United States Court of Appeals for the Federal Circuit

06-1102

ORTHO-MCNEIL PHARMACEUTICAL, INCORPORATED,

Plaintiff-Appellant,

v.

CARACO PHARMACEUTICAL LABORATORIES, LIMITED,

Defendant-Appellee.

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Appealed from: United States District Court for the Eastern District of Michigan

Judge George Caram Steeh

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DECIDED: January 19, 2007

Before SCHALL and GAJARSA, Circuit Judges, and MCKINNEY, Chief Judge. [*]

MCKINNEY, Chief Judge.

Plaintiff, Ortho-McNeil Pharmaceutical, Inc. ("Ortho"), appeals the district court's grant of defendant, Caraco Pharmaceutical Laboratories, Ltd's. ("Caraco's"), motion for summary judgment of non-infringement of claim 6 of U.S. Patent No. 5,336,691 ("the '691 patent"). See Ortho-McNeil Pharm. Inc. v. Caraco Pharm. Labs., Ltd. , No. 04-CV-73698, 2005 WL 2679788 (E.D. Mich. Oct. 19, 2005) ("District Court Opinion"). For the reasons set forth below, we affirm the judgment of the district court.

[*] Honorable Larry J. McKinney, Chief Judge of the United States District Court for the Southern District of Indiana, sitting by designation.

I.

BACKGROUND

A. The '691 Patent and Caraco's Abbreviated New Drug Application

The '691 patent has fifteen claims directed to a pharmaceutical composition comprising certain weight ratios of two known drugs, tramadol and acetaminophen. '691 Patent, col.11 l.18 to col.12 l.36. Both of these drugs act as pain relievers, i.e., analgesics. The '691 patent discloses that where these components are in certain ratios the pharmacological effects of the compositions are superadditive or synergistic. Id. Abstract. More specifically, the description of the invention reads:

> The [acetaminophen] and the tramadol material are generally present in a weight ratio of tramadol material to [acetaminophen] from about 1:1 to 1:1600. Certain ratios result in a composition which exhibits synergistic analgesic effects. For example, in a composition comprising a tramadol material and [acetaminophen], the ratio of the tramadol material: [acetaminophen] is preferably from about 1:5 to 1:1600; and, more preferably, from about 1:19 to 1:800.
>
> The most preferred ratios are from about 1:19 to 1:50. Compositions of a tramadol material and [acetaminophen] within these weight ratios have been shown to exhibit synergistic analgesic effects. In addition, the particular compositions wherein the ratio of the components are [sic] about 1:1 and about 1:5 are encompassed by the present invention.

Id. col.3 l.63 to col.4 l.8.

Figure 1 and Table 1 of the '691 patent report measured values, termed "ED50 values," that show the amount by weight of a combined dose of tramadol and acetaminophen needed to provide pain relief in 50% of the test subjects, in this case male mice. Id. col.8 ll.18-68 (describing the experimental design and the compilation of the data in Figure 1 and Table 1); id. Fig. 1; id. cols.9-12 (Table 1). The '691 patent

discloses that there are 95% confidence intervals around the ED50 values. Id. col.8 ll.61-64.

Caraco's Abbreviated New Drug Application ("ANDA") #77-184, as amended on or about July 26, 2005, evidences Caraco's intent to make and sell a pharmaceutical composition containing tramadol and acetaminophen with an average weight ratio of tramadol to acetaminophen of 1:8.67. Caraco's ANDA also expressly requires Caraco's formulation to have a weight ratio of no less than 1:7.5.[1] In response to Caraco's ANDA, Ortho alleged that Caraco infringed claim 6 of the '691 patent.

The only claim at issue is claim 6, a dependent claim, which, when read in conjunction with the two claims upon which it depends, states: "[A pharmaceutical composition comprising a tramadol material and acetaminophen], wherein the ratio of the tramadol material to acetaminophen is a weight ratio of about 1:5." Id. col.11 ll.19-34. As will be seen, the only claim construction dispute between the parties is the meaning of the phrase "about 1:5." The term "about" is used in all of the claims of the '691 patent to modify the weight ratios claimed therein. Id. col.11 l.19 to col.12 l.36.

B. Proceedings in the District Court

After Ortho sued Caraco for infringement of claim 6, in due course, Caraco moved for summary judgment of non-infringement. The only issue before the district court on summary judgment was infringement because the parties had stipulated to be bound by the outcome of Ortho-McNeil Pharmaceutical, Inc. v. Kali Laboratories, Inc.,

[1] Although expressing ratios in fractional form indicates that 1:8.67 is less than 1:7.5, the parties, their experts, and the record have adopted the terminology that compares the second number of the ratio. For simplicity, we do as well in this case. Therefore, for example, because 8.67 is greater than 7.5, we refer to the ratio 1:8.67 as greater than the ratio 1:7.5.

No. 02-CV-5707-JCL-MF (D.N.J.), and Ortho-McNeil Pharmaceutical, Inc. v. Teva Pharamceutical Industries, Ltd., No. 04-CV-886-HAA-GDH (D.N.J), on all issues relating to validity and enforceability.[2] A major point of contention between the parties was the proper construction of the term "about 1:5." Caraco argued that the proper construction is "approximately 1:5, subject perhaps to minor measuring errors of, say, 5 or 10%." Ortho argued that the proper construction is "approximately 1:5, and . . . encompasses a range of ratios of at least 1:3.6 to 1:7.1."

Under either claim construction, Caraco argued its ANDA-defined product did not literally infringe. With respect to infringement under the doctrine of equivalents, Caraco argued that the doctrine should not apply to broaden the scope of the "about 1:5" limitation beyond the range of ratios suggested by the confidence intervals in the patent because to do so would, alternatively, improperly expand a narrow claim limitation, improperly eliminate the 1:5 claim limitation, or improperly encompass the prior art disclosed in U.S. Patent No. 3,652,589 to Flick, et al. ("the Flick patent"). At argument in the district court, Caraco also stated that prosecution history estoppel should apply because, during reissue proceedings relating to the '691 patent, Ortho narrowed the "about 1:5" limitation to something very close to 1:5 when Ortho described the 1:5 limitation and clearly distinguished it from the 1:10 limitation disclosed in the Flick patent.

Ortho argued that, under its construction, there were issues of fact as to literal infringement. In addition, Ortho contended that its experts would opine that, under the

[2] Both of these cases are in their early stages. The defendant in each case has moved for summary judgment, but the district court has not yet ruled on the motions.

function-way-result test, Caraco's product with a tramadol to acetaminophen average weight ratio of 1:8.67 was indistinguishable from that with a ratio of 1:5. Ortho averred that this court's precedent precluded a finding that any limitation on the doctrine of equivalents was applicable.

The district court construed the "about 1:5" limitation of claim 6 to mean "approximately 1:5, encompassing a range of ratios no greater than 1:3.6 to 1:7.1." District Court Opinion at *4. In reaching this conclusion, the district court relied upon both intrinsic and extrinsic evidence. The intrinsic evidence upon which the district court relied included the claims and the specification. The extrinsic evidence upon which the court relied consisted, in part, of the opinions of Ortho's experts, Donald R. Stanski, M.D. ("Dr. Stanski"), and Eric Smith, Ph.D. ("Dr. Smith"), who opined that one of ordinary skill in the art would conclude that the "about 1:5" limitation would include a range of ratios that would extend up to and include 1:7.1. Id. at *3. The experts further opined that the lower end of the range of ratios that are statistically indistinguishable from the 1:5 ratio is 1:3.6. Id. (citing Stanski Inf. Rep., pp. 2, 7 ¶ 12; Smith Inf. Rep. p. 25).

The district court also considered evidence related to Ortho's application to reissue the '691 patent, which was pending while proceedings involving the '691 patent were ongoing in the district court.[3] In its January 20, 2004, application for reissue, Ortho stated that it "believe[d] the original patent to be wholly or partly inoperative or

[3] On January 20, 2004, Ortho applied for reissue of the '691 patent. On August 1, 2006, the '691 patent reissued as U.S. Reissued Patent RE39,221 E ("the '221 reissue patent"). Other than being rewritten in independent form, the claim asserted here, claim 6, survived reissue unchanged. Likewise, the relevant portions of the specification remain unchanged. Except where the context requires otherwise, we refer to the patent at issue as the '691 patent.

invalid . . . by reason of the patentee claiming more or less than patentee had the right to claim in the patent." The application retained claim 6, rewritten in independent form; canceled claims 1 through 5, and claims 7 through 14; and added claims 16 through 66. The new claims are written in a more narrow form than the original claims, using the phrase "comprising an active ingredient that consists essentially of," instead of the broader "comprising" language of the '691 patent. To illustrate, new claim 16 of the '221 reissue patent reads: "A pharmaceutical composition comprising an active ingredient that consists essentially of tramadol and acetaminophen, wherein the ratio of tramadol to acetaminophen is a weight ratio from about 1:1 to about 1:1600." Other than the more limiting language just noted, like the other cancelled claims, this claim is identical to claim 1 of the '691 patent. See '691 Patent, col.11 ll.19-22.

During the reissue proceedings, upon rejection by the examiner of all of the claims under 35 U.S.C. § 102(b) as anticipated by a disclosure of a tramadol-containing composition at column 12 of the Flick patent, Ortho distinguished the "about 1:5" limitation of claim 6. Specifically, Ortho stated:

> Although the text appearing at column 12, lines 66-75 [of the Flick patent] does refer to acetaminophen-containing tablets, such tablets are said to have a tramadol to acetaminophen ratio of 1:10, which differs from the ratios recited, respectively, in claims 6, 15, and 23 ("about 1:5"), claim 21 ("about 1:1"), and claims 55-66 ("about 1:19 to about 1:50").

As noted above, during this appeal, on August 1, 2006, the '691 patent reissued as U.S. Reissued Patent No. RE39,221 E ("the '221 reissue patent"). The claim at issue in this case, claim 6, issued as written in the reissue application.

Under its construction, the district court concluded that Caraco's ANDA-defined product did not literally infringe the '691 patent. District Court Opinion at *4. In addition,

the district court decided that there was no infringement under the doctrine of equivalents. Relying on the doctrine of claim vitiation, see Freedman Seating Co. v. Am. Seating Co., 420 F.3d 1350, 1362 (Fed. Cir. 2005), the court concluded that finding infringement by Caraco's formulation with an average weight ratio of 1:8.67 would render meaningless the "about 1:5" limitation. District Court Opinion at *5-6. The court thus rejected Ortho's claim of infringement under the doctrine of equivalents. In asserting infringement under the doctrine of equivalents, Ortho relied on its experts, Dr. Stanski and Dr. Smith. Dr. Stanski opined that under any doctrine of equivalents approach, a weight ratio of 1:8.76 is substantially similar to a weight ratio of 1:5. He claimed that he based his opinion on his own experience, one or more scientific principles associated with analgesics in general (which he did not identify), the '691 patent, and the conclusions of Dr. Smith's August 4, 2005, report. In his report, Dr. Smith stated that he "determined that a composition containing a ratio by weight of tramadol to acetaminophen of 1:5 is statistically indistinguishable from weight ratios of tramadol to acetaminophen ranging from 1:4.79 to 1:7.12" and that the "degree of synergy of a composition with a weight ratio of tramadol to acetaminophen of 1:5 is similar to the degree of synergy of a composition with a weight ratio of tramadol to acetaminophen of 1:8.67."

II.

DISCUSSION

A. Standard of Review

A district court's grant of summary judgment is reviewed de novo. Cook Biotech Inc. v. Acell, Inc., 460 F.3d 1365, 1372 (Fed. Cir. 2006). Summary judgment is

appropriate where there is no genuine issue of material fact and the moving party is entitled to a judgment as a matter of law. Id. (citing Fed. R. Civ. P. 56(c)).

Claim construction is also reviewed de novo. Id. "When interpreting claims, we inquire into how a person of ordinary skill in the art would have understood [the] claim terms at the time of the invention." Id. (quoting Pfizer, Inc. v. Teva Pharm. USA, Inc., 429 F.3d 1364, 1372-73 (Fed. Cir. 2005) (citing Phillips v. AWH Corp., 415 F.3d 1303 (Fed. Cir. 2005) (en banc))). A person of ordinary skill in the art is deemed to have read the claim term in the context of the entire patent, including the other claims, the specification and the prosecution history. Phillips, 415 F.3d at 1314.

"Infringement, whether literal or under the doctrine of equivalents, is a question of fact." Cook Biotech, 460 F.3d at 1373. In the summary judgment setting, the proper inquiry is whether or not, drawing all justifiable inferences in favor of the non-moving party, the evidence is such that a reasonable jury could return a verdict for the non-movant. Id. "Infringement under the doctrine of equivalents requires that any differences between the claim elements at issue and the corresponding elements of the accused product be insubstantial." Novartis Pharm. Corp. v. Eon Labs Mfg., Inc., 363 F.3d 1306, 1312 (Fed. Cir. 2004) (citing Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 39-40 (1997)). The court, as a matter of law, determines legal limitations on the application of the doctrine of equivalents. Abbott Labs. v. Dey, L.P., 287 F.3d 1097, 1103 (Fed. Cir. 2002).

B. Claim Construction

The central question in this case is the proper construction of the disputed claim limitation, "about 1:5." Although both the parties and the district court seem to agree

that the term "about" means "approximately," the parties and the district court disagree over the numerical limits that that term imparts to the limitation "1:5" in this case.

This court has looked at the meaning of the term "about," and similar qualifying words or phrases, in other cases and has developed an approach to the interpretation of such terms:

> [T]he word "about" does not have a universal meaning in patent claims, . . . the meaning depends upon the technological facts of the particular case.
>
> * * *
>
> The use of the word "about," avoids a strict numerical boundary to the specified parameter. Its range must be interpreted in its technological and stylistic context. We thus consider how the term . . . was used in the patent specification, the prosecution history, and other claims. It is appropriate to consider the effects of varying that parameter, for the inventor's intended meaning is relevant. Extrinsic evidence of meaning and usage in the art may be helpful in determining the criticality of the parameter . . . .

Pall Corp. v. Micron Separations, Inc., 66 F.3d 1211, 1217 (Fed. Cir. 1995) (citations omitted). See also Modine Mfg. Co. v. United States Int'l Trade Comm'n, 75 F.3d 1545, 1554 (Fed. Cir. 1996) (stating that "the usage [of the term 'about'] can usually be understood in light of the technology embodied by the invention"); Conopco, Inc. v. May Dep't Stores Co., 46 F.3d 1556 (Fed. Cir. 1994) (discussing the criticality of the claimed ratio to the invention and whether or not one of ordinary skill in the art would have read the modifier "about" expansively in light of the intrinsic evidence).

We must focus, then, on the criticality of the 1:5 ratio to the invention in claim 6 of the '691 patent. The intrinsic evidence points to a meaning for the term "about 1:5" that is narrow because the 1:5 weight ratio, along with the 1:1 weight ratio, is distinctly claimed and distinguished from other broader weight ratio ranges in the patent. There

are fifteen claims in the '691 patent, all of which use the term "about" to modify the weight ratio or weight ratio ranges of tramadol to acetaminophen.[4] '691 Patent, cols.11-12. There are two claims, claim 4 and disputed claim 6, that claim a single weight ratio; the other claims distinctly point out ranges of weight ratios. For example, independent claim 1 reads: "A pharmaceutical composition comprising a tramadol material and acetaminophen, wherein the ratio of the tramadol material to acetaminophen is a weight ratio from about 1:1 to about 1:1600." Id. col.11 ll.19-22. This leads to a conclusion that one of ordinary skill in the art would understand the inventors intended a range when they claimed one and something more precise when they did not.

The criticality of the "about 1:5" parameter to the claimed invention is also supported by other intrinsic evidence. As noted, in the specification, the inventors disclose the following:

> The [acetaminophen] and the tramadol material are generally present in a weight ratio of tramadol material to [acetaminophen] from about 1:1 to 1:1600. Certain ratios result in a composition which exhibits synergistic analgesic effects. For example, in a composition comprising a tramadol material and [acetaminophen], the ratio of tramadol material: [acetaminophen] is preferably from about 1:5 to 1:1600; and more preferably, from about 1:19 to 1:800.
>
> The most preferred ratios are from about 1:19 to 1:50. Compositions of tramadol material and [acetaminophen] within these weight ratios have been shown to exhibit synergistic analgesic effects. In addition, the particular compositions wherein the ratio of the components are [sic] about 1:1 and about 1:5 are encompassed by the present invention.

Id. col.3 l.63 to col.4 l.8. These paragraphs suggest that the qualifier "about" is narrow because to find otherwise would allow the scope of the more specifically identified ratio,

[4] This is identical to the treatment of weight ratios and weight ratio ranges in the '221 reissue patent. Both specific weight ratios and weight ratios in ranges are modified by the term "about." '221 Reissue Patent, cols.11-14.

1:5, to encompass a range of ratios that could potentially render meaningless another claim's limitation, namely the 1:1 limitation.

Furthermore, the data points from the experiments described in the specification support a conclusion that the more specifically identified ratio of 1:5 was meant to encompass compositions very close to that ratio. The experiments disclosed in the specification show data points for ratios of tramadol to acetaminophen in the lower ratio quadrant of 1:1, 1:3, 1:5, 1:5.7, and 1:15. '691 Patent, col.7 l.49 to col.8 l.68; id. Fig. 1 & Table 1. Yet, the patentees chose to specifically claim ratios of 1:1 and 1:5. If the data suggested to the inventors that a range of ratios in this lower ratio quadrant was desirable, they could easily have claimed a ratio range of "about 1:1 to about 1:5," or even a ratio range of "about 1:3 to about 1:5," but they did not. Instead, they chose a specific data point for claim 6 of precisely 1:5. Moreover, the identification of the 1:5 ratio in both claim 6 and the specification is especially important when the only other specifically identified ratio is close to it, 1:1, and the other claims point to a broad range of ratios. This dichotomy between the specific ratio of 1:5 and the broader ratio ranges of the other claims points to a narrow scope for the "about 1:5" limitation.

As discussed above, the district court relied in part upon Ortho's expert evidence to arrive at its claim construction. Ortho's expert, Dr. Stanski, noted that the data in the patent shows a synergistic analgesic effect for many ratios tested. In addition, he noted that the patent discloses statistical variability in the measured responses for each ratio. Dr. Stanski stated that "[b]ased on that statistical variability and [his] expertise, [he] can use statistical analyses to determine confidence bounds for the data in the patent, and [is] thus able to determine an upper bound and lower bound for the 1:5 weight ratio."

Dr. Stanski concluded that "the ratio of 'about 1:5' would not be statistically different from a ratio up to and including 1:7.1 and a ratio down to and including 1:3.6." In other words, Dr. Stanski opined that "about 1:5" means "about 1:5, which includes a ratio up to and including 1:7.1."

Considering the intrinsic and extrinsic evidence in this case, we see no error in the district court's construction of the term "about 1:5" to mean "approximately 1:5, encompassing a range of ratios no greater than 1:3.6 to 1:7.1."

C. Infringement

Under the district court's claim construction, with which we agree, there can be no literal infringement because Caraco's formulation must have a weight ratio of tramadol to acetaminophen of no less than 1:7.5. The issue we must decide then is whether the district court erred in granting summary judgment of non-infringement under the doctrine of equivalents. The district court determined that a holding that Caraco's product infringed claim 6 of the '691 patent under the doctrine of equivalents would impermissibly vitiate the limitation of claim 1 of a weight ratio of tramadol to acetaminophen of "about 1:5." We see no error in that determination.

As discussed above in connection with claim construction, the 1:5 parameter was critical to the invention. Moreover, the '691 patent points out the 95% confidence levels and makes them relevant to determining the scope of the invention. An infringement analysis that stretches the bounds of the "about 1:5" limitation beyond those confidence intervals directly conflicts with the patent's express claim to both the 1:1 and the 1:5 ratios. The patent specification distinctly identifies the 1:5 ratio versus all the other ratios or ratio ranges. Under this circumstance, whether or not the 1:5 ratio's analgesic

response is statistically different from that of other ratios is of no moment. The intrinsic evidence points to the desirability, and thus the criticality, of the 1:5 ratio versus other ratios.

Also relevant is the prosecution history of the ’691 patent and the ’221 reissue patent, described above. Ortho admitted that it claimed more than it was entitled to claim in the ’691 patent when, in its reissue application, it cancelled the broader “comprising” claims, except for claim 6. In sum, having so distinctly claimed the “about 1:5” ratio, Ortho cannot now argue that the parameter is broad enough to encompass, through the doctrine of equivalents, ratios outside of the confidence intervals expressly identified in the patent. We agree with the district court that to do so would eviscerate the limitation. The intrinsic evidence in this case points to the criticality of the “about 1:5” parameter, which necessitates a narrow claim construction and range of equivalents that does not encompass Caraco’s product. Similarly, we do not find Ortho’s other arguments persuasive.

III.

CONCLUSION

For these reasons, we conclude that the district court properly granted summary judgment of non-infringement in favor of defendant, Caraco Pharmaceutical Laboratories, Ltd., and against plaintiff, Ortho-McNeil Pharmaceutical, Inc.

AFFIRMED.