No. 2009-1368

IN THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

WYETH HOLDINGS CORPORATION and WYETH,

Plaintiffs-Appellants,

v.

Kathleen Sebelius, SECRETARY OF HEALTH AND HUMAN SERVICES, DEPARTMENT OF HEALTH AND HUMAN SERVICES, Dr. Margaret Hamburg, COMMISSIONER OF FOOD AND DRUGS, UNITED STATES FOOD AND DRUG ADMINISTRATION, David Kappos, UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY and DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE, and UNITED STATES PATENT AND TRADEMARK OFFICE,

Defendants-Appellees.

Appeal from the United States District Court For the District of Columbia
in Case No. 08-cv-00981, Judge Henry H. Kennedy, Jr.

BRIEF FOR DEFENDANTS-APPELLEES

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TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Cases:

Statutes:

Regulations:

Rules:

Legislative Materials:

Miscellaneous:

Statement of Related Cases

No other appeal in or from the present civil action has previously been before this or any other appellate court. Counsel is unaware any related case currently pending before this Court or any other court.

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STATEMENT OF JURISDICTION

This case involves a challenge to a patent term extension determination under 35 U.S.C. 156. The appellants, Wyeth Holdings Corporation and Wyeth (hereinafter "Wyeth"), invoked the jurisdiction of the district court under 28 U.S.C. 1331 and 1361. See JA 24 ¶ 6. The district court was also vested with jurisdiction by 28 U.S.C. 1338(a), which grants district courts jurisdiction "of any civil action arising under any Act of Congress relating to patents * * * ."

The district court entered a final judgment in favor of the appellees on March 23, 2009. JA 1. The appellants filed a notice of appeal on May 20, 2009 (JA 18), within the time allowed by Rule 4(a) of the Federal Rules of Appellate Procedure. The appellants invoke this Court's appellate jurisdiction pursuant to 28 U.S.C. 1295(a)(1), which gives this Court exclusive jurisdiction over appeals from final decisions by district courts exercising jurisdiction "in whole or in part" under 28 U.S.C. 1338(a). 28 U.S.C. 1295(a) provides this Court with jurisdiction to hear the appeal. See *Christianson v. Colt*, 486 U.S. 800, 810 (1988); *Biotechnology Industry Organization v. District of Columbia*, 496 F.3d 1362, 1366-1369 (Fed. Cir. 2007).

STATEMENT OF THE ISSUE

Whether the Food and Drug Administration (FDA) properly determined when an "application" for a new animal drug is "initially submitted" to FDA for approval for purposes of determining the length of a patent term extension under 35 U.S.C. 156(g)(4)(B).

STATEMENT OF THE CASE

A. Pertinent Statutory and Regulatory Provisions Involved

The pertinent statutory and regulatory provisions are contained in Addendum 2 of Wyeth's opening brief.

B. Patent Term Extensions for New Animal Drugs

1. FDA's Regulation of New Animal Drugs

a. Under the Federal Food, Drug, and Cosmetic Act (FDCA), a new animal drug is defined as "any drug intended for use for animals other than man, including any drug intended for use in animal feed * * *." 21 U.S.C. 321(v). The term "drug" is defined, in relevant part, as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and * * * articles (other than food) intended to affect the structure or any function of the body of man or other animals * * *." 21 U.S.C. 321(g)(1). Before a new animal drug can be legally marketed, a sponsor must submit, and FDA must approve, a new animal drug application (NADA).[1] 21 U.S.C. 360b(a). The approval process can be initiated by submitting what FDA calls either a traditional NADA or an administrative NADA, both of which are discussed in greater detail below. Without an approved NADA, a new animal drug is deemed unsafe and adulterated. 21 U.S.C. 360b(a)(1)(A) & 351(a)(5). See also n.1, *supra*.

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[1] The FDCA does provide additional ways a sponsor may legally market a new animal drug that are not at issue before the Court. A new animal drug shall be deemed to be safe if either: (1) it is conditionally approved for minor use or minor species or (2) it is granted an index listing as a legally marketed unapproved new animal drug for minor species. 21 U.S.C. 360b(a)(1)(B)-(C).

To obtain FDA approval of an NADA, a sponsor must demonstrate, among other things, that the drug is safe and effective for its intended uses. 21 U.S.C. 360b(b); 21 C.F.R. 514.1(b)(8). If the product is intended to be used in a food-producing animal, the sponsor must also demonstrate that food derived from animals treated with the new animal drug product is safe for human consumption. 21 U.S.C. 360b(d)(2); 21 C.F.R. 514.1(b)(7). To make the required showings, the sponsor must perform testing to generate data on the effects of the drug.

An application for a new animal drug is required to include, "as part of the application," all the information specified by 21 U.S.C. 360b(b)(1). Section 360b(b)(1) requires the application to include "full reports" of investigations regarding the safety and effectiveness of the drug; "a full list" of the drug components; "a full statement" of the drug composition; "a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the drug; samples of the drug and drug components, and of the edible portions or products of animals to which such drug is intended to be administered; specimens of the proposed labeling; a description of practicable methods for determining the quantity, if any, of the drug in or on food, and any substance formed in or on food, because of its use; and the proposed tolerance or withdrawal period or other use restrictions for the drug in order to assure that its

proposed use will be safe. See 21 U.S.C. 360b(b)(1)(A)-(H); see also 21 C.F.R. 514.1(b) (adding other required contents).

b. A sponsor may seek approval of a new animal drug through either traditional review or phased review. See JA 154-161 (Center for Veterinary Medicine (CVM) 2002 Draft Guidance # 132). Under traditional review, a sponsor first conducts the required investigation and testing of the drug; when this testing phase is complete, the sponsor submits a traditional NADA containing all the information required by 21 U.S.C. 360b(b)(1) and 21 C.F.R. 514.1(b). FDA then begins the approval phase of the NADA. 21 U.S.C. 360b(c).

Under phased review, the sponsor may submit portions or technical sections of information and data during the testing phase of the new animal drug. JA 156. Because submissions of investigational and testing data are made during the testing phase, they are submitted to what the FDA calls an Investigational New Animal Drug (INAD) file, pursuant to an investigational exemption under 21 U.S.C. 360b(j). *Ibid*. See also JA 63. As the technical sections are submitted to the INAD file, FDA reviews them, and if (in the view of the CVM section reviewing the data), a technical section meets the requirements of 21 C.F.R. 514.1, FDA issues a "complete letter" for that particular technical section. JA 159.

As noted, FDA refers to the application for a new animal drug submitted under phased review as an "administrative NADA." JA 156. The sponsor's administrative NADA must incorporate by reference any technical section the sponsor has previously submitted to the INAD file during the testing phase if the sponsor has received a "complete letter" for that technical section. JA 66, 230. Although the sponsor may submit a traditional NADA that complies with 21 U.S.C. 360b(b) at any time during the phased review process (JA 67), any NADA — whether traditional or administrative — must address all required technical sections or the application will be refused. JA 66-67, 159, 230, & 232. In any event, whether the sponsor uses traditional or phased review, an application is required to include all the information required by 21 U.S.C. 360b(b)(1) and 21 C.F.R. 514.1(b).

The time it takes to approve an administrative NADA under phased review usually will be shorter than the time it takes to approve a traditional NADA through traditional review. JA 161. The choice between traditional or phased review rests with the sponsor rather than with FDA, and a sponsor's decision to proceed by phased review is purely voluntary. JA 156.

2. The Patent Term Restoration Act

The Drug Price Competition and Patent Term Restoration Act of 1984 (known as the "Hatch-Waxman Amendments") enabled patent holders to extend the term of their patents for human drugs, medical devices, food additives, and color additives to recover some of the time lost due to regulatory review. See Pub. L. No. 98-417, 98 Stat. 1585 (1984). The Hatch-Waxman Amendments did not encompass animal drugs. *Ibid*. In 1988, Congress passed The Generic Animal Drug and Patent Term Restoration Act (GAD/PTR Act) to include animal drugs and veterinary biologics among those products eligible for patent term extensions. See Pub. L. No. 100-670, 102 Stat. 3971 (1988). The GAD/PTR Act used substantially similar language to the "Hatch-Waxman Amendments, and was intended to extend the existing statutory framework for human drugs to animal drugs." See H.R. Rep. No. 100-972, pt. 1, at 8 (1988) ("[the GAD/PTR Act] simply makes the additions to [Hatch-Waxman Amendments] necessary to include animal drugs and veterinary biologicals within the existing statutory framework"); H.R. Rep. No. 100-972, pt. 2, at 20 (1988) (stating the same); see also Patent Term Restoration Regulations (Proposed Rule), 56 Fed. Reg. 5784, 5785 (1991) (preamble to proposal for regulations later codified at 21 C.F.R. Part 60) ("The [GAD/PTR] Act (Pub. L. 100-670) achieved this goal in November 1988 by

amending the existing patent term restoration provisions at 35 U.S.C. 156 to include animal drug products and biologics.").

Under 35 U.S.C. 156, the patent term of an animal drug is eligible for an extension if, *inter alia*, the drug is subject to a "regulatory review period" prior to commercial marketing or use. 35 U.S.C. 156(a)(4). A "regulatory review period" consists of two periods of time: a "testing phase" and an "approval phase." 35 U.S.C. 156(g)(4)(B). 21 C.F.R. 60.22. For new animal drugs approved under 21 U.S.C. 360b(c), the "testing phase" begins on the earlier of (1) the effective date of an INAD exemption or (2) the date a major health or environmental effects test on the drug was initiated. 35 U.S.C. 156(g)(4)(B)(i); 21 C.F.R. 60.22(d)(1). The "testing phase" ends on "the date an application [is] initially submitted" to FDA under 21 U.S.C. 360b(b). *Ibid*. The "approval phase" begins on the same date and ends on the date the application is approved. 35 U.S.C. 156(g)(4)(B)(ii); 21 C.F.R. 60.22(d)(2). FDA's regulations provide that an application "is initially submitted on the date it contains sufficient information to allow FDA to commence review of the application." 21 C.F.R. 60.22(f).

FDA has determined that the approval phase for a new animal drug application using the phased review process begins when an "administrative NADA" (see p. 5, *supra*) is submitted. The administrative NADA constitutes "the

application" for FDA approval purposes because it is the first submission to contain *all* the information required by 21 U.S.C. 360b(b) and 21 C.F.R. 514.1(b) — including the corresponding technical section complete letters incorporating testing data in the INAD file — that allows FDA to make an approval decision. JA 156, 160-161, 232. FDA has consistently followed this approach. See, *e.g.*, Determination of Regulatory Review Period for Purposes of Patent Extension (Neutersol), 69 Fed. Reg. 40944 (2004) (Neutersol Notice); Determination of Regulatory Review Period for Purposes of Patent Extension (Anipryl), 63 Fed. Reg. 41578 (1998) (Anipryl Notice); Determination of Regulatory Review Period for Purposes of Patent Extension (Ivomec Eprinex Pour-On for Beef and Dairy Cattle), 63 Fed. Reg. 36922 (1998) (Ivomec Notice). See also JA 160-61.

Ordinarily, patent terms for animal drugs may be extended by the sum of (i) half of the length of the testing phase, and (ii) all of the length of the approval phase of the regulatory review period. 35 U.S.C. 156(c)(2) & 156(g)(4); 21 C.F.R. 60.22(d). As explained above, the date that "the application [is] initially submitted" marks the end of the testing phase and the beginning of the approval

phase. As a result, determining when an application is initially submitted has a direct impact on the length of the patent term extension.[2]

Finally, the United States Patent and Trademark Office (USPTO) and the FDA jointly determine the patent term extension. See *Astra v. Lehman*, 71 F.3d 1578, 1581 (Fed. Cir. 1995). While the USPTO receives the application for extension, calculates the extension based on the regulatory review period, and issues the certificate of extension, FDA is charged by statute with determining the actual length of the regulatory review period. *Ibid*.

STATEMENT OF FACTS

1. Factual background

a. Cydectin

Cydectin is an animal drug product approved to treat and control internal and external parasites in beef and dairy cattle. JA 32 ¶ 44. In April 1990, the USPTO issued U.S. Patent No. 4,916,154 ("the '154 patent," titled "23-Imino

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[2] The patent term extension statute imposes additional restrictions on the length of time an animal drug patent may be extended. First, if the applicant did not act with due diligence during the regulatory review period, the patent term extension must be reduced by the amount of time that the applicant caused undue delay. 35 U.S.C. 156(c)(1). Second, the patent term, as extended, cannot exceed fourteen years from the date of FDA's approval of the applicant's NADA. 35 U.S.C. 156(c)(3). Third, a patent term may not be extended by more than five years, even if the regulatory review period is longer than five years. 35 U.S.C. 156(g)(6)(A).

Derivatives of LL-F28249 Compounds"), which covers Cydectin. JA 32 ¶¶ 45, 49-51. The original expiration date of the '154 patent was April 10, 2007 (JA 32 ¶ 52), and Wyeth states that it is the current assignee of the '154 patent, and owner of all rights, title, and interests in and to the '154 patent (JA 3, 32 ¶ 48).

b. Cydectin's Testing Phase

Wyeth sought FDA approval for Cydectin pursuant to the phased review process, asking FDA to establish an INAD file on March 26, 1990. JA 3, 33 ¶¶ 55, 57. FDA established the INAD file in April 5, 1990, marking the date that the testing exemption under 21 U.S.C. 360b(j) became effective. JA 33 ¶ 56; JA 168 (Cydectin Notice).

Wyeth periodically submitted information and data to the INAD file during the testing phase of its new animal drug. JA 33-34 ¶¶ 58 & 61-65. Wyeth made its initial technical section submission of testing and investigational information (the "Residue Chemistry technical section") to the INAD file on August 8, 1995. JA 3, 23 ¶ 3, 33 ¶ 58. This submission of testing and investigational information to the INAD file was the first of many during Cydectin's testing phase. JA 33-34 ¶¶ 57, 59, & 61-65. For example, Wyeth submitted the final technical section ("Environmental Safety") on August 14, 1996. JA 3, 34 ¶¶ 65, 66. Wyeth amended that technical section on June 13, 1997. JA 184. Wyeth submitted

testing and investigational information to the INAD file as late as January 9, 1998, when it submitted the protocol pertaining to its residue depletion study in pre-ruminating calves. JA 149. Four days later, on January 13, 1998, Wyeth submitted its application — in the form of an administrative NADA — for Cydectin. JA 34 ¶ 68, 37 ¶ 84, 149, 232.

c. Cydectin's Approval Phase

On January 13, 1998, when Wyeth submitted its administrative NADA, FDA designated this application NADA 141-099, which triggered the beginning of the approval phase. JA 34 ¶ 68, 37 ¶ 84, 168-169, 230. FDA approved NADA 141-099 on January 28, 1998. JA 3, 33 ¶ 54, 34 ¶ 70, 169.

d. Wyeth's Patent Term Extension Application

Wyeth filed a Request for Extension of Patent Term with the USPTO for the '154 patent. JA 35 ¶ 71, 84-153. FDA advised the USPTO that Cydectin had undergone a regulatory review period and that the approval of Cydectin represented the first permitted commercial marketing or use of the product. JA 168. Shortly thereafter, the USPTO requested that FDA determine the length of the product's regulatory review period. *Ibid*.

FDA determined that the applicable regulatory review period for Cydectin was 2,857 days, consisting of a testing phase of 2,841 days and an approval phase

of 16 days. JA 3, 37 ¶ 82, JA 168. FDA determined that the testing phase began on April 5, 1990 (the date the INAD file was established) and ended on January 13, 1998 (the date Wyeth initially submitted administrative NADA 141-099); and the approval phase began on January 13, 1998 (the date Wyeth initially submitted its administrative NADA 141-099) and ended on January 28, 1998 (the date FDA approved administrative NADA 141-099). JA 3-4, 168-169.

Based on FDA's statutorily-mandated calculation (see p. 8, *supra*), the USPTO issued a notice of final determination indicating that Wyeth's '154 patent should be extended 1,434 days — an extension of approximately 3.9 years. JA 3-4, 37 ¶ 88. Therefore, the expiration of Wyeth's '154 patent was extended from April 10, 2007, to March 14, 2011. JA 3, 37 ¶ 89.

e. Wyeth's Request for Revision of the Regulatory Review Period

Wyeth filed a Request for Revision of the Regulatory Review Period with FDA. JA 4, 39 ¶ 96, 173-224. In Wyeth's view, "the [Cydectin] application was 'initially submitted' on August 8, 1995," and that "the approval phase of the regulatory review period began on that date." JA 189. Wyeth's position was that, because the first technical section (Residue Chemistry) was submitted to the INAD file on August 8, 1995, that date marked when Wyeth's NADA for Cydectin was initially submitted. JA 185. Although Wyeth acknowledged that a technical

section was amended as late as June 13, 1997, and that its testing and investigation of Cydectin continued into January 1998 (see JA 184; see also JA 149), Wyeth contended that August 8, 1995, was the point at which "there was 'sufficient information to allow FDA to commence review of the application.'" *Ibid*. (quoting 21 C.F.R. 60.22(f)). Wyeth's request for revision thus contended that the testing phase for Cydectin was 1,952 days and that the approval phase was 905 days. JA 189.

FDA denied Wyeth's request. JA 4, 228-232. FDA reiterated that when a sponsor seeks phased review of new animal drug products, the approval phase "begins when the administrative NADA, including all of the technical sections required for approval of the new animal drug under 21 C.F.R. 514.1 and the corresponding technical section complete letters, is submitted under section 512 of the Act [21 U.S.C. 360b(b)]." JA 232. Therefore, FDA concluded, January 13, 1998, was the date Wyeth initially submitted its application to begin the approval phase of Cydectin. *Ibid*.

FDA explained that the regulatory review determination for phased review of new animal drugs parallels the regulatory review determination for human drug applications, in that the applications submitted for human drugs "are not considered initially submitted until all required technical information is addressed

and available for FDA decision making to commence." *Ibid*. FDA also noted that the testing and investigational information in the form of technical sections were submitted to an INAD file, and that regulatory review under an INAD file (or investigational exemption) is conducted during the testing (or investigational) phase, not the approval phase, of the regulatory review period. *Ibid*. FDA stated that, although phased review "can result in a very short approval phase, it is most consistent with the idea that alternative drug development and review approaches are intended to permit the applicant to respond to FDA input as the application is developed, making FDA's review more efficient, and shortening the time required for review of the application." *Ibid*.

2. District court proceedings

Wyeth filed its complaint in June 2008, challenging under the Administrative Procedure Act (APA) FDA's determination that the testing phase ended and the approval phase began on January 13, 1998, when Wyeth initially submitted its administrative NADA for Cydectin. JA 20. Both sides moved for summary judgment. The government's principal argument was that a sponsor has not initially submitted an "application" until there is a submission containing all the documentation, samples, and specimens required under 21 U.S.C. 360b(b) and 21 C.F.R. 514.1(b). See JA 6-7. Thus, FDA contended, there was no

"application" until Wyeth submitted the administrative NADA on January 13, 1998, which triggered the end of the testing phase and the beginning of the 16-day approval phase. Wyeth argued that the "application" was "initially submitted" when Wyeth submitted the first technical section on August 8, 1995, or, alternatively, on August 14, 1996, when it submitted its last technical section ("Environmental Safety"). See JA 3, 4, 33 ¶ 58, & 36 ¶¶ 78-80.

The district court ruled that under *Chevron* step 1 there was no clear meaning to either 21 U.S.C. 360b(b) or 35 U.S.C. 156(g)(4)(B) with respect to the meaning of "application" — because that term was not defined in the statute — or when an application would be considered "initially submitted" for purposes of Wyeth's patent term extension application. JA 9-10. The court also found the legislative history unhelpful. JA 10. The court therefore moved to the analysis under *Chevron* step 2.

Considering the undisputed fact that Wyeth continued its investigation and testing of Cydectin through 1998, and that adopting Wyeth's interpretation would have the court declare that the testing phase ended when the bulk of the requisite testing remained to be done, the court found that 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." JA 12 (internal quotation marks and citation

omitted). The court therefore deferred to FDA's views as to when the testing phase ended and the approval phase began, finding that Wyeth had failed to carry its burden to show that the FDA's interpretation was unreasonable. JA 11-12.

SUMMARY OF ARGUMENT

1. Under 35 U.S.C. 156(g)(4)(B), a patent term extension may be granted to qualifying new animal drug products based on the length of the "regulatory review period." That period consists of a "testing phase" and an "approval phase," and the length of the patent term extension is equal to the sum of half the testing phase plus all of the approval phase. Thus, identifying the end of the testing phase and the beginning of the approval phase is central to calculating the patent term extension.

Subsection (ii) of Section 156(g)(4)(B) states that the approval phase begins "on the date the application [under 21 U.S.C. 360b(b)] was initially submitted for the approved animal drug product * * *." 21 U.S.C. 360b(b), in turn, sets out a specific list of information that an applicant "shall submit to the Secretary *as part of the application*" for a new animal drug approval. (Emphasis added.) Because an application must contain, *at a minimum*, the information specified by Section 360b(b), a submission that does not contain the specified information is not an "application" for purposes of that provision. Thus, the approval phase in 35

U.S.C. 156(g)(4)(B)(ii) is triggered only when a document containing (*at a minimum*) the information required in 21 U.S.C. 360b(b) is "initially submitted" to FDA for approval. A submission that does not contain the required information cannot trigger the approval phase in 35 U.S.C. 156(g)(4)(B) because it is not an application. In accordance with the foregoing, FDA correctly determined in this case that Cydectin's approval phase began on January 13, 1998, the date on which Wyeth submitted its administrative NADA.

Wyeth acknowledges that 21 U.S.C. 360b(b)(1) defines the elements of an application, but argues that, under 35 U.S.C. 156(g)(4)(B), "an application" is "initially submitted" when the first document containing *any* of the information required by Section 360b(b)(1) is submitted. According to Wyeth, by requiring submission of *all* the information in 21 U.S.C. 360b(b)(1), FDA improperly converts the term "initially submitted" to "finally submitted." But Wyeth's argument is inconsistent with the express terms of 21 U.S.C. 360b(b)(1), and otherwise finds no support in the statute.

Nor is there merit to Wyeth's argument that FDA's position emphasizes form over substance. FDA's reading is compelled by the language of the two statutory provisions at issue, 35 U.S.C. 156(g)(4)(B)(ii) and 21 U.S.C. 360b(b)(1). Morever, an application for purposes of the patent term extension provisions

relating to new animal drugs is the same whether the sponsor seeks approval under traditional or phased review. Yet, under Wyeth's view, a sponsor proceeding under phased review can trigger the approval phase by submitting only a fragment of what is required to be part of "the application," while a traditional-review sponsor achieves that result only by submitting an application and all the required information. Nothing in the statute authorizes such a difference in treatment.

Finally, Wyeth argues in the alternative, that the date of submission of its last technical section of data in August 1996 should mark the date its application was "initially submitted" on the theory that, by that date, it had submitted all the information required by statute and regulation. But this argument suffers from the same defective understanding of what constitutes an application as Wyeth's previous argument regarding the submission of the first technical section: even with the filing of the last *technical* section to the INAD file, Wyeth still had not submitted an application — a single submission containing or referencing all the required information. Moreover, FDA's reading of the statute is borne out by the record, which demonstrates that, even after the submission of the last technical section, Wyeth engaged in further testing and continued to submit information to FDA into early January 1998, just days before it submitted its application, the administrative NADA.

2. Even if the plain language of the statutory provisions did not compel FDA's reading, FDA's interpretation is entitled to deference because, for the reasons just stated, it is consistent with the statute. It is also consistent with the legislative history, the policy underlying the patent term extension provisions, and FDA's practice since the 1988 enactment of the patent term provisions pertaining to new animal drug products.

Wyeth wants the best of both worlds: it wants the quicker approval and earlier marketing that comes with phased review, but it also wants the longer patent term extension associated with the longer review period that comes with traditional review. At any time during phased review, Wyeth could have opted for traditional review, but it did not do so because, as it readily acknowledges, longer regulatory periods postpone the sponsor's recovery on its investment and creates the risk that competing drugs will emerge or gain market share. Having chosen the phased review option that minimized regulatory delay, Wyeth cannot insist on a patent term extension calculation that effectively disregards the expedition.

ARGUMENT

Introduction and Standard of Review

This Court reviews a district court's grant of summary judgment without deference to the lower court, applying the same standard as the district court. See

Lacavera v. Dudas, 441 F.3d 1380, 1382 (Fed. Cir. 2006); *Star Fruits, S.N.C. v. United States*, 393 F.3d 1277, 1281 (Fed. Cir. 2005). The Court also "'review[s] de novo whether [an agency's] interpretation of a governing statutory provision is in accordance with law,'" but it "'do[es] so within the framework established by *Chevron* [*U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 842-43 (1984)] * * *.'" *Ningbo Dafa Chemical Fiber Co., Ltd. v. U.S.*, 580 F.3d 1247, 2009 WL 2768491 (Fed. Cir. 2009) (ellipsis in original) (quoting *Agro Dutch Indus. Ltd. v. United States*, 508 F.3d 1024, 1029-30 (Fed. Cir.2007)). See also *Elkem Metals Co. v. United States*, 468 F.3d 795, 800 (Fed. Cir.2006).

Under *Chevron* step one, the Court must determine "'whether Congress has directly spoken to the precise question at issue. If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress.'" *Ningbo Dafa Chemical Fiber Co., Ltd.*, 2009 WL 2768491 at * 4 (quoting *Chevron*, 467 U.S. at 842-43). See also *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 132 (2000); *Agro Dutch*, 508 F.3d at 1030. Or, put another way, courts must initially decide "whether the statute unambiguously forbids the Agency's interpretation * * *." *Barnhart v. Walton*, 535 U.S. 212, 218 (2002).

If Congress has not "directly" addressed "the precise question at issue," the

Court may not "impose its own construction on the statute," *Chevron*, 467 U.S. at 843, but, rather, must determine under *Chevron* step two whether the agency's interpretation is based on "a permissible construction of the statute." *Ibid*. As long as "an agency's statutory interpretation promulgated under the authority delegated it by Congress is reasonable[,] it is binding [o]n the courts unless procedurally defective, arbitrary or capricious in substance, or manifestly contrary to the statute." *Wheatland Tube Co. v. United States*, 495 F.3d 1355, 1360 (Fed. Cir. 2007) (internal quotation marks and citation omitted; alteration in original). Thus, this Court extends deference to an agency's interpretation of a statute when, as here, it is charged with administering the statute. See *Cooper Technologies. v. Dudas*, 536 F.3d 1330 (Fed. Cir. 2008); 35 U.S.C. 156(d)(1)(C), 156(d)(2)(A)(ii), 156(d)(2)(B)(i), and 156(d)(2)(B)(ii). See also *Astra v. Lehman*, 71 F.3d at 1581 (discussed, *supra*, p. 10); and *Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1348 (Fed. Cir. 2003) ("FDA's interpretation of the statute is permissible and * * * therefore must be upheld."). Here, Congress specifically directed FDA to determine the regulatory review period from which the USPTO issues patent term extensions. Accordingly, if the Court reaches step two of the *Chevron* analysis, FDA's interpretation is entitled to deference as long as it is reasonable. See also *Gonzales v. Oregon*, 546 U.S. 243, 244 (2006) (deference applies when "Congress

delegated authority to the agency generally to make rules carrying the force of law.") (quoting *United States v. Mead Corp.*, 533 U.S. 218, 226-27 (2001)).

In this case, the district court declined to sustain the FDA's interpretation of 35 U.S.C. 156(g)(4)(B) under step one of *Chevron*, but held that the FDA's interpretation was reasonable and therefore entitled to deference under *Chevron* step two. As we now show, the FDA is entitled to prevail under both prongs of *Chevron*: FDA's interpretation is compelled by the plain language of the statute, and even if it were not, it is a manifestly reasonable implementation of the statutory language and the policies underlying the patent term extension provision.

I. THE PLAIN LANGUAGE OF 35 U.S.C. 156(g)(4)(B)(ii) AND 21 U.S.C. 360b(b) COMPELS FDA's DETERMINATION OF THE REGULATORY REVIEW PERIOD

1. Under 35 U.S.C. 156, a patent term extensions may be granted to qualifying new animal drug products based on the length of the "regulatory review period." 35 U.S.C. 156(g)(4)(B). See pp. 8-10, *supra*. The "regulatory review period" for a new animal drug product consists of —

> (i) the period beginning on the earlier of the date a major health or environmental effects test on the drug was initiated or the date an exemption under subsection (j) of section 512 became effective for the approved new animal drug product and ending on the date an application was initially submitted for such animal drug product under section 512, and

> (ii) the period beginning on the date the application was initially submitted for the approved animal drug product under subsection (b) of section 512 and ending on the date such application was approved under such section.

35 U.S.C. 156(g)(4)(B)(i) & (ii).

Subsection (i) describes the "testing phase" and subsection (ii) the "approval phase." See also 21 C.F.R. 60.22(d) (FDA regulation defining the "testing phase" and "approval phase".). The length of the patent term extension is equal to the sum of half the testing phase plus all of the approval phase. See 35 U.S.C. 156(c)(2) (only half of the testing phase is credited) & 156(g)(4)(B).[3] Thus, identifying the date on which the testing phase ends and the approval phase begins is central to the calculation of the patent term extension, and subsection (ii) controls the determination of that date: the approval phase begins (and thus the testing phase ends) "on the date the application was initially submitted for the approved animal drug product under subsection (b) of section 512 [of the FDCA, 21 U.S.C. 360b(b)]." 35 U.S.C. 156(g)(4)(B)(ii).[4]

As 35 U.S.C. 156(g)(4)(B)(ii) plainly states, the "application" referred to is

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[3] Other limitations are discussed at n.2 (p. 10), *supra*.

[4] 35 U.S.C. 156(g)(4)(B)(i), which addresses when the testing phase ends, contains similar wording. It states that the testing phase ends (and thus the approval phase starts) "on the date an application was initially submitted for such animal drug product under section 512 [of the FDCA, 21 U.S.C. 360b] * * *."

the "application" submitted under 21 U.S.C. 360b(b) — *i.e.*, Section 512 of the FDCA. In turn, 21 U.S.C. 360b(b) specifies the information that the sponsor "shall submit to the Secretary *as a part of the application* * * *." *Ibid*. (emphasis added). Thus, under the latter provision of the FDCA, *whether for traditional or for phased review* (see pp. 5-6, *supra*), the submission must contain *at least* the following information in order to constitute a new animal drug application: full reports of investigations regarding the safety and effectiveness of the drug; a full list of the drug components; a full statement of the drug composition; a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the drug; samples of the drug and drug components, and of the edible portions or products of animals to which such drug is intended to be administered; specimens of the proposed labeling; a description of practicable methods for determining the quantity, if any, of the drug in or on food, and any substance formed in or on food, because of its use; and the proposed tolerance or withdrawal period or other use restrictions for the drug in order to assure that its proposed use will be safe. See 21 U.S.C. 360b(b)(1)(A)-(H). A submission containing less than all of this information simply does not constitute

"the application" for purposes of the new animal drug approval process.[5] Thus, for example, a sponsor cannot claim to have submitted an "application" merely by tendering a statement of the drug's composition (*id.* § 360b(b)(1)(C)), or by submitting examples of labeling (*id.* § 360b(b)(1)(F)).

* * * * *

Based on the foregoing, FDA correctly determined that Cydectin's approval phase began on January 13, 1998. There is no dispute that on that date Wyeth initially submitted its administrative NADA, which was the submission containing all the information required by 21 U.S.C. 360b(b)(1) (and 21 C.F.R. 514.1(b)), by, among other things, its inclusion of technical section "complete" letters from FDA. See JA 34 ¶ 68, 37 ¶ 84, 166-170, 228-232.[6]

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[5] 21 U.S.C. 360b(b)(1) also states, in pertinent part, that "[t]he applicant shall file with the application" certain patent information, including "the patent number and the expiration date of any patent which claims the new animal drug * * *." Because the statute says the information in Section 360b(b)(1)(A)-(H) "shall" be submitted "as part of the application," the statute also establishes FDA's authority to require additional information in the application. See 21 C.F.R 514.1(b) (describing the contents of an application for a new animal drug). 21 C.F.R. 514.1(b) requires, for example, the submission of pertinent information identifying the applicant (21 C.F.R. 514.1(b)(1)); a table of contents and summary (21 C.F.R. 514.1(b)(2)); and a description of the applicant's commitments (21 C.F.R. 514.1(b)(11)).

[6] In addition, the record makes clear that Wyeth continued its testing of Cydectin into early 1998, as demonstrated by its continuous submission of testing

(continued...)

2. Wyeth acknowledges that 21 U.S.C. 360b(b)(1) defines the elements of an application, but argues nevertheless that "an application" is "initially submitted" under 35 U.S.C. 156(g)(4)(B) when *any* information required by Section 360b(b)(1) is submitted. See Wyeth Br. at 28-30, 30-32, 33-39; see also JA 3, 23 ¶ 3, 33 ¶ 58, 40 ¶ 102, 185. Wyeth's focus on "initially submitted" — to arrive at the conclusion the submission of *any* of the information prescribed in Section 360b)(b)(1)(A)-(H) constitutes initial submission of "the application" — is faulty, for at least two reasons.

First, 21 U.S.C. 360b(b)(1) plainly states that an application "shall" contain *at a minimum* the information listed in subsections (A)-(H). Anything less constitutes part of an application, not an application. Wyeth appears to have conceded as much at the administrative level when it stated that "the August 8, 1995 filing was sufficient to allow CVM to begin a substantive review of one section required *as part of the application*." JA 187 (emphasis added). Thus, filing of the first technical section clearly did not constitute the filing of an application under 21 U.S.C. 360b(b)(1).

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[6](...continued)
information to that point. See JA 12, 33-34 ¶¶ 54-70, 149, 184. For example, on January 9, 1998, Wyeth submitted the protocol pertaining to its residue depletion study in pre-ruminating calves. JA 149.

Second, the premise of Wyeth's argument — that the filing of the first technical section was "sufficient for FDA to begin its review," Wyeth Br. at 34 — is flawed. See also *id*. at 39-40 (arguing that, because FDA reviewed submissions while Wyeth was testing and investigating Cydectin, the submissions should count as the application). The statutory question is *not* when FDA is able to begin its review of partial testing data but, rather, when "the application" itself is "initially submitted" for FDA review.

Wyeth argues that its position is supported by the legislative history of the Hatch-Waxman Amendments upon which the GAD/PTR Act was engrafted. Wyeth Br. at 33-34. Wyeth points to a passage that states that "an *application* for agency review is considered to be 'initially submitted'" as long as the sponsor has "submit[ted] an application *containing all information necessary* for agency review to begin," *i.e.*, "[a]s long as the application was complete enough so that agency action could be commenced * * *." H.R. Rep. No. 98-857, pt. 1, at 44 (1984) (emphasis added). But, as noted by the italicized language, the legislative history is consistent with FDA's reading of the statute. An "application" is a submission that contains or references "all information necessary for agency review to begin," and given the phrasing, it is at least reasonable to understand the "review" referred to as "review" *of the application*. Similarly, in referring to a

submission that is "complete enough" to allow "agency action," it is more than reasonable to read that phrase as meaning "complete enough" to allow "approval." Nothing in the legislative history suggests that the mere submission of partial testing data can trigger the approval phase. This is especially true where, as here, the sponsor continued testing and submitting information to FDA up to four days prior to the submission of its application. See n.6, *supra*.

In a similar vein, Wyeth misplaces its reliance on 21 C.F.R. 60.22(f). See Wyeth Br. at 35 (the application "'is initially submitted on the date it contains sufficient information *to allow FDA to commence review of the application*.'") (quoting 21 C.F.R. 60.22(f); emphasis in Wyeth's Brief). That regulation refers to "review of the application," not review of part of the application (or the initial submission of partial data). Again, Wyeth simply misunderstands the concept of "the application," instead treating "the application" and a portion of the required testing data as the same thing. Similarly, when the regulation refers to "sufficient information," it is referring, at least, to the information required in 21 U.S.C. 360b(b)(1) and 21 C.F.R. 514.1(b).[7]

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[7] FDA's interpretation of its regulation is entitled to maximum deference. See *Federal Exp. Corp. v. Holowecki*, 128 S. Ct. 1147, 1155 (2008) ("Just as we defer to an agency's reasonable interpretations of the statute when it issues regulations in the first instance, * * * the agency is entitled to further deference when it adopts (continued...)

In any event, Wyeth is wrong to focus on "initially submitted" as the critical statutory issue because that phrase simply begs the question of what is being "initially submitted." 35 U.S.C. 156(g)(4)(B)(ii) makes clear that the reference to what is being "initially submitted" is "the application * * * submitted * * * under section (b) of section 512 [*i.e.*, 21 U.S.C. 360b(b)(1)] * * * ." Because it cannot be determined when an "application" is "initially submitted" without knowing what constitutes an "application," the essential statutory inquiry is what constitutes "the application." Consequently, Wyeth's reliance on the dictionary definition of "initially" (Wyeth Br. at 30) does not help its cause because that definition is irrelevant to the inquiry of *what* is being "initially" submitted. And, as noted, nothing in the plain language of 35 U.S.C. 156(g)(4)(B) allows Wyeth to exempt itself from submitting an application that complies with 21 U.S.C. 360b(b).

Although it upheld FDA's determination that Wyeth initially submitted its application for Cydectin on January 13, 2009, the district court was mistaken — as Wyeth is — when it stated that "initially submitted" "suggests something less than a complete or final application may be sufficient to trigger the Approval Phase."

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[7](...continued)
a reasonable interpretation of regulations it has put in force.").

JA 10. The approval phase can be triggered only by the filing of an application containing or referencing the submission of all the information required in the statute and regulation. In making this statement, moreover, the district court failed to appreciate that the structure of the review process itself gives meaning to the term "initially submitted." For example, if FDA were to request additional data from the sponsor after submission of the application, the application would still be considered "initially submitted" on the original date as long as the later-submitted data were considered minor. See, *e.g.*, JA 59 ("These changes, called Amendments to the Original NADA, can be of either major or minor consequence. If the information contained in the Amendment is major and may change the Agency's conclusions, then CVM will restart the review process."). See also H.R. Rep. No. 98-857, pt. 1, at 44 (1984) ("The Committee recognizes that the agency receiving the application might decide it needs additional information or other changes in the application. As long as the application was complete enough so that agency action could be commenced, it would be considered to be 'initially submitted.'"). Thus, it is untrue (see Wyeth Br. at 31-32) that FDA's position fails to give meaning to the term "initially submitted." Nor, for the reasons just stated, does FDA transform the term "initially submitted" into "'completely' submitted or 'finally' submitted" (*id*. at 33).

Wyeth argues that FDA's position elevates form over substance. See Wyeth Br. at 39 ("FDA appears to take the position that the submission of technical sections does not constitute the submission of an 'application' within the meaning of the statute because the agency chooses to call them something else."). To the contrary, as noted throughout, FDA's position is compelled by the language of 35 U.S.C. 156(g)(4)(B)(ii), and 21 U.S.C. 360b(b)(1). See also 21 C.F.R. 514.1(b). In addition, it is worth reiterating that the statute speaks only of "the application," and makes no reference to traditional-vs-phased review. Therefore, what constitutes "the application" is the same under both forms of review. See pp. 5-6, *supra*.[8] Under Wyeth's view, however, a sponsor proceeding under phased review could trigger the approval phase with a partial submission of testing information to an INAD file, whereas a traditional-review sponsor must submit the application and all the necessary information to achieve that result. Nothing in the statute authorizes such a difference in treatment.

Furthermore, in connection with its form-over-substance argument, Wyeth ignores the critical advantage to the sponsor that seeks approval through phased review over traditional review: in traditional review, the sponsor faces the

[8] To be clear, when Congress enacted the GAD/PTR Act, FDA had not yet instituted the concept of phased review. See n.13, *infra*.

prospect that its NADA will be rejected for deficiencies, which will send the sponsor back to the testing phase and require a subsequent refiling that will "restart the review process" (JA 52) and "reset the review clock" (*ibid*.). This cycle could repeat itself multiple times, each time postponing the "initially submitted" date and thus delaying the date of ultimate approval. Phased review facilitates efficient investigation, testing, and review through a process of continuous interaction between FDA and the sponsor, that avoids this problem. This process achieves approval at dates earlier than under traditional review. See, *e.g.*, JA 51, 52, 63 (1995 CVM Update). And Wyeth itself acknowledges the critical importance of early approval: "regulatory delays * * * postpone the sponsor's recovery on its investment and create the risk that competing drugs will emerge or gain market share." Wyeth Br. at 47.

Finally, Wyeth argues that, even if the submission of the first technical section did not start the approval phase, the submission of the last technical section on August 14, 1996, did. See Wyeth Br. at 22, 27, 33. See also JA 4. This argument suffers from the same defects as Wyeth's arguments regarding the August 1995 date. When Wyeth sent its last technical section to the INAD file, it still had not submitted an application — a submission containing or referencing all the information required by 21 U.S.C. 360b(b)(1) and 21 C.F.R. 514.1(b). There

was no such submission until the "administrative NADA" was initially submitted on January 13, 1998. See JA 3-4, 34 ¶ 68, 167-170, 228-232. And, as previously noted, the "administrative NADA" contained the same information that would have been required had Wyeth submitted a traditional NADA. See pp. 5-6, 32, *supra*. Furthermore, consistent with the foregoing (and contrary to Wyeth's contention, see Wyeth Br. at 30), the "complete letters" FDA issued in response to each technical section submitted by Wyeth were, on their face, responses to partial information. They were *not* responses to the application itself because, as stated, the application was not initially submitted until January 13, 1998.

In any event, as a general matter, submission of the last technical section, alone, does not mean that FDA has all the information required by statute and regulation. For example, here, as the district court found, after the last technical section was submitted in August 1996, "at least one other section (Public Safety) was still pending," and it was not until "January 1998 [that] Wyeth had submitted all the necessary technical information * * *." JA 3. In fact, as previously noted (see n.6, *supra*), Wyeth submitted the protocol pertaining to its residue depletion study in pre-ruminating calves as late as January 9, 1998, four days before it initially submitted its application. See JA 149. See also JA 141-149 (detailing submissions of additional information after submission of both the first *and* last

technical sections); JA 148 ("complete letter" for first technical section not issued until "12/10/07" after submission of additional information); JA 149 ("complete letter" for last technical section not issued until "12/23/07" after submission of additional information).[9]

Accordingly, Wyeth's submission of its "administrative NADA" on January 13, 1998, marked the date when "the application" referred to in 21 U.S.C. 360b(b)(1) was "initially submitted" for purposes of 35 U.S.C. 156(g)(4)(B)(ii). And, importantly, Wyeth was always aware that it could have submitted a traditional NADA that complied with 21 U.S.C. 360b(b) at any time during the phased review process. Had it followed that pathway, the NADA would have had to address all required technical sections in the same submission or FDA would have refused to file the application. 21 C.F.R. 514.110(b); see also JA 66-67 (1995 CVM Update).[10]

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[9] Furthermore, even if a "complete letter" issues, there is still the question whether the complete letters remain valid when the last complete letter is issued. For example, some "complete letters" are valid for a discrete period and obligate the sponsor to update the information after the expiration of that period if the FDA has not approved the drug product by that time. Also, deficiencies can appear when all the technical sections are evaluated together because it is not until submission of the administrative NADA that a single reviewer sees the entire application. See p. 46, *infra* (citing JA 52).

[10] See also JA 156 (2002 Draft Guidance # 132), 230, 232. In the 2002 Draft (continued...)

II. ALTERNATIVELY, IF THE STATUTORY LANGUAGE IS AMBIGUOUS, FDA's INTERPRETATION IS REASONABLE AND THE COURT SHOULD DEFER TO IT

If the Court finds the statutory language ambiguous, the Court should affirm the district court's holding that FDA's interpretation is reasonable because it is consistent with the statutory language, the legislative history and policy underlying the patent term extension provisions, and long standing agency precedent. The Court should therefore defer to FDA's interpretation.

A. FDA's Interpretation is Consistent with the Statutory Language and Legislative History

For the reasons discussed in Point I, the FDA's interpretation of 35 U.S.C. 156(g)(4)(B) and 21 U.S.C. 360b(b) is, at least, consistent with (if not compelled by) the language of both statutory provisions.

1. Wyeth argues that the term "'initially submitted,' by definition, contemplates further submissions." Wyeth Br. at 34.[11] But that argument clearly does not prove Wyeth's point: the minor amendments, corrections, or additions

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[10](...continued)
Guidance # 132, written after the events at issue here, FDA advised "sponsor[s] [to] consider whether seeking approval of a new animal drug under phased review will affect the extension of the patent term." JA 156 n.1.

[11] See also pp. 30-31, *supra* (in the district court's view, "initially submitted" could "suggest[] something less than a complete or final application may be sufficient to trigger the Approval Phase" (JA 10)).

that FDA often requires applicants to provide after an application has been submitted also qualify as "further submissions." Nothing in the term "initially submitted" compels the conclusion that the statute was intended to refer to anything more than such minor changes. Moreover, as we now demonstrate, nothing in the legislative history supports Wyeth's view. Instead, it supports FDA's position.

2. The district court thought the legislative history shed no light on the meaning of the statute. See JA 10. Even if that were true, FDA's interpretation should stand. But, in fact, the legislative history supports FDA's position. As noted above, the House Report accompanying the Hatch Waxman Amendments, in pertinent part, states:

> For purposes of determining the regulatory review period and its component periods, an *application* for agency review is considered to be 'initially submitted' if the applicant has made a deliberate effort *to submit an application containing all information necessary* for agency review to begin. As long as the application was complete enough so that agency action could be commenced, it would be considered to be "initially submitted."

H.R. Rep. No. 98-857, pt. 1, at 44 (1984) (emphasis added).[12] Congress's

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[12] The 1984 House Report pertains to the 1984 Hatch-Waxman Amendments, but the relevant portions of that statute and the GAD/PTR Act are indistinguishable with respect to the "initially submitted" terminology. Compare 35 U.S.C.

(continued...)

reference to an "application" as a submission "containing all information necessary for agency review to begin" is, at a minimum, consistent with FDA's view that review *of an application* does not commence until the submission of a document containing or referencing all the information required by statute and regulation. In any event, the legislative history clearly *does not compel* Wyeth's view that submission of partial testing data is sufficient to trigger the approval phase.

In Wyeth's view, the last sentence in the above quotation stands for the proposition that a partial submission of testing information or even a partial, incomplete application can trigger the approval phase. See Wyeth Br. at 34-35 (citing H.R. Rep. No. 98-857, pt. 1, at 44 (1984)); esp. *id*. at 34 ("The Report makes clear that an application is 'initially submitted' as soon as it contains sufficient information for the FDA to begin its review * * *."). The last sentence, however, is consistent with the remainder of the passage and with FDA's view that

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[12](...continued)
156(g)(1)(B), (2)(B), (3)(B), with subsection (g)(4)(B). In addition, the legislative history of the GAD/PRT Act makes clear that the patent term extension provisions covering animal drugs are to operate in the same way as the original provisions covering human drugs, medical devices, and food additives. See, *e.g.*, H.R. Rep. No. 100-972, pt. 1, at 8 (1988) (the GAD/PTR Act "simply makes the additions to [35 U.S.C. 156] necessary to include animal drugs and veterinary biologicals within the existing statutory framework"); *id*. pt. 2, at 20 (same).

there is a minimum amount of information that constitutes "an application," that this minimum amount of information must be submitted before agency review *of the application* can begin, and that Section 360b(b)(1)(A)-(H) specifies that information.

In any event, nothing in the last sentence *compels* Wyeth's contrary conclusion, namely, that Congress intended the submission of partial data to trigger the approval phase. Thus, the term "initially submitted" merely reflected the common understanding that, under traditional review (the only review existing in 1984 when the Hatch-Waxman Amendments were being debated), once the critical information was submitted (*i.e.*, the information required by 21 U.S.C. 360b(b)(1)(A)-(H)), the application would be considered "initially submitted" even if the agency later decided it needed additional information or other changes in the application. See also pp. 30-31, *supra*. In that circumstance, Congress did not want the start of the approval phase "reset," and nothing in the quotation on p. 37 *compels* a different conclusion. See H.R. Rep. No. 98-857, pt. 1, at 44.[13]

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[13] As noted, phased review did not exist in 1984 because FDA first introduced that concept in 1989. Thus, the legislative history could not have discussed phased review or what "initially submitted" meant in the context of such review. Wyeth nevertheless argues that "initially submitted" *could* have reflected Congress's awareness of the rolling application concept because of FDA's "fast track system" for review of certain new animal drugs established in 1980. See Wyeth Br. at 39 (continued...)

The legislative history, therefore, is consistent with FDA's long-standing practice that minor amendments or changes to an application that has been "initially submitted" to the agency do not "reset" the clock for the beginning of the approval phase. This history certainly does not compel Wyeth's contention that the submission of a single technical section (or multiple technical sections) — whether the first or last technical section — during the testing phase must trigger the approval phase. See Wyeth Br. at 27, 33; JA 36 ¶¶ 78-80. Either a traditional NADA or an administrative NADA must contain all the information — or a reference to all the information — necessary under 21 U.S.C. 360b(b) and 21 C.F.R. 514.1(b) to trigger the approval phase. After such a submission, situations may — and usually do — arise in which FDA requests additional minor information or other changes in the application, as Wyeth apparently recognizes. Wyeth Brief at 33-36. However, as long as the application includes or references

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[13](...continued)
n.15 (citing "'Fast Track' Drug Classification Guideline" at JA 237). There is no evidence that Congress knew of this "fast track system." More importantly, the "fast track system" has nothing at all to do with phased review. "Fast track" review refers to the prioritization for short review time frames of the rare animal drug product that can qualify as an important advance in animal health, not the phased submission of testing and investigational information to an INAD file, which is open to all sponsors under phased review. See http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/PoliciesProceduresManual/ucm046728.pdf . See also JA 53, 237.

all required information, the application may still be deemed to be "initially submitted."

B. FDA's Interpretation Is Consistent with the Policy Underlying Patent Term Restoration

The GAD/PTR Act provides patent term extensions for new animal drugs to make up for patent life lost during a period of regulatory review. Pub. L. No. 98-417, 98 Stat. 1585 (1984); Pub. L. 100-670, 102 Stat. 3971 (1988). Where the regulatory review is decreased, the length of the patent term extension will be commensurately decreased. FDA's interpretation of how phased review affects the trigger for the approval phase in 35 U.S.C. 156(g)(4)(B)(ii) is entirely consistent with this proposition and, thus, the policy underlying patent term extensions. See, *e.g.*, *Babbitt v. Sweet Home Chapter of Communities for a Great Oregon*, 515 U.S. 687, 707 (1995) (when interpretation of a statute involves a "complex policy choice," the court should be especially reluctant to substitute its judgment for the agency's).

The main purpose of phased review is to "enhance the efficiency of the drug development process." JA 63 (1995 CVM Update). See also JA 155 (2002 Draft Guidance # 132) (to "create greater efficiencies that facilitate the approval of new animal drugs"). It was FDA's prediction and intention that the more efficient and

shorter regulatory review periods would generally result in faster approvals and earlier product entries onto the market. See JA 161 (2002 Draft Guidance # 132) ("FDA intends that the time it takes to approve an application that qualifies as an Administrative NADA usually will be shorter than the time it takes to approve a traditional NADA"); JA 231 (quoting the same language). And that is precisely what occurred here. The brief, 16-day approval period was the direct result of the "interactive approach to the collection and review of data," JA 63 (1995 CVM Update), that occurred during phased review which, in turn, enabled Wyeth to begin marketing Cydectin earlier. Indeed, as previously noted (p. 33, *supra*), Wyeth has acknowledged the importance of prompt approval and early marketing. See Wyeth Br. at 47 ("regulatory delays * * * postpone the sponsor's recovery on its investment and create the risk that competing drugs will emerge or gain market share"). To be clear, neither Wyeth nor any other sponsor is under any obligation to choose phased over traditional review, see JA 156; the choice is up to the sponsor, and in this case, Wyeth chose phased review and should be held to the choice it made.

Wyeth, however, wants to have it both ways: it wants to receive the benefits of the more efficient phased review (that allowed Wyeth to market its product sooner), but it also wants a longer patent term extension even though its

regulatory review period was actually reduced because of the phased review process. Congress, however, wanted the patent term extension to be commensurate with the patent life lost because of the regulatory review period — *i.e.*, where the regulatory review period has been shortened by the phased review process, the patent term extension should be similarly shortened. Accordingly, a sponsor like Wyeth should not be allowed to submit virtually any amount of testing data to FDA and then claim that the submission of that data triggered the beginning of the approval phase, allowing the sponsor to obtain a longer patent term extension when, in fact, the sponsor is still collecting and submitting investigational data demonstrating that it is still within the testing phase. See n.6, *supra*.

Wyeth argues that the policy rationale just discussed is the post hoc rationalization of counsel advanced solely during this litigation and, therefore, should not be considered. Wyeth Br. at 46. But FDA advanced this very public policy rationale in denying Wyeth's "request for revision" of the regulatory review period, and it is that decision that Wyeth challenges as the final agency action in this case. See JA 41 ¶ 110, 230-232 (extensively addressing the policy discussion in FDA's 2002 Draft Guidance # 132). By quoting the Draft Guidance, FDA made clear that was the policy underlying phased review and that, therefore, those

who receive the benefit of the shorter phased review period were likely to receive shorter patent term extensions because of the shorter approval phase. JA 231-232 (quoting 2002 Draft Guidance #132 at JA 161). Ultimately, the policy goals of both patent term restoration and phased review were realized here because the approval phase for Cydectin was efficient (lasting merely 16 days) which, in turn, allowed for Cydectin's quick entrance onto the market as well as a nearly four-year patent term extension to recoup the patent life lost to the regulatory review process. JA 37 ¶¶ 82, 88.

Wyeth points to legislative history demonstrating that the credit for the testing phase was set at half the time spent in that phase because, at least in part, the sponsor has some control over the length of the testing phase; accordingly, Wyeth argues, FDA's interpretation is faulty because FDA "grants reduced compensation for periods of delay attributable to the agency, not the sponsor," where the sponsor has submitted technical sections during phased review. Wyeth Br. at 45 n.17. But, when the FDA conducts phased review during the testing phase, the time consumed by that review does not "cost" the sponsor anything in terms of the effective life of the patent because the days in question would be taken up with testing *even if no review were taking place*. And that is precisely what occurred here: Wyeth continued testing and submitting data up until four

days prior to filing its administrative NADA. See pp. 11-12 & 26-27 n.6, *supra*. Furthermore, since the time involved in conducting phased review during the testing phase does not add to the overall length of the regulatory review process, there is no reason to treat it as if it does, and there is no reason to treat those days any differently from any other days during which the sponsor is engaged in testing.

C. FDA's Interpretation Is Long-Standing And Has Been Consistently Applied

1. FDA's interpretation reflects a long-standing agency practice that has been applied consistently and thus is entitled to deference. See *Smiley v. Citibank (South Dakota), N.A.*, 517 U.S. 735, 740 (1996) ("To be sure, agency interpretations that are of long standing come before us with a certain credential of reasonableness, since it is rare that error would long persist."). In its 1995 CVM Update (JA 48-83), FDA stated that, with respect to the phased review of new animal drugs, "[t]he sponsor may [decide to] submit an NADA at anytime, but the NADA *must address all technical sections of the NADA* or CVM will refuse to file the application." JA 67 (emphasis added). At that point, "the sponsor must identify the submission(s) [already contained in the INAD file] and request incorporation into the NADA." *Ibid*. The 1995 CVM Update therefore made

abundantly clear that what constitutes an application for purposes of the NADA process — under phased review as well as traditional review — is a submission containing (or containing by reference) all the information covered by the technical sections spelled out in the statute and regulations, 21 U.S.C. 360b(b)(1)(A)-(H) and 21 C.F.R. 514.1.[14]

Moreover, the 1995 CVM Update advised that, in phased review, "there will be no one person in charge of [reviewing] the project in CVM until the NADA is filed * * * ." JA 52. Thus, it would only be when all of the required technical sections were in one submission (or combined by way of reference) and initially submitted as an NADA — whether traditional or administrative — that FDA could approve or deny "the application."[15] And FDA has unswervingly applied this interpretation. *See, e.g.*, Neutersol Notice, 69 Fed. Reg. 40944 (2004); Anipryl Notice, 63 Fed. Reg. 41578 (1998); Ivomec Notice, 63 Fed. Reg. 36922 (1998).

Although Wyeth argues that the 16-day approval phase for Cydectin was "unreasonably short," Wyeth Br. at 46; JA 23 ¶ 3, such a brief period is not

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[14] To reiterate, "partial information" — *i.e.*, separate technical sections — is sent to the INAD file and therefore is not the application. JA 60.

[15] Until that point, under phased review, the testing and investigational data submitted to the INAD file as separate technical sections would be reviewed by staff within CVM with expertise in the subject of the particular technical section. See JA 52. See also 2002 Guidance # 132 (JA 154-161).

unreasonable for phased review. See, *e.g.*, Neutersol Notice, 69 Fed. Reg. 40944 (the applicable regulatory review period for Neutersol was over 11½ years, but the approval phase took only 34 days); Anipryl Notice, 63 Fed. Reg. 41578 (the applicable regulatory review period for Anipryl was over 6 years, but the approval phase took only 54 days); Ivomec Notice, 63 Fed. Reg. 36922 (the applicable regulatory review period for Ivomec was over 6 years, but the approval phase took only 17 days). Thus, that the approval phase in the phased review process is only a tiny fraction of the total regulatory review period is neither unusual nor unreasonable.[16]

Wyeth argues that FDA treats the phased review process in animal and human drugs differently which, Wyeth contends, is arbitrary and capricious. For example, Wyeth asserts that Fuzeon, a human drug, underwent "phased review" but was treated differently than Cydectin. See Wyeth Brief at 32-33, 52-55; JA 38-39 ¶¶ 91-95. Wyeth is mistaken. See JA 12 n.9 (district court agrees that there is no inconsistency).

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[16] Contrary to the implication in Wyeth's brief (at pp. 42-43, 44, 50-51), the fact that Congress provided a day-for-day patent term extension for time spent in the approval phase does not provide any guidance as to whether Congress thought the approval phase would be long or short. Thus, the short approval phase that results from phased review is not inconsistent with congressional intent, and as noted, is unquestionably advantageous to a sponsor insofar as it provides earlier approval and marketing. See pp. 41-45, *supra*.

First, there is no such thing as "phased review" for human drugs. Fuzeon underwent "fast track" approval — which applies to human drugs and is authorized by statute, see 21 U.S.C. 356[17] — not "phased review." See Guidance For Industry, Fast Track Drug Development Programs – Designation, Development, and Application Review, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079736.pdf (Fast Track Guidance) at 3.[18]

Second, and more importantly, FDA treats the term "application" the same in both the "fast track program" and phased review in determining when the approval phase begins. In the "fast track program," a sponsor of a new human drug must provide "a schedule for submission of information necessary to make the application complete." 21 U.S.C. 356(c)(1)(A). See also Fast Track Guidance at 12-13. The sponsor then must receive FDA agreement to accept portions of the application on a rolling basis and agreement that the schedule is acceptable before

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[17] See CDER Fast Track Approvals, at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/FastTrackApprovalReports/ucm082380.htm.

[18] Under the statute, a new human drug must qualify for fast track review, whereas, as previously noted, any sponsor of a new animal drug may seek approval through phased review. To qualify for fast track, the new human drug must: (a) treat serious or life-threatening conditions, and (b) demonstrate the potential to address unmet medical needs. See 21 U.S.C. 356(a)(1); Fast Track Guidance at 3-7.

making any submission under the schedule. See Fast Track Guidance at 13. FDA does not begin the approval phase under the agreed schedule until the sponsor has informed FDA that the application is complete. See *ibid*. ("The review clock [under fast track review] will not begin until the applicant informs the Agency that a complete [application] has been submitted."). Although there is no administrative NADA under the fast track program, the sponsor's notice that the application is complete serves as the equivalent of an administrative NADA, and FDA calculates the regulatory review period for the "fast track program" in virtually the same way it does for phased review. *Compare* Fuzeon Notice, 71 Fed. Reg. 54996, 54997 (2006) ("It is FDA's position that the approval phase begins when the marketing application is complete."), *with* Cydectin Notice, 71 Fed. Reg. 54993 (2006) (JA 168-169) ("It is FDA's position that the approval phase begins when the marketing application is complete."). Thus, even though fast track review for human drugs and phased review for animal drugs are unrelated programs, FDA determines the regulatory review period for both under entirely consistent principles, and Wyeth's contrary contention is wrong.

CONCLUSION

For the foregoing reasons, the judgment of the district court should be affirmed.

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NOVEMBER 2009

CERTIFICATE OF SERVICE

I hereby certify that on November 12, 2009, I filed and served the foregoing BRIEF FOR DEFENDANTS-APPELLEES by causing an original and twelve copies to be delivered to the Clerk of the Court by hand delivery and by causing two copies to be delivered to the following counsel as indicated:

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OF THE FEDERAL RULES OF APPELLATE PROCEDURE

1. Pursuant to Fed. R. App. P. 32(a)(7), I certify that the attached BRIEF FOR DEFENDANTS-APPELLEES complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B). The brief contains **11,508** words, as counted by Corel Word Perfect X4, excluding the parts of the brief exempted by Fed. R. App. P. 32(a)(7)(B)(iii) and Federal Circuit Rule 32(b).

2. I also certify that this brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6). The brief has been prepared in a proportionally-spaced typeface using Word Perfect 12 in 14-point Times New Roman.

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