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Patent Term Extension Not A 1-Trick Pony For Animal Drugs

Law360, New York (August 18, 2016, 11:17 AM ET) --


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Drug innovators face a hurdle largely unseen in other technology spaces: regulatory marketing approval. Inherent to the regulatory review process is delay — delay associated with satisfying testing requirements and delay associated with review and approval of a new drug application. And this regulatory marketing approval delay is particularly acute for patent holders who typically seek patents for new drugs at early stages of development to exclude competitors, yet find themselves with limited patent term remaining once the approval process is completed.

As a trade-off for this delay, the law provides patent holders with extended patent term for time spent seeking U.S. Food and Drug Administration approval. And this patent term extension can have a significant economic impact depending on the drug product. Pharmaceutical and biotechnological patents often reach their peak value near the end of their patent terms. For example, during the last year of patent term covering Celgene's Revlimid, the drug enjoyed $5.8 billion dollars in sales.[1]

The animal drug and health industry is not immune from the regulatory marketing approval process seen in its companion human drug and health industry. Animal drug innovators, however, have options in how they apply for both FDA approval and patent term extension for their animal drug patents compared to their human counterparts.

To provide a guide for animal drug developers, this article will evaluate the different choices available when seeking regulatory approval and patent term extension. First, this article will outline what makes a patent eligible for PTE in the animal health context. Second, it will explain how to calculate the length of patent term extension for a patent generally. And third, this article will explore the traditional and phased review options available to patentees of animal drugs and biologics, explaining the implications for each on PTE.

When Is an Animal Drug Patent Eligible for PTE?

Section 156 of the Patent Act is a powerful tool for patentees who must obtain regulatory approval before marketing their patented products: The statute authorizes the U.S. Patent and Trademark Office to extend the patent terms of unexpired patents that are subject to a regulatory review period and cover products, the use of products, and methods of manufacturing products as defined in the statute. The statute defines covered "products" to include: (1) new drugs,

antibiotic drugs, human biological drugs;[2] and (2) new animal drugs or veterinary biological products "not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques."[3]

Unexpired[4] patents that have not previously been extended[5] are eligible for PTE. The applicant must file the application for extension within 60 days of receiving commercial marketing approval.[6] In most cases, Section 156 patent term extension is only available for the first period of FDA review — for the review period predicating the first permitted commercial marketing under the relevant drug regulatory regime.[7] But this rule is modified for therapeutics targeting food-producing animals. When a drug is pending for use in both food-producing and nonfood-producing animals and both are approved, the drug applicant can select to extend patent term based on the period of review for the food-producing animal use, even if the nonfood-producing use approval issued earlier.[8]

A peculiar rule applies solely to veterinary biologics produced via recombinant DNA technology: Congress did not include patent term extension for products manufactured using genetic manipulation, but Congress did include patent term extension for patents claiming the methods of manufacturing those products. In the case of the latter, the patent can only be extended under Section 156 if it is the first commercial marketing of a product made by the process claimed in the patent.[9]

While much less common in the human pharmaceutical industry, one patent typically covers the drug, use, and formulation for an animal drug or biologic.[10] This, in turn, simplifies the calculus for which patent to extend. But in cases where multiple patents cover the new drug or biologic in a so-called “patent thicket,” the patentee must choose which patent to extend, as only one extension will be granted per product per patent. This choice should be strategic: Patentees should consider patent strength, the patent’s expiration date, and design-around difficulty for a competitor.

How Is PTE Calculated?

Calculating PTE under Section 156 requires designating time as either part of the “testing” or “approval” phases.[11] In the testing phase, the applicant conducts testing and investigation of the drug over seven “technical sections.” These sections include: chemistry; manufacturing and controls; effectiveness; target animal safety; human food safety; environmental impact; labeling; freedom of information summary; and all other information. And in the approval phase, the FDA evaluates each technical section for approval.

Generally, PTE is available for: (1) all the time it takes the FDA to process and approve an application and (2) half of the time spent conducting testing relating to the application.[12] The "testing phase" begins on the earlier of: either the date major health or environmental effects tests are conducted or date of exemption under 512(j) (which covers investigational use exemptions). The testing phase ends when the application is submitted.[13] For biologics, the testing phase covers the date the applicant "had authority" to prepare the product under the Virus-Serum-Toxin Act until the date the license application was submitted under said act. For both drugs and biologics, the approval phase lasts during the pendency of the application and terminates on approval or grant of marketing license.[14]

PTE and Traditional and Phased Review

In the animal drug and biologics industry, there are two tracks under which an applicant can seek approval — traditional review and phased review. In traditional review, the applicant completes all of its testing before submitting one complete new animal drug application, similar to the traditional human pharmaceutical new drug application process. The testing phase ends when the sponsor completes its

investigation and submits all of the technical sections as its final NADA.[15]

Alternatively, if the applicant selects phased review, the applicant will submit its technical sections on a rolling basis into an investigational new animal dDrug file (INAD file).The FDA evaluates the sections on a rolling basis, issuing a complete letter for each one. Ultimately, the applicant submits an administrative NADA once each technical section is complete.[16] Applicants who opt for phased review may switch to traditional review by filing a NADA, and many sponsors find it useful to use the INAD structure early in development.[17]

Applicants can submit their NADA once it's complete under the "traditional review" system — and there is a clear distinction between the approval and testing phases of a traditional application. But the calculation of PTE becomes decidedly more complex if an applicant selects phased review. Phased review blurs the lines between the approval and testing phases, as applicants conduct testing concurrently with the FDA evaluating portions of their applications. Classifying time as part of the "testing" vs. "approval" phase dictates the length of potential patent-term extension. In Wyeth Holdings, the District of D.C. — affirmed by the Federal Circuit — clarified how to calculate PTE for phased review products.[18]

Wyeth Holdings: Phased-Review PTE Calculation

In Wyeth Holdings, Wyeth brought an action against the U.S. Department of Health and Human Services, the FDA and others under the Administrative Procedures Act seeking a longer patent term extension for the animal drug Cydectin, a drug used to treat and control parasites in beef and dairy cattle. Wyeth had selected Phased Review for Cydectin — establishing its INAD file in April of 1990. Wyeth submitted its first technical section, chemistry, in August of 1995.[19] Wyeth submitted its last technical section — environmental impact — in August of 1996, and the FDA issued a final complete letter in December 1997.[20] An earlier-submitted section — public safety — was still pending and received a final complete letter on Jan. 13, 1998. Wyeth submitted its administrative NADA on Jan. 13, 1998, as well. On Jan. 28, 1998, the FDA issued the marketing approval letter for Cydectin.[21]

The FDA determined that the testing phase began on April 5, 1990 — the date the INAD file was opened — and the approval phase began on Jan. 13, 1998 — the date that Wyeth submitted its Administrative NADA. Thus, the testing period was almost 3,000 days long, and the approval phase was only 16 days long. Based on the FDA's determinations, the PTO granted Wyeth PTE of almost four years.[22]

Wyeth disputed the FDA's calculation, however: It argued that the approval phase began upon the submission of the first technical section in August of 1995. Under Wyeth's calculation, it contended the PTE should have been ten months longer. Wyeth filed a request for revision of the regulatory review period with the FDA, but the FDA denied that request. Wyeth then filed an action in the District of D.C. seeking a court order setting aside the FDA's final determination of the regulatory review period for Cydectin.[23]

The District of D.C. applied Chevron deference: Under Chevron, the court first asks whether Congress has spoken directly to the precise question at issue. If Congress has not spoken to the issue, the court then determines whether the FDA's interpretation is based on a permissible construction of the statute.[24]

First, the court found that Congress had not spoken directly to the issue. The plain text of the statute was ambiguous, and the legislative history was inconclusive. Thus, the court held that 35 U.S.C. § 156(g)(4)(B)(ii) is "ambiguous based on its text, context, and legislative history."[25]

Second, the court found that Wyeth had not met its burden of proving that the FDA's interpretation was unreasonable. The court found the FDA's arguments to be more persuasive than Wyeth's: "Indeed, the FDA's construction runs true to the text and defines 'initially submitted' in a manner that is reasonable in light of the legislature's revealed design. Accordingly, the court cannot say that the FDA's interpretation is based on an impermissible construction of the statute, nor can the court find that the FDA's interpretation violates the APA."[26] Thus, the court granted summary judgment for the FDA.

Wyeth appealed the court's decision to the Federal Circuit, but the Federal Circuit affirmed. Judge Kimberly Moore, writing for the majority, reviewed the lower court's Chevron analysis and agreed that the statute was ambiguous and that the FDA's interpretation was appropriate.[27]

Because the District of D.C. and the Federal Circuit have both upheld the FDA's practice of calculating short approval phases for phased review, an animal drug applicant should be cognizant of what PTE may be available when selecting this review option.[28]

Implications for PTE

Depending on how the animal drug applicant structures its testing and application process, the choice of traditional or phased review could significantly affect the length of PTE available. In the majority of cases, choosing traditional review will yield longer PTE, but phased review can be an attractive choice from a business perspective. In phased review, the applicant is engaged in an ongoing conversation with the FDA and can more quickly adapt to meet the FDA's comments. NADA applicants would benefit from consulting with both regulatory and patent counsel before walking down either review path.

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[1] See Robert W. Esmond & Stephanie L. Elmer, USPTO Cancer Drug Pilot Program Not Likely to be Used Much, Law360, Jul. 21, 2016.

[2] 35 U.S.C. §156 (f)(2)(A).

[3] 35 U.S.C. § 156 (f)(2)(B).

[4] 35 U.S.C. § 156 (a)(1).

[5] 35 U.S.C. § 156 (a)(2).

[6] 35 U.S.C. § 156 (d)(2)(A).

[7] 35 U.S.C. § 156 (a)(5)(a)

[8] 35 U.S.C. § 156 (a)(5)(C).

[9] 35 U.S.C. § 156 (a)(5)(B).

[10] Portfolios With 4 Legs to Stand On: Animal Drug Patent Tips, D.A. Sterling, J.B. Frueauf, R. Hammond, Law360, 4/29/16.

[11] Wyeth Holdings Corp. v. U.S. Dep't of Health & Human Servs., 607 F. Supp. 2d 25 (D.D.C. 2009) aff'd sub nom. Wyeth Holdings Corp. v. Sebelius, 603 F.3d 1291 (Fed. Cir. 2010).

[12] 35 U.S.C. § 156(g)(4)

[13] 35 U.S.C. §156(g)(4).

[14] 35 U.S.C. § 156(g)(5).

[15] Wyeth Holdings Corp. v. U.S. Dep't of Health & Human Servs., 607 F. Supp. 2d 25, 27 (D.D.C. 2009), aff'd sub nom. Wyeth Holdings Corp. v. Sebelius, 603 F.3d 1291 (Fed. Cir. 2010).

[16] Id.

[17] Wyeth Holdings Corp. v. Sebelius, 603 F.3d 1291, 1294 (Fed. Cir. 2010).

[18] Wyeth, 607 F. Supp. at 25.

[19] Id.

[20] Id. at 28.

[21] Id.

[22] Id.

[23] Id.

[24] Id. at 29.

[25] Id. at 32.

[26] Id. at 33. (internal quotation marks omitted).

[27] Wyeth, 603 F.3d at 1296-1300.

[28] In its arguments at the district court level in Wyeth, the FDA pointed out that it had consistently determined that the Approval Phase begins upon submission of the Administrative NADA, and that such determinations have produced similarly short Approval Phases for the following animal drugs: Neutersol (34 days); Anipryl (54 days); Ivomec (17 days). Wyeth 607 F. Supp. at n. 8.