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In Re: Patent Term Extension
Application for
U.S. Patent No. RE40045
(Original U.S. Patent No. 5,270,305)

NOTICE OF FINAL DETERMINATION-INELIGIBLE

Glaxo Group Ltd ("Applicant"), the owner of record of U.S. Patent No. 5,270,305, now reissued as U.S. Patent No. RE40045 ("the '045 reissue patent"), filed an application ("PTE Application") for extension of the patent term of U.S. Patent No. 5,270;305 under 35 U.S.C. § 156 in the United States Patent and Trademark Office ("USPTO") on October 20, 2000. Applicant also filed a second supplement to the original PTE Application ("Second Supplement") on August 19, 2008 directing the USPTO's attention to the reissue and describing how the reissue patent claims the product which was subject to the regulatory review period. Applicant sought extension based upon the premarket review under section 505 of the Federal Food, Drug, and Cosmetic Act ("FFDCA") of the human drug product known by the tradename ADVAIR DISKUS®, having the active ingredients salmeterol xinafoate and fluticasone propionate. ADVAIR DISKUS® was approved for commercial use and sale by the Food and Drug Administration ("FDA") on August 24, 2000.

A determination has been made that the '045 reissue patent is INELIGIBLE for patent term extension under 35 U.S.C. § 156 based upon the regulatory review period of ADVAIR DISKUS® (salmeterol xinafoate and fluticasone propionate) because ADVAIR DISKUS® does not constitute the first permitted commercial marketing or use of the product ADVAIR DISKUS® (salmeterol xinafoate and fluticasone propionate) under the provision of law under which such regulatory review period occurred.

A single request for reconsideration of this FINAL DETERMINATION OF INELIGIBILITY may be made if filed by 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 PTE Application.

I. The PTE Application for the '045 Reissue Patent Fails to Comply with 35 U.S.C. § 156(a)(5)(A)

To qualify for a patent term extension under section 156, there are several requirements that must be satisfied. *See* 35 U.S.C. §§ 156 (a)(1)-(5) & (d)(1). Section 156(a)(5)(A) provides:

> (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—
>
> (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)(5)(A) (emphasis added). Based on this statutory language, one of the eligibility requirements for a patent term extension is that the permission for the commercial marketing or use of the product be the first permitted commercial marketing or use of the product.

The term "product" as used in section 156(a)(5) is defined as "drug product," *see* 35 U.S.C. § 156 (f)(1)(A), which in turn is defined as "the active ingredient of—(A) 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," *see* 35 U.S.C. § 156(f)(2)(A). Thus, by the explicit terms of section 156(f)(2), the term "product" as it relates to a human drug product means the active ingredient(s) of the new drug product.

Taking section 156(a)(5)(A) together with section 156(f)(2), a patent is eligible for a patent term extension if, *inter alia*, the active ingredient(s) of the product represents the first permitted commercial marketing or use of the active ingredient. Courts have confirmed this eligibility requirement in more than one case. *See, e.g., Fisons Plc v. Quigg*, 876 F.2d 99, 100-101 (D.C. Cir. 1989); *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 395 (Fed. Cir. 1990).

In this case, the PTE Application indicates that ADVAIR DISKUS® contains two active ingredients: salmeterol xinafoate and fluticasone propionate. The FDA official records indicate that salmeterol xinafoate and fluticasone propionate were each previously approved for commercial marketing or use before the approval of ADVAIR DISKUS®. Specifically, salmeterol xinafoate was first approved in New Drug Application ("NDA") No. 20-236 in the human drug product SEREVENT® on February 4, 1994. Regarding fluticasone proprionate, FDA official records indicate approval of NDA No. 20-121 on October 19, 1994 for FLONASE®, having as the active ingredient, fluticasone proprionate.

Because both active ingredients in ADVAIR DISKUS® have been previously approved for commercial marketing or use before the approval of ADVAIR DISKUS®, Applicant's approval of ADVAIR DISKUS® does not qualify as the first permitted commercial marketing or use of either active ingredient, as required by section 156(a)(5). Therefore, the '045 reissue patent is **ineligible** for patent term extension based on the regulatory review period of ADVAIR DISKUS®.

Applicant admits that both active ingredients of ADVAIR DISKUS® have been previously approved. *See* PTE Application at 4 (acknowledging that salmeterol xinafoate has been previously approved under section 505(b) of the FFDCA on February 4, 1994, and that fluticasone proprionate has been previously approved under section 505(b) of the FFDCA on March 27, 1996. Applicant argues, however, that since the product ADVAIR DISKUS® is a synergistic combination of salmeterol xinafoate and fluticasone propionate, it should be considered as a single active ingredient for patent term extension purposes. *See* PTE Application at 3-4. Applicant also presented evidence regarding the synergistic effect of the active ingredients salmeterol xinafoate and fluticasone propionate in the Supplement to Request for Extension of Patent Term under 35 U.S.C. 156 ("First Supplement") filed June 26, 2003. For support, Applicant apparently relies on the Manual of Patent Examining Procedure ("MPEP") which states: "Furthermore, an approved product having two active ingredients, which are not shown to have a synergistic effect or have pharmacological interaction, will not be considered to have a single active ingredient made of the two active ingredients." U.S. Patent & Trademark Off., MPEP § 2751 (8th ed. 2001, rev. Sept. 2007).

Applicant's argument is misplaced. The synergistic effect of the active ingredients salmeterol xinafoate and fluticasone propionate has no relevance in determining "first permitted commercial marketing or use of the product" as required by 35 U.S.C. § 156(a)(5)(A). The term "product" as used in 35 U.S.C. § 156 includes any new drug or antibiotic drug, "as a single entity or in combination with another active ingredient." 35 U.S.C. § 156 (f)(2). Section 156(f)(2) says nothing about if a combination of active ingredient is synergistic, it is treated as a single entity. *See Arnold Partnership v. Dudas*, 362 F.3d 1338, 1343 (Fed. Cir. 2004).

Furthermore, it is the Office's long-standing position that if a drug product contains two active ingredients, each of which has been previously approved individually, then regulatory approval of the combination drug product cannot be the basis for extension of a patent claiming the approved combination. *See In re Alcon Labs Inc.*, 13 USPQ2d 1115, 1118 (Comm'r of Pats. 1989) ("For a product which contains a plurality of active ingredients, as here, the statute [referring to 35 U.S.C. § 156(a)(5)(A)] must be analyzed with respect to each active ingredient."). The Federal Circuit confirmed that the Office's position is correct in *Arnold Partnership*. In that case, the Court considered whether a patent directed to a combination of active ingredients (ibuprofen and hydrocodone bitartrate) in the drug product VICOPROFEN® would qualify for a patent term extension under § 156 where each active ingredient had been previously approved separately. *Id.* at 1341. The Court explained that section 156(f) "requires this court to examine a drug product patent's eligibility for extension on a component-by-component basis." *Id.* Doing so, the Court reasoned that section 156(f)

> places a drug product with two active ingredients, A and B, in the same category as a drug product with a single active ingredient. In both instances, those active ingredients individually qualify for examination under the first permitted marketing requirement. **To extend the term of a patent claiming a composition comprising A and B, either A or B must not have been previously marketed**. In other words, at least one of the claimed active

ingredients must be new to the marketplace as a drug product.

Id. (emphasis added). The Court then concluded that the patent claiming VICOPROFEN® was ineligible for a patent term extension for failure to comply with 35 U.S.C. § 156(a)(5)(A) because the individual active ingredients of VICOPROFEN®, ibuprofen and hydrocodone bitartrate, had each been previously approved individually. *Id.* at 1342.

The facts here are analogous to those in *Arnold Partnership*. Like the active ingredients ibuprofen and hydrocodone bitartrate in the combination product VICOPROFEN® in *Arnold Partnership*, salmeterol xinafoate and fluticasone propionate each have been previously approved individually. As a result, the use of salmeterol xinafoate and fluticasone propionate in the combination product ADVAIR DISKUS® does not constitute the first permitted commercial marketing or use of ADVAIR DISKUS® as required by 35 U.S.C. § 156(a)(5)(A), just as the use of ibuprofen and hydrocodone bitartrate in the combination product VICOPROFEN® did not constitute the first permitted commercial marketing of VICOPROFEN® in *Arnold Partnership*. *See id.* at 1315. Accordingly, the '045 reissue patent is not entitled to a patent term extension under *Arnold Partnership*.

Applicant's reliance on MPEP § 2751 is misplaced. The statement in the MPEP does not require that the USPTO treat an alleged synergistic combination drug product with two active ingredients as a single active ingredient made up of the two active ingredients for patent term extension purposes. Rather, MPEP § 2751 merely explains that a product having two active ingredients, without synergy, will not be treated as a single active ingredient. This does not imply that a showing of synergy in a product having two active ingredients, each of which was previously approved for commercial marketing or use, must be considered to be a single active ingredient for patent term extension purposes. The USPTO construes 35 U.S.C. § 156(f)(2) by giving the plain meaning to each and every term of the provision. A "drug product" exists as a single entity, i.e., a drug product having one active ingredient, or the drug product is a combination of two or more active ingredients. No statutory language, regulation, court decision or legislative history account for synergy in the patent term extension context. As such, Applicant cannot point to any precedent which would require finding that a drug product having two active ingredients, which exhibit a synergistic effect, is a single entity within the meaning of section 156. Any commentary by the court supports the USPTO's determination, e.g., Federal Circuit made a statement in their decision in *Arnold Partnership* at 1343 regarding synergy, "[m]oreover, this court doubts that synergistic effects are an appropriate distinction for term extension policies, particularly where the statutory language does not distinguish at all between synergistic and nonsynergistic combinations."

II. Conclusion

For the above-stated reason, the PTE application for the '045 reissue patent is **DISMISSED**.

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. E-mail inquiries should be directed to Mary.Till@uspto.gov.

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