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# Patent Term Extension Considerations For Regulated Products

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The 1984 Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act,[1] includes Section 156, which provides for the extension of the term of a granted patent (PTE) under certain circumstances. The intent behind Section 156 is to extend patent life to compensate patent holders for patent term lost while developing their product and awaiting U.S. Food and Drug Administration approval.


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A patent eligible for PTE must claim a product (e.g., a human drug), a method of using the product, or a method of manufacturing the product, a medical device, food additive or color additive subject to regulation under the Federal Food, Drug and Cosmetic Act.[2] Section 156(a) sets forth conditions for granting PTE: "the term of the patent has not expired before an application is submitted;"[3] the term of the patent was never extended;[4] and the application for extension was submitted by the owner of the patent or its agent, within the 60-day period beginning on the date the product received permission for commercial marketing or use.[5],[6] In addition, "the product has been subject to a regulatory review period before its commercial marketing or use," and "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."[7] Thus, PTE is only available for delays incurred in obtaining regulatory approval for the first approved commercial marketing or use of the "product."

The statute defines the "product" as "a drug product" or "any medical device, food additive, or color additive" subject to regulation under the FFDCA.[8] Furthermore, the term "drug product" means "the active ingredient of a new drug, antibiotic drug, or human biological product ... or a new animal drug or veterinary biological product ... which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques, including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient."[9]

We address each of the "drug product" categories in turn.

**Salt and Ester**

For several years, the U.S. Patent and Trademark Office interpreted the term "product" in Section 156(a)(5)(A) to mean "active moiety," i.e., the molecule in a drug product responsible for pharmacological action, regardless of whether the active moiety is formulated as a salt, ester, or other noncovalent derivative, rather than an "active ingredient," i.e., the active ingredient physically found in the drug product. For example, under the PTO's old "active moiety" interpretation, a compound and a salt of the compound would be considered to be the same active moiety despite the fact that they are different compounds. This interpretation changed with PhotoCure ASA v. Kappos (2010) when the Federal Circuit held that the term "product" means the active ingredient present in the drug for which federal approval was obtained.[10]

After the PhotoCure decision, the USPTO framed the PTE eligibility determination for an approved drug product in four parts: (1) is the active ingredient physically present in the approved drug product, (2) was the active ingredient previously approved, (3) was a salt of the active ingredient previously approved, or (4) was an ester of the active ingredient previously approved.[11] If the answer to any question is yes, the permission to commercially market or use the drug product is not the first permitted commercial marketing or use of the product/active ingredient as required by section 156(a)(5)(A).

**Enantiomers**

The PTO and the FDA have consistently recognized that an enantiomer is a "different" drug product from its racemate, and is eligible for PTE. For example, escitalopram oxalate and citalopram hydrobromide are the active ingredients contained in Nexium and Celexa, respectively. Escitalopram oxalate is the S-enantiomer of citalopram. PTEs have been granted for patents covering both Nexium and Celexa. In Ortho-McNeil Pharmaceutical Inc. v. Lupin Pharmaceuticals Inc. (2010),[12] the Federal Circuit affirmed the PTO's and FDA's practice of granting PTEs for racemates and enantiomers of the same compound.[13]

**Combination Products**

For a drug product that contains more than one active ingredient, the Federal Circuit has held that at least one of the claimed active ingredients must be new to the marketplace as a drug product for a patent covering the drug product to be eligible for PTE.[14] The court also commented on whether synergistic combination drug patents qualify for PTE under Section 156. The court noted that the PTO has not taken a position on the effect of synergy on a combination drug patent's eligibility for a PTE, but "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 non-synergistic combinations."[15]

**Medical Devices**

Medical devices are subject to review under Section 156(f)(1)(B). Thus, patents covering medical devices may be eligible for PTE if delays are incurred in obtaining regulatory approval for the first approved commercial marketing or use of the product. For medical devices, Section 156(g)(3) limits the "medical review period" to periods of time related to product approvals under Section 515 of the FFDCA. Medical

device patents eligible for PTE are those covering medical devices approved under Section 515 of the FFDCA, the so called "Class III" medical devices.[16] Devices approved under other sections of the FFDCA are not eligible for PTE.[17]

Interestingly, the interpretation of "first approved commercial marketing or use" for a medical device is somewhat different from a drug product.[18]

**Food or Color Additive**

The PTO's analysis regarding "the first approved commercial marketing or use" of a food or color additive appears to be similar to that used for a drug product. Namely, the analysis is focused on whether the active ingredient contained in the food or color additive represents the first approved commercial marketing or use of the active ingredient by the FDA.[19]

**Human Biological Products**

A human drug product means the active ingredient of a new drug or human biologic product (as those terms are used in the FFDCA and the Public Health Service Act). The 1984 act excluded animal drug and veterinary biological products, but in 1988, Congress enacted the Generic Animal Drug and Patent Term Restoration Act, adding animal drugs and veterinary biologics to the list of products that may be eligible for PTE.[20] The term "product" includes a human biological product as defined in the PHSA.[21] The PHSA defines a biological product as a "virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, ... applicable to the prevention, treatment, or cure of a disease or condition of human beings."[22]

With respect to cellular and gene therapies, to date 11 cellular therapies have been approved by the FDA's Office of Cellular, Tissue and Gene Therapies.[23] One example is Azficel-T, an autologous cellular product composed of fibroblasts cells. A PTE of five years was granted for U.S. Patent No. 5,591,444 which claims a method of using and making Azficel-T. Similar to PTE applications for small molecule drugs, the PTE application for a human drug product includes all the requirements set forth in 37 C.F.R. §§ 1.740(a)(1)-(15).

**Scope of Protection During the Extended Period**

During the extended period, the scope of protection is limited to "any use approved for the product" if the patent claims a product, and to "any use claimed by the patent and approved for the product" if the patent claims a method of using a product.[24] In Merck & Co. Inc. v. Kessler (1996), the Federal Circuit indicated that "the restoration period of the patent does not extend to all products protected by the patent but only to the product on which the extension was based."[25]

However, in Pfizer v. Dr. Reddy's (2004),[26] the Federal Circuit held that the scope of protection during the extended period of a patent covers the particular active ingredient/moiety and any salt or ester thereof. It is not limited to solely the active ingredient contained in the approved drug product.[27]

The total extension period is limited to no more than five years if the patent was issued after the 1984 enactment of the Hatch-Waxman Act.[28] In addition, the effective patent term including the restoration period must not exceed 14 years following FDA approval of the new drug.[29] Also, the relevant regulatory review period for calculating the length of the PTE is the review period that occurred after issuance of the patent.[30]

**PTE and Terminal Disclaimers**

In Merck v. Hi-Tech Pharmacal Co., Inc. (2007),[31] the Federal Circuit addressed the question of whether a patent term extension under Section 156 may be applied to a patent subject to a terminal disclaimer under 35 U.S.C. § 253, filed to overcome an obviousness-type double-patenting rejection. The court held that PTE may be applied to a patent subject to a terminal disclaimer.[32]

**Interim Extensions**

In 1993, Section 156 was amended to provide for interim extension of a patent where a product claimed by the patent was expected to be approved, but not until after the original expiration date of the patent.[33] Section 156(e)(2) provides for interim PTE if the patent "would expire before a certificate of extension is issued or denied under paragraph (1) [Section 156(e)(1)]." Thus, to prevent a patent from expiring while an application for PTE is pending, the patentee can file for one or more interim extensions of up to one year each.[34] Together, all of the interim extensions cannot be longer than the extension that would be obtained under the normal patent term extension provisions. Section 156(d)(5) sets forth certain criteria that must be met for the PTO to grant an interim extension. Such an application must be submitted during the period beginning six months, and ending 15 days before the patent is due to expire.

**Strategic Considerations for Maximizing PTE**

As per PhotoCure, the order of drug product approval is important. For example, assuming other conditions of PTE are met, if a first drug product containing a compound was approved before a second drug product containing a salt of the compound, a patent covering the second drug product would be entitled to PTE as the compound contained in the first drug product is not a salt or ester of the salt contained in the second drug product. However, if the timing of approval of the first and second drug products were reversed, i.e., if a first drug product containing a salt of a compound was approved before a second drug product containing the compound, the patent covering the compound would not be entitled to PTE, because "a salt (or ester)" was previously approved.

Only one extension is granted per product per patent. In other words, if multiple patents cover an approved product, only one patent can be extended. The patent owner may submit multiple patent applications to the USPTO based on the same regulatory review period, but ultimately one patent must be chosen for PTE. If the patent owner fails to identify one patent, the PTO will extend the first patent to expire. The decision to extend a particular patent depends on a number of factors including the ability of the patent to withstand a challenge based on validity or unenforceability, the expiration date of the patent, the difficulty a competitor would have in avoiding the patent, i.e., the scope and ability to design around the patent claims.

Under certain (rare) circumstances, a company can pursue multiple PTEs for different patents covering the same product approved under separate new drug applications on the same first day of approval.[35] For a drug product covered by several patents, the USPTO may extend a different patent for each NDA approved on the same first day of approval (even when multiple NDAs share a common "testing phase" and "review phase"). In these situations, the USPTO considers each regulatory review period for an NDA to be distinct and thus available for PTE. Examples of such products include Omnicef, Lyrica, Mycamine and Vimpat.[36] Obviously, timing is critical in this situation.

In conclusion, patent term restoration is exceedingly important in maximizing market exclusivity, and the decision to apply for PTE must be carefully undertaken. Experienced patent practitioners who have a complete understanding of the nuances and interplay between PTE, FDA regulations, data exclusivity and the filing strategies undertaken by abbreviated new drug application or abbreviated biologics license application filers, are invaluable in aiding in this important decision.[37],[38]

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[1] Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 35 U.S.C. §§ 156 and 271.)

[2] The Federal Food, Drug and Cosmetic Act.

[3] 35 U.S.C. § 156 (a)(1).

[4] 35 U.S.C. § 156 (a)(2).

[5] To determine the date on which the product receives permission for commercial marketing or use, section 156 (d)(1) has been amended by the AIA, Section 37, to state that "if such permission is transmitted after 4:30 P.M., Eastern Time, on a business day, or is transmitted on a day that is not a business day, the product shall be deemed to receive such permission on the next business day."

[6] 35 U.S.C. §§ 156 (a)(3) and (d)(1).

[7] 35 U.S.C. §§ 156 (a)(4) and (5).

[8] 35 U.S.C. § 156(f)(1).

[9] 35 U.S.C. § 156(f)(2).

[10] See Glaxo Operations UK Ltd. V. Quigg, 894 F.2d 392 (Fed. Cir. 1990) and PhotoCure ASA v. Kappos, 603 F.3d 1372 (Fed. Cir. 2010).

[11] See e.g., PTO letters re. USP 6,034,267 and 5,362,718.

[12] Ortho-McNeil Pharmaceutical, Inc. v. Lupin Pharmaceuticals, Inc . 603 F.3d 1377 (Fed. Cir. 2010).

[13] The fact that the FDA required "full regulatory approval" for Levaquin® supported the court's conclusion that enantiomers are eligible for PTE.

[14] See Arnold Partnership v. Dudas, 362 F.3d 1338 (Fed. Cir. 2004).

[15] See id. at 1342.

[16] The FDA classifies medical devices based on the associated risks. Devices are classified into one of three categories — Class I, Class II, and Class III. Class I devices (e.g., dental floss) are deemed to be low risk and are only subject to "general controls" of the FFDCA that apply to all medical devices. Class II devices (e.g., condoms) are higher risk devices than Class I and additionally subject to "special controls." Class III devices (e.g., heart valves) are the highest risk devices. See Medical Devices, Regulatory Controls, available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/GeneralandSpecialControls/default.htm. Only class III devices are subject to approval of a Premarket Approval Application (PMA) under section 515 of the FFDCA by the FDA before they are marketed.

[17] As an example, the manufacturer of Sensor Pad® obtained FDA approval for commercial marketing of the product and filed a PTE application with the PTO. The PTO requested the FDA to confirm that Sensor Pad® had been subject to a regulatory review period within the meaning of Section 156(g) before its first commercial marketing or use. The PTO also indicated that based on its initial review, the patent would not be eligible for a PTE. In its reply, the FDA indicated that Sensor Pad® was approved under Section 510 of the FFDCA, not Section 515. The PTO subsequently denied the PTE application.

[18] Cardiac Pacemakers, Inc. v. St. Jude Medical, Inc., 381 F.3d 1371 (Fed. Cir. 2004).

[19] See the PTE application regarding U.S. Patent No. 4,600,706 for Nsure (natamycin).

[20] Public Law 100-670, sec. 201(a)-(h), 102 Stat. 3984 (Nov. 16, 1988).

[21] 35 U.S.C. § 156(f).

[22] 42 U.S.C. § 262.

[23] See http://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ApprovedProducts/default.htm

[24] See 35 U.S.C. §§ 156 (b)(1) and (2).

[25] Merck & Co., Inc. v. Kessler, 80 F.3d 1543, 1547 (Fed. Cir.1996). The court also noted several other limitations based on the language of Section 156: first, "[r]egardless of the time so lost, if a patent was issued and testing began before the 1984 enactment of the Hatch-Waxman Act, the total extension period may not exceed two years . . . otherwise the restoration period is limited to no more than five years. . . ." Further, "the effective patent term including the restoration period may not exceed 14 years following FDA approval of the new drug," and "the term of the patent may be given only one RESTORATION extension. . . . If the term of the patent has received such an extension, the patent may not be given another restoration extension even for another drug covered by the patent whose marketing also is delayed by reasons of FDA procedures."

[26] Pfizer v. Dr. Reddy's, 359 F.3d 1361 (Fed. Cir. 2004).

[27] Id., at 1366.

[28] 35 U.S.C. § 156(g)(6)(A).

[29] 35 U.S.C. § 156(c)(3).

[30] 35 U.S.C. § 156(c).

[31] Merck v. Hi-Tech Pharmacal Co., Inc., 482 F.3d 1317 (Fed. Cir. 2007).

[32] A terminal disclaimer can reduce patent term by limiting Patent Term Adjustment (PTA). 35 U.S.C. §§ 154(b)(2) and 253.

[33] Public Law 103-179, secs. 5, 6, 107 Stat. 2040, 2042 (Dec. 3, 1993).

[34] It appears that the USPTO has taken the position that only a single patent can receive interim PTE for the same (single) regulatory review period. See http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2008/05/looking-a-gift.html, which refers to the USPTO's decision granting interim PTE for U.S. Patent No. 5,407,914 but denying interim extensions for U.S. Patent Nos. 5,260,273 and 5,789,381 covering the drug product Surgaxin.

[35] For example, if two NDAs were approved on the same day for two indications of the same product, two PTEs may be applied for. See PTE for Lyrica®.

[36] http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2013/05/false-friends-fdas-gift-on-nesina-present-or-poison-it-may-depend-on-which-hatch-waxman-language-is-.html

[37] Contacts for information about the Patent Restoration Program. At the FDA: Beverly Friedman (Beverly.Friedman@fda.hhs.gov), 301-796-7900; at the USPTO: Mary Till (Mary.Till@uspto.gov), 571-272-7755; US Patent Terms Extended Under 35 USC 156 http://www.uspto.gov/patent/laws-and-regulations/patent-term-extension/patent-terms-extended-under-35-usc-156; At the EP, Supplementary Protection Certificates (SPCs) Guide For Applicants, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/309167/spctext.pdf

[38] For a patent that covers a drug product containing controlled substances that require approval by both the FDA and the Drug Enforcement Administration, the patent may be entitled to a longer PTE to compensate for the time required to obtain a final scheduling determination of the controlled substances under the Controlled Substance Act by the DEA. See http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2016/02/eisai-says-that-the-recently-enacted-irtnmta-should-result-in-a-longer-pte-for-fycompa-patent.html?utm_source=feedburner&utm_medium=email&utm_campaign=Feed%3A+FdaLawBlog+%28FDA+Law+Blog%29