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In re: Patent Term Extension
Application for
U.S. Patent No. 5,602,176

NOTICE OF FINAL DETERMINATION -- INELIGIBLE

Novartis AG ("Applicant"), is the owner of record of U.S. Patent No. 5,602,176 ("the '176 patent"). Applicant, through its subsidiary, Novartis Corporation, filed a Patent Term Extension Application ("PTE") Under 37 [sic] U.S.C. § 156 in the United States Patent and Trademark Office ("USPTO") on September 4, 2007. Extension was sought based upon the premarket review under § 505 of the Federal Food, Drug, and Cosmetic Act ("FFDCA") of a human drug product known by the tradename EXELON® PATCH having the active ingredient rivastigmine. EXELON® PATCH was approved for commercial use and sale by the Food and Drug Administration (FDA) on July 6, 2007. Because the grant of permission for commercial marketing and use of EXELON® PATCH does not constitute the first permitted commercial marketing or use of the "product" the '176 patent is **NOT** eligible for patent term extension.

A. Background

On September 4, 2007, Applicant filed the PTE Application under 35 U.S.C. § 156.

On January 8, 2008, the USPTO sent a letter to FDA, requesting the FDA's assistance in confirming that (1) the product identified in the PTE Application, EXELON® PATCH, having the active ingredient rivastigmine, was subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first permitted commercial marketing or use and (2) the PTE application was filed within sixty days of the product receiving FDA approval, as required by 35 U.S.C. § 156(d)(1).

On April 28, 2008, FDA responded to the USPTO stating (1) FDA's approval of the EXELON® PATCH, having the active ingredient rivastigmine, does not represent the first permitted commercial marketing or use of the "product," as defined under 35 U.S.C. § 156(f)(1), and as interpreted by the courts, and (2) the PTE Application was timely filed. Specifically, FDA's letter stated:

> A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). However, our records also indicate that it does not represent the first permitted commercial marketing or use of the product, as defined under 35 U.S.C. § 156(f)(1), and interpreted by the courts in Glaxo Operations UK Ltd. v. Quigg, 706 F. Supp. 1224 (E.D. Va. 1989), aff'd. 894 F. 2d 392 (Fed. Cir. 1990). The tartrate salt of rivastigmine, the active ingredient in Exelon Patch, has been previously

approved for commercial marketing or use in the Novartis Corporation products, Exelon oral capsules (NDA No. 20-823) and Exelon oral solution (NDA 21-025).

The Exelon Patch, NDA 22-083, was approved on July 6, 2007, which makes the submission of the patent term extension application on September 4, 2007, timely within the meaning of 35 U.S.C. 156(d)(1).

B. Analysis

1. The Plain Language of 35 U.S.C. § 156(f) Shows That EXELON® PATCH 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.

Apparently, Applicant attempts to distinguish the active ingredient in EXELON® PATCH from EXELON® by stating, at page 2 of the PTE that, (i) the active ingredient in EXELON® PATCH is rivastigmine, and (ii) ""[p]lease note that rivastigmine is a different active ingredient from rivastigmine tartrate, which is marketed as EXELON® (NDA 20-823)." Indeed, prior to the

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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.

approval of EXELON® PATCH, the FDA approved EXELON® (rivastigmine tartrate) . It is clear that rivastigmine is present in EXELON®, where rivastigmine is formulated as the tartrate salt. Consequently, the approved "product," as that term is defined in § 156, is the same in EXELON® PATCH and EXELON®, *i.e.*, rivastigmine and any salt or ester of rivastigmine. The later approved EXELON® PATCH 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 concludes that the PTE Application does not satisfy the requirements of section 156(a)(5)(A) and the '176 patent is not eligible for a patent term extension.

2. Judicial Precedent Confirms That EXELON® PATCH 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 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.

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. . . . [T]he text of the statute shows that it was not intended to be defeated by simply changing the salt.").

Here, before approving the EXELON® PATCH in 2007, the FDA granted permission for commercial marketing and use in 2000 of EXELON® in an oral capsule dosage form and an oral solution dosage form. As explained above, rivastigmine is the underlying molecule in both EXELON® PATCH and EXELON®. Rivastigmine is simply formulated differently in these two different drugs: as rivastigmine tartrate in EXELON®, and as the base itself in EXELON® PATCH. 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, EXELON® PATCH 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 EXELON®.

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. 37 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, rivastigmine is the "active ingredient" of not just EXELON®, but also of EXELON® PATCH; it is simply formulated as the base in EXELON® PATCH and as the tartrate salt in EXELON®.

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 determination that the '176 patent is ineligible for extension pursuant to section 156 is supported by, and consistent with, Glaxo.

In view of the above, the term of U.S. Patent No. 5,602,176 is not eligible for extension under 35 U.S.C. § 156 based upon the approval of the product EXELON®PATCH and the application for patent term extension, filed September 4, 2007, is dismissed.

C. Conclusion

In sum, based on the plain language of section 156(f)(2) and judicial precedent, the USPTO concludes and FDA has confirmed in their April 28, 2008 letter that the FDA's grant of permission for commercial marketing and use of EXELON® PATCH (rivastigmine) 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, as required by 35 U.S.C. § 156(a)(5)(A). Therefore, Applicant's application for patent term extension is **dismissed**.

A single request for reconsideration of this FINAL DETERMINATION OF INELIGIBILITY may be made if filed by the applicant within TWO MONTHS of the mailing date of this letter. The period for response may be extended pursuant to 37 C.F.R. 1.136. See 37 C.F.R. 1.750. A failure to respond to this letter will result in the application papers being placed into the patent file with no further action taken on the application for patent term extension.

Any correspondence with respect to this matter should be addressed as follows:

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Telephone inquiries related to this determination should be directed to the undersigned at (571) 272-7755.

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Attention: Beverly Friedman

RE: EXELON® PATCH
(rivastigmine)
FDA Docket No.: 2007E-0035