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Patent Term Extension for Drugs Not Limited to New Chemical Entities

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PTE affords a patent owner up to five additional years on a patent that covers a drug, biologic or class III medical device.

Patent term extension is a valuable tool that drug manufacturers should consider, even when their products are not new entities. Recent decisions from the U.S. Patent and Trademark Office, coupled with various court decisions, have granted patent term extensions (PTEs) for certain pharmaceuticals that do not qualify as new chemical entities (NCEs). The USPTO, however, has been inconsistent in determining eligibility. Among other requirements, to be eligible for PTE, a drug product must be the first permitted commercial marketing for which there was a regulatory review period. The "first permitted commercial marketing of the product" is not equivalent to the FDA's classifying the drug as an NCE. Although NCEs are eligible for PTE, manufacturers should note that there are other circumstances under which a non-NCE may still obtain PTE:

- New esters or salts of previously approved acids or bases are eligible for PTE.
- Combination drug products may be eligible for PTE.
- Combination drug-device products may be eligible for PTE.

Overview of PTE

PTE affords a patent owner up to five additional years on a patent that covers a drug, biologic or class III medical device.[1] Generally, to be eligible, the drug product must have been subject to regulatory review before its commercial marketing, and the drug product's approval must be the first approval of the drug by the FDA. The statute defines a "product," in part, as a human drug product, which is "the active ingredient of a new drug . . . including any salt or ester of the active ingredient, as a single entry or in combination with another active ingredient."[2]

In evaluating a drug's PTE eligibility, the "product" may be the "active ingredient," and not the entire composition of the drug product, based on the statute's plain language.[3] The Federal Circuit has remarked that PTEs were intended to be limited to NCEs — and not new uses and new doses of drugs already approved for commercial marketing[4] — but the definition of NCE has been expanding.[5] Even so, not all companies are seeking approval of an NCE. If they are not seeking NCE approval, are their products still eligible for PTE?

NCEs and New Esters or Salts

An NCE is a drug that contains "no active moiety that has been approved by FDA in any other" new drug application.[6] An active moiety is defined as "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance."[7]

In contrast, the PTE statute defines a drug product as "the active ingredient," including any salt or ester. The active ingredient of a drug product is the compound that is actually present in the drug (that gets administered) for which FDA approval was obtained.[8] If a product contains a new salt or ester of a previously approved acid, it may be eligible for PTE.[9] Similarly, if a product contains a new salt or ester of a previously approved salt or ester, it may be eligible for PTE.

The USPTO takes a different position. It says that if a product contains the acid of a previously approved salt or ester, it is not eligible for PTE, despite the fact that the compound present in the drug that gets administered is different.[10] In March 2017, the USPTO issued a decision denying PTE for buprenorphine because the FDA had previously approved a salt of buprenorphine (buprenorphine hydrochloride).[11] The USPTO denied PTE for buprenorphine, reasoning that the active ingredient buprenorphine was not the first commercial marketing of buprenorphine or a salt or ester of buprenorphine (since buprenorphine hydrochloride was previously approved) and relied on the decisions in *Glaxo v. Quigg*, 706 F. Supp. 1224 (E.D. Va. 1989), and *Hoescht*.

Combination Drug Products

For combination drug products, including fixed-dose combination products, PTE eligibility depends on whether at least one ingredient in the combination product would otherwise be eligible for PTE had it been developed as a monotherapy. In a combination product, if at least one ingredient is an NCE or is a new ester or salt of a previously approved acid, then the combination product will be eligible for PTE.[12] If none of the ingredients of the combination product falls into that category, then the combination product will not be eligible, despite the fact that the particular combination of drugs has never been approved before in that combination.

Combination Drug-Device Products

The FDA will review drug-device combination products as either a drug or a medical device for approval purposes. However, for purposes of classifying a product under the Hatch-Waxman Act, "it makes no difference whether the FDA reviews a product as a device, as a drug, as a biological product, or as a unicorn." This is because 35 U.S.C. § 156 enables a drug-device combination product to be classified as either a drug or a medical device for determining PTE eligibility.[13] Similar to combination drug products, if either the drug or the device would otherwise be eligible for PTE, the drug-device combination will be eligible for PTE.

Companies developing a new drug product, even if it is not an NCE, should consult with both patent and regulatory counsel to consider whether their product may be eligible for PTE and explore ways to increase the likelihood of obtaining and maximizing PTE.

This article is the first of a five-part series on PTE. Keep an eye on pepperlaw.com for more guidance on how to obtain and maximize PTE for your products.

Endnotes

[1] *See* 35 U.S.C. § 156.

[2] 35 U.S.C. § 156(f).

[3] *See Fisons plc v. Quigg*, 876 F.2d 99, 101 (Fed. Cir. 1989) (affirming the rejection of PTE for an innovative use or dosage form of cromolyn sodium, which had previously approved by the FDA in inhalation capsule form).

[4] *Id.*

[5] *See* Nemlekar, et al., "FDA Is Evolving on Qualifications for 'New Chemical Entity,'" Law360 (Sept. 7, 2016), https://www.law360.com/articles/836524/fda-is-evolving-on-qualifications-for-new-chemical-entity-.

[6] 21 C.F.R. § 314.108.

[7] 21 C.F.R. § 314.103.

[8] *See PhotoCure Asa v. Kappos*, 603 F.3d. 1372, 1375-76 (Fed. Cir. 2010) (holding that the drug product with the active ingredient MAL hydrochloride was eligible for PTE, even though MAL is the methyl ester of ALA and ALA hydrochloride had been previously approved by the FDA); *see also Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756, 759 n.3 (Fed. Cir. 1997); *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 393-95 (Fed. Cir. 1990).

[9] *See Glaxo Operations UK Ltd.*, 894 F.2d 392 (holding that cefuroxime axetil [an ester of cefuroxime] was a new product and eligible for PTE, despite the prior FDA approval of cefuroxime).

[10] *See* http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance /ucm069959.htm.

[11] *See* USPTO Notice of Determination of Ineligibility for Reissue Patent No. 41,571 (Mar. 2, 2017). The USPTO further reasoned that the decision in *PhotoCure* is also supported, but cautioned that *PhotoCure* did not provide additional criteria to confer eligibility — for example, that a drug was required to undergo full FDA review or has different pharmacological activities.

[12] *See Arnold P'ship v. Dudas*, 362 F.3d 1338 (Fed. Cir. 2004) (holding that the term of patent directed to combination of hydrocodone and ibuprofen for pain relief could not be extended under § 156, since both components have been available as separate drugs, even though the FDA evaluates the combination of drugs as a whole — not the individual active ingredients — when determining their safety and efficacy). "

[13] *See Angiotech Pharms. Inc. v. Lee*, 191 F. Supp. 3d 509, 524-25 (E.D. Va. 2016) ("When the FDA determines a

combination product's primary mode of action for purposes of FDCA review, the FDA is not identifying the nature of the product itself.").

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