

Federal Appeals Court Alters Availability Of Patent Term Extension

by George C. Best and Shaun R. Snader

The United States Court of Appeals for the Federal Circuit recently decided two cases that significantly impact both the availability of patent term extension and the scope of protection conferred by extension. Patent term extension is available, if certain conditions are met, to restore patent term lost to FDA review.

The meaning of “product,” as used in the patent term extension statute, 35 U.S.C. § 156, impacts patent term extension in terms of both eligibility and the scope of protection conferred. Prior to the Federal Circuit’s recent decisions, there were two competing ways “product” was construed. The Federal Circuit first employed a plain meaning construction in *Glaxo Operations U.K. Ltd. v. Quigg*, 894 F.2d 392 (Fed. Cir. 1990) by looking literally at the active ingredient of the drug. Close to 15 years later, the Federal Circuit employed an active moiety construction in *Pfizer Inc. v. Dr. Reddy’s Laboratories,*

Ltd., 359 F.3d 1361 (Fed. Cir. 2004), by looking at the biologically active species of the active ingredient of the drug. *Pfizer* failed to cite *Glaxo* despite arguably being in direct conflict.

The Federal Circuit was confronted with this conflict by appeals from two district court cases, *Photocure ASA v. Dudas*, 622 F. Supp. 2d 338 (E.D. Va. 2009), and *Ortho-McNeil Pharmaceuticals, Inc. v. Lupin Pharmaceutical, Inc.*, No. 06-4999, 2009 WL 1228448 (D.N.J. May 1, 2009). In *Photocure*, the district court used the plain meaning definition of “product,” while in *Ortho-McNeil* the district court used the active moiety definition. The Federal Circuit affirmed both decisions but endorsed the active moiety construction of the statute. *Photocure ASA v. Kappos*, No. 2009-1393 (Fed. Cir. May 10, 2010); *Ortho-McNeil Pharm., Inc. v. Lupin Pharms., Inc.*, No. 2009-1362 (Fed. Cir. May 10, 2010). In so doing, the Federal Circuit distinguished *Pfizer.*

By adopting the plain meaning construction of the statute as applied in *Glaxo*, the Federal Circuit’s decisions in *Photocure* and *Ortho-McNeil* resolve substantial ambiguity as to eligibility for patent term extension. Indeed, the decisions mean enantiomers, for example, will be eligible for patent term extension despite prior approval of racemates in most, if not all, cases. But the decisions leave uncertainty as to what compounds will fall within the ambit of a patent extended under § 156 and suggest that factors other than those enumerated by statute might come into play.

Patent Term Extension

The Drug Price Competition and Patent Term Restoration Act of 1984, popularly referred to as the Hatch-Waxman Act, generally addressed two problems. First, the regulatory review process for new drug products effectively shortened the terms of patents covering the products. Second, generic companies could not bring products into the market immediately after patent expiration because the approval process required infringing acts. The Hatch-Waxman Act addressed the former issue by enacting 35 U.S.C. § 156, which allows patent owners to extend the term of patents



Dr. Best is a Partner at Foley & Larder LLP in Palo Alto, CA.



Mr. Snader is an Associate in the IP Litigation practice at Wilson Sonsini Goodrich & Rosati in Washington, DC.

covering drugs subject to regulatory review if certain conditions are satisfied. Essentially, the statute allows a patent term to be extended to make up for some of the time taken for regulatory review of a product claimed by the patent.¹

The meaning of the term “product” is critical to both availability of extension and the scope of protection during the extended term. Section 156 defines “product” as a “drug product,” which is further defined as “the active ingredient of a new drug . . . including any salt or ester of the active ingredient.”² Thus, § 156 defines “product” as the “active ingredient” and any “salt” or “ester” of the “active ingredient.”

Among other requirements, the regulatory review process on which the extension is based must result in the product’s first approval for commercial marketing or use.³ Thus, the Act benefits new drugs rather than new uses for old drugs or new combinations of old drugs. In addition, only a single extension is available for any patent and “product.”⁴ These requirements have been summarized as “one patent extension per patent, one patent extension per product, and one product per patent extension.”⁵

The scope of protection available during the extended term of a patent claiming a “product” is limited to the “product” for approved uses of the “product.”⁶ In other words, the entire claim scope is not extended but only the scope covering the “product.”⁷ The protection applies to all approved uses.⁸

Prior Federal Circuit Decisions

The Federal Circuit addressed the issue of how to interpret “product” in the context of § 156 in *Glaxo Operations U.K. Ltd. v. Quigg*, 894 F.2d 392 (Fed. Cir. 1990). The patentee in *Glaxo* sought an extension for its patent covering cefu-

roxime axetil, an orally administered antibiotic compound commercially marketed as CEFTIN tablets.⁹ Cefuroxime axetil is an ester of cefuroxime, its parent organic acid and the biologically active moiety.¹⁰ The U.S. Patent and Trademark Office (USPTO) denied Glaxo’s request because FDA had previously approved drugs with salts of cefuroxime as their active ingredients. According to the USPTO, the “active ingredient” was the active moiety, cefuroxime.¹¹ Glaxo appealed to the district court, and the district court concluded that the USPTO’s interpretation of § 156 was “contrary to law,” based on a plain meaning construction of “product,” because the previously approved salts were not cefuroxime axetil and were not “salts” or “esters” of cefuroxime axetil.¹² The Federal Circuit affirmed, holding that the terms “active ingredient of a new drug . . . including any salt or ester of the active ingredient,” all have a plain meaning,” and that plain meaning is conclusive.¹³ That is, “active ingredient” means the actual active ingredient as opposed to the “active moiety of the active ingredient.” The court analyzed the legislative history of § 156 for a clearly expressed intention that the statute be construed contrary to its plain meaning.¹⁴ The USPTO cited specific House Report language and floor statements regarding the intent of § 156 to support its active moiety position.¹⁵ The Federal Circuit, however, rejected these arguments explaining that none of the legislative history spoke directly to the term the “product.”¹⁶ The Federal Circuit refused to consider which construction yields better policy because “[s]triking balances in legislative language is Congress’ job.”¹⁷

Just short of 15 years after *Glaxo*, the Federal Circuit applied the active moiety definition of “product” in the context of

the scope of an extended patent in *Pfizer Inc. v. Dr. Reddy’s Laboratories, Ltd.*, 359 F.3d 1361, 1366 (Fed. Cir. 2004). *Pfizer* stemmed from Dr. Reddy’s Laboratories Ltd.’s and Dr. Reddy’s Laboratory, Inc.’s (collectively “Dr. Reddy’s”) attempt to market an amlodipine salt, amlodipine maleate, for treatment of heart disease.¹⁸ Pfizer previously obtained approval for NORVASC that contained as an active ingredient another amlodipine salt, amlodipine besylate.¹⁹ Pfizer owned a patent covering amlodipine and its maleate and besylate salts.²⁰ Based on the regulatory review of NORVASC, Pfizer sought and obtained an extension of its patent covering amlodipine and the two salts.²¹ During this extended term, Dr. Reddy’s sought regulatory approval for amlodipine maleate, and asserted that the extended term of Pfizer’s patent would not encompass amlodipine maleate.²²

Thus, the court had to decide whether a patent term extension for the drug product amlodipine besylate (NORVASC) extended protection to amlodipine maleate. The district court held that it did not because Pfizer’s approved “product” was amlodipine besylate rather than the biologically active moiety (amlodipine), based on the plain meaning of the statute. The district court relied on *Glaxo* as rejecting Pfizer’s contention that the “active ingredient” of a drug product means the “active moiety.”

The Federal Circuit reversed in an opinion that did not include a single citation to *Glaxo*. The Federal Circuit noted that the therapeutically active agent *in vivo* was amlodipine regardless of whether the besylate or maleate salt was administered.²³ The court reasoned that the “statute foresaw variation in the salt or ester of an active ingredient, and guarded against the very loophole [] urged.”²⁴ In addition, the court noted

that it was unfair that Dr. Reddy's should be afforded the benefit of Pfizer's data while depriving Pfizer of term extension covering the proposed new drug.²⁵ The court also cited FDA regulations defining "active ingredient" as "active moiety."²⁶ Thus, the court held that the "product" was amlodipine, *i.e.*, the active moiety. Pfizer's term extension, therefore, covered both the maleate and besylate salts of amlodipine.

Glaxo considered the availability of extension, and *Pfizer* considered the scope of protection conferred. But both decisions turned on the identical statutory language, the meaning of "product" in § 156.

Ortho-McNeil and Photocure

Ortho-McNeil

The patent owner in *Ortho-McNeil*, Daiichi Sankyo, obtained an extension of its patent based on the regulatory review of an enantiomer branded as Levafloxacin when the corresponding racemate was previously approved.²⁷ Lupin Pharmaceuticals, Inc. alleged that its generic version of Levafloxacin would not infringe after the original term of the extended patent because the grant of the extension was improper.²⁸

The district court rejected Lupin's challenge, holding that Lupin was unable to show by clear and convincing evidence that the USPTO acted contrary to § 156.²⁹ The district court reasoned that the USPTO and FDA had consistently held that the enantiomers were "products" different from their racemates for purposes of § 156.³⁰ The district court cited *Glaxo* for the proposition that courts must give "great deference to this determination by the PTO" and determined that Lupin was unable to carry its burden.³¹ It is interesting to note that *Glaxo* rejected the USPTO's request for deference with

respect to its interpretation of "product" because the question was one of statutory construction.³²

The Federal Circuit affirmed and reasoned that the long-standing practice of considering an enantiomer to be a drug product that is distinct from its racemate is "in accordance with *Glaxo*, where the court held that 'product' as used in §156(a) is the active ingredient present in the drug."³³ Thus, the Federal Circuit endorsed the plain meaning construction of § 156. Although not directly related to the construction of § 156, the court also noted that the enantiomer enjoyed "separate patentability" from the racemate and was treated separately by FDA.³⁴

Ortho-McNeil did not directly address *Pfizer*; that distinction belongs to *Photocure*.

Photocure

Photocure stemmed from the USPTO's refusal to extend a patent covering methyl aminolevulinate hydrochloride ("MAL hydrochloride") in view of prior approval of another related drug, aminolevulinic acid hydrochloride ("ALA hydrochloride").³⁵ MAL hydrochloride and ALA hydrochloride share the same parent acid, aminolevulinic acid ("ALA").³⁶ ALA hydrochloride is an ALA salt, while MAL hydrochloride is the salt of an ALA ester.³⁷ The USPTO refused the extension because in its view, "the underlying molecule, or active moiety, [of a drug] and all of its salts and esters qualify as the same 'product.'"³⁸

Photocure challenged the USPTO's decision, and the district court agreed that the USPTO's active moiety interpretation of the term "product" was legally incorrect.³⁹ The district court noted *Glaxo* and *Pfizer* "are clearly in conflict."⁴⁰ But because *Glaxo* was decided before *Pfizer* and had not been overturned *en banc*, the district court applied *Glaxo* as the

controlling precedential opinion.⁴¹ Moreover, the district court reasoned that *Glaxo* was the proper result because the plain text of the statute did not support the USPTO's active moiety construction of "product."⁴²

The Federal Circuit affirmed because the USPTO's position was premised on an "incorrect statutory interpretation."⁴³ That is, the court determined that the USPTO's construction of § 156, which equates "active ingredient" with "active moiety," cannot be reconciled with the plain language of § 156. Interestingly, the Federal Circuit noted that "even on the USPTO'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."⁴⁴ *Photocure*, therefore, suggests that separate patentability is at least a factor to consider when determining whether a drug is distinct from a previously approved drug for § 156 purposes.

Photocure distinguished *Pfizer*, noting that "[t]he issue in *Pfizer* was whether infringement of an extended patent on the drug amlodipine was avoided by changing the salt."⁴⁵ According to *Photocure*, "*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."⁴⁶ Rather, "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."⁴⁷

Ramifications of Photocure and Ortho-McNeil

Photocure and *Ortho-McNeil* provide substantial clarification for applicants

seeking patent term extension and expand the ability to obtain patent term extension. Prior to *Photocure* and *Ortho-McNeil*, uncertainty existed as to whether “active ingredient,” as used in § 156, means just that, *i.e.*, the actual active ingredient in a drug, or the biologically “active moiety” of the active ingredient. This uncertainty stemmed in large part from the Federal Circuit’s arguably conflicting positions in *Glaxo* and *Pfizer*. But *Photocure* and *Ortho-McNeil* distinguish *Pfizer* and, consistent with *Glaxo*, reject the USPTO’s active moiety application of the statute. Thus, the Federal Circuit has opened the door for applicants to obtain extensions based on drugs that share an active moiety with previously approved drugs as long as the active ingredients are different.

Interestingly, both *Photocure* and *Ortho-McNeil* suggest that separate patentability of the drug for which extension is sought is a consideration relevant in applying § 156. Indeed, *Photocure* suggests that separate patentability alone could justify finding a drug product distinct from a previously approved product for § 156 purposes.⁴⁸ On the other hand, *Photocure* and *Ortho-McNeil* do not discuss what the absence of separate patentability may mean for patent term extension eligibility. For example, if a salt is not separately patentable over a previously approved ester, can the salt be eligible for patent term extension? Under the plain meaning of the statute, the answer is seemingly yes, but the Federal Circuit’s reliance on separate patentability suggests that it may be open to arguments otherwise.

While largely clarifying the law in terms of eligibility, *Photocure* and *Ortho-McNeil* create questions as to how § 156 will be construed in terms of enforcement. That is, *Photocure* and *Ortho-McNeil* in view of *Pfizer* leave uncertain the scope of protection afforded by patent term extension. *Photocure* distinguished *Pfizer*, in part, by reasoning that “*Pfizer* did not concern a different, separately patented product requiring full regulatory approval.”⁴⁹ Nonetheless, the product found to infringe the extended patent in *Pfizer* arguably had a different “active ingredient,” based on the plain meaning of the term “product” endorsed by *Photocure* and *Ortho-McNeil*. Thus, at least in some cases, a product can infringe a patent extended under § 156 even if the product’s approval would give rise to separate eligibility for patent term extension.

Further litigation will surely clarify the application of § 156 in terms of both eligibility and enforcement. But the promise of future answers provides little comfort to pharmaceutical companies struggling to protect or obtain market share. ▲

1 The patent must claim the product rather than be merely infringed by the product. *Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756, 759 (Fed. Cir. 1997). For example, a patent claiming a metabolite of a drug product is not eligible for extension based on the approval process for the product that infringes upon administration. *Id.*
 2 35 U.S.C. § 156(f)(1) & (2).
 3 35 U.S.C. § 156(a)(5).
 4 See *Fisons v. Quigg*, No. 86-1804, 1988 U.S. Dist. LEXIS 10935 (D.D.C. 1988); *Arnold P’ship v. Rogan*, 246 F. Supp. 2d 460 (E.D. Va. 2003).
 5 *Cardiac Pacemakers, Inc. v. St. Jude Med., Inc.*, No. 96-1718-c H/G, 2001 U.S. Dist. LEXIS 5753, *26 (S.D. Ind. 2001).

6 35 U.S.C. § 156(b).
 7 *Id.*
 8 35 U.S.C. § 156(b).
 9 *Id.* at 394.
 10 *Id.* at 393.
 11 *Id.* at 395.
 12 *Id.*
 13 *Id.* at 395-96.
 14 *Id.*
 15 *Id.* at 397-98.
 16 *Id.* at 398.
 17 *Id.* at 399.
 18 *Id.* at 1364.
 19 *Id.* at 1363.
 20 *Id.* at 1364.
 21 *Id.* at 1364.
 22 Dr. Reddy’s was able to rely on Pfizer’s approval process data because Pfizer submitted data on both amlodipine besylate and amlodipine maleate. *Id.* at 1363-64. Pfizer chose amlodipine besylate because it proved to be the more effective compound. *Pfizer*, 2002 WL 31833744, *7 (D.N.J. 2002).
 23 *Id.* at 1365.
 24 *Pfizer Inc. v. Dr. Reddy’s Labs., Ltd.*, 359 F.3d 1361, 1366 (Fed. Cir. 2004)
 25 *Id.* at 1366.
 26 *Pfizer*, 359 F.3d at 1365 (citing Abbreviated New Drug Application Regulations: Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338, 50,358 (F.D.A. Oct. 3, 1994)).
 27 *Ortho-McNeil Pharm., Inc. v. Lupin Pharms., Inc.*, Civ. No. 06-4999, slip op. at 5-6 (D.N.J. Apr. 30, 2009).
 28 *Id.* at 7.
 29 *Id.* at 10.
 30 *Id.* at 11.
 31 *Id.* at 11-12.
 32 *Glaxo*, 894 F.2d at 399.
 33 *Ortho-McNeil Pharm., Inc. v. Lupin Pharms., Inc.*, 603 F.3d 1377, 1381 (Fed. Cir. 2010).
 34 *Id.* at 1380.
 35 *Photocure ASA v. Dudas*, 622 F. Supp. 2d 338, 342 (E.D. Va. 2009).
 36 *Id.* at 341.
 37 *Id.* at 341-42.
 38 *Id.* at 342 (citations omitted).
 39 *Id.* at 347-48.
 40 *Id.* at 347.
 41 *Id.* at 347.
 42 *Id.* at 348.
 43 *Photocure ASA v. Kappos*, 603 F.3d 1372, 1375 (Fed. Cir. 2010).
 44 *Id.*
 45 *Id.* at 1376.
 46 *Id.*
 47 *Id.*
 48 *Photocure ASA v. Kappos*, 603 F.3d 1372, 1376 (Fed. Cir. May 10, 2010).
 49 *Id.*