United States Court of Appeals for the Federal Circuit

2009-1362

ORTHO-MCNEIL PHARMACEUTICAL, INC.,
and ORTHO-MCNEIL, INC.,

Plaintiffs-Appellees,

and

DAIICHI SANKYO CO., LTD.,

Plaintiff-Appellee,

v.

LUPIN PHARMACEUTICALS, INC.
and LUPIN LTD.,

Defendants-Appellants.

George F. Pappas, Covington & Burling LLP, of Washington, DC, for plaintiffs-appellees Ortho-McNeil Pharmaceutical, Inc. et al. With him on the brief were Jeffrey B. Elikan and Gary Rubman.

Henry B. Gutman, Simpson Thacher & Bartlett LLP, of New York, New York, argued for plaintiff-appellee Daiichi Sankyo Company, Ltd. With him on the brief were Robert A. Bourque and Noah M. Leibowitz. Of counsel on the brief were Mark Boland, Michael R. Dzwonczyk and Keiko K. Takagi, Sughrue Mion, PLLC, of Washington, DC.

Robert F. Green, Leydig, Voit & Mayer, Ltd., of Chicago, Illinois, argued for defendants-appellants. With him on the brief was Christopher T. Griffith.

Howard S. Scher, Trial Attorney, Appellate Staff, Civil Division, United States Department of Justice, of Washington, DC, for amicus curiae United States. With him on the brief were Tony West, Assistant Attorney General, and Scott R. McIntosh, Attorney. Of counsel on the brief were James A. Toupin, General Counsel, Office of the General Counsel, United States International Trade Commission, of Washington, DC, and Raymond T. Chen, Deputy General Counsel and Solicitor, Office of the Solicitor, United States Patent and Trademark Office, of Arlington, Virginia.

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

Chief Judge Garrett E. Brown, Jr.

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Defendants-Appellants.

Appeal from the United States District Court for the District of New Jersey in Case No. 06-CV-4999, Chief Judge Garrett E. Brown, Jr.

DECIDED: May 10, 2010

Before NEWMAN, RADER and LINN, Circuit Judges.

NEWMAN, Circuit Judge.

Lupin Pharmaceuticals, Inc. and Lupin Ltd. (together "Lupin") appeal the judgment of the United States District Court for the District of New Jersey, sustaining the extension of the term of United States Patent No. 5,053,407 ("the '407 patent"), assigned to Daiichi

Sankyo Co. and exclusively licensed to Ortho-McNeil Pharmaceutical, Inc. and Ortho-McNeil, Inc. (collectively "Ortho").[1] The '407 patent is directed to an enantiomer of a racemic compound that had previously been approved by the Food and Drug Administration (FDA). On cross-motions for summary judgment, the district court agreed with the positions of the Patent and Trademark Office (PTO) and the FDA, and held that the statutory requirements for term extension were met for the '407 patent.

The district court enjoined Lupin from infringement during the extended term of the patent. We affirm the district court's judgment.

BACKGROUND

The '407 patent is for an antimicrobial compound having the common name levofloxacin. Levofloxacin is the levorotatory enantiomer (also designated the S(-) enantiomer) of the racemate ofloxacin, which is a known antimicrobial product. A racemate consists of equal amounts of spatial isomers called enantiomers, molecules that are mirror images of each other. Due to their spatial orientation, enantiomers are optically active and are characterized by whether they rotate plane-polarized light clockwise (dextrorotatory) or counter-clockwise (levorotatory). Although enantiomers and their racemates have the same chemical composition, they may differ in their physical, chemical, or biological properties. See, e.g., Sanofi-Synthelabo v. Apotex, Inc., 550 F.3d 1075, 1081 (Fed. Cir. 2008) (discussing possible differences among enantiomers and their racemates).

The record states that the inventors at Daiichi Sankyo tried unsuccessfully, over several years, to separate the constituent enantiomers from the racemate ofloxacin.

[1] Ortho-McNeil Pharm., Inc. v. Lupin Pharm., Inc., Civ. No. 06-4999, 2009 WL 1228448 (D.N.J. May 1, 2009).

They eventually produced the substantially pure enantiomers by direct synthesis from stereospecific starting materials. The inventors then determined that levofloxacin has properties that are significantly superior to those of ofloxacin. The '407 patent describes this synthesis, and presents data showing that levofloxacin is more effective as an antimicrobial agent, more rapidly available for biological effectiveness, and has lower acute toxicity and thus may be administered in higher doses than ofloxacin. See Ortho-McNeil Pharm. Inc. v. Mylan Labs., Inc., 348 F. Supp. 2d 713, 754 (N.D.W. Va. 2004) ("[L]evofloxacin is pharmaceutically superior to ofloxacin in virtually every relevant aspect."), aff'd, 161 F. App'x 944 (Fed. Cir. 2005).

The '407 patent issued on October 1, 1991. In 1996, after Ortho satisfied the regulatory requirements, the FDA approved levofloxacin for commercial marketing and use as the product having the brand name Levaquin®. Daiichi Sankyo then applied for extension of the patent term, in accordance with 35 U.S.C. §156. The PTO consulted with the FDA, as provided in their Memorandum of Understanding, 52 Fed. Reg. 17,830 (FDA May 12, 1987) (observing that "while it is the responsibility of the Commissioner of Patents and Trademarks to decide whether an applicant has satisfied these six conditions [of 35 U.S.C. §§156(a)(1)–(5) and 156(d)(1)], FDA possesses expertise and records regarding" some of these conditions). The FDA duly advised the PTO that regulatory approval for levofloxacin had been granted, stating that:

> A review of the Food and Drug Administration's official records indicates that this product [LEVAQUIN] was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. §156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of the product, as defined under 35 U.S.C. §156(f)(1), and interpreted by the courts in Glaxo Operations UK Ltd. v. Quigg, 706 F. Supp. 1224 (E.D. Va. 1989), aff'd, 894 F.2d 392 (Fed. Cir. 1990).

Ortho-McNeil, Civ. No. 06-4999, slip op. at 6 (alteration in original). The PTO concluded that extension of the patent term was warranted, and the PTO and FDA collaborated in calculation of the applicable extension of 810 days, in accordance with §156(d)(2)(A). See In re Patent Term Extension Application for U.S. Patent No. 5,053,407 (PTO Aug. 4, 1999).

Lupin invoked the litigation procedures of 21 U.S.C. §355(j)(2)(A)(vii)(IV) (Paragraph IV certification). In the district court, Lupin stipulated to the validity, enforceability, and infringement of the '407 patent, contesting only whether the '407 patent is entitled to the term extension.[2] The district court held that the extension was properly granted.

DISCUSSION

The grant of summary judgment receives plenary review on appeal. Int'l Visual Corp. v. Crown Metal Mfg. Co., 991 F.2d 768, 770 (Fed. Cir. 1993). Similarly, statutory interpretation receives plenary review. Madison Galleries, Ltd. v. United States, 870 F.2d 627, 629 (Fed. Cir. 1989). The relevant statutory provisions include:

> 35 U.S.C. §156(a) The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section . . . , if--
>
> * * * *
>
> (a)(4) the product has been subject to a regulatory review period before its commercial marketing or use;
>
> (a)(5)(A) except as provided in subparagraph (B) or (C) [not here relevant], the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred;
>
> * * * *
>
> §156(f) For purposes of this section:
>
> (1) The term "product" means:
>
> (A) A drug product.

[2] Validity of the '407 patent had previously been sustained. See Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 348 F. Supp. 2d 713 (N.D.W. Va. 2004), aff'd., 161 F. App'x 944 (Fed. Cir. 2005).

* * * *

> (2) The term "drug product" means the active ingredient of—
>
> (A) a new drug, antibiotic drug, or human biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act), . . .
>
> including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient.

The '407 patent claims the enantiomer levofloxacin as a new product and for use as an antimicrobial agent. Regulatory review of the drug product containing levofloxacin as active ingredient was required by the FDA, and permission for sale and use had been granted. The issue is whether this was the first permitted commercial marketing or use of levofloxacin, as required by 35 U.S.C. §156(a)(5)(A), for the racemate had previously been marketed. The district court held that the extension was in conformity with the practices of the PTO and the FDA with respect to enantiomers, and that the PTO's determination that levofloxacin is a different "product" than the racemate ofloxacin must be afforded "great deference," see Glaxo Operations UK Ltd. v. Quigg, 894 F.2d 392, 399 (Fed. Cir. 1990) ("[W]e will give great deference to the Commissioner's determinations as to which patented chemical compounds fall within Congress' definition of 'products,' but little or no deference to the Commissioner's surmise of Congress' intent in framing its definition.").

Lupin argued in the district court, and again on this appeal, that the PTO and the FDA have incorrectly interpreted the statute insofar as enantiomers are concerned. Lupin argued that an enantiomer is half of its racemate, and thus that the enantiomer levofloxacin was an "active ingredient" or component of the previously marketed racemate ofloxacin. Thus Lupin argued that levofloxacin is the same "drug product" as ofloxacin, and that since ofloxacin had been previously approved by the FDA, permission to market and use

levofloxacin was not "the first permitted commercial marketing or use of the product" as required by §156(a)(5)(A).

Ortho responded that an enantiomer has consistently been recognized, by the FDA and the PTO, as a different "drug product" from its racemate. Ortho pointed out that levofloxacin was viewed by the FDA as a new product requiring full regulatory approval, and that levofloxacin was viewed by the PTO as separately patentable. The FDA practices were explained by Dr. David Lin, a former acting Division Director in the FDA's Division of New Drug Chemistry, declaring that "in each and every instance in which it has considered the question, the FDA has described a racemate as a single active ingredient, distinct from its enantiomers, and each enantiomer as a single active ingredient distinct from the other and from the racemate," Lin Decl. ¶20, J.A. 1280 (including examples and Orange Book descriptions, at Lin Decl. Ex. C, J.A. 1278-1439). Nor does Lupin challenge the separate patentability of the enantiomer levofloxacin. Lupin also does not dispute that the federal approval for Levaquin® is the first permitted marketing of levofloxacin as a separate enantiomer. We discern no basis for challenging these established FDA and PTO practices. The FDA and PTO practices are in accordance with Glaxo, where the court held that "product" as used in §156(a) is the active ingredient present in the drug. See 894 F.2d at 393–95 (extending term of patent on a new separately patentable ester, although salts of the same acid had previously been approved).

Lupin presses the argument that the status of enantiomers with respect to eligibility for term extension was legislatively changed in 2007, in the statute that changed the FDA policy concerning data exclusivity for new enantiomer products. See 21 U.S.C. §355(u)(1) (Supp. II 2008). The new provision authorizes an applicant "for a non-racemic drug

containing as an active ingredient (including any ester or salt of the active ingredient) a single enantiomer that is contained in a racemic drug approved in another application" to, under certain conditions, "elect to have the single enantiomer not be considered the same active ingredient as that contained in the approved racemic drug." Id. Lupin argues that by specifically allowing an applicant to "elect" this separate treatment for enantiomers, Congress expressed its understanding that enantiomers were the same active ingredient as the racemate for all other purposes, including patent term extension.

No support for this theory appears in the legislative record, or elsewhere. Lupin's interpretation would change the long-standing term-extension policy of the FDA and the PTO; such a far-reaching change is not achieved by legislative silence. See Young v. Cmty. Nutrition Inst., 476 U.S. 974, 983 (1986) ("This failure to change the scheme under which the FDA operated is significant, for a congressional failure to revise or repeal the agency's interpretation is persuasive evidence that the interpretation is the one intended by Congress." (internal quotation marks omitted)); Daewoo Electronics Co. v. Int'l Union of Electronic, Electrical, Technical, Salaried & Machine Workers, 6 F.3d 1511, 1522 (Fed. Cir. 1993) (unrelated amendments to a statute without change in the provisions at issue is "evidence that the policy of the [agency] comports with congressional intent").

We affirm the district court's ruling that the '407 patent on levofloxacin was properly granted the statutory term extension, for the enantiomer is a different drug product from the racemate ofloxacin, and was subject to regulatory approval before it could be commercially marketed and used.

II

Based on Lupin's admissions of infringement, validity, and enforceability, the district court granted Ortho's motion to enjoin Lupin from making, using, offering to sell, selling, or importing levofloxacin in bulk or tablet form during the extended term of the '407 patent. Lupin argues that the injunction is improperly broad. Ortho states, and Lupin does not contradict, that Lupin did not object to the scope of the injunction when it was presented to the district court as a proposed order, and did not move for modification or raise any other objection when the order was entered by the district court. Although Lupin appears to have waived objection to the injunction, in the interest of completeness we have reviewed Lupin's challenge.

The grant of an injunction and its scope are reviewed for abuse of discretion. Ortho Pharm. Corp. v. Smith, 959 F.2d 936, 945 (Fed. Cir. 1992). Lupin argues that the extension of a patent term under 35 U.S.C. §156(b) applies only to sale and use of the patented product, and that the extended term does not encompass any other exclusionary patent rights, such as making or importing the patented product. Thus Lupin argues that the district court's injunction is improper as a matter of law.

It is recognized that an extended patent term does not apply to unrelated uses of an FDA-approved product. See Pfizer Inc. v. Dr. Reddy's Labs., Ltd., 359 F.3d 1361, 1366 (Fed. Cir. 2004) ("The 'rights derived' provision of §156(b) specifically limits the extension to 'any use approved for the product,' which means that other, e.g., non-pharmaceutical uses, are not subject to the extension."). Lupin does not assert that levofloxacin has any non-pharmaceutical uses. The district court did not abuse its discretion in issuing an injunction commensurate with the patent rights of exclusion, see 35 U.S.C. §271(a) (infringement

includes making, using, selling, and importing the patented invention). The scope of the injunction is sustained.

AFFIRMED