Arnall Golden Gregory LLP

Client Alert

Contact Attorneys Regarding This Matter:

Clark G. Sullivan
404.873.8512 - direct
404.873.8513 - fax
clark.sullivan@agg.com

David E. Huizenga, Ph.D.
404.873.8518 - direct
404.873.8519 - fax
david.huizenga@agg.com

Robert A. Hodges, Ph.D.
404.873.8670 - direct
404.873.8671 - fax
bob.hodges@agg.com

Alan G. Minsk
404.873.8690 - direct
404.873.8691 - fax
alan.minsk@agg.com

Arnall Golden Gregory LLP
Attorneys at Law
171 17th Street NW
Suite 2100
Atlanta, GA 30363-1031
404.873.8500
www.agg.com

CONFUSION PERSISTS AROUND DRUG EXCLUSIVITY AND PATENT TERM EXTENSIONS FOR NEW CHEMICAL ENTITIES

When has an active ingredient in a drug product been previously approved by the U.S. Food and Drug Administration (FDA)? That question, and conflicting precedent from the U.S. Court of Appeals for the Federal Circuit discussing that question, were addressed recently in a lawsuit filed in the Eastern District of Virginia against the Commissioner of the United States Patent Office, after the Commissioner refused to grant a patent term extension (PTE) to Photocure ASA. See Photocure ASA v. Dudas.[1]

Whether an active ingredient has previously been approved is critical to drug companies in the United States because it determines whether an extension of patent term is available to the drug company, and whether the drug qualifies for exclusivity as a new chemical entity (NCE). Unfortunately, the legal situation is not always clear due to conflicting decisions from the U.S. Court of Appeals for the Federal Circuit. This lack of clarity is especially pronounced when evaluating different salts and esters of a previously approved drug product.

The U.S. Patent Laws provide that a patent for a drug that has been delayed from market by FDA approval requirements may have its term extended if the FDA approval is "the first permitted commercial marketing or use of the product."[2] A "product" is defined to include "the active ingredient of a new drug, including any salt or ester of the active ingredient."[3] Thus, a patent term extension is only available if FDA has not previously approved the same active ingredient or a salt or ester of the active ingredient.

Similar language governs the availability of new chemical entity exclusivity under the Federal Food Drug and Cosmetic Act (FFDCA). With limited exceptions, if FDA approves a new drug having an "active ingredient (including any ester or salt of the active ingredient)" that has not been previously approved, FDA will not accept another application for the same drug for five years.[4] As with PTEs, NCE exclusivity is only available if FDA has not previously approved the same active ingredient or a salt or ester of the same active ingredient.

The similarity in language should come as no surprise to practitioners in this area because both provisions were included in the original 1984 legislation enacting the Waxman Hatch Act.[5] But that is where the similarity ends. The Patent Office has interpreted the language in the Patent Laws differently than FDA has interpreted the FFDCA, and different court decisions have interpret-

[1] Photocure ASA v. Dudas et al., __ F.Supp.2d __ (E.D. Va. 2009).
[2] 35 U.S.C. § 156(a).
[3] 35 U.S.C. § 156(f).
[4] 21 U.S.C. §§ 355(c)(3)(E)(ii) and 355(j)(5)(F)(ii).
[5] Pub. L. No. 98-417, 98 Stat. 1585 (1984).

ed the language in the Patent Laws differently.

FDA's interpretation of the NCE provisions has been consistent ever since the Hatch Waxman Act was first enacted. FDA considers the "active moiety" to be the active ingredient in a drug, and awards NCE exclusivity to the drug only if FDA has not previously approved the "active moiety" or a salt or ester form of the active moiety.[6] FDA effectively substitutes "active moiety" for "active ingredient" in its interpretation of the law.

While this approach does not follow the strict language of the law, it does reflect FDA's experience with drug approvals, during which FDA focuses on the active form of the drug after it has been administered and metabolized. In the case of a salt, which consists of the active moiety appended to a counter-ion, the active moiety is revealed after the drug is dissolved and the counter-ion disassociates from the active moiety. In the case of an ester, which consists of the active moiety appended to an ester function, the active moiety is revealed after enzymes cleave the ester function from the active moiety in the bloodstream.

Unlike FDA, the Patent Office has not been consistent in its interpretation of the PTE laws over the years, perhaps as a consequence of conflicting court decisions it has endured. These conflicts and inconsistencies culminated earlier this year in a lawsuit filed by Photocure ASA, when the Patent Office applied FDA's active moiety approach and denied Photocure a patent term extension for its Metvix® chemotherapy product.[7]

Against this backdrop were two conflicting decisions from the U.S. Court of Appeals for the Federal Circuit, the appeals court created in 1982. In a 1990 decision in Glaxo v. Quigg,[8] a three-judge panel at the Federal Circuit had applied the literal terms of the Patent Laws and held that the axetil ester of cefuroxime was entitled to a patent term extension, even though two salts of cefuroxime had previously been approved, because FDA had not previously approved cefuroxime axetil or "any salt or ester of cefuroxime axetil."

In 2004, a different three judge panel at the Federal Circuit reached a contradictory result in Pfizer v. Dr. Reddy's.[9] Applying the active moiety approach, the court held that Pfizer's patent term extension for the besylate ester of amlodipine extended to all esters of amlodipine, including the maleate ester under development by Dr. Reddy's, because the active moiety of both molecules was the same. Remarkably, the Federal Circuit did not refer to its earlier decision in Glaxo v. Quigg, or make any effort to reconcile the two decisions even though both cases interpreted the exact same definition of "drug" in the Patent Laws.

Once the Photocure v. Dudas court appreciated the conflict that the Federal Circuit's decisions had created, it had little difficulty resolving the conflict in Photocure's favor. When decisions of two different panels of the same appeals court conflict, the first decision usually takes precedence over the second.[10]

The Photocure v. Dudas court also had little difficulty resolving the Patent Office's conflicting policies on the issue. While the Patent Office urged the court to defer to its judgment on the issue, the court had dif-

[6] 21 C.F.R. § 314.108. "*New chemical entity* means a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the act."
[7] Photocure, __ F.Supp.2d at __. The active ingredient in Metvix® is an ester form of aminolevulinic hydrochloride; FDA had previously approved a product containing the same active moiety as Metvix® -- aminolevulinic acid.
[8] Glaxo Operations UK Ltd. v. Quigg, 894, F.2d 392 (Fed. Cir. 1990).
[9] Pfizer, Inc. v. Dr. Reddy's Labs., Ltd., 359 F.3d 1361 (Fed. Cir. 2004).
[10] Newell Companies, Inc. v. Kennedy Manufacturing Co., 864 F.2d 757 (Fed. Cir. 1988).

ficulty accepting the Patent Office's argument because the Patent Office had not been consistent on the issue. To the contrary -- as of the 2008 printing of the Manual of Patent Examining Procedure (MPEP), the Patent Office was reportedly applying the Federal Circuit's literal interpretation of the statute in Glaxo v. Quigg, stating: "the ester form is a different active ingredient from the salt form. Both the ester and the salt active ingredient may each support an extension of patent term of different patents provided the [base active moiety] itself has not previously been approved."[11] Because of the conflict between the interpretation advised in MPEP § 2751 and the active moiety approach used to deny Photocure's PTE, the court refused to give the Patent Office's decision any deference, and ordered the Patent Office to approve the patent term extension.[12]

The district court's Photocure v. Dudas decision is currently on appeal to the Federal Circuit. Unless the Patent Office can persuade the Federal Circuit to hear the appeal *en banc*, your authors predict that the district court's decision will stand, and Photocure's patent term extension will be granted. After all, as the district court so aptly observed, it is the first appellate decision on the issue that has precedential value, unless and until the court of appeals reconsiders its precedent through an *en banc* hearing.[13]

[11] MPEP § 2751 (2008).
[12] Photocure, __ F.Supp.2d at __.
[13] Id. at __. One complicating factor is precedent from the Federal Circuit holding that a new panel of Federal Circuit judges need not follow precedent from an earlier panel when there is a new agency interpretation of the law. Tunik v. Merit Systems Protection Board, 407 F.3d 1326, 1338 (Fed. Cir. 2005). The Photocure v. Dudas court distinguished this precedent by holding that the statutory mandate at 35 U.S.C. § 156(a) is unambiguous. Photocure, __ F.Supp.2d at __ .