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Office of Regulatory Policy
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 51, Rm. 6222
Silver Spring, MD 20993-0002

APR - 1 2008

Attention: Beverly Friedman

Dear Ms. Axelrad:

Transmitted herewith is a copy of the application for patent term extension of U.S. Patent No. 5,817,338 (the '338 patent). The application was filed on August 19, 2003, under 35 U.S.C. § 156.

The patent claims a product that was subject to regulatory review under the Federal Food, Drug and Cosmetic Act. Subject to final review, the subject patent may be eligible for patent term extension. Thus, a determination by your office of the applicable regulatory review period is necessary. Accordingly, notice and a copy of the application are provided pursuant to 35 U.S.C. § 156(d)(2)(A).

Prior to determining the regulatory review period, however, the USPTO has two inquiries with respect to the eligibility of the patent for patent term extension based on the regulatory review period of Prilosec OTC®. The first inquiry relates to timeliness of the filing of the patent term extension application, while the second inquiry relates to whether the approval of Prilosec OTC® constitutes the first permitted commercial marketing or use of the active ingredient of Prilosec OTC®, namely, omeprazole magnesium.

With respect to the first inquiry, it is the position of the USPTO that the subject patent term extension was not timely filed based on a plain reading of the statutory language of 35 U.S.C. § 156(d)(1) and the USPTO's implementing regulations at 37 C.F.R. § 1.720(f).

Specifically, FDA approval triggers the time period specified in 35 U.S.C. § 156(d)(1), which requires that an application for patent term extension of a patent which claims a product, a method of using such product, or a method of manufacturing such product, wherein the product was subject to premarket regulatory review by a regulating agency, must be submitted, "within the sixty-day period beginning on the date the product received permission under the provision of law under which the applicable regulatory review period occurred for commercial marketing or use." See 35 U.S.C. § 156(d)(1) (emphases added). Additionally, the USPTO's implementing regulations mirror the language of section 156(d)(1): "[t]he application is submitted within the sixty-day period beginning on the date the product first received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred . . . ." See 37 C.F.R. § 1.720(f) (emphases added).

Moreover, the phrases used in section 156(d)(1) to define the time period, i.e., "within" and

"beginning on" are clear. *See, Unimed, Inc. v. Quigg*, 888 F.2d 826, 828 (Fed. Cir. 1989) (characterizing the language used in section 156(d)(1) as "crystal clear"); *see also, United States v. Inn Foods, Inc.*, 383 F.3d 1319, 1322 (Fed. Cir. 2004) (explaining, in the context of a statute of limitation, that terms such as "within [a particular time period]" and "beginning on" clearly specify a time period and need no further analysis). Thus, under both 35 U.S.C. § 156(d)(1) and 37 C.F.R. § 1.720(f), a PTE applicant has sixty days to submit a PTE application, and the first day of that sixty-day period begins on the FDA approval date.

In the present case, the FDA approved NDA No. 021229 on June 20, 2003. The absolute deadline for filing a PTE application was sixty days from June 20, 2003, starting the count of that sixty day period on June 20, 2003. The sixtieth day of that time period was August 18, 2003 (a Monday). Since the subject PTE application was filed on August 19, 2003, it is untimely.

With respect to the second inquiry, it is the position of the USPTO that U.S. Patent No. 5,817,388 is not eligible for extension because Applicant has not complied with 35 U.S.C. § 156(a)(5)(A). Specifically, permission for the commercial marketing or use of the product, Prilosec OTC®, does not constitute the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred.

The USPTO's rationale for this position is as follows:

The Plain Language of 35 U.S.C. § 156(f) Shows That Prilosec OTC® (omeprazole magnesium) Is Not the First Permitted Commercial Marketing or Use of the "Product" As Required by 35 U.S.C. § 156(a)(5)(A)

Section 156(a) of Title 35 sets forth several requirements that must be met before the Director can extend the term of a patent. See 35 U.S.C. §§ 156 (a)(1)-(a)(5), (d)(1), & (e)(1). Section 156(a)(5)(A) requires that

> the permission for the commercial marketing or use of the product . . . [be] 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)(5)(A) (emphasis added). The term "product" as used in section 156(a)(5)(A) is defined in section 156(f)(1) as a "drug product," and the term "drug product" is defined in section 156(f)(2) 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) (emphasis added). Hence, by the explicit terms of section 156(f)(2), the term "product" as used in section 156 includes: (i) a non-salified and non-esterified form of a molecule (*i.e.*, the "active ingredient"); (ii) a salt of the molecule (*i.e.*, the "salt . . . of the active ingredient"); and (iii) an ester of the molecule (*i.e.*, the " . . . ester of the

active ingredient").[1] Because a "product" includes all three forms, a non-salified, non-esterified form of a molecule is statutorily the same "product" as a salt or ester of that molecule for purposes of the patent term extension provisions in section 156.

Applicant states at page 2 bridging to page 3 of the PTE Application that (i) "the active ingredient in the Approved Product is omeprazole magnesium," and (ii) "[p]lease note that omeprazole magnesium is a different active ingredient from omeprazole, which is marketed as Prilosec® (NDA 019810), for which patent term extension has previously been granted." Indeed, as admitted by Applicant, prior to the approval of Prilosec OTC® (omeprazole magnesium), the FDA approved Prilosec® (omeprazole). It is clear that omeprazole is present in Prilosec®, where omeprazole is formulated as a base. Consequently, the approved "product," as that term is defined in § 156, is the same in Prilosec® and Prilosec OTC®, *i.e.*, omeprazole and any salt or ester of omeprazole. The later approved Prilosec OTC® (omeprazole magnesium) thus does not represent the first permitted commercial marketing or use of the "product" under the provision of law under which such regulatory review occurred. The USPTO therefore believes that the PTE Application does not satisfy the requirements of section 156(a)(5)(A) and the '338 patent is not eligible for a patent term extension.

Judicial Precedent Confirms That Prilosec OTC® (omeprazole magnesium) Is Not the First Permitted Commercial Marketing or Use of the "Product" As Required by 35 U.S.C. § 156(a)(5)(A)

Judicial precedent confirms that the USPTO's understanding and application of the definition of "product," as that term is used in section 156(a)(5)(A), is correct. In Fisons v. Quigg, 1988 WL 150851 (D.D.C. 1988) ("Fisons I"), the district court construed section 156(a)(5)(A) in a straightforward way:

> In the definitional provision of Section 156, the term "product" is defined as a "human drug product." 35 U.S.C. § 156(f)(1)(A). This term is further defined in the next subparagraph 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) (emphasis added in original). Substituting this definition directly back into Section 156(a)(5)(A) yields the statement that a patent is ineligible for extension if it is not the first permitted commercial marketing or use of the active ingredient contained in that approved patented product.

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[1]The plain language of section 156(f) makes clear that the same definition of "product" is to be applied throughout section 156. Section 156(f) explicitly states that its provisions are "for purposes of this section." Thus, the term "product" as used throughout 35 U.S.C. § 156—for eligibility under section 156(a) and for enforcement under section 156(b)—has but one meaning.

Id. at *5.

The Federal Circuit affirmed the district court's interpretation. Fisons v. Quigg, 876 F.2d 99 (Fed. Cir. 1989) ("Fisons II"). The Federal Circuit stated: "In sum, we hold that the district court correctly applied the definition given in 35 U.S.C. § 156(f) to the term 'product' used in section 156(a)(5)(A). We are convinced that such an interpretation comports with the intent of Congress as expressed in the statute." Fisons II, 876 F.2d at 102.

The Federal Circuit later interpreted the term "active ingredient" in Pfizer, Inc. v. Dr. Reddy's Labs., Ltd., 359 F.3d 1361 (Fed. Cir. 2004). There, the Federal Circuit accepted the FDA's definition of the term "active ingredient" as meaning "active moiety." Id. at 1366 (citing Abbreviated New Drug Application Regulations: Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338, 50,358 (F.D.A. Oct. 3, 1994)). It likewise accepted that "active moiety" means "the molecule or ion excluding those appended portions of the molecule that cause the drug to be an ester, salt . . . responsible for the physiological or pharmacological action of the drug substance," based upon the FDA's regulations. Id. (quoting 21 C.F.R. § 314.108(a)) (omission in original). Hence, the Federal Circuit has construed the term "active ingredient" as used in section 156(f)(2) to mean the underlying molecule, *i.e.*, the molecule or ion responsible for the physiological or pharmacological action of the drug, excluding those appended portions of the molecule that cause the drug to be an ester or salt.

Substituting this definition for the word "active ingredient" as it appears in section 156, the term "drug product" in section 156(f)(2) must mean the underlying molecule as well as any salt or ester of the underlying molecule, since it is defined as "active ingredient . . . including any salt or ester of the active ingredient." Further, because "product" is defined as "drug product" in section 156(f)(1)(A), "product" likewise must mean the underlying molecule as well as any salt or ester of the underlying molecule. That definition conforms with the plain language of section 156(f). What is more, the Federal Circuit confirmed in Pfizer that only the first approval for any given "active ingredient" can trigger a patent term extension under 35 U.S.C. § 156, regardless of whether that first approval was for an underlying molecule, a salt of the underlying molecule, or an ester of the underlying molecule. Pfizer, 359 F.3d at 1366 ("The statute [referring to 35 U.S.C. § 156] foresaw variation in the salt or ester of an active ingredient, and guarded against the very loophole now urged").

Here, before approving Prilosec OTC® (omeprazole magnesium) in 2003, the FDA approved Prilosec® (omeprazole) in 1989. As explained above, omeprazole is the underlying molecule in both Prilosec® and Prilosec OTC® . Omeprazole is simply formulated differently in these two different drugs: as omeprazole itself in Prilosec®, and as the magnesium salt of omeprazole in Prilosec OTC®. However, the salt formulation difference does not matter for purposes of section 156. The statutory definition of "product" includes the underlying molecule as well as any salt or ester of the underlying molecule. Accordingly, Prilosec OTC® (omeprazole magnesium) is not the first permitted commercial marketing or use of the "product" as required by 35 U.S.C. § 156(a)(5)(A) because of the earlier approval of Prilosec® (omeprazole).

Finally, the FDA has issued a regulation defining the term "active ingredient" of a pharmaceutical "product" for purposes of patent term extension under 35 U.S.C. § 156. Specifically, 21 C.F.R. § 60.1(a) states that "[t]his part [referring to Part 60] sets forth procedures and requirements for the [FDA]'s review of applications for the extension of the term of certain patents under 35 U.S.C. § 156." That provision further states that "[FDA] actions in this area include [inter alia] [a]ssisting the [USPTO] in determining eligibility for patent term restoration." 21 C.F.R. § 60.1(a)(1). Section 60.3 then provides a series of definitions to be used in Part 60 in addition to the definitions already contained in 35 U.S.C. § 156. 21 C.F.R. § 60(b)(2) defines "active ingredient" for purposes of a patent extension to mean a drug's active moiety, *i.e.*, its therapeutically active component. It states:

> Active ingredient means any component that is intended to furnish pharmacological activity or other direct effects in the diagnosis, cure, mitigation, treatment or prevention of disease, or to affect the structure or function of the body of man or of animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.

21 C.F.R. § 60.3 (b)(2). Applying the FDA's regulations in this case, omeprazole is the "active ingredient" of not just Prilosec® (omeprazole), but also of Prilosec OTC® (omeprazole magnesium); it is simply formulated as a magnesium salt in Prilosec OTC®.

The USPTO recognizes that Glaxo Operations UK, Ltd v. Quigg, 894 F.2d (Fed. Cir. 1990), also concerns section 156(f). However, the USPTO observes that Glaxo is factually distinguishable because the Federal Circuit did not address the definition of "active ingredient" in that case. Rather, the Federal Circuit focused on the USPTO's argument that the term "product" did not have the literal meaning set forth in section 156(f)(2), but instead meant "any 'new chemical entity,' *i.e.*, 'new active moiety.'" Rejecting that argument, the Federal Circuit explained that Congress provided a definition of the term "product" in section 156(f)(2) and that Congress "selected terms with narrow meanings that it chose from among many alternatives." Glaxo, 894 F.2d at 399 (footnoting as examples of other possible words "new molecular entity," "active moiety," and "new chemical entity"). The Federal Circuit did not discuss the definition of the term "active ingredient" because, unlike here, the determination of the active ingredient was not in dispute in Glaxo.

The most that can be said about Glaxo is that the Federal Circuit acknowledged that the term "product" was not expressly defined by Congress to mean "active moiety," since those words do not appear in section 156(f)(2). However, Glaxo does not hold that the term "active ingredient" as used in section 156(f)(2) does not mean "active moiety." In fact, the Federal Circuit later accorded the term "active ingredient" with that precise definition in Pfizer. See Pfizer, 359 F.3d at 1366. Accordingly, the USPTO's initial determination is that the '338 patent is ineligible for extension pursuant to section 156 as supported by, and consistent with, Glaxo.

Inquiries regarding this communication should be directed to the undersigned at (571) 272-7755 (telephone) or (571) 273-7755 (facsimile).

Mary C. Till
Legal Advisor
Office of Patent Legal Administration
Office of the Deputy Commissioner
for Patent Examination Policy

cc: Leslie Morioka
Patent Department
White and Case
1155 Avenue of the Americas
New York, NY 10036-2787

RE: Prilosec OTC® (omeprazole magnesium)
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