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Leslie Morioka, Esq.
Patent Department
White & Case LLP
1155 Avenue of the Americas
New York, NY 10036-2787

In Re: Patent Term Extension
Application for
U.S. Patent No. 5,674,860

NOTICE OF FINAL DETERMINATION-INELIGIBLE

AstraZeneca AB ("Applicant"), the owner of record of U.S. Patent No. 5674,860 ("the '860 patent"), filed an application ("PTE Application") for extension of the patent term of the '860 patent under 35 U.S.C. § 156 in the United States Patent and Trademark Office ("USPTO") on September 19, 2006. 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 SYMBICORT®, having the active ingredients, formoterol fumarate dihydrate and budesonide. SYMBICORT® was approved for commercial use and sale by the Food and Drug Administration ("FDA") on July 21, 2006.

A determination has been made that the '860 patent is INELIGIBLE for patent term extension under 35 U.S.C. § 156 based upon the regulatory review period of SYMBICORT® (formoterol fumarate dihydrate and budesonide) because (1) SYMBICORT® does not constitute the first permitted commercial marketing or use of the product SYMBICORT® (formoterol fumarate dihydrate and budesonide) under the provision of law under which such regulatory review period occurred, and (2) the PTE Application was not timely filed.

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 '860 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 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 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 SYMBICORT® contains two active ingredients: formoterol fumarate dihydrate and budesonide. The FDA official records indicate that formoterol fumarate dihydrate and budesonide were each approved for commercial marketing or use before the approval of SYMBICORT®. In a letter dated December 6, 2007, FDA stated:

However, our records also indicate that the marketing of the combination product, Symbicort Inhalation Aerosol (formoterol fumarate dihydrate and budesonide), under NDA 21-929 does not represent the first permitted commercial marketing or use of either of the active ingredients in this “product.” For purposes of patent term extension in relation to new drug approval, “product” is defined under 35 U.S.C. § 156(f)(2) as “the active ingredient. . . including any salt or ester of the active ingredient. . . .” FDA has previously approved several new drugs containing formoterol fumarate or budesonide. The new drugs include Novartis Pharmaceuticals’ Foradil and Dey LP’s Perforomist with the active ingredient of formoterol fumarate and Astra Zeneca’s Entocort EC, Pulmicort and Rhinocort with budesonide as the active ingredient.

Because both active ingredients in SYMBICORT® have been previously approved for commercial marketing or use before the approval of SYMBICORT®, Applicant’s approval of SYMBICORT® does not qualify as the first permitted commercial marketing or use of either

active ingredient, as required by section 156(a)(5). Therefore, the '860 patent is ineligible for patent term extension based on the regulatory review period of SYMBICORT®.

Applicant admits that both active ingredients of SYMBICORT® have been previously approved. See PTE Application at 5 (acknowledging that formoterol has been previously approved for use in Foradil® (marketed by Novartis) and that budesonide has been previously approved for use in products such as Pulmicort Respules®, Rhinocort® and Entocort® EC (all marketed by AstraZeneca)). Applicant argues, however, that since the product SYMBICORT® is a synergistic combination of formoterol fumarate dihydrate and budesonide, it should be considered as a single active ingredient for patent term extension purposes. See PTE Application at 3-5 (presenting evidence regarding the synergistic effect of the active ingredients formoterol fumarate dihydrate and budesonide); see also *id.* at Exhibit D (same). 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 incorrect. The synergistic effect of the active ingredients formoterol fumarate dihydrate and budesonide 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 whether a combination is synergistic. See *Arnold Partnership v. Dudas*, 362 F.3d 1338, 1343 (Fed. Cir. 2004) (“Moreover, 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.”).

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 relied upon 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 the active ingredients had each 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*, formoterol fumarate dihydrate and budesonide each have been previously approved individually. As a result, the use of formoterol fumarate dihydrate and budesonide in the combination product SYMBICORT® does not constitute the first permitted commercial marketing or use of the SYMBICORT® 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 '860 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.

II. The PTE Application for the '860 Patent Fails to Comply with 35 U.S.C. § 156(d)(1)

As explained above, there are several statutory requirements that must be satisfied in order for a patent to be eligible for extension under 35 U.S.C. § 156. Apart from the requirement in section 156(a)(5)(A), section 156(d)(1) requires the patent term extension application, containing sufficient information to determine entitlement to the extension, be submitted to the USPTO "**within the sixty-day period beginning on the date the product received permission under the provision of law under which such regulatory review period occurred for commercial marketing or use.**" 35 U.S.C. § 156 (d)(1) (emphases added). Additionally, the USPTO's

regulation implementing section 156(d)(1) mirrors the language of section 156(d)(1): “The 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) (emphasis added).

Based on the plain language of section 156(d)(1) and Rule 1.720(f), the FDA’s grant of permission for commercial marketing or use triggers the time period for submission of a patent term extension application. The phrases used in section 156(d)(1) and Rule 1.720 to define the time period for submitting a patent term extension application, *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 section 156(d)(1) and Rule 1.720(f), a PTE applicant has sixty days to submit a PTE application; the first day of that sixty day period begins on the date granted permission for commercial marketing or use of the product which was subject to the applicable regulatory review period.

In the present case, the FDA letter of December 6, 2007, indicated that “the FDA granted permission for commercial marketing or use of NDA 21-929 for SYMBICORT® (formoterol fumarate dihydrate and budesonide) on July 21, 2006.” The absolute deadline for filing the PTE Application was sixty days from July 21, 2006, starting the count of that sixty day period on July 21, 2006. The sixtieth day of that time period was September 18, 2006 (a Monday). Applicant failed to meet the statutory deadline, because it filed the PTE Application on September 19, 2006, one day late.

Applicant claims that the last day within the sixty day period permitted for submission of the PTE Application under 35 U.S.C. § 156 in compliance with 37 C.F.R. § 1.740(a)(5) is September 19, 2006. See PTE Application at 5. In particular, Applicant asserts: “This application is timely filed, pursuant to 35 U.S.C. § 156(d)(1) and 37 C.F.R. 1.720(f), within the permitted sixty-day (60-day) period **that began on July 21, 2006, the date the product received permission under 21 U.S.C. § 355(b)**, and that will expire on September 19, 2006.” (Emphasis added). It is unclear how Applicant, who specifically correctly indicated that the first day of the sixty-day period “began on July 21, 2006,” calculated that the end point of the sixty-day period was any day other than September 18, 2006.

Because Applicant has miscalculated the relevant time period and thus failed to file the PTE application by the absolute deadline of September 18, 2006, the PTE Application is untimely filed under section 156(d)(1) and Rule 1.720(f) and therefore the '860 patent is **ineligible** for extension.

III. Conclusion

For the above-stated two separate reasons, the PTE application for the '860 patent is **DISMISSED**.

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

By mail: Mail Stop Hatch-Waxman PTE
P.O. Box 1450
Alexandria, VA 22313-1450

By FAX: (571) 273-7755

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.



Mary C. Till

Legal Advisor

Office of Patent Legal Administration

Office of Deputy Commissioner for Patent Examination Policy

Commissioner for Patents

cc: Office of Regulatory Policy
Food and Drug Administration
10903 New Hampshire Ave., Building 51, Room 6222
Silver Spring, MD 20993-0002

RE: SYMBICORT®
(formoterol fumarate dihydrate
and budesonide)

Attn: Beverly Friedman

cc: Dr. Allen Giles, Esq.
Principal Patent Attorney
AstraZeneca Global Intellectual Property
Alderly Park
Macclesfield
Cheshire SK10 4TG
United Kingdom