NOTE: This disposition is nonprecedential.

# United States Court of Appeals for the Federal Circuit

2006-1564

DAIICHI SANKYO CO., LTD.
(formerly known as Daiichi Pharmaceutical Co., Ltd.)
and DAIICHI SANKYO, INC. (formerly known as
Daiichi Pharmaceutical Corporation),

Plaintiffs-Appellees,

v.

APOTEX, INC. and APOTEX CORP.,

Defendants-Appellants.

Brian P. Murphy, Morgan, Lewis & Bockius LLP, of New York, New York, argued for plaintiffs-appellees. With him on the brief were David Leichtman, Daniel Murphy, and Oren D. Langer. Of counsel on the brief was James P. Flynn, Epstein, Becker & Green, PC, of Newark, New Jersey.

Robert B. Breisblatt, Welsh & Katz, Ltd., of Chicago, Illinois, argued for defendants-appellants. With him on the brief were A. Sidney Katz, Julie A. Katz, Philip D. Segrest, Jr., and Michael A. Krol. Of counsel on the brief was Steven Gerber, Adorno & Yoss, LLP, of Wayne, New Jersey.

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

Senior Judge William G. Bassler

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DECIDED: July 11, 2007

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Before MICHEL, Chief Judge, ARCHER, Senior Circuit Judge, and DYK, Circuit Judge.

ARCHER, Senior Circuit Judge.

Apotex, Inc. and Apotex Corp. (collectively "Apotex") appeal the judgment of the United States District Court for the District of New Jersey that Apotex infringes U.S. Pat. No. 5,401,741 ("the '741 patent") and that the '741 patent is not invalid or unenforceable. Daiichi Pharm. Co. v. Apotex, Inc., 441 F. Supp. 2d 672 (D.N.J. 2006) ("Validity Determination"). Because the invention of the '741 patent would have been obvious in view of the prior art, we reverse.

I

The ’741 patent is drawn to a method for treating bacterial ear infections by topically administering the antibiotic ofloxacin into the ear.[1] Claim 1 is representative and states “[a] method for treating otopathy which comprises the topical otic administration of an amount of ofloxacin or a salt thereof effective to treat otopathy in a pharmaceutically acceptable carrier to the area affected with otopathy.” ’741 Patent, col.6 ll.36-39.

Apotex filed an Abbreviated New Drug Application (“ANDA”) seeking approval to manufacture a generic ofloxacin ear drop, including a ¶ IV certification that the ’741 patent was invalid and/or not infringed. Following receipt of the ANDA, Daiichi, owner of the ’741 patent, sued Apotex for infringement. Following a Markman hearing, the district court construed the claim term “effective to treat” as “efficacious and safe.” Based on this construction and following a bench trial, the court concluded that the ’741 patent was not invalid. The court also found that Daiichi did not intend to deceive the Patent and Trademark Office during prosecution of the ’741 patent. Finally, because Apotex stipulated that the subject matter of its ANDA fell within the scope of the claims of the ’741 patent, the court found that Apotex infringed the ’741 patent.

Apotex appeals, and we have jurisdiction pursuant to 28 U.S.C. 1295(a)(1).

II

Obviousness is a question of law based on underlying questions of fact. Winner Int’l Royalty Corp. v. Wang, 202 F.3d 1340, 1348 (Fed. Cir. 2000). Thus, we review the

[1] The ’741 patent has an effective filing date of April 8, 1988.

ultimate determination of obviousness by a district court de novo and the underlying factual inquiries for clear error. Id.

The underlying factual inquiries in an obviousness analysis include: "(1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness." In re Dembiczak, 175 F.3d 994, 998 (Fed. Cir. 1999). In this case, we begin our analysis with the question of the level of ordinary skill in the prior art.

The district court concluded that the ordinary person skilled in the art pertaining to the '741 patent "would have a medical degree, experience treating patients with ear infections, and knowledge of the pharmacology and use of antibiotics. This person would be . . . a pediatrician or general practitioner—those doctors who are often the 'first line of defense' in treating ear infections and who, by virtue of their medical training, possess basic pharmacological knowledge." Daiichi Pharm. Co. v. Apotex, Inc., 380 F. Supp. 2d 478, 485 (D.N.J. 2005) ("Claim Construction Order"). Apotex argues that the district court clearly erred in this determination and that one having ordinary skill in the relevant art is properly defined as "a person engaged in developing new pharmaceuticals, formulations and treatment methods, or a specialist in ear treatments such as an otologist, otolaryngologist, or otorhinolaryngologist who also has training in pharmaceutical formulations."

"Factors that may be considered in determining level of ordinary skill in the art include: (1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in

the field." Envtl. Designs, Ltd. v. Union Oil Co., 713 F.2d 693, 696 (Fed. Cir. 1983) (citing Orthopedic Equip. Co., Inc. v. All Orthopedic Appliances, Inc., 707 F.3d 1376, 1381-82 (Fed. Cir. 1983)). These factors are not exhaustive but are merely a guide to determining the level of ordinary skill in the art.

In making its determination regarding the level of skill in the art, the district court noted that the parties had provided "little more than conclusory arguments concerning this issue in their briefs." As a result, the court looked to other decisions involving patents for a method of treating a physical condition for guidance. Only one case cited by the district court is binding on us, Merck & Co., Inc. v. Teva Pharm. USA, Inc., 347 F.3d 1367 (Fed. Cir. 2003). The district court was correct that in that case we affirmed the trial court's conclusion that a person having ordinary skill in the relevant art was a person having a medical degree, experience treating patients with osteoporosis, and knowledge of the pharmacology and usage of biphosponates—the compounds at issue in Merck. However, in Merck the level of skill in the art was not disputed by the parties. Thus, we simply accepted the district court's finding. That clearly is not the case before us. Therefore, the district court's reliance on the level of skill in the art stated in Merck was improper.

The art involved in the '741 patent is the creation of a compound to treat ear infections without damaging a patient's hearing. The inventors of the '741 patent were specialists in drug and ear treatments—not general practitioners or pediatricians. At the time of the invention, Inventor Sato was a university professor specializing in otorhinolaryngology; Inventor Handa was a clinical development department manager at Daiichi, where he was involved with new drug development and clinical trials; and

Inventor Kitahara was a research scientist at Daiichi engaged in the research and development of antibiotics. Additionally, others working in the same field as the inventors of the '741 patent were of the same skill level. See Daiichi Material for [C]onference on Development, Nov. 11, 1987 (stating that "there are many voices among medical persons concerned with otorhinolaryngology for demanding development of an otic solution making use of [ofloxacin]").

Further, the problem the invention of the '741 patent was trying to solve was to create a topical antibiotic compound to treat ear infections (otopathy) that did not have damage to the ear as a side effect. '741 Patent, col.1 ll.23-34. Indeed, most of the written description details the inventors' testing ofloxacin on guinea pigs and their findings that ototoxicity did not result from the use of their compound. Such animal testing is traditionally outside the realm of a general practitioner or pediatrician. Finally, while a general practitioner or pediatrician could (and would) prescribe the invention of the '741 patent to treat ear infections, he would not have the training or knowledge to develop the claimed compound absent some specialty training such as that possessed by the '741 patent's inventors. Accordingly, the level of ordinary skill in the art of the '741 patent is that of a person engaged in developing pharmaceutical formulations and treatment methods for the ear or a specialist in ear treatments such as an otologist, otolaryngologist, or otorhinolaryngologist who also has training in pharmaceutical formulations. Thus, the district court clearly erred in finding otherwise.

We now turn to the question of whether the invention of the '741 patent would have been obvious to one of ordinary skill in the art at the time of the invention. The district court's error in determining the level of ordinary skill in the art of the '741 patent

tainted its obviousness analysis. In view of the correct level of skill in the art and the evidence of record, we conclude that as a matter of law the '741 patent is invalid as obvious.

The district court construed "effective to treat" to include not only efficacy but safety. We need not decide whether safety is a positive limitation, because the evidence demonstrates that in view of the correct level of skill in the art using a topical formulation of ofloxacin to treat ear infections was not only obvious but safe.

An article published in 1986, taught the successful use of ear drops containing ciprofloxacin to treat middle ear infections. Gyrase inhibitor in local treatment of middle ear radical cavities chronically infected with problem microorganisms, HNO vol. 34, 511 (1986) (teaching a lack of ototoxicity for ciprofloxacin administered topically) ("Ganz"). This article explained that ciprofloxacin "would definitely have to be suitable for use as eardops" because ciprofloxacin, a gyrase inhibitor, was not subject to the drawbacks normally associated with local treatment of the ear with antibiotics, such as ototoxicity. Id. The subjects' ear infections were treated locally with a ciprofloxacin solution, and "[i]n not one case were side effects of any kind observed." Id. at 512.

The district court dismissed this finding of no side effects, and thus no ototoxicity, because the article reported that use of gyrase inhibitors "should be used only in difficult cases and exclusively by the otologist." Because an otologist was outside the level of ordinary skill in the art as determined by the district court, the district court found that the reference did not support Apotex's argument that ofloxacin, a gyrase inhibitor like

ciprofloxacin, was effective and safe to treat bacterial ear infections topically.[2] As explained above, the district court's determination of the level of ordinary skill in the art was incorrect; thus, so, too, was its dismissal of the teaching of the Ganz reference.

When testifying as to the relevance of the Ganz reference in 1988, Apotex's expert explained that ciprofloxacin is an antibiotic that is in the same family as ofloxacin, and thus "[o]ne would understand that a very close relative to Ciprofloxacin [sic] was safe and effective in treatment of middle ear disease, otitis media." Trial Tr. Vol. 3, 73-74 Nov. 3, 2005. When asked specifically what the Ganz reference would teach to one of ordinary skill in the art with regard to ofloxacin, he further opined that "someone of ordinary skill in the art would be taught that Ofloxacin [sic] would be very likely equally as effective as Ciprofloxacin [sic] when used topically to treat middle ear infections" and "one would also think it would be highly likely that Ofloxacin [sic] could be used in the middle ear with safety." Id. at 77. This testimony was based on the Ganz reference's statement that no side effects were observed combined with the fact that ofloxacin and ciprofloxacin were both from the same drug family (gyrase inhibitors). Id. at 77, 61. This testimony was not disputed by Daiichi's expert except on the basis that the Ganz reference did not convey the same teaching to one of lower skill in the art such as a practicing physician.

Daiichi's expert opined that the Ganz reference disclosed "nothing at all" relevant. This opinion was based on the fact that the article was directed at "a highly, highly subspecialized physician . . . which would be the otologist or the ear doctor" not a primary care physician or general practitioner. Trial Tr. Vol. 7, 72-73 Nov. 11, 2005. He

[2] Presumably, this explains why the district court did not refer to ofloxacin's similarity to ciprofloxacin in its opinion.

further explained that the article did not render the invention of the '741 patent obvious "most importantly because those of ordinary skill are defined as a population . . . of physicians that are completely different than the audience Dr. Ganz [the author] was writing to." Id. at 73-74. Thus, Daiichi's evidence as to why this reference did not render the invention of the '741 patent obvious was based on an improper determination of the level of skill in the art.[3]

Accordingly, the evidence demonstrates that a reasonable jury would have no other choice than to conclude that, in view of the Ganz reference, it would have been obvious to a person engaged in developing pharmaceutical formulations and treatment methods for the ear or to a specialist in ear treatments who also has training in pharmaceutical formulations to use ofloxacin in ear drops to topically treat ear infections.[4]

III

Because the invention of the '741 patent would have been obvious to one having ordinary skill in the art at the time of the invention, the judgment of the district court[5] is reversed.

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[3] Daiichi's only evidence with respect to this reference that does not rely on the level of skill in the art is its expert's conclusory statement that "[o]ne cannot extrapolate a safety profile for one antibiotic to another." This unsupported statement cannot refute the detailed testimony of Apotex's expert.

[4] Claim 4 of the '741 patent recites a concentration range for the ofloxacin in the compound—"about 0.05 to about 2% w/v." One of the prior art references, U.S. Patent No. 4,551,456, teaches the use of ofloxacin in antibiotic compounds where ofloxacin makes up "0.03 to 3% and especially 0.15% to 0.5%" of the compound. Col.1 ll. 37-39. Thus, the range claimed in the '741 patent falls within the scope of the prior art.

[5] Because we hold the '741 patent invalid as obvious, we need not reach Apotex's arguments that the '741 patent was anticipated or procured through inequitable conduct.