No. 2009-1393

IN THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

PHOTOCURE ASA,

Plaintiff-Appellee,

v.

JOHN J. DOLL, ACTING UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY and ACTING 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. 08cv718, Judge Liam O'Grady

BRIEF FOR DEFENDANT-APPELLANT

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Statement of Related Cases

No other appeal in or from the present civil action has previously been before this or any other appellate court. Counsel is aware of the following related case currently pending before this Court: *Ortho-McNeil Pharmaceutical, Inc. et al. v. Lupin Pharmaceutical, Inc.*, et al., No. 2009-1362, which is scheduled for oral argument in September. Both cases potentially involve the correct interpretation of the term "active ingredient" in 35 U.S.C. 156.

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BRIEF FOR DEFENDANT-APPELLANT

STATEMENT OF JURISDICTION

This case involves a challenge to a patent term extension determination by the United States Patent and Trademark Office (USPTO) under 35 U.S.C. 156. A28. The plaintiff (PhotoCure ASA or PhotoCure) invoked the jurisdiction of the district court, *inter alia*, under 28 U.S.C. 1331, 1338, and 1361. A7, A29. On March 31, 2009, the district court entered an order granting PhotoCure's motion for summary judgment, denying the USPTO's motion for summary judgment, and remanding the case to the USPTO for further proceedings consistent with the

court's opinion. A1. The USPTO filed a timely notice of appeal on May 29, 2009. A1067; Fed. R. App. P. 4(a)(1). This Court has jurisdiction over the appeal under 28 U.S.C. 1295(a)(1), and the district court judgment is appealable under *Sullivan v. Finkelstein*, 496 U.S. 617 (1990), and *Travelstead v. Derwinski*, 978 F.2d 1244 (Fed. Cir. 1992). This Court will exercise jurisdiction over an order remanding a case to the agency where that judgment "terminated the action, set aside the agency's determination, and would be effectively unappealable at a later stage." *Hyatt v. Dudas*, 492 F.3d 1365, 1368 (Fed. Cir. 2007). Such an appealable judgment is presented here, because the district court "interpreted a rule of law * * * and its remand to the agency compel[s] the agency to act contrary to its prior ruling." *Ibid.*

STATEMENT OF THE ISSUES

Pursuant to 35 U.S.C. 156, the USPTO is authorized to extend the term of a patent protecting an innovative drug to compensate for the length of the Food and Drug Administration's (FDA's) new drug approval process. Under this scheme, a patent protecting a drug is not eligible for a term extension if, *inter alia*, the drug's "active ingredient" or "any salt or ester of the active ingredient" has previously been approved for marketing by the FDA. 35 U.S.C. 156(a)(5)(A), (f)(1)(A), (f)(2). The questions presented are:

1. Whether *Pfizer Inc. v. Dr. Reddy's Laboratories, Ltd.*, 359 F.3d 1361 (Fed. Cir. 2004), establishes that the term "active ingredient" in 35 U.S.C. 156 means the active moiety in a drug — *i.e.*, the portion of the molecule (excluding those portions that make the drug, *e.g.*, a salt or ester) that gives the drug its therapeutic effect.

2. Whether, if this case is not controlled by *Pfizer*, the USPTO persuasively interpreted "active ingredient" to mean active moiety and, accordingly, determined that PhotoCure's drug product, Metvixia, was not eligible for a term extension in light of the FDA's prior approval of Levulan.

STATEMENT OF THE CASE

A. Pertinent Statutory Provision Involved.

The pertinent sections of 35 U.S.C. 156 are contained in Addendum A to this brief.

B. Section 156(b) Patent Term Extensions.

At issue in this case are provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act. Pub. L. No. 98-417, 98 Stat. 1585 (1984), *codified at* 21 U.S.C. 355, 360cc, and 35 U.S.C. 156, 271, 282. The Hatch-Waxman Act has dual goals: (1) increasing the number of lower-cost generic drugs on the market and (2) preserving the incentive for

manufacturers to perform the research and development necessary to create new pioneer drugs. See H.R. Rep. No. 857 (Part I), 98th Cong., 2d Sess. at 14-15 (1984), *reprinted in* 1984 U.S.C.C.A.N. at 2647. See also *Pfizer Inc. v. Dr. Reddy's Laboratories, Ltd.*, 359 F.3d at 1364-65.

Title I of the Act was intended "to make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962." H.R. Rep. No. 857 at 14-15. Title II was intended to provide a new incentive for the research and development of pioneer drugs by providing "restoration of some of the time lost on patent life while the product is awaiting pre-market approval." *Id.* at 15. See also, *e.g.*, *Fisons v. Quigg*, 1988 WL 150851, at *3 (D.D.C. Aug. 19, 1988) (Congress recognized "that the effective market lives" of certain patented inventions — particularly, pharmaceutical products — "were being eroded by excessively long periods of regulatory review by the Food and Drug Administration"), *aff'd*, 876 F.2d 99 (Fed. Cir. 1989). The statutory scheme crafted by Congress represents a delicate balancing of these two policy goals. See *Pfizer*, 359 F.3d at 1364-65; *Tri-Bio Labs, Inc. v. United States*, 836 F.2d 135, 139 (3d Cir. 1987), *cert. denied*, 488 U.S. 818 (1988). See generally *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990).

This case involves the patent term extension provisions of Title II, codified in 35 U.S.C. 156. Section 156 authorizes the USPTO to extend the term of a patent protecting a particular drug if certain statutory requirements are met. The term of a drug patent qualifies for an extension under Section 156 where, *inter alia*, the patent "claims a product" (subsection (a)) that "has been subject to a regulatory review period before its commercial marketing or use" (subsection (a)(4)), and "the permission for the commercial marketing or use * * * after [the] regulatory review period is the first permitted commercial marketing or use of the product [under the statutory scheme establishing the regulatory review period]" (subsection (a)(5)). In short, the FDA's approval of the drug product supporting the patent term extension application must represent the first FDA approval of the "product," as that term is defined in the statute.

C. The USPTO's Interpretation of Section 156.

Because a patent is not eligible for a patent term extension if the claimed "product" has previously been approved for marketing by the FDA, the meaning of "product" is critical to the scope and operation of the patent term extension provision. Section 156(f)(1)(A) defines "product" to mean "drug product." In turn, Section 156(f)(2) provides in relevant part that "drug product" means "the *active ingredient* * * * of a new drug, * * * including *any salt or ester of the*

active ingredient * * * ." (Emphasis added). Thus, eligibility for a patent term extension turns on whether the "active ingredient" of the drug, or "any salt or ester of the active ingredient," has previously been approved for marketing by the FDA.

The Hatch-Waxman Act does not define "active ingredient." However, the USPTO has construed the term in the course of administering the patent term extension provisions of the Hatch-Waxman Act. The USPTO interprets "active ingredient" — consistent with the holding in *Pfizer*, *supra* — to mean "active moiety." As discussed further below, this Court's decision in *Pfizer* likewise construes "active ingredient" in Section 156 to mean active moiety. See *Pfizer*, 359 F.3d at 1365-66.

Generally speaking, the active moiety of a drug product is the portion of the drug product (excluding those parts that cause it to be, *e.g.*, a salt or ester) that produces the pharmacological effect. The FDA, as *Pfizer* noted, has defined "active moiety" more precisely as "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester [or] salt * * *, responsible for the physiological or pharmacological action of the drug substance," 359 F.3d at 1366 (quoting 21 C.F.R. 314.108(a)), and the USPTO

applies the same definition. See A743-44.[1] Thus, if the active moiety of the drug product that is the basis for extension of a patent term is the same active moiety of a drug product previously approved by the FDA, then the USPTO will deny the application.

In this regard, by rendering a drug molecule in the form of a salt or ester, a drug manufacturer may modify certain characteristics of the molecule, but it generally does not change the basic pharmacologic or toxicologic properties of the molecule. Depending on the drug in question, a particular salt or ester may affect the drug's solubility and rate of absorption; increase stability; regulate the rate of release; improve transdermal solubility of topical preparations; reduce pain at an injection site; or make an orally administered drug more palatable. See, *e.g.*, Richard B. Silverman, *The Organic Chemistry of Drug Design and Drug Action* 505-516 (2d ed. 2004); John H. Block & John M. Beale, Jr. (eds.), *Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry* 145, 147 (11th ed. 2004); P. Heinrich Stahl & Camille G. Wermuth (eds.), *Handbook of Pharmaceutical Salts: Properties, Selection, and Use* 1-5, 95, 107 (2008).

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[1] The USPTO has not promulgated any formal regulation regarding the meaning of "active ingredient." The FDA's regulation includes more than salts and esters as derivatives, but this case involves only the salt and ester portion of the definition.

However, "the formation of a salt * * * or of an ester, is not intended to, and generally cannot, alter the basic pharmacologic or toxicologic properties of the molecule (except for possible local toxicity)." Letter from Ronald G. Chesemore, Acting Associate Commissioner for Regulatory Affairs, FDA, to John D. Siegfried, M.D. Executive Director for Pharmaceutical Affairs, McNeil Pharmaceutical, p. 12 & n.5 (July 26, 1989) (available online at <http://www.regulations.gov/fdmspublic/ContentViewer?objectId=09000064809c33d6&disposition=attachment&contentType=pdf>). By the time the molecule reaches its therapeutic target, its salt or ester group generally has been metabolically or chemically removed from the molecule, and therefore cannot contribute to the molecule's activity at the target site. *Id.* at 12 n.5 (portions of molecules that cause them to be salts "are designed to be separated from the 'active moiety' before the drug is absorbed into the circulation" and "do not travel to, or act on, the site of the drug action"; similarly, "the ester portion [of a drug molecule] is cleaved from the 'active moiety'" "before, or just after, absorption by gut or blood esterases," and "only the active moiety travels to, and acts on, the receptor site"); Stahl & Wermuth at 128 ("As a rule, it may be assumed that, because of electrolytic dissociation in the aqueous media, only the active entity * * * and not the complete salt reaches the therapeutic target."); Silverman at 501

("esterases are ubiquitous [in human systems], so metabolic regeneration of the drug [through removal of the ester group] is a facile process").

D. The FDA's Market Exclusivity Provisions.

As an additional incentive for innovative drugs, the Hatch-Waxman Act provides non-patent related market exclusivity to qualifying drug products. For example, 21 U.S.C. 355(j)(5)(F)(ii), in pertinent part, states:

> If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section * * *.

The reward of market exclusivity, therefore, turns on language — "active ingredient (including any ester or salt of the active ingredient)" — virtually identical to the language in 35 U.S.C. 156 that rewards innovative drugs with patent term extensions.

STATEMENT OF FACTS

1. Factual background.

In March 2000, the USPTO issued U.S. Patent No. 6,034,267 (the "'267 patent"). The '267 patent claims both a pharmaceutical compound called methyl

aminolevulinate hydrochloride ("MAL hydrochloride"), which has the brand name Metvixia. Metvixia is both an ester and salt of aminolevulinic acid (ALA), specifically, the methyl ester of the hydrochloride salt. The '267 patent also claims a method of using that compound to treat actinic keratosis — essentially skin cancer or premalignant warty lesions that can become skin cancer — through a technique called photochemotherapy. PhotoCure is the assignee of the patent. A3.

Because Metvixia qualified as a "new drug" under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 321(p), it required FDA approval before PhotoCure could begin commercially marketing it. The FDA granted approval in July 2004. A5.

In September 2004, PhotoCure filed a patent term extension application with the USPTO for the '267 patent based on the period of the FDA's approval of Metvixia. The USPTO reviewed the application and made a preliminary determination that the '267 patent was ineligible for extension on the grounds that the active ingredient in Metvixia had been previously approved by the FDA in the drug Levulan, which is the brand name for aminolevulinate hydrochloride ("ALA hydrochloride") — or, put differently, that Levulan is a hydrochloride salt of ALA.

Thus, the USPTO found that the FDA's approval of Metvixia was not the first FDA approval of the product. A5, 515-520.

After making its preliminary determination, the USPTO sought input from the FDA as to whether, in accordance with Section 156(a)(5)(A), "permission for the commercial marketing or use of [Metvixia] * * * is the first permitted commercial marketing or use of the product * * * ." In response to the USPTO's request for assistance, the FDA determined that Metvixia was not the first FDA approval of the "product." See A515-17. The FDA's letter, in pertinent part, stated as follows:

> The active ingredient in Metvixia, methylaminolevulinate hydrochloride, is an ester of aminolevulinic acid hydrochloride, an active ingredient that has been previously approved for commercial marketing or use as Levulan, NDA 20-965.

A517.

Following the FDA's input, the USPTO dismissed the application (A518-20), and PhotoCure requested reconsideration (A521-26). In its reconsideration decision, the USPTO interpreted Section 156(a)(5)(A) to mean that the underlying molecule, or active moiety, and all of its salts and esters separately qualify as the "product" for purposes of the patent term extension provisions of the Hatch-Waxman Act. United States Patent and Trademark Office, Final Decision

Regarding Patent Term Extension Application under 35 U.S.C. § 156 for U.S. Patent No. 6,034,267 (May 13, 2008). A741-49. Applying that interpretation to the particular chemistries of Metvixia and Levulan, the USPTO determined that Metvixia was not the first permitted commercial marketing or use of the product in light of the FDA's prior approval of Levulan. A6, A743-44. The USPTO reasoned that the two drugs have the same active moiety and explained:

> ALA is simply formulated differently in the two different drugs: as a hydrochloride salt of its methyl ester in Metvixia[], and as a hydrochloride salt in Levulan[]. However, the difference in formulation does not matter for purposes of defining a product in Section 156.

A745. Thus, the USPTO denied PhotoCure's request for a patent term extension. A6, 741-49.

2. The district court proceedings.

PhotoCure brought suit to challenge the USPTO's decision, and the district court reversed the USPTO and remanded for further proceedings consistent with its decision. A1. The district court believed (A10-14) that the Federal Circuit had addressed the meaning of the statutory terms at issue here in two cases: *Glaxo Operations UK Limited v. Quigg*, 894 F.2d 392 (Fed. Cir. 1990), and *Pfizer Inc. v. Dr. Reddy's Laboratories, Ltd.*, 359 F.3d 1361 (Fed. Cir. 2004). The district court read the two opinions to adopt conflicting interpretations of "active ingredient,"

with *Glaxo* rejecting the "active moiety" interpretation in 1990 and *Pfizer* subsequently approving it in 2004. A14-15.

The district court also noted that the Federal Circuit "has adopted the rule that prior decisions of a panel of the court are binding precedent on subsequent panels unless and until overturned in banc" and that, "[w]here there is a direct conflict, the precedential decision is the first." A14 (internal quotations marks and citations omitted). Thus, the district court ruled that it was bound by *Glaxo*. Applying that case, which the district court said defined "active ingredient" to mean the compound "physically present" in the administered drug, it found that the active ingredient in Metvixia is MAL hydrochloride, whereas the active ingredient in Levulan is ALA hydrochloride. Because the court found Metvixia does not have the same active ingredient as Levulan, it rejected the USPTO's determination and directed the USPTO to grant a term extension to the '267 patent. A15-16.[2]

The court went on to state that it would have reached the same result had the issue been one of first impression, "believ[ing] that a plain meaning interpretation of the § 156(f)(2) 'active ingredient' requires the actual presence of a compound

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[2] The district court reached its conclusion by comparing the "active ingredient" of Levulan with the "product" of Metvixia, though the statute appears to require a comparison of the product of Levulan to the product of Metvixia.

qualifying as the 'active ingredient' in the drug." A16. To adopt the active moiety approach, the court said, would entail construing the term "active ingredient" to allow a compound to qualify as an ingredient of a drug even when the compound is not actually present in the drug. A16. Here, for example, while MAL hydrochloride is an ester and salt of ALA, ALA in its non-salified, non-esterified form is not itself physically present in Metvixia. Construing "active ingredient" to mean active moiety would be permissible, the court said, only if there were support for that construction in the legislative history, but there was none. A16. Therefore, the court stated that it would not construe "active ingredient" contrary to what the court regarded as its plain meaning. A16.

SUMMARY OF ARGUMENT

1. In *Pfizer*, this Court interpreted "active ingredient" in Section 156 to mean "active moiety." *Pfizer* is the governing precedent in this Circuit, and it compels reversal of the district court decision. The district court held that *Glaxo* governs, but it is clear, as we demonstrate below, that *Glaxo* had no occasion to address the meaning of "active ingredient" and did not do so. Consequently, the "active moiety" interpretation in *Pfizer* governs, and the USPTO's denial of PhotoCure's patent term extension application should be sustained.

2. a. Even if *Pfizer* were not controlling, and because *Glaxo* did not address the meaning of "active ingredient," the USPTO's interpretation of "active ingredient" in 35 U.S.C. 156 as "active moiety" is persuasive and should be upheld. 35 U.S.C. 156(f)(2)(A) defines "drug product" to mean (in pertinent part) "the active ingredient of * * * a new drug, * * * including any salt or ester of the active ingredient," but it does not define "active ingredient." The USPTO reads the definition of "drug product" to encompass three categories of molecules: (1) a non-salified and non-esterified form of a molecule, (2) any salt of that molecule; and (3) any ester of that molecule. Parsing the language, the USPTO interprets "active ingredient" to refer to the first category of molecule, which is the active moiety — the pharmacologically active molecule to which components are added to make it a salt or ester. In *Pfizer*, the Court reasoned similarly, reading the reference to "any salt or ester of the active ingredient" as an indication that Congress did not conceive of individual salts and esters as themselves constituting distinct active ingredients.

In isolation, "active ingredient" is an ambiguous term that could bear more than one meaning. But the definition of "drug product" in Section 156(f)(2) does not use "active ingredient" in isolation. Instead, it refers to, and distinguishes between, "active ingredient" and "any salt or ester of the active ingredient." This

language strongly suggests that salts and esters are not themselves to be regarded as active ingredients, and that "active ingredient" refers instead to the non-salified and non-esterified form of the therapeutically active molecule — in other words, the active moiety. While the district court believed that the USPTO's interpretation was inconsistent with the plain text of the statute, no definition of active ingredient is provided in the statute, and when Congress enacted the Hatch-Waxman Act, there was no formal or established definition of "active ingredient" as used in the phrase at issue here — namely, "active ingredient * * * including any salt or ester of the active ingredient." 35 U.S.C. 156(f)(2).

As added support for the reasonableness of the USPTO's interpretation, it is significant that the FDA, which is faced with virtually identical statutory language in administering the market exclusivity provisions of Title I of the Hatch-Waxman Act, adopted the same reading of "active ingredient" for those provisions that the USPTO employs here.

Finally, the USPTO's interpretation is entirely consistent with Congress's goal to reward true innovation. The district court's interpretation, on the other hand, produces the odd result that the eligibility for a patent term extension could turn on the sequence of drug approvals rather than innovation. For example,

if the drug product seeking a patent term extension is the acid, and a salt or ester of the acid had previously been approved, the application will denied (because a salt or ester of the active ingredient was previously approved). However, if the drug product seeking a patent term extension is the salt or ester, and only the acid had previously been approved, the application will be granted (because neither the salt nor ester was previously approved). There is no apparent legislative purpose for this odd, asymmetrical result.

b. Applying its interpretation of "active ingredient" to mean "active moiety" as was done in *Pfizer*, the USPTO correctly determined that the '267 patent protecting Photocure's drug Metvixia is not entitled to a term extension. Because Metvixia (which is MAL hydrochloride) and Levulan (which is ALA hydrochloride) have the same active moiety (ALA), and because the FDA approved Levulan before Metvixia, Metvixia is not the first permitted commercial marketing or use of the product. The USPTO's determination in this regard is entitled to "great deference" as it turns on which patented chemical compounds fall within the definition of products and therefore should be sustained.

ARGUMENT

THE USPTO'S DENIAL OF A PATENT TERM EXTENSION, BASED ON THE "ACTIVE MOIETY" INTERPRETATION OF "ACTIVE INGREDIENT," IS CORRECT AND SHOULD BE UPHELD.

A. Standard of Review

This Court reviews a district court's grant of summary judgment without deference to the lower court, applying the same standard as the district court. See *Lacavera v. Dudas*, 441 F.3d 1380, 1382 (Fed. Cir. 2006); *Star Fruits, S.N.C. v. United States*, 393 F.3d 1277, 1281 (Fed. Cir. 2005). Where, as here, a court addresses the meaning of a statutory provision that is administered by a federal agency and has been interpreted by the agency, the agency's interpretation of ambiguous language is entitled to *Skidmore* deference based on the adequacy and persuasiveness of the agency's reasoning. See *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944); *Merck v. Kessler*, 80 F.3d 1543, 1550 (Fed. Cir. 1996). Once statutory issues are resolved, the USPTO is entitled to "great deference" in determining which compounds qualify for patent term extension. *Pfizer, Inc. v. Ranbaxy Labs Ltd.*, 457 F.3d 1284, 1290 (Fed. Cir. 2006) (hereinafter "*Ranbaxy*") (quoting *Glaxo*, 894 F.2d at 399)).

B. Contrary To The District Court's Conclusion, *Pfizer* Governs The Outcome In This Case.

1. In *Pfizer*, this Court squarely held that "active ingredient" in Section 156 means "active moiety." See 359 F.3d at 1365-66. As a matter of *stare decisis*, that holding governs this appeal and compels reversal of the district court's decision.

Pfizer involved a patent term extension on a patent protecting the drug Norvasc, which has the chemical name amlodipine besylate. Amlodipine besylate is a salt of the underlying molecule, amlodipine. Dr. Reddy's sought to market amlodipine maleate, a different salt of the same underlying molecule. Pfizer sued Dr. Reddy's for infringement, and Dr. Reddy's defended by arguing that the patent term extension was limited to the particular salt approved by the FDA, amlodipine besylate. Pfizer, in contrast, argued that its patent term extension covered amlodipine and all of its salt forms. This Court agreed with Pfizer, holding that "the active ingredient is amlodipine" — the active moiety of both drugs — and that "[t]he statutory definition of 'drug product' is met by amlodipine and its salts." 359 F.3d at 1366.

Parsing the statutory language, *Pfizer* reasoned that, by "defining the term 'product' as 'including any salt or ester of the active ingredient,'" 35 U.S.C. 156(f)

"clearly provides" that the active ingredient itself cannot be a salt or an ester. 359 F.3d at 1365-66. Instead, the Court held that "active ingredient" means active moiety. *Id.* at 1366.

The Court looked to regulations promulgated by the FDA to implement the marketing exclusivity provisions of the Hatch-Waxman Act. In these regulations, where "active ingredient" is modified by the parenthetical, "including any ester or salt of the active ingredient," the FDA equates "active ingredient" with "active moiety," and defines "active moiety" as "'the molecule or ion, *excluding those appended portions of the molecule that cause the drug to be an ester [or] salt* * * * responsible for the physiological or pharmacological action of the drug substance.'" *Id.* at 1366 (quoting 21 C.F.R. § 314.108(a)) (emphasis added).

Pfizer also observed that "[t]he statute foresaw variation in the salt or ester of an active ingredient, and guarded against the very loophole now urged [by Dr. Reddy's]" by including salts and esters of the active ingredient within the definition of "drug product." 359 F.3d at 1366, citing 35 U.S.C. 156(f) (patent term extension) and 21 U.S.C. 355(j)(4)(D)(i) and (v) (1994) (now codified as 21 U.S.C. 355(j)(5)(F)(i) and (v)) (marketing exclusivity). The operation of the patent term extension provision, the Court said, "was not intended to be defeated by simply changing the salt [or ester]." *Id.* at 1366. To permit otherwise would

allow Dr. Reddy's to obtain approval of its own product based on Pfizer's "approved uses and data" by merely changing a salt or ester and, at the same time, "ba[r] [Pfizer's] extension of patent coverage of the drug product whose approvals and data" were the basis for Dr. Reddy's product approval. *Id.* at 1366.[3]

In short, *Pfizer* squarely addresses the meaning of "active ingredient" in Section 156 and construes it to refer to the drug's active moiety. That is precisely the interpretation that USPTO employs, and the agency correctly relied on that interpretation in denying PhotoCure's patent term extension application in this case. See also discussion, *infra*, at pp. 24-29, 35-37.

2. The district court believed that *Glaxo*, not *Pfizer*, governs as to the meaning of "active ingredient." See A14-15. But the meaning of "active ingredient" was not in dispute in *Glaxo*. To the contrary, the parties in *Glaxo* agreed about the active ingredient in that case, and the appeal was litigated on the basis of that common understanding. As a consequence, this Court reviewed the USPTO's patent term extension decision in *Glaxo* without ever addressing the

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[3] The *Pfizer* Court agreed with Pfizer "that a changed salt does not affect the therapeutically active agent, which is the same amlodipine, whatever the salt," 359 F.3d at 1365, and agreed "that the active ingredient is amlodipine, and that it is the same whether administered as the besylate salt or the maleate salt." 359 F.3d at 1366. Cf. *Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 347 F.3d 1367 (Fed. Cir. 2003) (finding "active moiety" key to patent infringement and patent term extension issues).

meaning of "active ingredient."

Glaxo sought a patent term extension for cefuroxime axetil — an ester of the acid cefuroxime. 894 F.2d at 393-94. Today, the USPTO's position would be that cefuroxime, the underlying molecule of the ester, is the "active ingredient." At the time of the *Glaxo* appeal, however, the USPTO took the position that the active ingredient was cefuroxime axetil, the ester of the active moiety. *Id.* at 394.[4] For its part, Glaxo took precisely the same position. *Ibid.*

Because the USPTO and Glaxo were in agreement that the "active ingredient" was cefuroxime axetil, the parties' arguments focused solely on whether the term "product" in Section 156(a)(5) — limiting a term extension to the "the [first] commercial marketing or use of the product after such regulatory review period" — meant the precise product approved by the FDA. *Ibid.* ("It is undisputed that cefuroxime axetil is the active ingredient of CEFTIN tablets.') Thus, the Court focused solely on whether cefuroxime axetil, Glaxo's "product,"

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[4] In the proceedings before the district court in *Glaxo*, the USPTO did advance the active moiety reading of "active ingredient." See *Glaxo Operations UK Limited v. Quigg*, 706 F. Supp. 1224, 1226 (E.D. Va. 1989), *aff'd*, 894 F.2d 392 (Fed. Cir. 1990). However, the USPTO had not relied on that reading at the administrative stage. See 706 F. Supp. at 1226. On appeal, the USPTO acknowledged that *Chenery* principles (see *SEC v. Chenery Corp.*, 332 U.S. 194, 196-197 (1947)) foreclosed the agency from relying on a post hoc interpretive rationale, and therefore did not seek to defend its administrative decision on the basis of the active moiety interpretation.

was the same as a product previously approved by the FDA for commercial marketing. The Court noted that the products previously approved by the FDA were salts of cefuroxime, whereas Glaxo's product (cefuroxime axetil) was an ester of cefuroxime. See *id.* at 393-94. The Court decided, therefore, that cefuroxime axetil had not been previously approved by the FDA, and affirmed the district court's order granting a patent term extension which had overruled the USPTO's denial of the extension. In so doing, this Court addressed neither the meaning of "active ingredient" nor the precise role that that definition plays in the patent term extension regime. *Id.* at 394-400. Indeed, as previously noted, the Court treated the identification of the active ingredient as "undisputed." *Id.* at 394.

It is telling in this regard that the Court's decision in *Pfizer* never mentions *Glaxo*. This omission can hardly have been an oversight, for the appellate briefs,[5] the petition for rehearing en banc,[6] and the rehearing response[7] all featured *Glaxo* prominently, with the generic manufacturer in *Pfizer* arguing that *Glaxo* was

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[5] See 2003 WL 24032076 (appellant's opening brief), 2003 WL 24032075 (appellee's brief), and 2003 WL 24032077 (appellant's reply brief).

[6] See 2004 WL 3261083.

[7] See 2004 WL 3261016.

controlling and Pfizer arguing the opposite. The fact that *Glaxo* was never mentioned in *Pfizer* — not even in Judge Mayer's dissent — confirms that *Glaxo*, properly understood, does not address the meaning of "active ingredient" in Section 156, and hence that *Pfizer* is the controlling precedent as to the meaning of that term. Thus, the district court's conclusion here that *Glaxo* is controlling because the later *Pfizer* decision could not overrule *Glaxo* (see A14-15) is without merit; there was nothing in *Glaxo* for *Pfizer* to overrule.

C. Even if *Pfizer* Does not Control, the USPTO's Interpretation Should be Upheld.

1. a. Even if *Pfizer* were not considered controlling, and because *Glaxo* clearly did not address the meaning of "active ingredient," the USPTO's interpretation of "active ingredient" in 35 U.S.C. 156 is persuasive and should be upheld.[8] As noted above, 35 U.S.C. 156(f)(2)(A) defines "drug product" to mean (in pertinent part) "the active ingredient of * * * a new drug, * * * including any salt or ester of the active ingredient," but it does not define "active ingredient." The USPTO reads the definition of "drug product" to encompass three categories of

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[8] The USPTO is entitled to *Skidmore* deference based on the adequacy and persuasiveness of the analysis set forth in the agency's final decision (see A741-49), an analysis supported by *Pfizer*, the FDA's interpretation of virtually identical language in the market exclusivity provision of Title I of the Hatch-Waxman Act (see, *infra*, at pp. 26-28), the legislative history, and public policy (see discussion, *infra*, at 31-33).

molecules: (1) a non-salified and non-esterified form of a molecule, (2) any salt of that molecule; and (3) any ester of that molecule. A743. Parsing the language, the USPTO interprets "active ingredient" to refer to the first category of molecule, which is the "active moiety" of the drug — the pharmacologically active molecule to which components can be added to make it a salt or ester. *Ibid.* In *Pfizer*, this Court reasoned similarly, reading the reference to "any salt or ester of the active ingredient" as an indication that Congress did not conceive of individual salts and esters as themselves constituting separate active ingredients. *Pfizer*, 359 F.3d at 1365-66. See also discussion, *supra*, at 19-21.

Viewed in isolation, "active ingredient" is an ambiguous term that could bear more than one meaning. But the definition of "drug product" in Section 156(f)(2) does not use "active ingredient" in isolation. Instead, it refers to, and distinguishes between, "active ingredient" and "any salt or ester of the active ingredient." This language strongly suggests that salts and esters are not themselves to be regarded as active ingredients, and that "active ingredient" refers instead to the non-salified and non-esterified form of the therapeutically active molecule — in other words, the active moiety. Thus, the USPTO's interpretation of "active ingredient" draws meaning and support from the terms that accompany the term "active ingredient" in the statute, and reads them in a consistent and

coherent manner. See *United States v. Santos*, 128 S. Ct. 2020, 2024 (2008) ("context gives meaning"); *Fort Stewart Schools v. Federal Labor Relations Authority*, 495 U.S. 641, 645-46 (1990) ("[the term in question] is not in isolation, but forms part of a paragraph whose structure, as a whole, lends support to the [agency's] * * * reading.").

The USPTO's interpretation of "active ingredient" ensures that molecules with the same pharmacological activity are treated as the same drug product, rather than treating molecules as different "active ingredients" on the basis of features that do not contribute to or alter the activity of the molecules. As explained above (see pp. 7-9, *supra*), while the behavior of a drug molecule may be modified in certain respects by administering it in the form of a salt or ester, the pharmacological activity of the molecule generally does not depend on the salt or ester group. Under the district court's interpretation, different salts and esters with the same active moiety are treated as different active ingredients, and hence different drug products, even though the differences have no effect on the activity of the drugs. The USPTO's interpretation, in contrast, hews more closely to the statutory text by treating molecules with the same *activity* as having the same "active ingredient."

As further support for the persuasiveness of the USPTO's interpretation, it

is significant that the FDA, which is faced with virtually identical statutory language in administering the market exclusivity provisions of Title I of the Hatch-Waxman Act, has adopted the same reading of "active ingredient" that the USPTO employs here. The FDA is required to grant periods of marketing exclusivity to a newly approved drug if that drug contains no "active ingredient (including any ester or salt of the active ingredient)" that has received prior FDA approval. See 21 U.S.C. 355(j)(5)(F)(i), (ii), and (v) (formerly 355(j)(4)(D)(i), (ii), and (v)). In that context, where the statutory language refers to "active ingredient" in conjunction with the parenthetical "any ester or salt of the active ingredient," the FDA has expressly interpreted "active ingredient" to mean "active moiety." See 59 Fed. Reg. 50338, 50358 (1994).

Notably, the FDA adopted its current "active moiety" approach after, and in response to, *Abbott Labs. v. Young*, 920 F.2d 984 (D.C. Cir. 1990), where the D.C. Circuit addressed and rejected the FDA's original approach to Hatch-Waxman marketing exclusivity. See *id.* at 988. The FDA stated that the "active moiety" approach in the context of the phrase, "active ingredient (including any ester or salt of the active ingredient)," was not foreclosed by the D.C. Circuit, explaining as follows:

> Although the court of appeals appeared to agree with the agency's conclusion that exclusivity should be limited to the first approved product containing the active moiety, the court found the agency's parsing of the operative statutory phrase "active ingredient (including any salt or ester of the active ingredient)" to be linguistically impermissible as set forth in the agency's administrative decision denying 10-year exclusivity to *Abbott*. Rather than interpret the term "active ingredient" broadly to include the concept of active moiety, the agency interpreted the term narrowly to refer to the form of the moiety in the product, but interpreted the parenthetical phrase "(including any salt or ester of the active ingredient)" broadly to include all active ingredients that are different but contain the same active moiety. *Although the court noted that the agency had, subsequent to the administrative decision, voiced the more linguistically permissible construction (interpreting the term "active ingredient" to refer to active moiety), the court found that it could not consider this construction because it was not relied upon in the administrative decision.*

59 Fed. Reg. at 50357-58 (emphasis added). Revisiting the issue on remand, the FDA concluded that the "active ingredient," as used in the phrase "active ingredient (including any salt or ester of the active ingredient)," is the "active moiety," *id.* at 50358. That position remains in effect today, and no drug manufacturer has directly challenged the FDA's regulatory approach in litigation in the intervening fifteen years.

The FDA's interpretation is significant for two reasons. First, the relevant language in the marketing exclusivity provisions of Title I (see, *e.g.*, pp. 5-6, *supra*) and the corresponding language in the patent term extension provisions of

Title II are essentially identical. Compare 21 U.S.C. 355(j)(5)(F)(ii) ("active ingredient (including any ester or salt of the active ingredient)"), with 35 U.S.C. 156(f)(2) ("active ingredient * * * , including any salt or ester of the active ingredient"). Second, the marketing exclusivity provisions and the patent term extension provisions are closely related provisions with the same underlying legislative purpose — to provide additional incentives for genuinely innovative drugs. See discussion, *infra*, at pp. 31-32 (legislative history). The consistency in the USPTO's and FDA's approach therefore is a strong indicator of the persuasiveness of the USPTO's position.[9]

b. The district court offered two related reasons for rejecting the "active moiety" approach: one, that "active ingredient" had a settled administrative meaning when the Hatch-Waxman Act was enacted (A12-13); and, two, that "'active moiety' was indisputably well-known at the time Congress drafted the statute," A16, yet Congress chose to use "active ingredient," not "active moiety."

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[9] The FDA promulgated 21 C.F.R. 60.3(b)(2) in connection with its role in the patent term extension application process, and defined "[a]ctive ingredient" as "any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or of animals." That regulation, however, predated the FDA's analysis during the *Abbott Labs.* remand in which the FDA explained that "active ingredient," when juxtaposed with the salt/ester parenthetical in the FDA's market exclusivity provisions, means active moiety. See pp. 27-28, *supra*.

Neither point defeats the agency's interpretation.

First, contrary to the district court's belief, there was no formal or established meaning of "active ingredient" in the context presented here prior to the enactment of the Hatch-Waxman Act. The only definition of "active ingredient" was found in the FDA's Good Manufacturing Practices (GMP) regulations, 21 C.F.R. 210.3(b)(7).[10] There was formal or established meaning of the term "active ingredient" where "active ingredient" is juxtaposed with the parenthetical, "including any ester or salt of the active ingredient." This point is critical because, since the enactment in 1984 of the Hatch-Waxman Act, the FDA has construed "active ingredient" in the context of the "salt or ester" parenthetical differently from "active ingredient" in provisions *without* the parenthetical. See, *e.g.*, 21 U.S.C. 355(j)(2)(A)(ii)(I) ("An abbreviated application for a new drug shall contain * * * information to show that the active ingredients of the new drug are the same as those of the listed [innovator] drug."). In the latter context, the FDA has construed "active ingredient" to mean "the active ingredient in the finished drug product *prior to its administration,*" 54 Fed. Reg. 28872, 28881

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[10] "Active ingredient means any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure of any function of the body of man or other animals." 21 C.F.R. 210.3(b)(7). See also n.9, *supra*.

(1989) (2d col.) (1989) (emphasis added), which *may not necessarily be* the "active moiety" (*i.e.*, the molecule (excluding the parts that make it a salt or ester) that causes the pharmacological effect *after* administration). In the former, it has consistently treated "active ingredient" to mean "active moiety" (the same interpretation employed by the USPTO in the virtually identical patent term extension provisions of Title II of the Hatch-Waxman Act). Accordingly, contrary to the district court's view (A12-13), there was no settled administrative understanding of what "active ingredient" meant in the specific statutory context presented in this case that compels an interpretation from different than that accorded by the USPTO.

Second, while Congress used "active ingredient" rather than "active moiety," the use of "active ingredient" does not prove that Congress did not have "active moiety" in mind or that "active moiety" would *not* be a permissible understanding of what Congress meant, particularly in the absence of a settled administrative interpretation of "active ingredient." In fact, the legislative history supports the "active moiety" approach.

While the legislative history does not directly address the meaning of "active ingredient," at a more general level it strongly suggests that Congress wanted to reward *only* truly innovative research — involving "new chemical

entities" — and did not intend to reward patents claiming drug products with patent term extensions where the approval of those products was based merely on new uses, dosage forms, or formulations of previously approved drug products. See A744. In *Fisons v. Quigg*, 1988 WL 150851 (D.D.C. 1988), *aff'd*, 876 F.2d 99 (Fed. Cir. 1989), the district court noted:

> Upon examination, the specific purpose of Section 156(a)(5)(A) appears to have been relatively narrow — to restore lost patent life only for "pioneer" drugs. A report by the Congressional Office of Technology Assessment ("OTA") to the 97th Congress provided the factual foundation for the restriction of patent restoration benefits to new chemical entities. The OTA report stated: "Although important pharmaceutical innovations may result from new therapeutic applications of existing chemicals * * * many of the pharmaceutical breakthroughs that have occurred have resulted from NCE (new chemical entity) research and the development of NCEs generally has required more time and money than other types of innovation and has involved greater risks." The House Committee on Energy and Commerce explained that the bill "requires extensions to be based on the first approval of the product because the only evidence available to Congress showing that patent time has been lost is data on so-called class I, new chemical entity drugs."

1988 WL 150851 at *7. Thus, "Congress's intent was to restore patent life only to new chemical entities." *Ibid.*[11]

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[11] In 21 C.F.R. 314.108(a), the FDA defines a "[n[ew chemical entity" as "a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) [21 U.S.C. 355(b)] of the act."

In the USPTO's view, rewarding a patent claiming a drug product with a patent term extension where its "active moiety" is the same as that of a previously approved drug is not rewarding genuine innovation, and therefore would be inconsistent with clearly expressed congressional intent. Accord: *Pfizer*, 359 F.3d at 1366 ("None of the aspects offered to the district court or on this appeal suggests a statutory intent to provide the generic producer with access to the pioneer's approved uses and data while barring extension of patent coverage of the drug product whose approvals and data are provided."). Accordingly, while Congress did not expressly use the term "active moiety," that term precisely expresses what Congress intended.

Further, if "active ingredient" were not construed to mean "active moiety," the eligibility for a patent term extension could turn on the sequence of drug approvals rather than innovation. For example, as noted by the *Glaxo* district court, a patent term extension would be granted where the new drug approval is for an ester, even though a salt or acid related to the ester had been previously approved, and would be denied where the new approval is for an acid if the salt or ester form of the acid had been previously approved. See, *e.g.*, *Glaxo*, 706 F. Supp. at 1229-30 n.12. There is no apparent legislative purpose for such an odd, "asymmetrical" result. *Ibid.* See also *Abbott Labs. v. Young*, 920 F.2d 984, 989

(D.C. Cir. 1990) (to have patent term extensions depend on the sequence of drug approvals "fail[s] to serve any conceivable statutory purpose"). Indeed, as previously noted, it contradicts Congress's intent to reward only truly innovative research. Construing "active ingredient" to mean active moiety avoids this irrational regulatory asymmetry.

c. The district court assumed that the definition of the term "ingredient" requires that the active ingredient actually be physically present in the administered drug product. See A16, citing 7 Oxford English Dictionary 963-64 (2d ed. 1989) (an "ingredient" is "[s]omething that enters into the formation of a compound or mixture; a component part, constituent or element."). See also A11 (referring to the *Glaxo* district court's similar conclusion, 706 F. Supp. at 1227-28). In the court's view, based on the definition of "ingredient," a plain meaning interpretation of "active ingredient" requires the actual presence of a compound qualifying as the "active ingredient" in the administered drug product. The court, however, was wrong.

The court misunderstood the dictionary definition of "ingredient." An "ingredient" is a component that "*enters into the formation* of a compound or

mixture," 7 Oxford English Dictionary at 963-64 (emphasis added).[12] Nothing in the definition suggests that a component is not an ingredient of a drug product *unless* it is physically present in the finished product. For example, a bottle of beer does not contain hops or yeast, yet no one would dispute that hops and yeast are ingredients of beer, since they are two of the principal components used to create it. Thus, the district court's contention that a component must be physically present in the final product to qualify as an "ingredient" misapprehends the nature of what an "ingredient" is. In any event, it is accurate to say that active moiety is contained in the final compound in that it is present in the form of the particular salt or ester of the moiety.[13]

2. a. The district court declined to give the USPTO's interpretation

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[12] See also, *e.g.*, The American College Dictionary (1970) at 625 ("ingredient" is "something that enters as an element into a mixture").

[13] In *Hoechst-Roussel v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997), this Court stated that "[f]or purposes of patent term extension, th[e] active ingredient must be present in the drug product when administered." *Id.* at 759 n.3, citing *Glaxo*, 706 F. Supp. at 1227-28 (E.D.Va.1989), *aff'd* 894 F.2d 392 (Fed. Cir.1990). The language in *Hoechst-Roussel* is dicta because the Court was addressing whether the patent at issue "claimed" the drug product, not the meaning of "active ingredient * * * including any salt or ester of the active ingredient," for purposes of the patent term extension provisions of the Hatch-Waxman Act. Moreover, even if the statement in the *Hoechst-Roussel* footnote were regarded as controlling here, the USPTO would still prevail because, as just noted above, the active moiety is present in the final compound.

deference because it found the "active moiety" approach to be inconsistent with the agency's Manual of Patent Examining Procedures (MPEP) in effect when the agency issued its final decision in this case. See A16-20. Section 2751 of the MPEP provided: "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 acid itself has not previously been approved." A19. Even so, the agency is not disqualified from receiving deference solely because of inconsistency. As long as the agency's current interpretation is adequately and persuasively explained, it is entitled to at least *Skidmore* deference. See *Merck*, 80 F.3d at 1550 ("Such deference as we owe to the PTO's interpretive 'Final Determination' * * * thus arises * * *, *inter alia*, the thoroughness of its consideration and the validity of its reasoning, *i.e.*, its basic power to persuade if lacking power to control.") (citing *Skidmore*, 323 U.S. at 140).

Here, the agency's "active moiety" approach is clearly explained in its final decision. See A743-44 and discussion, *supra*, at 24-26. The agency also informed the district court that it was in the process of revising the MPEP to reflect the "active moiety" approach that the agency had been employing. A19. The agency is therefore entitled to *Skidmore* deference because of the adequacy and persuasiveness of the analysis in its final decision, see A741-749, an analysis all

the more persuasive because of its consistency with *Pfizer*, the FDA's interpretation of virtually identical language in the market exclusivity provision of Title I of the Hatch-Waxman Act (see discussion above at pp. 27-29), and the legislative history of, and public policy supporting, the Hatch-Waxman Act (see discussion above at pp. 31-33).

b. After intepreting "active ingredient" to mean "active moiety" as was done in *Pfizer*, the USPTO correctly determined that the '267 patent protecting Photocure's drug Metvixia is not entitled to a term extension. Both Metvixia and the earlier FDA approved drug Levulan are different formulations of ALA. Metvixia is the methyl ester of the hydrochloride salt of ALA, while Levulan is the hydrochloride salt of ALA. See A4 & n.3, A743-46; and pp. 11-12, *supra*. The active moiety in both drugs is ALA, *i.e.*, it the portion of both drugs (excluding those parts that make the drugs a salt and/or ester) that gives the drugs their therapeutic effect. *Ibid.* Accordingly, because Levulan was approved by the FDA before Metvixia, the latter is not the first FDA approval of the product. The USPTO's determination in this regard is entitled to "great deference" and should be sustained. *Ranbaxy*, 457 F.3d at 1290, quoting *Glaxo*, 894 F.2d at 399 ("[W]e will give great deference to the Commissioner's determinations as to which patented chemical compounds fall within Congress' definition of 'products.'").

CONCLUSION

For the foregoing reasons, the judgment of the district court should be reversed.

Respectfully submitted,

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JULY 2009

DISTRICT COURT ORDER AND OPINION

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF VIRGINIA
Alexandria Division

PHOTOCURE ASA,	)	
	)	
	)	
Plaintiff,	)	
	)	
v.	)	Civil Action No.: 1:08-cv-718
	)	
JON W. DUDAS, *et al.*,	)	
	)	
	)	
Defendants.	)	

JUDGMENT ORDER

In accordance with the accompanying Memorandum Opinion, Plaintiff's Motion for Summary Judgment (Dkt. no. 12) is GRANTED, and Defendants' Motion for Summary Judgment (Dkt. no. 21) is DENIED.

The Court declares that Plaintiff's application for a patent term extension for Patent No. 6,034,267 satisfies each requirement of § 156(a). Specifically, the parties do not dispute that §§ 156(a)(1)-(4) are satisfied. Section 156(a)(5)(A) is satisfied for the reasons stated in the accompanying Memorandum Opinion.

Accordingly, this matter is remanded to the Director for a ruling on the '267 patent term extension application in a manner consistent with this opinion. The parties are to bear their own costs.

ENTERED this 31st day of March, 2009.

Alexandria, Virginia

/s/
Liam O'Grady
United States District Judge

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF VIRGINIA
Alexandria Division

PHOTOCURE ASA,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Civil Action No.: 1:08-cv-718
	)	
JON W. DUDAS, *et al.*,	)	
	)	
Defendants.	)	

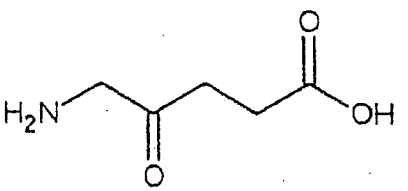
MEMORANDUM OPINION

In this action, Plaintiff PhotoCure seeks to extend the term of its drug patent, which was effectively shortened by the lengthy Food and Drug Administration ("FDA") approval process. 35 U.S.C. § 156 (2006) permits patent term extensions in such circumstances, provided that the applicant meets specific statutory elements. One such element requires that the drug be the first permitted commercial marketing or use of "the product." 35 U.S.C. § 156(a)(5)(A) (2006). On May 13, 2008, the Defendants, employees of the United States Patent and Trademark Office ("USPTO"), denied PhotoCure's application for a patent term extension under "the product" provision. PhotoCure now appeals this decision. The question presented herein is whether the patented drug supporting the term extension application at issue meets the requirement of § 156(a)(5)(A) that the use of "the product" following FDA approval constitutes the first commercial marketing or use. The Court holds that the patented drug in this case meets the above statutory requirement.

I. BACKGROUND

On March 7, 2000, the USPTO issued U.S. Patent No. 6,034,267 (the "'267 patent") entitled "Esters of 5-Aminolevulinic Acid as Photosensitizing Agents in Photochemotherapy." The patent lists Plaintiff PhotoCure as the assignee. The '267 patent claims both a pharmaceutical compound called methyl aminoevulinate hydrochloride ("MAL hydrochloride"), and a method of using that compound to treat actinic keratoses through a technique called photochemotherapy.[1] Claims 8 and 9 of the '267 patent cover the MAL hydrochloride compound itself, while claims 1 and 3-7 cover the method of using that compound in conjunction with performing photochemotherapy.

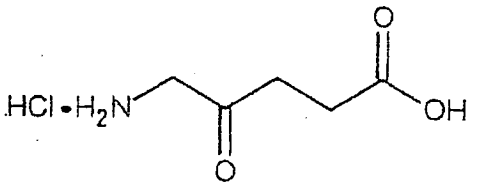
MAL hydrochloride is an "ester" of the organic acid called aminolevulinic acid ("ALA"). An organic acid is a compound consisting of either a hydrogen or organic chemical group covalently bonded to an acid group. The specific acid group found in ALA is called the carboxyl group, which is represented by the chemical formula COOH. The chemical formula for ALA as a whole is $C_5H_9NO_3$. The chemical structure is diagrammed below:



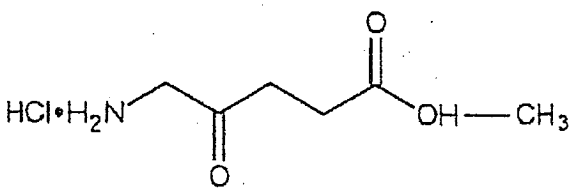
When hydrochloric acid ("HCl") is added to an organic acid, a salt of that organic acid is formed. Thus, when HCl is added to ALA, the resultant compound is a salt of ALA, called aminolevulinic acid hydrochloride (ALA hydrochloride). The chemical formula for ALA

[1] Actinic keratoses are premalignant lesions on sun-exposed skin having the ability to develop into carcinomas.

hydrochloride is $C_5H_9NO_3HCl$. A diagram showing the chemical structure for ALA hydrochloride, which reflects the addition of HCl, is shown below:



When the hydrogen atom (H) is removed from the COOH group of an organic compound and replaced with an organic chemical group, an ester of that organic compound is formed. Therefore, in the case of ALA hydrochloride, if the H from the COOH group is replaced with the organic chemical group CH_3, the resultant compound is an ester of ALA hydrochloride called MAL hydrochloride.[2] The chemical formula for MAL hydrochloride is $C_6H_{11}NO_3HCl$. The chemical structure is:



Worth noting is that ALA hydrochloride and MAL hydrochloride both have ALA as their base organic acid, or underlying molecule. In other words, ALA hydrochloride and MAL hydrochloride share the same parent acid, ALA. ALA hydrochloride and MAL hydrochloride are just two members of a large family of salts and esters that derive from the parent acid ALA.[3]

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[2] In addition to being an ester of ALA hydrochloride, MAL hydrochloride can be characterized as both an ester and a salt of the base organic acid ALA.

[3] A term used to describe the underlying molecule, or parent acid, of a large salt and ester family is "active moiety." Therefore, ALA hydrochloride and MAL hydrochloride also can be said to share the same active moiety.

The commercial embodiment of the '267 patent is the drug Metvixia™ ("Metvixia"), which contains MAL hydrochloride as its key ingredient.[4] Metvixia was the first commercial drug to contain MAL hydrochloride as its key ingredient. However, a commercial drug predating Metvixia called Levulan™ ("Levulan") implemented ALA hydrochloride as its key ingredient. As a result, the key ingredients in both Metvixia and Levulan share the same active moiety, ALA.[5]

Because Metvixia qualified as a "new drug" under § 201(p) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 321(p) (2006), it required approval by the FDA before it could be commercially marketed and sold. In an attempt to obtain this FDA approval, PhotoCure submitted a New Drug Application on September 26, 2001. On July 27, 2004, the Metvixia drug was approved for commercial and marketing use.

Due to the inability of PhotoCure to obtain FDA approval until more than four years after the USPTO issued the '267 patent, a significant portion of time elapsed between when PhotoCure gained patent rights and when it could profit from those patent rights by commercially marketing and selling the drug. In order to aid patent holders in PhotoCure's position, Congress passed 35 U.S.C. § 156 (2006), commonly referred to as the Hatch-Waxman Act, which permits patent term extensions for patent holders who have their terms reduced by the FDA regulatory process.

Not every patent having its term shortened by the FDA regulatory process, however, qualifies for an extension. Extensions are only appropriate if the statutory requirements of §

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[4] Metvixia also contains other chemical compounds that serve as inactive ingredients.

[5] Despite sharing the same active moiety, PhotoCure asserts that substantial differences exist in the effects that MAL hydrochloride and ALA hydrochloride have on the human body. In support of this assertion, PhotoCure points to data and expert opinion suggesting that these differences are as follows: selectivity of uptake by target lesions; penetration of target lesions; (unwanted) systemic distribution of the active ingredient; pain resulting from use in PDT; and mechanisms by which cells take up the active ingredient. J.A. 422, 642.

156(a) are met. One such requirement provides that an extension may only be granted if the drug covered by the patent is the "first permitted commercial marketing or use of the product." 35 U.S.C. § 156(a)(5)(A) (2006).[6] Section 156(f) further defines the term "product" to mean the "active ingredient" of the drug, as well as any salt or ester of the active ingredient. 35 U.S.C. § 156(f)(2) (2006).

On September 22, 2004, PhotoCure timely filed a patent term extension application with the USPTO for the '267 patent. This application was denied. On November 13, 2007, PhotoCure filed a "Request for Reconsideration of Final Determination of Ineligibility for Patent Term Extension." The USPTO issued its final agency decision on May 13, 2008.

In this decision, the USPTO interpreted § 156(a)(5)(A) to mean that the underlying molecule, or active moiety, and all of its salts and esters qualify as the same "product." United States Patent and Trademark Office, *Final Decision Regarding Patent Term Extension Application under 35 U.S.C. § 156 for U.S. Patent No. 6,034,267*, 3 (May 13, 2008) [hereinafter "USPTO Decision"]. Because Levulan's key ingredient (ALA hydrochloride) and Metvixia's key ingredient (MAL hydrochloride) share the same active moiety (ALA), Levulan and Metvixia contain the same "product" under this interpretation, which is ALA. And because Levulan earned FDA approval before Metvixia, the USPTO held that "the [FDA] approval of METVIXIA™ (methyl aminolevulinate hydrochloride) [did] not constitute the first permitted commercial marketing or use of the 'product'" under § 156(a)(5)(A). USPTO Decision at 1. As a result, PhotoCure's request for a patent term extension was denied.

PhotoCure now appeals the USPTO's decision. In its complaint, PhotoCure alleges that the USPTO's decision was contrary to law (Count I), as well as arbitrary and capricious and not in accordance with law (Count II).

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[6] The remaining requirements are outlined in Section IV.A., infra.

II. JURISDICTION AND VENUE

Subject matter jurisdiction exists pursuant to 28 U.S.C. § 1331 (2006) because this action arises under federal law; 28 U.S.C. § 1338(a) (2006) because this action arises under an "Act of Congress relating to patents"; and 28 U.S.C. § 1361 (2006), which provides district court jurisdiction over a "mandamus to compel an officer or employee of the United States or any agency thereof to perform a duty owed to the plaintiff."

The relief requested is authorized by 28 U.S.C. §§ 2201-2202 (2006), which permit declaratory judgment when an actual controversy exists. The parties do not dispute that an actual controversy exists. The relief requested is also authorized by 5 U.S.C. §§ 701-705 (2006), which outline a framework for judicial review of agency decisions.

Finally, venue is proper under 28 U.S.C. § 1391(e) (2006).

III. STANDARD OF REVIEW

Because this case involves judicial review of a final agency decision, the Administrative Procedure Act ("APA") provides the applicable standard of review. *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 395 n.4 (Fed. Cir. 1990). Under the APA, agency action may be set aside if the court finds that the agency action was "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). In making this determination, "the focal point for judicial review should be the administrative record already in existence, not some new record made initially in the reviewing court." *Camp v. Pitts*, 411 U.S. 138, 142 (1973).

Here, the parties agree that no factual disputes exist and that the undisputed facts of the case are contained in the administrative record. Accordingly, PhotoCure moved for summary judgment on October 14, 2008, and Defendants Jon Dudas and John Doll of the USPTO moved

for summary judgment on November 4, 2008. Because this action presents no disputed issues of material fact, the Court will resolve it at the summary judgment stage under Fed. R. Civ. P. 56. The Court, using the facts found in the administrative record, will base its decision on whether the USPTO's action was "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A).

IV. ANALYSIS

A. Statutory Framework

A patent can only qualify for a term extension under § 156 if the following five conditions are met:

> (1) the term of the patent has not expired before an application is submitted under subsection (d)(1) for its extension;
> (2) the term of the patent has never been extended under subsection (e)(1) of this section;
> (3) an application for extension is submitted by the owner of record of the patent or its agent and in accordance with the requirements . . . of subsection (d);
> (4) the product has been subject to a regulatory review period before its commercial marketing or use;
> (5)(A) except as provided in subparagraph (B) or (C), 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[.]

35 U.S.C. § 156(a) (2006) (emphasis added).

Defendants do not dispute that Plaintiff's '267 patent meets the first four conditions of § 156(a). The lone contested issue is whether the fifth condition, § 156(a)(5)(A), is met. . Resolution of this issue requires the court to decide which compound of the drug being used to support the patent term extension request qualifies as the "the product." Congress, in the statute, supplied further definition for "the product" term. Section 156(f)(1)(A) defines "product" as "a drug product," which, in turn, is defined as "the *active ingredient* of . . . a new drug, antibiotic

drug, or human biological product . . . including *any salt or ester of the active ingredient*, as a single entity or in combination with another active ingredient." 35 U.S.C. § 156(f)(2) (2006) (emphasis added). Therefore, identifying which compound in the drug qualifies as "the product" for § 156(a)(5)(A) purposes requires the court to determine the drug's "active ingredient." That active ingredient, along with the entire group of salts and esters that derive from it, constitute "the product."

The court then must determine whether the active ingredient, or any of its salts or esters, (i.e. "the product") were previously approved by the FDA. If so, the relevant patent term extension application must be denied. Applying this statutory framework to the facts of the present case, if the active ingredient of Metvixia, or any one of its salts or esters, were previously approved by the FDA for commercial marketing or use, then the '267 patent cannot be granted a term extension.

PhotoCure argues that the active ingredient in Metvixia is MAL hydrochloride, since that is the critical compound in Metvixia that enables the drug to work effectively. If PhotoCure's view is accepted, MAL hydrochloride and all of the salts and esters that derive from it would qualify as "the product." ALA and ALA hydrochloride would not qualify as "the product" under this approach, because neither are salts or esters of MAL hydrochloride. This would mean that Levulan, whose key ingredient is ALA hydrochloride, also would not be covered by "the product" language and could not bar the '267 patent from an extension. Instead, under the PhotoCure interpretation, the '267 patent would satisfy § 156(a)(5)(A) because Metvixia would be the first permitted commercial marketing or use of a drug containing "the product" MAL hydrochloride.[7]

[7] The USPTO acknowledged that that neither MAL hydrochloride nor any of its salts or esters have been previously approved by the FDA for commercial marketing or use. USPTO Decision at 7.

On the other hand, the USPTO argues that the active ingredient must always be the underlying molecule of the salt and ester family in its non-esterified and non-salified form (i.e., the active moiety approach). Adopting the active moiety approach in this case would lead to ALA qualifying as the "active ingredient" of Metvixia. As a result, ALA, and all of its salts and esters, including ALA hydrochloride and MAL hydrochloride, would qualify as "the product." Under this reasoning, ALA, and all of its salts and esters, would also qualify as "the product" of Levulan. Thus, under the active moiety approach, Levulan and Metvixia would be viewed as containing the same product. Because Levulan would earn FDA approval before Metvixia under the active moiety approach, Metvixia, would not qualify as the first permitted commercial marketing or use of a drug containing "the product" ALA, which means that the patent covering Metvixia would not qualify for a term extension. In short, the outcome of this case turns on whether the active moiety approach or the PhotoCure approach is adopted.

B. Case Law

i. Glaxo I & II

This Court previously addressed the issue of how to interpret §§ 156(a)(5)(A) and 156(f)(2) in *Glaxo Operations UK Ltd. v. Quigg*, 706 F.Supp. 1224 (E.D. Va. 1989) ("*Glaxo I*"). The facts of *Glaxo I* are nearly identical to those of this case. The patent holder in *Glaxo I* sought a term extension for its patent covering cefuroxime axetil, an orally administered antibiotic compound commercially marketed as Ceftin Tablets. *Glaxo I*, 706 F.Supp. at 1225. Cefuroxime axetil is an ester of cefuroxime, its parent organic acid and active moiety. *Id.* at 1225. But because two salts of cefuroxime had been the active ingredients of drugs earning FDA approval before the Ceftin Tablets, the USPTO denied the application for a term extension. *Id.* at 1225-26. Specifically, the USPTO applied the active moiety approach and explained:

> [F]or the purpose of eligibility for patent term extension, an active ingredient in the acid, salt or ester form is treated as the same drug product . . . [I]t must be concluded that the active ingredient in CEFTIN is an ester of cefuroxime. A sodium salt of cefuroxime has been approved for commercial marketing or use by the FDA prior to the approval of CEFTIN. Accordingly, the permission for commercial marketing or use of the product (i.e., the active ingredient cefuroxime axetil) after the regulatory review period was not the first permitted commercial marketing or use of the product (cefuroxime as a salt or ester) . . . .

Id. at 1226 (citing *In re Glaxo Operations UK Ltd.*, Request for Patent Term Extension under 35 U.S.C. § 156 for U.S. Patent No. 4,267,320 at 3-4 (Sept. 9, 1988)).

Judge Ellis, however, reversed the USPTO's decision, explaining that the Office's interpretation of § 156 ignored the plain meaning of the statute by permitting a compound to qualify as the "active ingredient" when that compound was not physically present in the drug. *Id.* at 1227. Specifically, Judge Ellis reasoned that:

> Cefuroxime itself is not present at all in Ceftin Tablets; it is therefore not an "ingredient." This conclusion is inescapable given the plain and unambiguous language of the statute. An ingredient is a "constituent element of a mixture or compounds." *Webster's Second University Dictionary* (1984). It must be something found in the mixture or compound, not just something that can be derived from it or from which the mixture or compound can be derived. Simply because the ester cefuroxime axetil may be derived from the acid cefuroxime through esterification is no basis for concluding that cefuroxime is some how an "ingredient." One might as well say that a caterpillar is an ingredient of a butterfly. This is palpably not so. To be sure, a butterfly comes from, or derives from, a caterpillar in metamorphosis as does the ester from the acid in esterification.

Id. at 1227-28.

Judge Ellis also found significance in the fact that the statute used the term "ingredient" instead of "moiety":

> [N]either this Court, nor the Commissioner is at liberty to ignore . . . the fact that the statute uses "ingredient," not "moiety." Equating "active moiety" with "active ingredient" . . . results in reading out of the statute the plain meaning of the phrase Congress chose. This is unwarranted for "'[a] fundamental canon of statutory construction is that, unless otherwise defined, words will be interpreted as taking their ordinary, contemporary, common meaning.'" *Ethicon, Inc. v. Quigg*, 849

F.2d 1422, 1426 (Fed.Cir.1988) (quoting *Perrin v. United States*, 444 U.S. 37, 42 (1979)).

Id. at 1228.

Finally, after an extensive review of the legislative history, Judge Ellis noted that nothing in the legislative history discusses the terms "active ingredient" or "active moiety." *Id.* at 1228. As a result, he concluded that the legislative history provides no basis for reading the term "active ingredient" contrary to its plain meaning to include ingredients not physically present in the drug.

On appeal of *Glaxo I*, the Federal Circuit affirmed Judge Ellis's ruling, stating that "the district court correctly construed and properly applied the operative terms of § 156(a)." *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 393 (Fed. Cir. 1990) (*Glaxo II*). The court in *Glaxo II*, similar to Judge Ellis's approach, extensively analyzed the legislative history of § 156 to determine whether it clearly expressed an intention that the statute be construed contrary to its plain meaning. *Glaxo II*, 894 F.2d at 395-96. The USPTO had cited specific House Report language and floor statements in *Glaxo II* in hopes of persuading the court that the legislative history should be construed contrary to its plain meaning and that the active moiety approach was what Congress intended. *Id.* at 397-98. But the court rejected these arguments, explaining that none of the legislative history spoke directly to the term "the product." *Id.* at 398.

As a result, the court concluded that the terms of the statute should be interpreted according to their plain meaning. *Id.* at 395. In reaching this conclusion, the court reasoned that "the terms 'active ingredient,' 'salt,' and 'ester' had well-defined, ordinary, common meanings when Congress enacted the Act" and merit legal consequence. *Id.* at 395. The court refrained from deciding whether its plain meaning approach, or the USPTO active moiety approach, was

better from a policy standpoint, explaining that "[s]triking balances in legislative language is Congress' job." *Id.* at 399.

ii. Pfizer I & II

The Federal Circuit addressed the issue of how to interpret §§ 156(a) and (f) again in *Pfizer, Inc. v. Dr. Reddy's Labs., Ltd.*, 359 F.3d 1361 (Fed. Cir. 2004) (*Pfizer II*). In that case, Pfizer owned a patent covering the base molecule amlodipine and two of its salts, amlodipine besylate and amlodipine maleate. *Pfizer II*, 359 F.3d at 1363. Pfizer obtained FDA marketing approval for a drug called Norvasc, which contained amlodipine besylate as its key ingredient. *Id.* at 1364-65; *see also Pfizer, Inc. v. Dr. Reddy's Labs., Ltd.* 2002 WL 31833744, at *1 (D. N.J. 2002) (*Pfizer I*). After obtaining approval, Pfizer applied for and was granted a term extension for the patent covering the Norvasc drug. *Id.* at 1364.

Also after Pfizer's FDA approval, Dr. Reddy's applied for its own FDA approval of a drug containing amlodipine maleate as its key ingredient. *Pfizer II*, 359 F.3d at 1364. Attempting to convince the court that its drug was not covered by Pfizer's patent term extension, Dr. Reddy's argued that the "active ingredient" of Pfizer's Norvasc drug was amlodipine besylate and not the underlying parent molecule amlodipine. *Id.* at 1364. Pfizer, on the other hand, asserted the "active moiety" argument, which would result in amlodipine qualifying as the "active ingredient" of Norvasc. *Id.* 1365. Under the active moiety interpretation, Pfizer's patent term extension would cover both amlodipine besylate and amlodipine maleate because both compounds are salts of the "active ingredient" amlodipine.

The court, reversing the district court which had applied *Glaxo II*, applied the active moiety approach and held that amlodipine was the § 156 "active ingredient" of Norvasc. Under this statutory construction, Pfizer's patent term extension covered amlodipine, amlodipine

besylate, and amlodipine maleate. *Pfizer II*, 359 F.3d at 1367. The court explained why it adopted the active moiety approach:

> The statute foresaw variation in the salt or ester of an active ingredient, and guarded against [this] loophole . . . . [T]he Hatch-Waxman Act established a balance whereby the patent term extension is offset by facilitating generic entry when the extended term expires, yet preserving the innovation incentive. Whether or not this bargain achieved "perfect symmetry"—Dr. Reddy's argues that it was not intended to do so, but was designed to favor the generics—the text of the statute shows that it was not intended to be defeated by simply changing the salt.

Id. at 1366 (internal citations omitted).

iii. The Glaxo II/Pfizer II Conflict

Interestingly, the Federal Circuit in *Pfizer II* did not cite *Glaxo II* or *Glaxo I*, even though *Pfizer II* and those cases are clearly in conflict. *Glaxo I* and *II* stand for the proposition that a compound can only qualify as the "active ingredient" of a drug if that compound itself is present in the drug.[8] *See Glaxo II*, 894 F.2d at 393; *Glaxo I*, 706 F.Supp. at 1227-28. *Pfizer II*, in contrast, supports the active moiety approach, which results in automatically naming the base molecule the "active ingredient" in any instance where a salt or ester of that base molecule is the key ingredient in the drug. *Pfizer II*, 359 F.3d at 1367. The active moiety approach does not require that the active ingredient be a compound physically present in the drug.

The Court must determine whether it is required to follow *Glaxo II* or *Pfizer II*. Importantly, *Pfizer II* postdated *Glaxo II* and was a panel decision that the Federal Circuit declined to hear *en banc*. "[The Federal Circuit] has adopted the rule that prior decisions of a panel of the court are binding precedent on subsequent panels unless and until overturned *in banc*. Where there is a direct conflict, the precedential decision is the first." *Newell Companies,*

[8] *Glaxo II* does not expressly state that the compound must be present in the drug in order to qualify as the "active ingredient." However, the *Glaxo II* court's interpretation of § 156, in combination with its affirmance of *Glaxo I* persuades this Court that *Glaxo II* must be read to incorporate this concept.

Inc. v. Kenney Manufacturing Co., 864 F.2d 757, 765 (Fed. Cir. 1988) (internal citations omitted); *see Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1371 (Fed. Cir. 2008). Therefore, this court is bound by *Glaxo II*.[9]

C. Application

Applying *Glaxo II* to the facts of this case, the active ingredient in Metvixia is MAL hydrochloride and not the active moiety ALA, because MAL hydrochloride is the ingredient physically present in Metvixia that permits the drug to work effectively. ALA does not exist in Metvixia in any capacity besides its esterified form of MAL hydrochloride. Therefore, MAL hydrochloride, and any salt or ester deriving from it, constitute "the product" under § 156. ALA and ALA hydrochloride, on the other hand, are not covered by "the product" language.

As a result, Levulan, whose key ingredient is ALA hydrochloride, does not contain the same "product" as Metvixia. It necessarily follows that Levulan cannot qualify as the first permitted use of a drug containing "the product" at issue in this case. Instead, Metvixia is the first permitted commercial marketing or use of a drug containing "the product" MAL hydrochloride. *See* 35 U.S.C. § 156(a)(5)(A) (2006). Therefore, this Court holds that the '267 patent covering Metvixia satisfies § 156(a)(5)(A), and that the USPTO's decision to apply the active moiety interpretation and deny PhotoCure a patent term extension under this provision was contrary to the plain meaning of the statute and thus not in accordance with law. *See* 5 U.S.C. § 706(2)(A).

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[9] The Court is aware of the *Tunik v. Merit Systems Protection Board* case where the Federal Circuit stated the following: "where an earlier panel decision on statutory construction was based on deference to an agency interpretation, a later panel of this court is free to consider whether a new agency interpretation is reasonable without en banc reconsideration of the earlier panel decision." 407 F.3d 1326, 1338 (Fed. Cir. 2005). This rule does not apply to the present case, however, because the USPTO interpretation in *Glaxo II* (i.e. the "earlier panel decision") was accorded no deference, and because, as explained below in Section IV.D, the USPTO interpretation in this case merits no deference, as well.

Even though this holding is compelled by *Glaxo II*, the Court would reach the same result had the issue been one of first impression. The primary definition of the term "ingredient" requires that the ingredient actually be contained in the compound. *See* 7 Oxford English Dictionary 963-64 (2d ed.1989) (an "ingredient" is "[s]omething that enters into the formation of a compound or mixture; a component part, constituent or element."). Therefore, the Court believes that a plain meaning interpretation of the § 156(f)(2) "active ingredient" term requires the actual presence of a compound qualifying as the "active ingredient" in the drug.

To adopt the active moiety approach would entail construing the term "active ingredient" in such a manner that permits compounds to qualify as ingredients of drugs even when those compounds are not actually present in the drug. To adopt such a construction would be permissible, in this Court's view, only if there was support in the legislative history. But the Court could find no legitimate support for the active moiety approach in the § 156 legislative history. Therefore, the Court will not construe the "active ingredient" term against its plain meaning by adopting a construction that permits compounds not present in the drug to qualify as the "active ingredient."

Also worth emphasizing is that the term "active moiety" was indisputably well-known at the time Congress drafted the statute. If Congress desired to infuse the "active moiety" concept into §§ 156(a) and (f), it could have done so easily by including the term somewhere in either of those two provisions.

D. Agency Deference

The USPTO argues that its active moiety interpretation of § 156 is entitled to *Chevron* and *Skidmore* deference. *Chevron* established a two-step test for determining the amount of

deference accorded to agency actions having the force of law.[10] *See Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984); *Citizens Exposing Truth about Casinos v. Kempthorne*, 492 F.3d 460, 466 (D.C. Cir. 2007). Under the first step, the court must determine "whether Congress has directly spoken to the precise question at issue." *Chevron*, 467 U.S. at 842. If so, then "that is the end of the matter; for the court, as well as the agency must give effect to the unambiguously expressed intent of Congress." *Chevron*, 467 U.S. at 842-43. However, if the statute is silent (i.e., "left a gap") or ambiguous with respect to a specific issue, then the analysis proceeds to "Step Two." *Chevron*, 467 U.S. at 842-44. Under Step Two, the court must give the agency's interpretation deference unless it is "arbitrary, capricious, or manifestly contrary to the statute." *Id.* at 843.

The controlling statutory terms in this case are "product," "drug product," and "active ingredient." As explained above, the terms "product" and "drug product" are further defined by the "active ingredient" language of § 156(f)(2). Congress, however, did not supply a statutory definition for the "active ingredient" term. Therefore, if *Chevron* deference is appropriate in this case, it would apply most directly to the USPTO's interpretation of the undefined "active ingredient" term and not the further defined "product" and "drug product" terms.

The *Glaxo II* court addressed the issue of whether Congress "left a gap" in or ambiguously drafted the terms in § 156(f)(2). Specifically, the court stated that "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. Accordingly, we need not defer to any reasonable interpretation of the Commissioner." *Id.* at 398. In other words, because the statutory terms in § 156(f)(2) (e.g., "active ingredient") are

[10] The USPTO interpreted § 156(f)(2) in its formal adjudication of the '267 patent term extension case. Because this interpretation came through formal adjudication, it clearly has the force of law and is ripe for a *Chevron* analysis.

unambiguous, the *Chevron* analysis ends at Step One and the Court must give effect to the intent of Congress. Following the *Glaxo II* reasoning, this Court concludes that the USPTO's formal active moiety interpretation of the § 156(f)(2) "active ingredient" term merits no *Chevron* deference.

The USPTO also argues that it is entitled to *Skidmore* deference, a lesser and different form of deference than that of *Chevron*. *See Skidmore v. Swift & Co.*, 323 U.S. 134 (1944); *United States v. Mead Corp.*, 533 U.S. 218, 227-28 (2001). Unlike *Chevron* deference, *Skidmore* deference can apply to agency interpretations not having the force of law, such as those contained in opinion letters, policy statements, agency manuals, and enforcement guidelines. *Christensen v. Harris County*, 529 U.S. 576, 587 (2000) (internal citations omitted). Such agency interpretations are "'entitled to respect' . . . but only to the extent that those interpretations have the 'power to persuade.'" *Id.* (internal citations omitted).

The amount of deference that an agency interpretation of a statute warrants under *Skidmore* varies with the circumstances. *Mead*, 533 U.S. at 228; *Cathedral Candle Co. v. United States Int'l Trade Comm'n*, 400 F.3d 1352, 1365-66 (Fed. Cir. 2005). One factor courts consider in determining how much deference to award is "the writer's thoroughness, logic, and expertise." *Cathedral Candle*, 400 F.3d at 1366 (citing *Mead*, 533 U.S. at 235.). Additionally, the Federal Circuit has explained:

> [W]e believe the Supreme Court intends for us to defer to an agency interpretation of the statute that it administers if the agency has conducted a careful analysis of the statutory issue, if the agency's position has been consistent and reflects agency-wide policy, and if the agency's position constitutes a reasonable conclusion as to the proper construction of the statute, even if we might not have adopted that construction without the benefit of the agency's analysis.

Cathedral Candle Co., 400 F.3d at 1366.

The USPTO first argues that it warrants *Skidmore* deference because it has consistently applied the same principles to patent term extension applications. The Court disagrees. For example, the USPTO clearly applied the active moiety approach at the formal agency adjudication stage of this case. Yet at the time the agency decision issued on May 13, 2008, § 2751 of the Manual of Patent Examining Procedures (MPEP), one of the most prominent documents published by the USPTO, stated the following: "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 acid itself has not previously been approved." Even more, this language was contained under the USPTO's definition of "drug product" and cited both *Glaxo I* and *Glaxo II*. *See* MPEP § 2751. This MPEP language does not comport with the "active moiety" approach. The USPTO stated as much in its brief, writing that "the guidance in MPEP § 2751 about the patent term extension eligibility for salts and esters is admittedly incorrect, and the agency is revising it." Reply Brief for Defendants at 8-9, *PhotoCure v. Dudas, et al.*, 1:08-cv-718 (E.D. Va. 2008).

Because of the conflict between the interpretation advised in MPEP § 2751 and the "active moiety" approach used in the formal adjudication, the Court is not persuaded that the USPTO should merit any deference under *Skidmore* for being "consistent" in constructing and "careful" in analyzing §§ 156(a) and (f). *See Cathedral Candle Co.*, 400 F.3d at 1366.

Furthermore, the USPTO does not merit deference for its active moiety construction of §§ 156(a) and (f) being a "reasonable conclusion as to the proper construction of the statute." *See id.* Once more, the USPTO's interpretation of "active ingredient" in this case runs afoul of the plain meaning of the statute and finds no legitimate support in the legislative history. Such an interpretation, in the Court's view, is not reasonable.

Finally, the USPTO asserts that its expertise in understanding the chemistry of drug products calls for a high level of *Skidmore* deference. Any amount of deference earned as a result of such expertise, however, would be insufficient to convince the Court to follow the USPTO in adopting an inconsistent and unreasonable statutory construction contrary to plain meaning. *See Garcia v. U.S.*, 469 U.S. 70, 75 (1984) (quoting *TVA v. Hill*, 437 U.S. 153, 187 n.33 (1978)) ("[w]hen we find the terms of a statute unambiguous, judicial inquiry is complete, except in rare and exceptional circumstances") (internal quotations omitted). For these reasons, the Court will not defer to the USPTO's interpretation of § 156(a). Instead, the Court's holding in Section IV.C stands.

V. CONCLUSION

For the foregoing reasons, the Court shall grant Plaintiff's Motion for Summary Judgment on Counts I and II. Accordingly, the Court shall deny Defendants' Motion for Summary Judgment on those same counts.

Entered this 31st day of March, 2009.

Alexandria, Virginia

/s/
Liam O'Grady
United States District Judge

CERTIFICATE OF SERVICE

I hereby certify that on July 21, 2009, I filed and served the foregoing BRIEF FOR DEFENDANT-APPELLANT by causing an original and twelve copies to be delivered to the Clerk of the Court by hand delivery and by causing two copies to be delivered to the following counsel as indicated:

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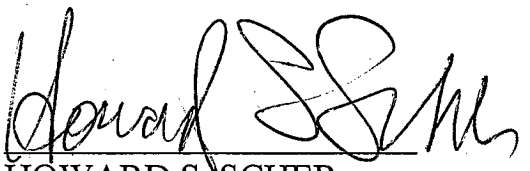
CERTIFICATE OF COMPLIANCE WITH RULE 32(a)
OF THE FEDERAL RULES OF APPELLATE PROCEDURE

1. Pursuant to Fed. R. App. P. 32(a)(7), I certify that the attached BRIEF FOR DEFENDANT-APPELLANT complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B). The brief contains **8,511** words, as counted by Word Perfect 12, excluding the parts of the brief exempted by Fed. R. App. P. 32(a)(7)(B)(iii) and Federal Circuit Rule 32(b).

2. I also certify that this brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6). The brief has been prepared in a proportionally-spaced typeface using Word Perfect 12 in 14-point Times New Roman.



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ADDENDUM A

Pertinent Statutory Provision

35 U.S.C. 156, in pertinent part, provides as follows:

(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 from the original expiration date of the patent, which shall include any patent term adjustment granted under section 154(b), if —

(1) the term of the patent has not expired before an application is submitted under subsection (d)(1) for its extension;

(2) the term of the patent has never been extended under subsection (e)(1) of this section;

(3) an application for extension is submitted by the owner of record of the patent or its agent and in accordance with the requirements of paragraphs (1) through (4) of subsection (d);

(4) the product has been subject to a regulatory review period before its commercial marketing or use;

(5)(A) except as provided in subparagraph (B) or (C), 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 * * *.

* * *

(f) For purposes of this section:

(1) The term "product" means:

(A) A drug product.

(B) Any medical device, food additive, or color additive subject to regulation under the Federal Food, Drug, and Cosmetic Act.

(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), or

(B) a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Virus-Serum-Toxin Act) which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques,

including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient.