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Unique Active Ingredient in Drug Product Can Mean Patent Term Extension

The U.S. Court of Appeals for the Federal Circuit recently affirmed two separate district court decisions finding that patents on newly approved pharmaceutical active ingredients are eligible for patent term extension under 35 U.S.C. § 156(a)(5)(A), to account for time lost during Food and Drug Administration (FDA) regulatory review. In both *Photocure ASA v. Kappos* and *Ortho-McNeil Pharm., Inc. v. Lupin Pharm., Inc.*, the Federal Circuit reasoned that new active ingredients that are separately patentable and subject to regulatory review over related compounds may satisfy the § 156 requirement as the first permitted commercial marketing of the drug product following regulatory approval.

The new drug product in the *Photocure* case was METVIXIA[®], a prodrug (methyl ester) of a previously approved active moiety of LEVULAN KERASTICK[®]. The new drug product LEVAQUIN[®] in the *Lupin* case was a single enantiomer of a previously approved racemate sold as FLOXIN[®]. These holdings represent a shift in how the Federal Circuit views unique pharmaceutical compounds and appear to open the door to extending patent term for new drug products that are related to previously approved drugs, such as polymorphs, protected forms, and different stereoisomeric combinations.

The Patent Term Extension statute allows the term of a patent that claims a drug product, a method for using a drug product, or a method of manufacturing a drug product to be lengthened by up to five years if the drug product was subject to regulatory review before commercial marketing or use. The statute was intended “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.” *Photocure* at *1 (citing H.R. Rep. No. 98-857, at 15 (1984)). Patent term extension is possible if the product has been subject to a regulatory review period before its commercial marketing or use, and the permission sought is for the first commercial marketing or use of the product.

The key issue in both of these cases was whether the drug “product” was first being sought for FDA approval. Due to the inartful drafting of the relevant statutory provisions, prior cases had treated the definition of drug “product” inconsistently. For example, in *Fisons v. Quigg*, 876 F.2d 99 (Fed. Cir. 1989) (developing a new use of same compound), and *Pfizer Inc. v. Dr. Reddy’s Labs.*, 359 F.3d 1361 (Fed. Cir. 2004) (“*Pfizer II*”) (later product was a salt included in the earlier patent claims) the Federal Circuit supported the U.S. Patent and Trademark Office (USPTO) interpretation of the term “product” in 35 U.S.C. § 156(a)(5)(A) to broadly mean the “active moiety” such that first approval was for the active portion of the molecule in a drug product responsible for pharmacological action, regardless of whether the active moiety is later formulated as a salt, ester, or other non-covalent derivative.

On the other hand, the Federal Circuit’s decision in *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392 (Fed. Cir. 1990) (“*Glaxo II*”) (relating to a later ester of a previously approved drug), had construed the term “product” in 35 U.S.C. § 156(a)(5)(A) to mean “active ingredient” such that first approval was limited to only the specific structure physically found in the product, which would not include any salt, ester, or other non-covalent derivative of the active ingredient physically found in the drug product as defined in § 156(f)(2). The more recent decisions discussed in this article adopt this position.

In *Photocure* (*Photocure ASA v. Kappos*, No. 2009-1393, 2010 WL 1838653 (Fed. Cir. May 10, 2010)), the Federal Circuit affirmed the decision of the U.S. District Court for the Eastern District of Virginia that

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reversed the USPTO's ruling denying extension for U.S. Patent No. 6,034,267 ("the `267 patent") covering the drug product METVIXIA[®], methyl aminolevulinate hydrochloride ("MAL"). MAL is the methyl ester of the previously approved drug product LEVULAN KERASTICK[®], aminolevulinic acid hydrochloride ("ALA"), indicated for similar skin treatments. MAL was a new chemical compound separately patentable on the basis of its improved therapeutic properties as compared to ALA, and also had to undergo full FDA approval before commercial marketing or use. The USPTO incorrectly held that MAL was the same product as ALA because the underlying molecule of MAL is ALA, and therefore, did not meet the first commercial marketing or use requirement of § 156. The district court and the Federal Circuit disagreed with the USPTO, reasoning that since MAL was separately patentable and required FDA approval, MAL met the statutory requirements for patent term extension. In following the reasoning of *Glaxo II*, the Federal Circuit held that 35 U.S.C. § 156 was correctly applied to extend the patent term of the `267 patent by two years.

In *Ortho-McNeil (Ortho-McNeil Pharm., Inc. v. Lupin Pharm., Inc.*, No. 2009-1362, 2010 WL 1838655 (Fed. Cir. May 10, 2010)), the Federal Circuit sustained the extension of patent term for U.S. Patent No. 5,053,407 ("the `407 patent"), assigned to Daiichi Sankyo Co. and licensed to Ortho-McNeil, for the antibiotic LEVAQUIN[®] that contained the levorotatory enantiomer, levofloxacin, of the racemate ofloxacin, previously sold as FLOXIN[®]. Lupin argued that the enantiomer levofloxacin was a separate "active ingredient" of the previously marketed racemate ofloxacin, and since ofloxacin was previously approved by the FDA, permission to market levofloxacin was not the first permitted commercial marketing as required by § 156(a)(5)(A). Ortho-McNeil argued that levofloxacin was viewed by the FDA as a new product requiring full approval, and that levofloxacin was viewed by the USPTO as separately patentable. The Federal Circuit affirmed the district court's ruling that the `407 patent was properly granted a statutory term extension because an enantiomer is a different active ingredient than the racemate. As a result, the patent term for LEVAQUIN[®] was extended by more than two years.

These holdings represent a shift in how the Federal Circuit views related compounds and may provide opportunities for patentees to extend patent term for new drug products related to previously patented and approved drug products. In light of these decisions, care should be taken to file separate patents for drug candidates with different physical, chemical, biological, or pharmacological properties, especially if each drug candidate would need to undergo separate regulatory approval, and even if the drug candidates are related as polymorphs, protected forms, and different stereoisomeric combinations of a previously patented and approved product.



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