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In re: Patent Term Extension
Application for
U.S. Patent No. 4,868,179

NOTICE OF FINAL DETERMINATION OF INELIGIBILITY AND DENIAL OF REQUEST FOR INTERIM EXTENSION

An application for extension of the patent term of U.S. Patent No. 4,868,179 (the '179 patent) under 35 U.S.C. § 156 was filed in the United States Patent and Trademark Office (PTO) on August 19, 2005. The application was filed by NitroMed, Inc. (Applicant), an authorized agent of the patent owner of record. 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 BiDIL® and having the active ingredients hydralazine hydrochloride and isosorbide dinitrate. The application indicated that BiDIL® (hydralazine hydrochloride and isosorbide dinitrate) had been approved for commercial use and sale by the Food and Drug Administration (FDA) on June 23, 2005.

On September 12, 2005, the PTO sent a letter to the FDA stating, "Our review of the application to date indicates that the subject patent would not be eligible for extension of the patent term under § 156 because both hydralazine hydrochloride and isosorbide dinitrate were previously approved under section 505 of the Federal Food, Drug and Cosmetic Act (FFDCA)." The PTO requested the FDA's assistance in determining whether BiDIL® (hydralazine hydrochloride and isosorbide dinitrate) had been subject to a regulatory review period in accordance with § 156(g).

In a letter dated today and transmitted electronically from the FDA to the PTO (FDA letter), the FDA indicated that BiDIL® (hydralazine hydrochloride and isosorbide dinitrate) had been subject to regulatory review under new drug application (NDA) 20-727 in accordance with section 505 of the FFDCA, and confirmed that NDA 20-727 did not represent the first permitted commercial marketing or use of the active ingredients of BiDIL® (hydralazine hydrochloride and isosorbide dinitrate).

A. U.S. Patent No. 4,868,179 Is Not Eligible for Patent Term Extension

A determination has been made that the '179 patent is **NOT** eligible for patent term extension under § 156 based upon the regulatory review period of BiDIL® (hydralazine hydrochloride and isosorbide dinitrate).

The FDA official records indicate that each of the two active ingredients comprising BiDIL® (hydralazine hydrochloride and isosorbide dinitrate) has been previously approved for commercial marketing or use, prior to the approval of BiDIL® (hydralazine hydrochloride and isosorbide dinitrate). In the FDA letter, the FDA stated:

> Approvals of NDAs for new drugs containing hydralazine occurred prior to Title II's enactment in September 1984, including in 1982, 1983, and May 1984. NDAs have also been approved for other new drugs containing hydralazine and ISDN after enactment of Title II but prior to approval of BiDil, in 1985, 1986, 1997 and 2001 for hydralazine, and in 1987, 1988, 1991, 1993, 1995, 1998, 1999, 2000 and 2005 for ISDN.

Under § 156(a) a term of a patent which claims a product shall be extended if, *inter alia*, the product has been subject to a regulatory review period before its commercial marketing or use. In addition, § 156(a)(5)(A) provides in pertinent part that "the permission for the commercial marketing or use of the product . . . is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred." (Emphases added.)

Thus, whether the '179 patent is eligible for patent term extension turns on the requirement in § 156(a)(5)(A) that the permission for the commercial marketing or use is the first permitted commercial marketing or use of the product.

The term "product" is defined in § 156(f) as follows:

> (f) For purposes of this section:
> (1) The term "product" means:
> (A) A drug product . . .
> (2) The term "drug product" means 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. (Emphasis added.)

By the explicit terms of § 156(f)(2), the term "product" as it relates to a human drug product means the active ingredient of the new drug product. See In re Fisons Pharmaceuticals Limited, 231 USPQ 305 (Comm'r Pats. 1986); aff'd, Fisons plc v. Quigg, 8 USPQ2d 1491 (DDC 1988); aff'd, 10 USPQ2d 1869 (Fed. Cir. 1988) (holding that the term "product" as used in § 156(f) refers to the active ingredient); Glaxo Operations UK Ltd. v. Quigg, 13 USPQ 1628 (Fed. Cir. 1990) (holding that the term "product" as used in § 156(f) refers to the active ingredient); Arnold P'ship v. Dudas, 362 F.3d 1338, 1341 (Fed. Cir. 2004) (holding that a composition comprised of multiple active ingredients is eligible for patent term extension only if at least one of the active ingredients complies with the first commercial marketing requirement of § 156(a)(5)(A)). The

active ingredients in the approved product BiDIL® are hydralazine hydrochloride and isosorbide dinitrate.[1] As noted in the FDA letter, the active ingredients hydralazine hydrochloride and isosorbide dinitrate had each been approved for commercial marketing and use prior to the approval of BiDIL®. Furthermore, the prior approval of each of the active ingredients hydralazine hydrochloride and isosorbide dinitrate by the FDA occurred under section 505 of the FFDCA, the same provision of law under which regulatory review of the product BiDIL® (hydralazine hydrochloride and isosorbide dinitrate) occurred.

Applying the definition of "product" provided in § 156(f) to the extension requirement of § 156(a)(5)(A), Applicant's product BiDIL® (hydralazine hydrochloride and isosorbide dinitrate) does not qualify as the first permitted marketing or use of either active ingredient. Since the approval of BiDIL® was not the first permitted marketing or use of at least one of the active ingredients thereof, hydralazine hydrochloride or isosorbide dinitrate, the patent is not eligible for patent term extension based upon the regulatory review of BiDIL®.

The Applicant for patent term extension has argued, via letters from Fox Kiser to the FDA dated November 4, 2005 and February 22, 2006, that the '179 patent is entitled to an extension under § 156 because each of the various amended versions of section 505 of the FFDCA constitutes a different "provision of law" as that phrase appears in § 156(a)(%)(A). According to Fox Kiser, the term of the '179 patent should be extended because the version of section 505 under which BiDIL® (hydralazine hydrochloride and isosorbide dinitrate) was approved was textually different from the versions of section 505 under which the active ingredients of BiDIL® (hydralazine hydrochloride and isosorbide dinitrate) had previously been approved.

Applicant is mistaken in its reading of § 156(a)(5)(A). As explained at page 2 of the FDA letter, the phrase "provision of law" refers "to the statutory provision under which the regulatory review occurs for a particular class of products that is eligible for patent term restoration, regardless of whether that statutory provision is amended." The FDA also states, and the PTO concurs, that the phrase is unambiguous on its face. However, as explained in the FDA letter, even if the phrase is ambiguous, this interpretation is permissible in light of legislative intent, public policy concerns, and applicable case law. There is no suggestion in the legislative history that the phrase "first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred" as used in § 156(a)(5)(A) is intended to treat amended versions of section 505 as different provisions of law. Rather, as explained by the FDA at page 6 of the FDA letter, to treat each different amended version of section 505 as a

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[1]In accordance with § 156(f), the active ingredient of a new drug includes salts of the active ingredient, so prior approval of hydralazine would preclude subsequent extension of a patent based on approval of hydralazine hydrochloride. See Pfizer Inc. v. Dr. Reddy's Labs., Ltd., 359 F.3d 1361, 1366, 69 U.S.P.Q.2d 2016, 2018 (Fed. Cir. 2004) (concluding "that the active ingredient is amlodipine, and that it is the same whether administered as the besylate salt or the maleate salt. The statutory definition of 'drug product' is met by amlodipine and its salts.")

different provision of law would contravene the legislative intent of Congress by allowing the term of more than one patent to be extended if a product received more than one approval as a member of a particular class of products. Additionally, as to public policy concerns, the FDA points out at page 7 that if Fox Kiser's interpretation were adopted, there would be marketplace uncertainty and applicants for patent term extension could be treated inequitably as a result of the timing of amendments to section 505. Furthermore, the FDA points out at pages 8-9 that the only federal court decision to have addressed the question at issue, Westwood Pharms., Inc. v. Quigg., 1989 WL 205631, 13 U.S.P.Q.2d 2067 (D.D.C. 1989), supports the interpretation of the FDA and the PTO. Finally, the Supreme Court in Eli Lilly and Co. v. Medtronic, Inc., 496 U.S. 661, 667, 674, 15 USPQ2d 1121, 1125-26, 1128 (1990), while making a distinction between the term "law" as broadly construed and a "provision of law," identified 21 U.S.C. § 355 (the codification of section 505), as a "provision" of the FFDCA under which new drugs are subject to premarket approval.

In view of the foregoing reasons, as well as the remaining reasons stated in the FDA letter, the term of the '179 patent is not eligible for extension under § 156 based upon the regulatory review period and approval of the human drug product BiDIL® (hydralazine hydrochloride and isosorbide dinitrate).

B. The Request for Interim Extension of U.S. Patent No. 4,868,179 Is Denied

On January 25, 2007, Applicant filed a request for interim extension for a period of one year of the term of the '179 patent under § 156(e)(2). Because the patent is not eligible for patent term extension, the request for interim extension must be denied.

If a patent will expire before the Director has made a determination to issue or deny an application for patent term extension, § 156(e)(2) provides for an interim patent term extension of up to one year:

> If the term of a patent for which an application has been submitted under subsection (d)(1) would expire before a certificate of extension is issued or denied under paragraph (1) respecting the application, the Director shall extend, until such determination is made, the term of the patent for periods of up to one year if he determines that the patent is eligible for extension.

§ 156(e)(2) (emphasis added).

Based on the express language of §156(e)(2), certain conditions must be satisfied in order to permit the Director to issue an interim extension. Specifically, the language "before a certificate of extension is issued or denied" in § 156(e)(2) indicates that an interim extension may be granted only during the period of time prior to the Director's determination either to issue the certificate or deny the applicant's request. Furthermore, the language "if he determines that the patent is eligible for extension," which follows the aforementioned language, instructs the

Director to grant an interim extension only if the patent is eligible for patent term extension. If the patent is not eligible, then § 156(e)(2) explicitly prohibits the Director from granting an interim extension.

The legislative history of the Hatch-Waxman Act is consistent with this interpretation. There are two committee reports that address § 156. The Committee on Energy and Commerce prepared a report for the House version of the Act (H.R. 3605), giving a general explanation for how the provision would operate in practice:

> It is possible that the original term of the patent for which extension is sought could expire before a final decision by the Commissioner to issue a certificate of extension. This might occur, for instance, because the determination of due diligence by the Secretary of HHS or Agriculture has not been completed.
>
> In such circumstances, the Commissioner is required to determine whether the patent is eligible for extension under section 156(a), and if it is, to issue a certificate of extension for a period of up to one year. The length of this interim extension is discretionary with the Commissioner, but is intended to provide time for the completion of any outstanding requirements. If the Commissioner determined that subsequent interim extensions were necessary, and consistent with the objectives of section 156(e)(2), they could be granted as well. In no event could these interim extensions be longer than the maximum period of extension to which the application is thought to be eligible.

H.R. Rep. No. 857(I), 98th Cong., 2d Sess. (June 21, 1981), reprinted in 1984 U.S.C.C.A.N. 2647 at 29. The Committee on the Judiciary likewise prepared a separate report on H.R. 3605 and explained even less about § 156(e)(2):

> Proposed section 156(e) provides that the Commissioner's determination that a patent is eligible for extension is to be made solely on the basis of information contained in the application. If it is determined that the patent is eligible for an extension, the Commissioner shall issue a certificate of extension, under seal, for the period determined, in accordance with procedures authorized by subsection (c). The certificate shall be recorded in official patent files and becomes a part of the original patent.
>
> In the event that the original term of the patent for which extension is sought will expire before a final decision by the Commissioner on that extension, the Commissioner may issue an interim extension certificate for a period of up to one year.

H.R. Rep. No. 857(II), 98th Cong., 2d Sess. (Aug. 1, 1984) (emphasis added).

The Committee on Energy and Commerce's discussion supports reading § 156(e)(2) as permitting an interim extension only if the Director determines that the patent is eligible for a patent term extension. In particular, the portion that states "and if it is" implies that an interim extension should not be granted if a patent is not eligible for extension under § 156(a). While the Committee on the Judiciary did not specifically state that eligibility is a prerequisite for an interim extension, such an interpretation is not inconsistent with this report.

It does not appear that the conditions for an interim extension under § 156(e)(2) have ever been the subject of litigation in a federal court. There are, however, two decisions addressing interim extensions by the Commissioner of Patents & Trademarks that shed light on the meaning of § 156(e)(2). In In re Reckitt, 230 USPQ 369 (Comm'r of Pat. & Trademarks 1986), a patent owner filed a patent term extension application on August 26, 1985, for its drug product. 230 USPQ at 369. Thereafter, while the patent owner's patent term extension was pending, a licensee filed a citizen's petition with the FDA, asserting that the drug product received FDA approval on June 28, 1985. Id. The FDA nevertheless determined that the drug product was approved on December 29, 1981, and informed the USPTO of this date. Id. at 370. Upon receiving this information, the USPTO rejected the patent owner's patent term extension application as untimely filed. Id. Meanwhile, the licensee filed suit against the FDA in district court, seeking a declaration of its rights under the patent. Id. The district court found in favor of the licensee that the correct approval date was June 28, 1985. Id. Following this district court decision, the patent owner requested reconsideration of the denial of its patent term extension application and requested an interim extension under § 156(e)(2) since its patent was due to expire before an appeal of the district court case could be heard. Id. at 369.

The Commissioner granted an interim extension for a limited period "in the interest of justice." Id. at 372. Specifically, the Commissioner explained: "By granting an interim extension, there would be no hiatus in the term of the patent. Moreover, the length of any interim extension can be tailored to deal with relevant events which necessarily must take place at some future date, if at all." Id. The Commissioner also observed that

> [b]y granting the interim extension, the USPTO would be acting in harmony with a decision of a district court (albeit the decision is not final). . . . However, in doing so [the patent owner] must recognize that the final determination in the [] litigation could render the interim extension herein granted invalid should it ultimately turn out that FDA approved the NDA for [the drug product] more than sixty days prior to the date [the patent owner] filed its patent term extension application.

Id.

When the Commissioner indicated that the grant of an interim extension under § 156(e)(2) comports with the district court decision, he implied that if that decision was correct, then (1) the patent term extension application was timely filed; (2) the timeliness requirement at issue for

granting a patent term extension was satisfied; and (3) an interim extension under § 156(e)(2) is permissible. That implication is supported by the Commissioner's later statement that if an appellate court determines that the FDA approved the drug product more than sixty days before the applicant filed its patent term extension application, then the timeliness requirement was not satisfied and any interim extension was invalid. Thus, the Commissioner appears to imply that an interim extension under § 156(e)(2) may be granted only where the patent eligible for patent term extension.

In In re Alcon, 13 USPQ 2d 1115 (Comm'r Pat. & Trademarks 1989), the Commissioner expressly confirmed this implication. There, the applicant applied for a patent term extension application on its drug product. While that application was pending, the applicant applied for a one-year interim extension under § 156(e)(2) as its patent was set to expire before the applicant expected a decision on its application. The Commissioner denied the interim extension request and proffered two reasons for doing so: (1) the PTO made a decision to deny the application before expiration of the patent because the drug product was not the first commercial marketing of the active ingredient as required under § 156(a)(5)(A); and (2) "an interim extension can be granted only in those circumstances, unlike the present case, where the Commissioner has determined that the patent is eligible for extension." Alcon, 13 USPQ 2d at 1123. Through the second reason, the Commissioner in Alcon makes clear that an applicant whose patent is set to expire before the patent term extension application process is complete is entitled to an interim patent extension under § 156(e)(2) only if the patent is eligible for patent term extension under § 156(a).

Consistent with Reckitt and Alcon, the Manual of Patent Examining Procedure (MPEP) explains that an applicant is entitled to an interim extension only if the patent meets the requirements for a patent term extension set forth in § 156(a). U.S. Pat. & Trademark Off., Manual of Patent Examining § 2755 (8th ed. 2001, rev. Oct. 2005). Specifically, MPEP § 2755.01 states: "An applicant who has filed a formal application for extension in compliance with § 1.740 may request one or more interim extensions for periods of up to one year each pending a final determination on the application pursuant to § 1.750." Id. at § 2755.01. MPEP § 2755.01 then discusses when such a request should be granted: "If the original term of the patent for which extension is sought will expire before a final determination to issue a certificate of extension can be made, and a determination is made that the patent is eligible for extension, § 156 provides that the Director may issue an interim extension of the patent term for up to one year pending a final decision on the application for extension." Id. This sentence clarifies that the Director should grant an interim extension request where the patent is eligible for extension under § 156(a) and that the Director, in turn, should deny a request where the patent is ineligible. Additionally, MPEP § 2755.01 removes all doubt as to whether an interim extension can be granted if the patent is not eligible for extension, stating: "Where a determination is made that the patent is not eligible for patent term extension, an interim extension of the patent term is not warranted under § 156(e)(2). . . . Where an interim extension has been granted and it is subsequently determined that the patent is not eligible for patent term extension, the interim extension may be vacated *ab initio* as ineligible under § 156(e)(2)." MPEP § 2755.01 (citing Alcon and Reckitt). Hence, the MPEP follows both the Reckitt and Alcon decisions in terms of when an interim extension may

be granted under § 156(e)(2).

Thus, because the '179 patent is not eligible for patent term extension, the request for interim extension under § 156(e)(2) is denied.

THIS DECISION MAY BE VIEWED AS A FINAL AGENCY ACTION.

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

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Re: BiDIL® (hydralazine hydrochloride and isosorbide dinitrate)

FDA Docket No. 2006E-0003

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