United States Court of Appeals for the Federal Circuit

2009-1393

PHOTOCURE ASA,

Plaintiff-Appellee,

v.

DAVID J. KAPPOS, Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office,

Defendant-Appellant.

John W. Bateman, Kenyon & Kenyon LLP, of Washington, DC, argued for plaintiff-appellee. With him on the brief were Richard L. DeLucia and Lawrence H. Frank, of New York, New York.

Scott R. McIntosh, Trial Attorney, Appellate Staff, Civil Division, United States Department of Justice, of Washington, DC, argued for defendant-appellant. With him on the brief were Tony West, Assistant Attorney General, Dana Boente, Acting United States Attorney, and Howard S. Scher, 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 Eastern District of Virginia

Judge Liam O'Grady

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DAVID J. KAPPOS, Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office,

Defendant-Appellant.

Appeal from the United States District Court for the Eastern District of Virginia in Case No. 1:08-CV-718, Judge Liam O'Grady.

DECIDED: May 10, 2010

Before NEWMAN, RADER and LINN, Circuit Judges.

NEWMAN, Circuit Judge.

This case concerns the applicability of the statute governing patent term extension, 35 U.S.C. §156, to the drug product having as its active ingredient the chemical compound methyl aminolevulinate hydrochloride ("MAL hydrochloride"), brand name Metvixia®. The Director of the United States Patent and Trademark Office (PTO) denied the extension, and Photocure sought review in the district court under the Administrative Procedure Act, 5

U.S.C. §702. The United States District Court for the Eastern District of Virginia held that the PTO's ruling was "not in accordance with law," and that the patent on MAL hydrochloride is subject to term extension.[1] The Director appeals, stating that the district court did not correctly define or apply the statutory terms "drug product" and "active ingredient." We affirm the decision of the district court.

DISCUSSION

The Patent Term Extension statute was enacted in recognition of the lengthy procedures associated with regulatory review of a new drug product, for the patent term continues to run although the product cannot be sold or used until authorized by the Food and Drug Administration (FDA). The statute was designed to restore a portion of the patent life lost during the period of regulatory review, in order to preserve the economic incentive for development of new therapeutic products. See H.R. Rep. No. 98-857, at 15 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2670 (discussing policy purposes of patent term extension). The following provisions are relevant to this case:

> 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--
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> * * * *
>
> (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;
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> * * * *
>
> §156(f) For purposes of this section:
>
> (1) The term "product" means:
>
> (A) A drug product.

[1] PhotoCure ASA v. Dudas, 622 F. Supp. 2d 338 (E.D. Va. 2009).

* * * *

> (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 drug product Metvixia®, whose active ingredient is MAL hydrochloride, is used in photochemotherapy or photodynamic therapy to treat actinic keratoses, which are precancerous cell growths on the skin. When the Metvixia® cream is applied to the skin, the MAL hydrochloride concentrates in the cells to be treated. The cells use MAL hydrochloride to form an excess amount of a naturally-occurring, light sensitive compound called protoporphyrin IX ("Pp"). On exposure to light, the Pp is activated and a chemical reaction ensues that kills the precancerous cells.

MAL hydrochloride was a new chemical compound, and was patented in U.S. Patent No. 6,034,267 ("the '267 patent") on the basis of its improved therapeutic properties as compared with the known compound aminolevulinic acid hydrochloride ("ALA hydrochloride"). MAL is the methyl ester of ALA. ALA hydrochloride had previously received FDA approval for the same therapeutic use. The specification of the '267 patent discusses and exemplifies the biological and physiological advantages of the MAL product over the ALA product; MAL is characterized as "better able to penetrate skin and other tissues," as a "better enhancer[] of Pp production than ALA," and as providing "improved selectivity for the target tissue to be treated." '267 patent col. 4 l.59–col. 5 l.1. Separate patentability of the MAL product and its use is not disputed.

The product containing MAL hydrochloride was a "new drug" in terms of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §321(p), and required full FDA approval. The

clinical and other tests for demonstration of safety and efficacy of the MAL hydrochloride product consumed four and a half years. After FDA approval was received, Photocure applied for the statutory extension of the term of the '267 patent. The PTO consulted with the FDA, in accordance with the Memorandum of Understanding, 52 Fed. Reg. 17,830 (FDA May 12, 1987). The FDA advised that MAL hydrochloride had received regulatory approval for the designated use. The FDA also pointed out that MAL hydrochloride is an ester of the previously FDA-approved ALA hydrochloride, and proposed that the requirements of §156(a)(5)(A) were not met.

The PTO then denied the requested term extension, stating that "active ingredient" in §156(f)(2) does not mean the product that was approved by the FDA, but rather means the "active moiety" of that product. The PTO held that MAL hydrochloride is the "same 'product'" as ALA hydrochloride because the "underlying molecule" of MAL is ALA, and the PTO stated that "ALA is simply formulated differently in the two different drugs." Final Decision Regarding Patent Term Extension Application Under 35 U.S.C. §156 For U.S. Patent No. 6,034,267 at 3, 5 (May 13, 2008). The PTO held that since a drug product containing ALA hydrochloride was previously approved by the FDA, the FDA's marketing approval of the MAL hydrochloride product was not the first commercial marketing or use of that "product."

Applying the provisions of the patent term extension statute, the district court considered the separate chemical composition, the separate patentability, and the separate FDA approval of MAL, and held that MAL hydrochloride is the active ingredient of a new drug product that required FDA approval, §156(f)(2)(A); that the MAL hydrochloride product was subject to a full regulatory review period before commercial marketing and use was

permitted, §156(a)(4); that this review permitted the first commercial marketing and use of the MAL hydrochloride product, §156(a)(5)(A); and therefore that the statutory requirements for term extension were met.

The PTO argues that the district court erred, and that the statutory term "active ingredient" does not mean the product that is present in the approved drug, but only the "active moiety" of the product, that is, the part responsible for the pharmacological properties. However, even on the PTO's incorrect statutory interpretation MAL would meet the criteria for term extension, for, as the '267 patent illustrates, the pharmacological properties of MAL differ from those of ALA, supporting the separate patentability of the MAL product. MAL hydrochloride is a different chemical compound from ALA hydrochloride, and it is not disputed that they differ in their biological properties, warranting separate patenting and separate regulatory approval, although their chemical structure is similar. Thus the district court held that MAL hydrochloride and ALA hydrochloride are different "products" with different "active ingredients," as the terms are used in §156, explaining that "a compound can only qualify as the 'active ingredient' of a drug if that compound itself is present in the drug," citing Glaxo Operations UK Ltd. v. Quigg, 894 F.2d 392, 393 (Fed. Cir. 1990). Photocure, 622 F. Supp. 2d at 347.

In Glaxo this court held that "product" in §156(a) means the product that is present in the drug for which federal approval was obtained. 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); Hoechst-Roussel Pharms., Inc. v. Lehman, 109 F.3d 756, 759 n.3 (Fed. Cir. 1997) ("For purposes of patent term extension, this active ingredient must be present in the drug product when administered."). The PTO argues that Glaxo did not

address the meaning of the term "active ingredient," and is therefore not in conflict with this court's decision in Pfizer Inc. v. Dr. Reddy's Laboratories, Ltd., 359 F.3d 1361 (Fed. Cir. 2004), which the PTO states supports its statutory interpretation. We agree that the decisions are not in conflict, but for a different reason, for Pfizer did not concern the Glaxo ruling that the active ingredient is the ingredient in the drug product as administered.

The issue in Pfizer was whether infringement of an extended patent on the drug amlodipine was avoided by changing the salt. This court held that the incentive purpose of term extension "was not intended to be defeated by simply changing the salt," id. at 1366, the court observing that the changed salt had no effect on the activity of the product, for the "active moiety" of the product was unchanged. Pfizer did not hold that extension is not available when an existing product is substantively changed in a way that produces a new and separately patentable product having improved properties and requiring full FDA approval. To the contrary, the disputed product in Pfizer was a salt that was included in the Pfizer patent claims and for which Pfizer had provided data to the FDA. The decision in Pfizer did not change the law of §156, and Pfizer did not concern a different, separately patented product requiring full regulatory approval.

The PTO argues that even if its view of Pfizer is not accepted, the agency's interpretation is entitled to deference in accordance with the persuasiveness of the agency's reasoning, citing Skidmore v. Swift & Co., 323 U.S. 134 (1944). In the district court, the Director also cited Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc., 467 U.S. 837 (1984), for the rule that when a statute is ambiguous the court should defer to the interpretation by the agency charged with administering the statute. The district court observed that Chevron does not apply because the statute is unambiguous,

and that Skidmore deference is not warranted because the PTO's interpretation is neither persuasive nor consistent. We agree with the district court. As this court held in Glaxo, "section 156(f)(2)'s operative terms, individually and as combined in the full definition, have a common and unambiguous meaning, which leaves no gap to be filled in by the administering agency." 894 F.2d at 398. Even if some level of deference were owed to the PTO's interpretation, neither Chevron nor Skidmore permits a court to defer to an incorrect agency interpretation. See Eldredge v. Dep't of the Interior, 451 F.3d 1337, 1343 (Fed. Cir. 2006) (declining to defer to the agency's "counterintuitive reading of the statute").

The PTO's statutory interpretation, which would exclude MAL hydrochloride from term extension, is contrary to the statutory purpose, for MAL is the active ingredient of a new and improved drug product. The district court correctly applied 35 U.S.C. §156 to extend the term of the patented product that is subject to regulatory review. We affirm the ruling that the patent on MAL hydrochloride is subject to term extension.

AFFIRMED