign counterparts to the '893 patent are irrelevant to claim construction because they were made in response to patentability requirements unique to Danish and European law. See TI Group Auto. Sys. (N. Am.), Inc. v. VDO N. Am. LLC, 375 F.3d 1126, 1136 (Fed. Cir. 2004). Likewise, statements made during prosecution of the later, unrelated '995 patent cannot be used to interpret claims of the '893 patent. See Goldenberg v. Cytogen, Inc., 373 F.3d 1158, 1167-68 (Fed. Cir. 2004) (finding statements in another patent or its prosecution history irrelevant to claim construction "[a]bsent a formal relationship or incorporation during prosecution" of the patent at issue); cf. Abbott Labs. v. Dey L.P., 287 F.3d 1097, 1104-05 (Fed. Cir. 2002) (finding arguments made during prosecution of a commonly-owned but unrelated patent did not create prosecution history estoppel). Finally, insofar as Ranbaxy restates the same argument under the guise of judicial estoppel, we are not persuaded.

Because claim 1 was correctly construed to include the enantiomeric trans-forms of the compounds of structural formula I, we affirm the finding of infringement.

2. Term Extension.

Under the Hatch-Waxman Act, if a patented product has been subject to a regulatory review period before its commercial marketing or use, an extension of the

patent term may be obtained. 35 U.S.C. § 156(c). In applying for a patent extension, the patentee has a duty of candor and good faith towards the PTO and must disclose any "material information adverse to a determination of entitlement to the extension sought." 37 C.F.R. § 1.765(a). The Director of the PTO is charged with deciding whether the patent is entitled to term extension, a decision which is given "great deference." Glaxo Operations UK Ltd. v. Quigg, 894 F.2d 392, 399 (Fed. Cir. 1990).

On appeal, Ranbaxy asserts that, when correctly construed, the '893 patent does not cover enantiomeric atorvastatin calcium, i.e., the active ingredient in Lipitor®, so it was not eligible for a patent term extension under 35 U.S.C. § 156. In the alternative, Ranbaxy argues that the term extension is invalid due to inequitable conduct because Pfizer failed to disclose the statements Warner-Lambert made during prosecution of the '995 patent and the foreign counterparts to the '893 patent.

Ranbaxy's first argument depends on its proffered claim construction, which we have already rejected. As to its allegations of inequitable conduct, the district court found that the allegedly withheld information was not material, and consequently did not need to be disclosed to the PTO, because those statements were "irrelevant to a determination of the scope of the claims of the '893 patent." Pfizer, 405 F. Supp. 2d at 512. This factual finding was not clearly erroneous. We thus agree that Ranbaxy failed to establish by clear and convincing evidence that the term extension was invalid.

B. '995 Patent.

With respect to the '995 patent, numerous issues have been raised on appeal. Rather than considering them in the order presented by the appellants, we first direct our attention to the question of validity under 35 U.S.C. § 112, ¶ 4, which provides:

> Subject to the following paragraph [concerning multiple dependent claims], a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

As described above, Pfizer only asserted dependent claim 6 of the '995 patent. This claim reads: "The hemicalcium salt of the compound of claim 2." Claim 2, in turn, is dependent on claim 1, which recites the following compounds: (1) atorvastatin acid; or (2) atorvastatin lactone; or (3) pharmaceutically acceptable salts thereof. Claim 2 itself, however, only recites atorvastatin acid. Notably, it does not include the pharmaceutically acceptable salts of atorvastatin acid.[6] Ranbaxy asserts that the district court erred in refusing to invalidate claim 6, even though it does not "incorporate by reference all the limitations of the claim to which it refers" and "then specify a further limitation of the subject matter," as required by § 112, ¶ 4. In other words, claim 6 does not narrow the scope of claim 2; instead, the two claims deal with non-overlapping subject matter.

The district court explicitly recognized that "there may be a technical problem in the drafting of claim 6." Pfizer, 405 F. Supp. 2d at 508. Yet, it declined to find that "this drafting problem is sufficient to render the claim invalid if the claim is read consistently with its meaning to those skilled in the art" because it was unable to find any Federal Circuit precedent applying § 112, ¶ 4 to invalidate a patent. Id. at 508-09. The district court understood § 112, ¶ 4 "to be limited to matters of form, rather than matters of

[6] Theoretically, a claimed acid could be liberally construed to include the corresponding salts. See Merck & Co., Inc. v. Teva Pharms. USA, Inc., 347 F.3d 1367, 1372 (Fed. Cir. 2003). But here, given the absence of the "pharmaceutically acceptable salts thereof" language which was used in claim 1, the intrinsic evidence would not have supported such an interpretation of claim 2.

substance," noting that the PTO treats a claim that fails to comply with this provision "as a matter to be addressed through an objection" rather than rejected as unpatentable. Id. at 509. In any event, it emphasized that no objections were made to claim 6, (or any of the other similarly-worded dependent claims), during prosecution. Id. at 509 n.7.

It is true that at the time the district court wrote its opinion, there was no applicable Federal Circuit precedent. More recently, however, we have suggested that a violation of § 112, ¶ 4 renders a patent invalid just as violations of other paragraphs of § 112 would. Curtiss-Wright Flow Control Corp., 438 F.3d 1374, 1380 (Fed. Cir. 2006). In Curtiss-Wright, the issue was one of claim differentiation. The court reasoned that "reading an additional limitation from a dependent claim into an independent claim would not only make that additional limitation superfluous, it might render the dependent claim invalid" for failing to add a limitation to those recited in the independent claim, as required by 35 U.S.C. § 112, ¶ 4. Id. Indeed, "[i]nvalidity of the patent or any claim in suit for failure to comply with any requirement of sections 112 or 251 of this title" is expressly included among the available defenses to an infringement suit. 35 U.S.C. § 282(3) (emphasis added).

We recognize that the patentee was attempting to claim what might otherwise have been patentable subject matter.[7] Indeed, claim 6 could have been properly drafted either as dependent from claim 1 or as an independent claim—i.e., "the hemicalcium salt of atorvastatin acid." But, we "should not rewrite claims to preserve

[7] The district court found that claim 6 was unambiguous to the extent that the patentee intended to claim the hemicalcium salt of atorvastatin acid. Pfizer, 405 F. Supp. 2d at 507. The court further recognized that "[a]s a matter of standard chemical nomenclature, chemists typically refer to a salt of an acid, even though they are aware that the complete acid is technically no longer present in the salt form." Id. at 508.

validity." Nazomi Commc'ns, Inc. v. Arm Holdings, PLC, 403 F.3d 1364, 1368 (Fed. Cir. 2005); see also Rhine v. Casio, Inc., 183 F.3d 1342, 1345 (Fed. Cir. 1999) ("[I]f the only claim construction that is consistent with the claim's language and the written description renders the claim invalid, then . . . the claim is simply invalid."). Ranbaxy correctly argues that claim 6 fails to "specify a further limitation of the subject matter" of the claim to which it refers because it is completely outside the scope of claim 2. We must therefore reverse the district court with respect to this issue and hold claim 6 invalid for failure to comply with § 112, ¶ 4.

Although the district court was reluctant to find the fourth paragraph of § 112 to be an invalidating provision, doing so does not exalt form over substance. Rather, it is consistent with the overall statutory scheme that requires applicants to satisfy certain requirements before obtaining a patent, some of which are more procedural or technical than others. See, e.g., 35 U.S.C. § 102(b) & (d) (establishing statutory one-year bars to patentability); 35 U.S.C. § 111(a)(2)(C) (requiring submission of an oath by the applicant); 35 U.S.C. § 111(a)(3) (requiring submission of a fee with the application); 35 U.S.C. § 116 (requiring joint inventors to apply for a patent jointly).

In light of this holding, appellants' remaining arguments concerning the '995 patent are rendered moot. We therefore decline to reach the remaining issues raised.

III. CONCLUSION

For the aforementioned reasons, we affirm-in-part, reverse-in-part and remand so the district court can modify the permanent injunction in a manner consistent with this opinion.

AFFIRMED-IN-PART, REVERSED-IN-PART and REMANDED.