2009-1368

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 APPELLANTS

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August 27, 2009

CERTIFICATE OF INTEREST

Counsel for Plaintiffs-Appellants Wyeth Holdings Corporation and Wyeth certifies the following:

1. The full names of every party or amicus represented by me are:

Wyeth Holdings Corporation and Wyeth

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

Not applicable

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the parties represented by me are:

Appellant Wyeth Holdings Corporation: Wyeth

Appellant Wyeth: None

4. The names of all law firms and the partners or associates who appeared for the parties now represented by me in the trial court or are expected to appear in this Court are:

In the trial court: Jeffrey Paul Kushan, Peter S. Choi, Daniel E. Troy, and Gary L. Veron, all of Sidley Austin LLP

In this Court: Randolph D. Moss, Brian M. Boynton, and Brian H. Fletcher, all of Wilmer Cutler Pickering Hale and Dorr LLP

Dated: August 27, 2009

Randolph D. Moss

Counsel for Appellants Wyeth Holdings Corporation and Wyeth

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STATEMENT OF RELATED CASES

No other appeal in or from the same civil action in the district court has previously been before this or any other appellate court, and counsel is not aware of any related cases pending in this or any other court.

JURISDICTIONAL STATEMENT

The district court had jurisdiction under 28 U.S.C. § 1331 (federal question) and § 1338(a) (civil actions relating to patents). This Court has jurisdiction under 28 U.S.C. § 1295(a)(1) (appeals from final decisions by district courts exercising jurisdiction under § 1338(a)). The district court entered a final judgment on March 23, 2009. JA14. Plaintiffs-Appellants filed a timely notice of appeal on May 20, 2009. JA18; *see* Fed. R. App. P. 4(a)(1)(B).

INTRODUCTION

Every new animal drug must be approved by the Food and Drug Administration ("FDA") before it can be commercially marketed. This requirement ensures the safety and effectiveness of the animal drug supply, but it has the unintended consequence of substantially shortening the effective term of a patent covering a new animal drug. FDA-mandated testing and the agency's review of a New Animal Drug Application ("NADA") last several years, during which the inventor derives no commercial benefit from its patent. If left unremedied, this de facto reduction in patent life would frustrate the goals of the patent system by significantly reducing the incentives to develop innovative new veterinary medicines.

In 1988, Congress recognized this problem and provided a remedy: Subject to limitations not at issue here, the holder of a patent covering a new animal drug is

entitled to an extension of its patent term equal to half of the period it spent conducting the tests necessary to support its NADA (the "testing phase") plus the entire period during which the application was under FDA review (the "approval phase"). Underscoring its desire to provide full compensation for administrative delays, Congress explicitly provided that the approval phase begins as soon as an application is "initially submitted" to the FDA. 35 U.S.C. § 156(g)(4)(B).

The meaning of the term "initially submitted" is uncontroversial when an applicant files its entire NADA on a single day: Although the applicant may submit amendments or supplements in response to the FDA's comments, it is clear that the application is "initially submitted" on that day. In 1989, however, the FDA established a "Phased Review" program that encourages applicants to submit the component parts of an NADA—known as the "technical sections"—on a rolling basis. The FDA begins reviewing each technical section upon receipt and issues a "technical section complete letter" once it has determined that the section satisfies the statutory requirements. The FDA reviews the technical sections concurrently—*i.e.*, the applicant need not wait for the FDA to complete its review of one technical section before submitting the next one. After the FDA has approved all of the necessary technical sections, the applicant submits a ministerial filing—which the agency now calls an "Administrative NADA"—containing the complete letters and certain other administrative details. Final approval of the

NADA follows shortly thereafter—usually in a matter of days or weeks. This Phased Review process benefits both applicants and the FDA by allowing the agency to process applications more efficiently.

The FDA, however, has now taken the position that an application under the Phased Review program is not "initially submitted" until the applicant submits its so-called "Administrative NADA"—that is, until after the applicant has already submitted all of the technical sections containing the information required by statute for an NADA and the agency has both reviewed and approved those submissions. This interpretation is flatly contrary to the statutory text. Moreover, it contradicts Congress's intent to provide patent holders with full compensation for administrative delays because it shifts virtually all of the time that the FDA spends *reviewing* an application into the *testing* phase, which provides only a half-day extension for each day's delay.

In this case, for example, Appellants Wyeth Holdings Corporation and Wyeth ("Wyeth") submitted the first technical section of an NADA in August 1995 and submitted the last technical section in August 1996. The FDA began its review as soon as Wyeth submitted the first technical section and was continuously reviewing one or more technical sections until January 13, 1998, when it signed off on the final technical section. Wyeth submitted an "Administrative NADA" that same day, and the FDA issued its formal approval just days later, on January 28.

Although the agency spent roughly *two and a half years* reviewing Wyeth's application—a year and a half of which elapsed after Wyeth had filed *all* of the required technical sections of its NADA—the FDA has taken the position that the approval phase consisted of only the *16 days* starting January 13 and ending January 28. By shifting all of the substantive review of the technical sections into the testing phase, the FDA's interpretation reduced Wyeth's patent term extension by at least eight months.

The FDA's interpretation of § 156(g)(4)(B) cannot be squared with the statute's text, legislative history, or purpose. This Court should reject the agency's position and set aside the erroneous determination of the length of the patent term extension available to Wyeth.

STATEMENT OF ISSUES

The sole issue presented in this appeal is whether the FDA's determination that Wyeth's NADA was not "initially submitted" until Wyeth filed its "Administrative NADA" was arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.

STATEMENT OF THE CASE

On January 28, 1998, the FDA approved Wyeth's new animal drug CYDECTIN® (moxidectin) Pour-On ("Cydectin") for commercial marketing. JA169. On March 27, 1998, Wyeth filed with the U.S. Patent and Trademark

Office ("PTO") a timely request for extension of U.S. Patent No. 4,916,154 ("the '154 Patent"), which claims moxidectin, the active ingredient of Cydectin. JA86; *see* 35 U.S.C. § 156(d)(1). Pursuant to 35 U.S.C. § 156, the PTO determined that the '154 Patent was eligible for an extension because of the FDA's premarket review of Cydectin and asked the FDA to determine the length of the relevant regulatory review period. JA165. On September 20, 2006, the FDA determined that the regulatory review period was 2,857 days, with 2,841 days occurring during the testing phase and only 16 days occurring during the approval phase. JA168. Wyeth filed a timely request for reconsideration of the FDA's determination on November 20, 2006. JA173. The FDA denied that request on May 7, 2008. JA228.

On June 6, 2008, Wyeth filed a suit in the U.S. District Court for the District of Columbia seeking review of the FDA's determination of the regulatory review period. JA20. After granting their motion to dismiss, or, in the alternative, for summary judgment, JA1, the district court entered a final judgment in favor of Defendants on March 23, 2009, JA14. *See Wyeth Holdings Corp. v. HHS*, 607 F. Supp. 2d 25 (D.D.C. 2009).

STATEMENT OF FACTS

Congress Provides For Extensions To Restore Patent Terms Effectively Lost As A Result Of Administrative Delays

A new animal drug may not be commercially marketed until the FDA has determined that it is safe and effective for its intended use. *See* 21 U.S.C. §§ 331(a), 351(a)(5), 360b(b)(1). To obtain this premarket approval, an applicant (also called a sponsor) must first obtain the FDA's permission to begin clinical testing of the drug. *Id.* § 360b(j); 21 C.F.R. § 511.1(b)(4). When the FDA receives such a request, it opens an "Investigational New Animal Drug" ("INAD") file. The sponsor then conducts extensive trials to verify that the drug is safe and effective in the target animal, to assess its effects on food safety and the environment, to determine the proper dosage, and to satisfy other statutory and regulatory requirements. The sponsor eventually incorporates the results of these tests into an NADA. *See* 21 U.S.C. § 360b(b); 21 C.F.R. § 514.1. To satisfy the FDA's rigorous standards, an NADA must include extensive reports on clinical tests and vast amounts of other data. In this case, for example, the Cydectin application and supporting data ultimately comprised 28 linear feet of documents. JA121.

Unsurprisingly, the process of producing, assembling, and reviewing such large amounts of data typically takes many years. A review of the FDA's regulatory review period determinations for animal drugs published since

August 1, 2004 reveals that the average delay between the beginning of clinical testing and final marketing approval is approximately 2,950 days—or more than eight years.[1]

This lengthy delay substantially reduces the effective terms of patents covering new animal drugs. In theory, a patent grants an inventor the exclusive right commercially to exploit an invention from the time the patent is granted until 20 years after the patent application was filed. *See* 35 U.S.C. § 154(a)(2). But as the Supreme Court has explained, patents covering products subject to premarket approval requirements confer much less of a benefit in practice:

> When an inventor makes a potentially useful discovery, he ordinarily protects it by applying for a patent at once. Thus, if the discovery relates to a product that cannot be marketed without substantial testing and regulatory approval, the "clock" on his patent term will be running even though he is not yet able to derive any profit from the invention.

Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661, 669-670 (1990); *see also Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1357 (Fed. Cir. 2003).

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[1] When a patent holder applies for a patent term extension, the FDA must determine the regulatory review period and publish it in the Federal Register. *See* 35 U.S.C. § 156(d)(2)(A). This figure is the average of the 12 regulatory review periods for new animal drugs published by the FDA between August 2004 and August 2009. *See* 74 Fed. Reg. 10,744 (2009); 74 Fed. Reg. 10,597 (2009); 74 Fed. Reg. 10,596 (2009); 74 Fed. Reg. 6,639 (2009); 72 Fed. Reg. 30,594 (2007); 72 Fed. Reg. 14,280 (2007); 72 Fed. Reg. 14,119 (2007); 71 Fed. Reg. 57,978 (2006); 71 Fed. Reg. 54,993 (2006); 71 Fed. Reg. 44,032 (2006); 71 Fed. Reg. 5,859 (2006); 70 Fed. Reg. 43,701 (2005).

This "unintended distortion[] of the … patent term," *Eli Lilly & Co*, 496 U.S. at 669, not only harms the individual inventor, but also frustrates the goals of the patent system. That system "embodies a carefully crafted bargain for encouraging the creation and disclosure of new, useful, and nonobvious advances in technology and design in return for the exclusive right to practice the invention for a period of years." *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 150-151 (1989). By reducing effective patent terms, premarket approval requirements reduce the incentive for the creation of new and beneficial drugs.

Congress first addressed this problem in the context of human drugs by passing the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, commonly known as the Hatch-Waxman Act.[2] Title II of the Act provides that the holder of a patent covering a drug subject to premarket approval is entitled to an extension of its patent term to compensate for the period of time the premarket approval requirement barred commercial marketing of the product. The purpose of the statute was "to further encourage new drug research by restoring some of the patent term lost while drug products undergo testing and await FDA pre-market approval." *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 396 (Fed. Cir. 1990); *see also* H.R. Rep. No. 98-857, pt. 1,

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[2] The Hatch-Waxman Act also covers medical devices and food additives, which are subject to similar premarket approval requirements. *See* 35 U.S.C. § 156(f)(1).

at 15 (1984) ("The purpose of Title II of the Bill is to create a new incentive for increased expenditures for research and development of certain products which are subject to premarket government approval.").[3]

In 1988, Congress amended the Hatch-Waxman Act to provide the same restoration of lost patent terms to the holders of patents covering new animal drugs. *See* Generic Animal Drug and Patent Term Restoration Act, Pub. L. No. 100-670, 102 Stat. 3971 (1988) ("GAD/PTR Act"). The evidence before Congress at the time suggested that "on the average, almost six years of patent life expired before FDA … approval [of a new animal drug] could be obtained." *GAD/PTR Act: Hearing on H.R. 4982 Before the Subcomm. on Courts, Civil Liberties, and the Admin. of Justice of the H. Comm. on the Judiciary*, 100th Cong. 103 (1988) (statement of Eugene I. Lambert, General Counsel, Animal Health Institute). Congress explained that this delay "can have the effect of reducing incentive to

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[3] The Hatch-Waxman Act was a compromise between the interests of pioneer drug makers and generic drug makers. Pioneer drug makers had long sought patent term extension legislation like that contained in Title II, whereas generic drug makers wanted relief from another unintended consequence of stringent premarket approval requirements: The time and expense associated with obtaining FDA approval deterred generic manufacturers from entering the market for a drug even after the patent covering that drug had lapsed. *See Warner-Lambert*, 316 F.3d at 1357. Accordingly, Title I of the Hatch-Waxman Act provides that a generic version of an approved drug may be approved without new tests demonstrating its safety and effectiveness so long as "the generic is the same as the original drug or so similar that FDA has determined that the differences do not require safety and effectiveness testing." H.R. Rep. No. 98-857, pt. 1, at 14-15; *see generally* 21 U.S.C. § 355(b)(2)-(3).

develop new animal drugs" and that, as with human drugs, "[p]atent term restoration will restore these important incentives." H.R. Rep. No. 100-972, pt. 1, at 3 (1988); *see also id.* pt. 2, at 16 (same).

The Available Extension Depends On The Date An Application Was "Initially Submitted" To The FDA

The length of the patent term extension available under the Hatch-Waxman Act, as amended by the GAD/PTR Act, is calculated based on the "regulatory review period" to which a new animal drug was subjected. The statute divides that period into two parts, known as a "testing phase" and an "approval phase." The testing phase begins on the date the FDA granted the sponsor permission to begin clinical testing or the date on which "a major health or environmental effects test on the drug was initiated," whichever is earlier, and ends on the date "an application was initially submitted" to the FDA. 35 U.S.C. § 156(g)(4)(B)(i). The approval phase, in turn, begins "on the date the application was initially submitted" and ends "on the date such application was approved." *Id.* § 156(g)(4)(B)(ii). In setting this dividing line, Congress recognized that testing often continues during the approval phase as the applicant responds to FDA questions or comments. *See* H.R. Rep. No. 98-857, pt. 1, at 44 (recognizing that the FDA "might decide it needs additional information or other changes in the application" even after the application is "initially submitted").

Congress determined that a patent holder should receive a "year-for-year matching extension … for any time in the drug approval process that the drug spends awaiting a decision by the FDA." H.R. Rep. No. 98-857, pt. 2, at 6. Accordingly, the statute provides for an extension equal to the entire period of the approval phase. *See* 35 U.S.C. § 156(c). By contrast, the statute limits the extension to half the length of the testing phase. *See id.* § 156(c)(2).[4] The Act's differential treatment of the testing and approval phases means that the date on which an application is "initially submitted" is crucial: It marks the start of the day-for-day extension that Congress provided to compensate for those periods during which the patent holder is "awaiting a decision by the FDA."

The FDA's "Phased Review" Program For New Animal Drug Applications

The question presented in this appeal arises from the interaction between the patent term extension provisions of § 156—specifically, the term "initially submitted"—and the FDA's "Phased Review" program. Under what the agency calls "Traditional Review," the sponsor of a new animal drug submits all of the components of an NADA at the same time. In such circumstances, there is rarely any significant dispute over the date on which the application is "initially

[4] The length of the available extension is also subject to two upper limits. First, no patent term extension may be longer than 5 years. *See* 35 U.S.C. § 156(g)(6)(A). Second, an extension may not extend the effective patent term—the period between FDA approval and patent expiration—beyond 14 years. *See id.* § 156(c)(3).

submitted." Beginning in 1989, however, the FDA began "encourag[ing]" sponsors to forego Traditional Review in favor of Phased Review. JA63; *see also* JA191-195. A sponsor participating in the Phased Review program submits the component parts of an NADA—which the agency calls "technical sections"—on a rolling basis. The agency currently recognizes eight technical sections: (1) Chemistry, Manufacturing, and Controls; (2) Effectiveness; (3) Target Animal Safety; (4) Human Food Safety; (5) Environmental Impact; (6) Labeling; (7) Freedom of Information Summary; and (8) All Other Information. JA157-158.[5] The FDA reviews each technical section as it is submitted and then issues a "technical section complete letter" once the agency has determined that the section satisfies the statutory requirements. *See* JA159. Because the various technical sections are reviewed by different subject-matter experts within the FDA, they can be reviewed concurrently. JA66.

Importantly, the FDA reviews the technical sections of an NADA submitted via Phased Review in the same manner, and using the same standards, as the technical sections of an NADA submitted via Traditional Review. Each technical section submitted for Phased Review must "meet the quality standards of [a

[5] These are the technical sections set forth in a draft guidance document issued by the FDA in 2002. Earlier agency documents organized the technical sections somewhat differently. *See* JA63-64 (1995 FDA guidance document listing six technical sections); JA192-194 (1989 staff manual listing six slightly different technical sections).

traditional] application" and must be accompanied by "all appropriate information and declarations" required by the statute and regulations governing the corresponding portions of a traditional NADA. JA71; *see also* JA65; JA156. The FDA will not start its review of a technical section submitted via Phased Review unless it contains enough information for a "valid and meaningful" evaluation. JA65-66.

When the agency has issued complete letters for all of the necessary technical sections, the sponsor submits an administrative filing requesting formal approval of its application—a filing that the FDA now calls an "Administrative NADA." JA159.[6] Because the technical sections contain all of the information required by statute to be included in an NADA, the "Administrative NADA" is a largely ministerial filing consisting of the agency's own complete letters, a summary of the previously submitted data, and administrative details such as the sponsor's name and address. The FDA then "evaluates whether all the data for all technical sections viewed as a whole support approval." JA159. But because the agency has already determined that all of the technical sections that make up the NADA satisfy the statutory standards, the agency's review of an "Administrative NADA" is usually very brief—lasting days or weeks, in contrast to the years

[6] The FDA appears to have used the term "Administrative NADA" for the first time in a draft guidance document issued in 2002. JA154-161.

typically spent reviewing the technical sections. *See, e.g.*, 71 Fed. Reg. 57,978 (2006) (37 days); 69 Fed. Reg. 40,944 (2004) (34 days); 63 Fed. Reg. 36,922 (1998) (17 days).

Wyeth Seeks Premarket Approval For Cydectin Using Phased Review

Cydectin is an animal drug product used to control internal and external parasites in beef and dairy cattle. JA32. Its active ingredient moxidectin is claimed by the '154 Patent, which was issued on April 10, 1990 and assigned to Wyeth's predecessor, the American Cyanamid Company. JA98; JA112.[7] On April 5, 1990, the FDA opened an INAD file for Cydectin and Wyeth began conducting the tests required to prepare its NADA. JA168.

On August 8, 1995, Wyeth submitted the first technical section of the marketing application for Cydectin. JA184. The accompanying cover letter stated that the submission included "all information and data comprising the 'Residue Chemistry and Regulatory Methods' technical section for review and final acceptance" by the Center for Veterinary Medicine ("CVM")—the division of the FDA responsible for reviewing NADAs—"under the Phased Review Submission Policy." JA185 (internal quotation marks omitted). The submission contained a total of 4,790 pages.

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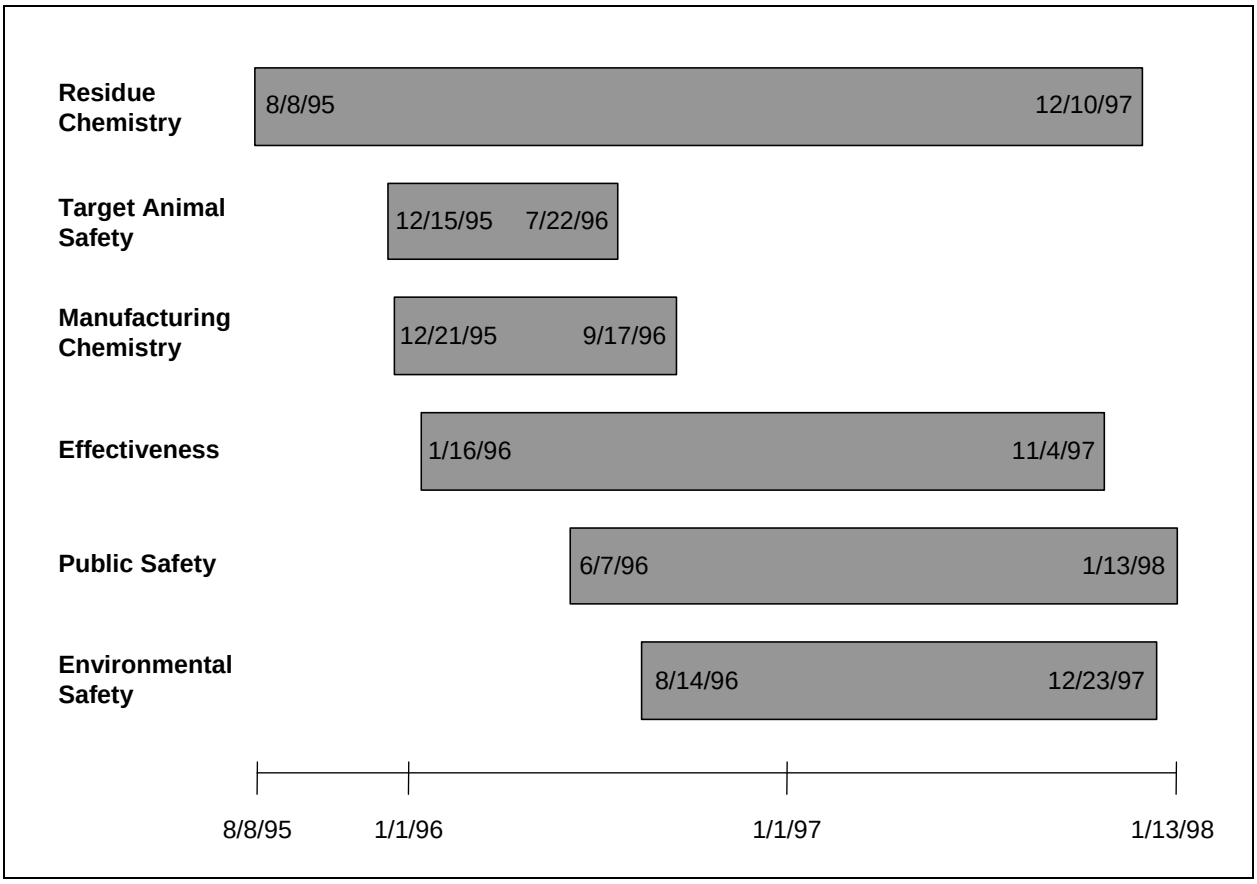
[7] For simplicity, we hereinafter refer to American Cyanamid as "Wyeth."

The FDA began review of the Residue Chemistry section immediately, *see* JA186 (quoting a 1996 letter from the FDA stating that the agency had "proceeded with [its] review" of the Residue Chemistry section), and ultimately issued a "complete letter" on December 10, 1997, JA184. Before the FDA had finished its review of that section, Wyeth submitted five other technical sections, culminating with the Environmental Safety section on August 14, 1996. JA184; *see generally* JA132-149 (full regulatory chronology listing all correspondence between Wyeth and the FDA). The FDA issued complete letters for each of these sections, with the last one issuing on January 13, 1998. JA184. This final letter was issued only a month after the FDA issued a complete letter for the Residue Chemistry section; thus, FDA review of the first technical section that Wyeth submitted spanned almost the entire period of regulatory review. JA184. The following chart illustrates the timing of the FDA's review of the six technical sections:



Wyeth submitted the "Administrative NADA" for Cydectin on January 13, 1998, the same day that the FDA issued the final complete letter. JA168-169. The FDA approved Cydectin for commercial marketing just 16 days later, on January 28, 1998. JA169.

Wyeth's Patent Term Extension Application

On March 27, 1998, Wyeth filed a request with the PTO to extend the term of the '154 Patent based on the regulatory review of Cydectin. JA86; *see* 35 U.S.C. § 156(d)(1). This was the first patent term extension request based on an NADA submitted via Phased Review. JA36.

At the time Wyeth's request was filed, the FDA had not addressed the question of when an NADA submitted under Phased Review would be deemed "initially submitted" within the meaning of § 156(g)(4)(B). The agency had explained its Phased Review policy in a 1989 staff manual and a 1995 guidance document, but neither explanation addressed this question. *See* JA48-83; JA191-195. In 2002, the FDA published a "Draft Guidance" document on the Phased Review program. The document stated for the first time that if an application is submitted "as part of the phased review process, [the FDA] intends to consider the NADA submitted when it receives an Administrative NADA." JA160. But it was not issued until several years *after* Wyeth submitted its patent term extension request raising the "initially submitted" issue. And in any event, the 2002 draft—which apparently has never been finalized—prominently states that it was "distributed for comment purposes only," JA154, and "does not bind the [FDA] or the public," JA155.

Because Wyeth was aware that the FDA had not yet passed on this issue, it included a detailed analysis in an exhibit to its patent term extension request. *See* JA115-131. Wyeth's request explained that its application was "initially submitted" when it filed the first technical section of its NADA on August 8, 1995, because that was the date on which the FDA commenced its substantive review of the application. JA124-125. Calculating the regulatory review period based on

this interpretation would have yielded a testing phase of 1,952 days and an approval phase of 905 days. After reducing the testing phase by 6 days to exclude the period prior to the issuance of the '154 patent, *see* 35 U.S.C. § 156(c), these figures would have yielded a patent term extension of 1,878 days (905 + ((1,952 - 6) / 2) = 1,878). But because the statute caps the term of any extended patent at 14 years from the date on which the FDA approved the underlying drug product, *see* 35 U.S.C. § 156(c)(3), the maximum extension available to Wyeth was 1,754 days.

In the alternative, Wyeth observed that at the very latest its application was "initially submitted" when it filed its *last* technical section on August 14, 1996 because on that date the FDA had all of the information that would have been included in a traditional NADA. JA125-127. Calculating the regulatory review period based on this interpretation would have resulted in a testing phase of 2,324 days and an approval phase of 533 days. These figures would have yielded a patent term extension of 1,692 days (533 + ((2,324 - 6) / 2) = 1,692).[8]

[8] These two calculations of the proper patent term extension differ slightly (by a half day and a single day, respectively) from those set forth in Wyeth's initial filing with the PTO. *See* JA96; JA130. The calculations in the text exclude the day on which the patent was granted from the testing phase, *see* 37 C.F.R. § 1.778(c), and include the date on which the application was initially submitted to the FDA in the approval phase, *see id.* § 1.778(d)(1)(i).

The FDA Adopts An Interpretation Of "Initially Submitted" That Substantially Reduces Wyeth's Patent Term Extension

By statute, the PTO and the FDA share responsibility for deciding applications for patent term extensions: If the PTO determines that a patent is eligible for an extension, it asks the FDA to determine the length of the applicable regulatory review period and then uses that determination to calculate the length of the available extension. *See* 35 U.S.C. § 156(c); *see generally Astra v. Lehman*, 71 F.3d 1578, 1581 (Fed. Cir. 1995).

Because it took the FDA almost six years just to confirm that Cydectin had been subject to a regulatory review period, *see* JA162-164,[9] the PTO did not determine that the '154 Patent satisfied all of the eligibility requirements for an extension until June 21, 2004, *see* JA165. At that point, the PTO referred Wyeth's request back to the FDA for a determination of the regulatory review period. *Id.* The FDA must act on such requests within 30 days. *See* 35 U.S.C. § 156(d)(2)(A); 21 C.F.R. § 60.28(a). In this case, however, it did not respond until September 7, 2006—more than two years late, and more than eight years after Wyeth had filed its request for a patent term extension. JA171.

[9] The PTO's original letter to the FDA requesting confirmation that Cydectin had been subject to regulatory review (dated May 5, 1998) is not included in the administrative record compiled by the FDA but is available in the online docket for the '154 Patent in the PTO's Patent Application Information Retrieval system, http://portal.uspto.gov/external/portal/pair (last visited August 27, 2009).

In its September 7, 2006 response to the PTO, the FDA rejected both of Wyeth's proffered interpretations of the phrase "initially submitted." Without addressing Wyeth's extensive analysis, the agency determined that Wyeth's application had not been "initially submitted" until after the FDA had reviewed and approved all of the technical sections and Wyeth filed its "Administrative NADA" on January 13, 1998. JA168-169. Under this interpretation, virtually the entire regulatory review period—2,841 days—occurred during the testing phase, and only 16 days occurred during the approval phase. Accordingly, the FDA's interpretation yielded a patent term extension of only 1,434 days—roughly ten months shorter than the extension Wyeth had requested and roughly eight months shorter than the extension that would have been due under Wyeth's alternative interpretation. Under the FDA's interpretation, the '154 Patent will expire on March 14, 2011.

Wyeth filed a request for reconsideration with the FDA. JA173; *see* 21 C.F.R. § 60.24(a). Once again, Wyeth's request included a lengthy discussion of the proper interpretation of § 156(g)(4)(B), including a detailed analysis of the statute's text, legislative history, and purpose. *See* JA175-189. But the FDA adhered to its position without meaningfully addressing these arguments, offering only two conclusory paragraphs of justification. First, it simply asserted without explanation that "it is the FDA's position that the approval phase for purposes of

patent term extension begins when the marketing application is complete, including *all* technical sections and the CVM complete letters." JA232. Second, the FDA sought to bootstrap from its own filing practices, claiming that the technical sections are not an "application" under the statute because they "are submitted for FDA review not to the NADA [file], but to the INAD [file]." *Id.*

The District Court Finds The Statute Ambiguous And Defers To The FDA

On June 6, 2008, Wyeth filed a suit in the U.S. District Court for the District of Columbia seeking review of the FDA's determination of the regulatory review period for Cydectin. The district court granted Defendants' motion to dismiss, or in the alternative, for summary judgment, denied Wyeth's cross-motion for summary judgment, and entered judgment in favor of Defendants. JA1-14. The court applied the two-step framework for reviewing an administrative interpretation of a statute set forth in *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). At *Chevron* step one, the court held that § 156(g)(4)(B) was ambiguous. JA10. The court then concluded that it was obliged to defer to the FDA's interpretation at *Chevron* step two because it could not "say that the FDA's interpretation was based on an impermissible construction of the statute." JA12. But the court's step-two analysis was extremely cursory. It simply identified the "policy arguments" made by both parties and then concluded, without explanation, that the agency's interpretation was reasonable because it

found "the FDA's arguments to be more persuasive than those made by Wyeth." JA12.

SUMMARY OF THE ARGUMENT

The FDA contends that an "application" to market a new animal drug is not "initially submitted" under 35 U.S.C. § 156(g)(4)(B) until after (1) all of the substantive sections of an application under the Phased Review process are submitted to the agency, (2) the FDA both reviews and signs off on each section, and (3) an "Administrative NADA" collecting the FDA approval letters is submitted to the agency. The validity of this interpretation is a question of first impression; the district court's opinion in this case was the first judicial decision to consider the issue.

This Court should reject the FDA's interpretation. The statute's text, legislative history, and purpose demonstrate that at the very latest, an application is "initially submitted" when the applicant submits the *last* technical section. Indeed, these sources make clear that an application is "initially submitted" as soon as the applicant submits the *first* technical section and the FDA can begin its review.

1. The FDA's interpretation fails at both *Chevron* step one and *Chevron* step two because it is contrary to congressional intent clearly expressed in the statute's text and legislative history. First, 35 U.S.C. § 156(g)(4)(B) refers to the submission of "an application … under [21 U.S.C. § 360b(b)]." Section

360b(b)(1), in turn, provides an exhaustive definition of an "application." All of the elements of an "application" under § 360b(b)(1) are submitted in the technical sections, not the subsequent "Administrative NADA." Accordingly, when an applicant submits its last technical section, it has unquestionably submitted an "application" in the relevant sense. Moreover, the statute provides that the approval phase begins as soon as an application is "*initially* submitted." The legislative history makes clear that Congress chose the word "initially" because it intended the approval phase to begin as soon as an application contains enough information for FDA review to begin. Under Phased Review, this occurs when the applicant submits the *first* technical section. That submission thus marks the point at which an application is "initially submitted" within the meaning of the statute.

2. This Court should also reject the FDA's interpretation because it is contrary to the purpose of § 156. As the context and legislative history of the statute make abundantly clear, Congress sought to compensate patent holders for reductions in their effective patent terms due to the delays associated with FDA review and carefully crafted the statutory provisions to achieve this goal. In particular, Congress provided a day-for-day extension for the approval phase because it wanted to ensure that patent holders were fully compensated for time spent "awaiting a decision by the FDA." Under the FDA's view, however, the vast majority of the time the agency spends reviewing an application is pushed to the

testing phase, which provides only a half-day's compensation for each day of the period. The agency's interpretation thus upsets the careful balance struck by Congress and fails to provide adequate incentives for innovation.

3. The FDA has also failed to explain its inconsistent interpretation of the term "initially submitted" in the context of animal and human drugs. In some cases, human drugs may be submitted through a "fast track" process that, like Phased Review, permits rolling submission and review of the component parts of a marketing application. For these human drugs, however, the FDA takes the position that an application is "initially submitted" as soon as the agency receives the last component of the application—not, as with respect to animal drugs, after the FDA has reviewed and approved all of the components. The agency acted arbitrarily and capriciously by failing to acknowledge—much less explain—this inconsistency. This provides an independent reason to set aside the agency's action.

STANDARD OF REVIEW

This Court reviews a district court's grant of summary judgment *de novo*, applying the same standard as the district court. *Hoechst Aktiengesellschaft v. Quigg*, 917 F.2d 522, 526 (Fed. Cir. 1990). In this case, the material facts are undisputed, JA4, and the only question before the Court is whether the FDA's determination of the regulatory review period for Cydectin was "arbitrary,

capricious, an abuse of discretion, or otherwise not in accordance with law," 5 U.S.C. § 706(2)(A).

For purposes of this case, the parties have assumed that the FDA's interpretation of 35 U.S.C. § 156(g)(4) should be reviewed under the two-step *Chevron* framework. At step one, the question is "whether Congress has directly spoken to the precise question at issue." *Chevron U.S.A. Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 843 (1984). If so, then "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." *Id.* at 842-843. But "if the statute is silent or ambiguous," then the inquiry proceeds to step two, where the reviewing court must uphold the agency's interpretation if it is a "permissible construction of the statute." *Id.* at 843. Even at *Chevron* step two, however, "the courts are the final authority on the issues of statutory construction" and "must reject administrative constructions … that are inconsistent with the statutory mandate or that frustrate the policy Congress sought to implement." *Hoechst Aktiengesellschaft*, 917 F.2d at 526 (internal quotation marks omitted).

Moreover, even if an agency's action is based on a permissible construction of the statute for *Chevron* purposes, it still must be set aside as arbitrary and capricious if the agency failed to engage in "reasoned decisionmaking." *Motor Vehicle Mfrs. Ass'n of the U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S.

29, 52 (1983); *see also Arnold P'ship v. Dudas*, 362 F.3d 1338, 1340 (Fed. Cir. 2004). For example, if an agency adopts inconsistent interpretations of the same statutory language, its action cannot stand unless the agency "provid[ed] a reasonable explanation for the inconsistency." *NSK Ltd. v. United States*, 390 F.3d 1352, 1358 (Fed. Cir. 2004).

ARGUMENT

The FDA contends that an NADA is not "initially submitted" until the agency has both *reviewed* and *approved* all of its components and the sponsor has effectively resubmitted those components by filing an "Administrative NADA" incorporating them by reference. This interpretation is foreclosed by the statute's text, legislative history, and purpose. The FDA's interpretation thus fails at both steps of the *Chevron* analysis: An administrative interpretation must be set aside at *Chevron* step one if the "traditional tools of statutory construction" reveal that "Congress did not intend" the reading adopted by the agency. *INS v. Cardoza-Fonseca*, 480 U.S. 421, 446 (1987). And an interpretation that is "contrary to the statute" is, by definition, not a "permissible" interpretation within the meaning of *Chevron* step two. *See, e.g., GHS Health Maint. Org. v. United States*, 536 F.3d 1293, 1297 (Fed. Cir. 2008).

I. THE FDA'S INTERPRETATION IS FORECLOSED BY THE STATUTORY TEXT AND LEGISLATIVE HISTORY

Under *Chevron*, a court must begin by attempting to discern Congress's intent using the "traditional tools of statutory construction." 467 U.S. at 843 n.9. "The first and foremost 'tool' to be used is the statute's text, giving it its plain meaning." *Timex V.I., Inc. v. United States*, 157 F.3d 879, 882 (Fed. Cir. 1998). "[I]f the text answers the question, that is the end of the matter," but if the text alone does not provide a clear answer, a court must also consult the other "traditional tools" of statutory construction, including the relevant legislative history. *Id.*

In this case, both the text and the legislative history demonstrate that the FDA's interpretation is contrary to Congress's intent. At the very latest, a Phased Review "application" is "initially submitted" when the applicant submits the *last* technical section. Indeed, the statute's text and legislative history demonstrate that an application is initially submitted as soon as the applicant files the *first* technical section.

A. At The Very Latest, An "Application" Is "Initially Submitted" When The Sponsor Submits The Last Technical Section

1. The crucial date in 35 U.S.C. § 156(g)(4)(B) is the date on which an "application … under [21 U.S.C. § 360b(b)]" is initially submitted. Section 360b(b)(1), in turn, includes an exhaustive list of the elements of an

"application."[10] For example, it provides that a sponsor must submit, "as part of the application," "full reports of investigations which have been made to show whether or not [the] drug is safe and effective for use" and "a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of [the] drug."

The FDA takes the position that § 360b(b)(1) defines an "application" for purposes of § 156(g)(4)(B). *See* JA6-7. But when an application is submitted via Phased Review, the technical sections contain all of the information required by

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[10] The relevant portion of § 360b(b)(1) provides:

> Any person may file with the Secretary an application with respect to any intended use or uses of a new animal drug. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe and effective for use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof, of any animal feed for use in or on which such drug is intended, and of the edible portions or products (before or after slaughter) of animals to which such drug (directly or in or on animal feed) is intended to be administered, as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, or in case such drug is intended for use in animal feed, proposed labeling appropriate for such use, and specimens of the labeling for the drug to be manufactured, packed, or distributed by the applicant; (G) a description of practicable methods for determining the quantity, if any, of such drug in or on food, and any substance formed in or on food, because of its use; and (H) the proposed tolerance or withdrawal period or other use restrictions for such drug if any tolerance or withdrawal period or other use restrictions are required in order to assure that the proposed use of such drug will be safe.

§ 360b(b)(1). *See* JA156 (2002 FDA draft guidance document stating that an "Administrative NADA" is "submitted after all of the technical sections that fulfill the requirements for approval of the new animal drug under 21 CFR 514.1"—the regulation implementing § 360b(b)—"have been reviewed"); JA71 (1995 FDA guidance document stating that technical sections "must meet the quality standards of an application, and contain all appropriate information and declarations"). When an applicant submits the last technical section, it has thus submitted an "application" as that term is defined in the statute.

The FDA, however, does not recognize an application as being "initially submitted" at this point. Instead, it waits until the agency has reviewed and approved all of the technical sections and the applicant has submitted an "Administrative NADA." But an "Administrative NADA" does not provide the FDA with any new component of an "application" as that term is defined in § 360b(b)(1). Indeed, the agency's own guidance documents make clear that an "Administrative NADA" does not contain any new information at all.[11] The FDA

[11] The FDA's 2002 draft guidance specifies the contents of an "Administrative NADA" as follows: "a cover letter, [a] signed FDA Form 356V, a table of contents, [a] summary, a copy of each technical section complete letter, complete facsimile labeling, and the [Freedom of Information ('FOI')] summary." JA159. But when a sponsor files an "Administrative NADA," the facsimile labeling and FOI summary have already been submitted as technical sections. *See* JA158. And Form 356V is a short administrative filing that contains no new substantive information. *See* FDA, *Application for Approval of a New Animal Drug*, *available at* http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/

effectively admitted as much in its denial of Wyeth's request for reconsideration. The agency explained that "for phased review applications, it is FDA's position that the approval phase for purposes of patent term extension begins when the marketing application is complete, including all technical sections *and the CVM complete letters*." JA232 (emphasis altered). But the "CVM complete letters" are letters issued *by the FDA* certifying that the agency has completed its review of the technical sections submitted by an applicant. They are the FDA's *responses* to an application, not parts of that application. A sponsor thus submits a complete "application" as that term is defined in § 360b(b) when it submits the last technical section. The FDA can maintain otherwise only by defining the contents of an "application" in a manner contrary to both the statute and common sense.

2. The FDA's interpretation also cannot be reconciled with Congress's use of the word "initially." Where, as here, a statute does not define a word, that word must be given its "ordinary, contemporary, common meaning." *NTP, Inc. v. Research In Motion, Ltd.*, 418 F.3d 1282, 1314-1315 (Fed. Cir. 2005) (internal quotation marks omitted). And the ordinary meaning of "initially" is "at the beginning." *Webster's Third New International Dictionary* 1164 (1971); *see also*

AnimalDrugForms/UCM048749.pdf (last visited August 27, 2009) (the current version of Form 356V). (The FDA's 1995 guidance, which was in effect when Wyeth submitted its NADA, did not identify the FOI summary and labeling as separate technical sections. Instead, it simply required that each technical section include "the applicable portions of the labeling [and] FOI summary." JA65.)

Dodd v. United States, 365 F.3d 1273, 1279 (11th Cir. 2004) ("There is no reason to read the unambiguous term 'initially' as signifying anything other than its common-sense and ordinary meaning of 'from the beginning.'"). The FDA's view is that an application is not "initially submitted" until the applicant has submitted the application materials (in the form of the technical sections), the FDA has actually reviewed those materials, and the applicant has then submitted an "Administrative NADA" that "incorporate[s]" the technical sections "by reference." JA67. This is hardly the "beginning" of the submission; to the contrary, the FDA's interpretation effectively replaces "initially submitted" with "*submitted, reviewed,* and then *re-submitted*."

The FDA's interpretation is thus contrary to the "cardinal principle of statutory construction" that "a statute ought, upon the whole, to be so construed that, if it can be prevented, no clause, sentence, or word shall be superfluous, void, or insignificant." *Duncan v. Walker*, 533 U.S. 167, 174 (2001) (internal quotation marks omitted); *see also, e.g., United States v. Menasche*, 348 U.S. 528, 538-539 (1955). An administrative interpretation that violates this fundamental principle must be rejected. *See, e.g., Natural Res. Def. Council v. EPA*, 489 F.3d 1364, 1373 (D.C. Cir. 2007). In order to survive scrutiny, then, the FDA must—at a minimum—adopt a reading of the statute that gives some effect to the word "initially." And the latest date on which an application can possibly be said to

have been "initially" submitted is the date on which the sponsor submits the last technical section of the NADA.

3. Indeed, the FDA itself appears to have recognized this point in the human drug context. Under § 156, human drugs are subject to the same patent term extension standards as animal drugs. Most importantly, the patent term extension provision governing human drugs also states that the approval phase begins when an application is "initially submitted" to the FDA. 35 U.S.C. § 156(g)(1)(B). The FDA does not have a "Phased Review" program for human drugs. But certain human drugs are eligible for an analogous program known as "fast track" review. *See* 21 U.S.C. § 356; *see generally* FDA, *Guidance for Industry: Fast Track Drug Development Programs—Designation, Development, and Application Review* (2006), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079736.pdf ("*Fast Track Guidance*"). Like an applicant using Phased Review, a human drug applicant using the fast track system submits its application on a rolling basis. *See Fast Track Guidance* 12-13. In the fast track context, however, the FDA recognizes that an application is "initially submitted" as soon as the "final module of the marketing application [is] submitted," 71 Fed. Reg. 54,996, 54,997 (2006)—that is, as soon as the sponsor has submitted the equivalent of the last technical

section of an NADA. The agency's contrary interpretation of the same statutory language in the animal drug context must be rejected.[12]

B. In Fact, The Text And Legislative History Demonstrate That An Application Is "Initially Submitted" When The Sponsor Submits The First Technical Section For Review

The foregoing discussion demonstrates that an application is initially submitted no later than the date the last technical section is filed because at that point the sponsor has submitted all of the elements listed in the statutory definition of an application. As noted above, however, the statute does not provide that the approval phase begins when an application is "completely" submitted or "finally" submitted. Instead, it provides that the approval phase begins as soon as the application is "*initially* submitted." 35 U.S.C. § 156(g)(4)(B) (emphasis added). Congress's use of the term "initially" indicates that the approval phase in fact begins as soon as an applicant submits the first technical section for review, as Wyeth did in August 1995.

The FDA rejected this view because it takes the position that "the approval phase begins"—that is, that an application is "initially submitted"—only "when the marketing application is *complete*." JA168-169 (emphasis added); *see also* JA232 ("[I]t is FDA's position that the approval phase for purposes of patent term

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[12] The FDA's inconsistent treatment of fast-track human drugs is also an independent ground for vacating its decision as arbitrary and capricious. *See infra* Part III.

extension begins when the marketing application is complete…."). But the ordinary meaning of the term makes clear that an application is *initially* submitted before it is complete. Indeed, the term "initially submitted," by definition, contemplates further submissions.

This interpretation is confirmed by the legislative history of the phrase "initially submitted." The House Report on the Hatch-Waxman Act explains that Congress chose the term "initially submitted" rather than the term "filed" because "an application is often not considered to be filed, even though agency review has begun, until the agency has determined that no other information is needed." H.R. Rep. No. 98-857, pt. 1, at 44 (1984).[13] The Report makes clear that an application is "initially submitted" as soon as it contains sufficient information for the FDA to begin its review:

> For purposes of determining the regulatory review period and its component periods, an application for agency review is considered to

[13] This Report refers to the Hatch-Waxman Act as passed in 1984, but the relevant portions of the original statute are materially identical to the relevant portions of the 1988 amendment covering animal drugs: Both provide that the approval phase begins when an application is "initially submitted." *Compare* 35 U.S.C. § 156(g)(1)(B), (2)(B), (3)(B), *with id.* § 156(g)(4)(B). Moreover, the legislative history of the 1988 amendment makes clear that Congress intended the patent term extension provisions covering animal drugs 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).

> be "initially submitted" *if the applicant has made a deliberate effort to submit an application containing all information necessary for agency review to begin*. 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."

Id. (emphasis added).

This Court has routinely considered this House Report to be an authoritative source on the meaning of the Hatch-Waxman Act. *See, e.g., Eli Lilly & Co. v. Teva Pharms. USA, Inc.*, 557 F.3d 1346, 1350 (Fed. Cir. 2009); *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1366 (Fed. Cir. 2008). And the FDA itself has endorsed the Report's interpretation. The agency's rules state: "For purposes of determining the regulatory review period for any product, a marketing 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) (emphasis added).

The FDA now contends, however, that a phased review application is not "initially submitted" until the sponsor files an "Administrative NADA." But by that point, the FDA has not only *begun* its substantive review of the application, it has effectively *completed* it. In this case, for example, the FDA spent 890 days—from August 8, 1995 until January 13, 2008—reviewing the technical sections of Wyeth's application and only 16 days reviewing its "Administrative NADA." The

agency's interpretation thus cannot be reconciled with Congress's intent that an application be deemed "initially submitted" as soon as FDA review can begin. And this Court "owe[s] … no deference" to an administrative interpretation that is "contrary to the intent of Congress, as divined from the statute and its legislative history." *Muwwakkil v. OPM*, 18 F.3d 921, 925 (Fed. Cir. 1994).

The legislative history of § 156(g)(4)(B) not only demonstrates that the FDA's interpretation is wrong, but also shows that an application is "initially submitted" as soon as the sponsor submits the first technical section. Congress explained that it intended for the "initial submission" to be the date on which the FDA could begin its substantive review. But it is undisputed that when an application is submitted via Phased Review, the FDA reviews the technical sections on a rolling basis. Indeed, the name of the program—"Phased Review"—reveals that the FDA's review occurs as each technical section is submitted. But that means that an application includes "all information necessary for agency review to begin," H.R. Rep. No. 98-857, pt. 1, at 44, as soon as the applicant submits the first technical section. In this case, for example, the FDA's review of Wyeth's application began as soon as Wyeth submitted the residue chemistry section in August 1995—and review of that first technical section continued until approximately a month before the FDA issued its *final* complete letter. During this

time, the FDA was also concurrently reviewing the five additional technical sections submitted by Wyeth.

The FDA's administrative decisions did not even acknowledge this legislative history, much less attempt to reconcile the agency's interpretation with the congressional intent it expresses. The agency did offer two belated arguments on this point in the district court, but neither is persuasive.

First, the FDA placed great weight on the House Report's statement that an application is "initially submitted" when "the applicant has made a deliberate effort to submit an application *containing all information necessary* for agency review to begin." JA8 (emphasis in original). The FDA argued that the italicized language "evidenc[ed] Congress's intent that the submission of partial information … such as one technical section, could not begin the Approval Phase." JA9. The district court, in turn, relied on this sentence in concluding that the legislative history may be read "to support either of [the parties'] interpretations." JA10. But Congress did not require that an application contain all information necessary for agency review *to be completed*, but rather "all information necessary for agency review *to begin*." H.R. Rep. No. 98-857, pt. 1, at 44 (emphases added).[14] And, as explained above, the FDA "begin[s]" its review of an application submitted via Phased

[14] Indeed, Congress specifically contemplated that "additional information or other changes in the application" would be required even after the application was initially submitted. H.R. Rep. No. 98-857, pt. 1, at 44.

Review as soon as it receives the first technical section. Here, Wyeth's first technical section unquestionably had enough information to permit FDA review to begin when it was submitted on August 8, 1995: The record shows that the agency accepted the section and "proceeded with [its] review." JA186.

Second, the FDA argued that reliance on the legislative history of § 156(g)(4)(B) is misplaced because "the House Report was issued in 1984 and pertains only to Traditional Review considering that Phased Review was not initiated until five years later in 1989." JA9. The district court did not rely on this argument, and this Court should not do so either. The FDA's administrative decision to adopt Phased Review has no bearing on what Congress intended when it passed the statute in 1984 and amended it in 1988. The House Report makes clear that Congress intended for the approval phase to begin as soon as the FDA commences its substantive review of an application. The fact that the agency subsequently chose to make its process for reviewing the parts of an NADA more efficient cannot change the meaning of the statute. The agency must work within the boundaries set by Congress, not the other way around. *Cf. Pennsylvania Dep't of Corr. v. Yeskey*, 524 U.S. 206, 212 (1998) ("[T]he fact that a statute can be

applied in situations not expressly anticipated by Congress does not demonstrate ambiguity." (internal quotation marks omitted)).[15]

C. The FDA Cannot Change The Meaning Of The Statute Through Administrative Formalisms

The FDA's decision denying Wyeth's request for reconsideration offered one other justification for its interpretation. The agency explained that "the technical sections of the administrative NADA are submitted for FDA review not to the NADA [file], but to the INAD [file]"—that is, to the file that the FDA maintains for a drug during the testing phase. JA232. In other words, the 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.

It is true that the FDA has chosen to file the technical sections submitted during a Phased Review to an INAD file. As a formal matter, the "Administrative

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[15] In any event, the FDA's argument also rests on a false premise. The agency assumes that Congress could not have anticipated the possibility that the FDA would review applications on a rolling basis because the Phased Review program did not begin until 1989. But as early as 1980, the FDA allowed some new animal drug applicants to obtain review of the substantive portions of their applications prior to formal submission. JA237. The agency explained that under this policy, known as the "fast track system," "formal processing of the NADA"—like the processing of an "Administrative NADA"—"should then require only a minimum amount of time and primarily involve administrative matters." JA237-239. The existence of the program forecloses any argument that Congress could not have anticipated rolling review of applications when it passed the Hatch-Waxman Act in 1984 and then extended it to animal drugs in 1988.

NADA" then incorporates those technical sections into an NADA file by reference. JA67. But these administrative formalities cannot change the meaning of the statute. If what Wyeth submitted was an "application" within the meaning of § 360b(b), the FDA cannot avoid the statutory consequence—*i.e.*, the commencement of the approval phase—by calling it something different. And the agency has never denied that the technical sections include all of the information required to be submitted in an NADA or that it reviews those technical sections under the same standards that it applies to NADAs submitted via Traditional Review. The technical sections submitted under the FDA's Phased Review program *are* the application contemplated by the statute and the "Administrative NADA" is merely an administrative formality.

II. THE FDA'S INTERPRETATION FRUSTRATES CONGRESS'S POLICY GOALS

In addition to contradicting the text and legislative history of § 156(g)(4)(B), the FDA's interpretation also frustrates the purpose of the patent term extension statute and therefore should be rejected. *See Shays v. FEC*, 528 F.3d 914, 925 (D.C. Cir. 2008) ("[Courts] must reject administrative constructions of [a] statute ... that frustrate the policy that Congress sought to implement." (second alternation and omission in original; internal quotation marks omitted)); *see also Star-Glo Assocs., LP v. United States*, 414 F.3d 1349, 1356 (Fed. Cir. 2005) (*Chevron*

deference is inappropriate if "the context and legislative history of the statute clearly indicate the congressional purpose").

A. The FDA's Interpretation Is Contrary To The Purpose Of The Hatch-Waxman Act And The GAD/PTR Act

As this Court has repeatedly recognized, the purpose of the patent term extension provisions of the Hatch-Waxman Act was to preserve "the incentive to develop and market products that require lengthy pre-marketing approval" by "restoring a portion of the patent term that is consumed during the approval phase." *Pfizer Inc. v. Dr. Reddy's Labs., Ltd.*, 359 F.3d 1361, 1364 (Fed. Cir. 2004).[16] Congress was concerned that without these compensating extensions, the patent laws would not provide sufficient incentives to "encourage[] drug manufacturers to assume the increased costs of research and development of certain products which are subject to premarketing clearance." H.R. Rep. No. 98-857, pt. 2, at 11. In amending the Hatch-Waxman Act to cover animal drugs, Congress was motivated by the same concern. *See* H.R. Rep. No. 100-972, pt. 2, at 16 (1988) (the amendment was necessary because "animal drug innovators

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[16] *See also, e.g.*, *Telectronics Pacing Sys., Inc. v. Ventritex, Inc.*, 982 F.2d 1520, 1524 (Fed. Cir. 1992) (Congress sought "[t]o avoid th[e] unintended distortion of the purposes of the Patent Act" that was "created by the legal requirements for premarket FDA approval of drugs and medical devices, and the lengthy delays often attendant on this approval"); *Hoechst Aktiengesellschaft v. Quigg*, 917 F.2d 522, 526 (Fed. Cir. 1990) (the purpose of the Act is "to compensate drug patent owners who lost part of their patent term due to the protracted FDA approval process and thereby provide incentive for the pharmaceutical industry to develop new drugs").

typically lose years of patent protection because of FDA's scientific testing requirements and regulatory review"); *see also id.* pt. 1, at 3 (FDA delays "can have the effect of reducing incentives to develop new animal drugs" and "[p]atent term restoration will restore these important incentives"). The FDA's interpretation of § 156(g)(4)(B) contradicts this purpose in two ways.

1. Congress made clear that in order to provide adequate incentives for innovation, it intended to grant a "year-for-year matching extension … for any time in the drug approval process that the drug spends *awaiting a decision by the FDA*." H.R. Rep. No. 98-857, pt. 2, at 6 (emphasis added). But under the FDA's interpretation, a patent holder receives only a half day's extension for the majority of the time it spends waiting for the agency to act. In this case, for example, Wyeth submitted its first technical section on August 8, 1995—two and a half years before the FDA approved the drug. JA131. That section remained pending before the agency until December 10, 1997. *Id.* And as of the submission of the last technical section on August 14, 1996, *all* elements of the application were before the FDA—where they remained until the agency issued the final complete letter 17 months later. Yet under the FDA's interpretation, Wyeth receives only a half day's patent term extension for each day of this period spent awaiting agency action. That result cannot be squared with Congress's intent—implicit in the statute itself and made explicit in the legislative history—that a patent holder

receive day-for-day compensation for the periods "the drug spends awaiting a decision by the FDA." H.R. Rep. No. 98-857, pt. 2, at 6.

2. More broadly, the FDA's interpretation upsets Congress's careful balancing of the competing interests implicated by patent term extensions. Congress precisely calibrated the length of the patent term extensions available under § 156 by subdividing the regulatory review period into two phases that are treated differently, *see* 35 U.S.C. § 156(c)(2), by excluding periods in which the applicant did not act with diligence, *see id.* § 156(c)(1), by imposing a 5-year cap on any extension, *see id.* § 156(g)(6)(A), and by limiting any extended patent to 14 years of effective patent life after the date on which the NADA was approved, *see id.* § 156(c)(3). *See generally Unimed, Inc. v. Quigg*, 888 F.2d 826, 829 (Fed. Cir. 1989) (the "scope of the relief" provided by § 156 was "explicitly and precisely limited" by Congress).

This highly reticulated scheme was the result of a "compromise between two competing sets of interests: those of innovative drug manufacturers," who sought longer extensions to preserve adequate incentives for innovation, "and those of generic drug manufacturers," who strongly supported the Abbreviated New Drug Application scheme contained in Title I of the Hatch-Waxman Act but sought to keep the patent term extensions granted in Title II as short as possible. *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1358 (Fed. Cir. 2003).

Indeed, the statute's treatment of the testing phase was a specifically negotiated compromise. A previous version of the patent term extension bill—without the accompanying Abbreviated New Drug Application provision—had passed the Senate, but failed in the House. *See* 127 Cong. Rec. S7354-7356 (daily ed. July 9, 1981); 128 Cong. Rec. H6986-6987 (daily ed. Sept. 15, 1982). That bill had provided for a day-for-day patent term extension to compensate for the *full* regulatory review period, including the testing phase. *See* 127 Cong. Rec. at S7356. The current provision granting only a half day's extension for each day of the testing phase was a compromise between the interests of pioneer and generic producers reached during the subsequent negotiations over the combined Hatch-Waxman bill. *See Innovation and Patent Law Reform: Hearings on H.R. 3285, H.R. 3286, and H.R. 3605 Before the Subcomm. on Courts, Civil Liberties, and the Admin. of Justice of the H. Comm. on the Judiciary*, pt. 1, 98th Cong. 402 (1984) (testimony of Gerald J. Mossinghoff, Assistant Secretary of Commerce and Commissioner of Patents and Trademarks) ("[O]ne of the compromises reached in the bill in front of us … says that there are two phases to this regulatory review, a testing phase and the actual review phase.").

The FDA's interpretation of § 156(g)(4)(B) greatly alters the effect of this compromise because it shrinks the approval phase to just a few weeks—if not days—and increases the testing phase by a corresponding amount. The result is

that for any given period of total regulatory delay, the FDA's interpretation produces a significantly shorter patent term extension than Congress would have contemplated. This across-the-board shift upsets the balance that Congress struck between the interests of generic drugmakers and pioneer drug producers. Moreover, by reducing the patent term extensions available to pioneer drugmakers, the FDA's interpretation also prevents the statute from restoring "important incentives" for innovation to the degree that Congress deemed necessary. H.R. Rep. No. 100-972, pt. 2, at 3.[17]

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[17] The legislative history suggests two possible further explanations for § 156(g)(4)(B)'s differential treatment of the testing and approval phases. Both support Wyeth's reading rather than the FDA's. First, some critics of past bills had argued that providing day-for-day extensions during the testing phase was inappropriate because the sponsor exercised some control over the length of the testing phase. *See, e.g.*, *The Patent Term Restoration Act of 1981: Hearing on S. 255 Before the S. Comm. on the Judiciary*, 97th Cong. 123 (1981) (statement of William F. Haddad, Director of the Generic Pharmaceutical Industry Association). But by extending the testing phase to cover the period after the submission of the first technical section—and particularly the period after the submission of the *last* technical section—the FDA's interpretation grants reduced compensation for periods of delay that are attributable to the agency, not the sponsor. Second, the Commissioner of Patents and Trademarks testified that the reduced compensation for the testing phase was based "[o]n the theory that some testing would obviously have to be done by any responsible company" even without the premarket approval requirement. *Innovation and Patent Law Reform: Hearings on H.R. 3285, H.R. 3286, and H.R. 3605 Before the Subcomm. on Courts, Civil Liberties, and the Admin. of Justice of the Comm. on the Judiciary*, pt. 1, 98th Cong. 402 (1984) (testimony of Gerald J. Mossinghoff, Assistant Secretary of Commerce and Commissioner of Patents and Trademarks). A deduction of half of the testing phase was presumably intended to be a rough proxy for the amount of time that the sponsor would have spent on testing anyway. But the FDA's interpretation greatly expands the testing phase simply because an application is submitted via Phased

B. The FDA Cannot Salvage Its Unreasonable Interpretation With *Post Hoc* Policy Arguments

In deferring to the FDA's interpretation as "reasonable" at *Chevron* step two, the district court apparently relied in part on a number of "policy arguments" that the FDA advanced in its district court briefs. JA11 & n.7. To the extent that the FDA seeks to raise these arguments again on appeal, they should be rejected for two reasons.

1. At the outset, the FDA's arguments are not cognizable here because they were not articulated in either its initial determination of the regulatory review period or in its decision on reconsideration. Those decisions gave *no* policy justification for the agency's interpretation, *see* JA166-170; JA231-232, and the agency has never articulated such a justification in any forum outside of this litigation. But it is a fundamental principle of administrative law that a court "may not accept appellate counsel's *post hoc* rationalizations for agency action." *Motor Vehicle Mfrs. Ass'n of the U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 50 (1983); *see also Morgan Stanley Capital Group Inc. v. Public Util. Dist. No. 1 of Snohomish County*, 128 S. Ct. 2733, 2745 (2008) (a court may not uphold an agency's statutory interpretation at *Chevron* step two "where the agency has offered a justification in court different from what it provided in its opinion");

Review—a fact that has nothing to do with the length of time that the sponsor would have spent testing in the absence of FDA requirements.

Parker v. OPM, 974 F.2d 164, 166 (Fed. Cir. 1992) (*post hoc* rationalizations "will not create a statutory interpretation deserving of deference"). Accordingly, this Court should not even consider the agency's belated explanations for its decision.

2. In any event, both of the FDA's policy arguments are unpersuasive even on their own terms.

First, the FDA argues that under Wyeth's interpretation patent holders could abuse the system by rushing to submit their first technical sections and then delaying submission of the remaining sections while still enjoying the benefits of day-for-day patent term restoration. But this concern is wholly implausible. As a threshold matter, sponsors have no reason to delay FDA review and every incentive to get their drugs to market as quickly as possible. Even day-for-day patent term extensions provide only partial compensation for regulatory delays because those delays still postpone the sponsor's recovery on its investment and create the risk that competing drugs will emerge or gain market share. Moreover, the statute caps the available patent term extension at 5 years. *See* 35 U.S.C. § 156(g)(6)(A). A sponsor that sought to prolong the FDA's review would run the risk of being denied full compensation by this cap.

In addition to these powerful incentives against delay, the statute and administrative procedures also contain safeguards against the sort of dilatory behavior that the FDA fears. For one thing, the agency's own guidance documents

make clear that it will not begin its review of a technical section if the sponsor "submits less than the necessary package for review." JA51; *see also* JA66. Accordingly, there is no risk that sponsors will be able to trigger the start of the approval phase by submitting grossly incomplete first technical sections.

Moreover, a patent term extension is reduced by any periods of time during which it is shown that the applicant "did not act with due diligence." 35 U.S.C. § 156(c)(1). Due diligence is defined as the "degree of attention, continuous directed effort, and timeliness as may reasonably be expected from, and are ordinarily exercised by, a person during a regulatory review period." *Id.* § 156(d)(3). In the unlikely event that an applicant sought to manipulate the system by delaying the submission of its technical sections, it would thus receive *no* patent term extension for the periods attributable to its delay.

Finally, even if the FDA's concern had merit, it would not support the agency's interpretation of the statute. At most, it would provide a reason to hold that an application is initially submitted when the sponsor files the *last* technical section. At that point, the sponsor has submitted the information required by the statute and has no ability to manipulate the system. There is thus no justification for further postponing the start of the approval phase until the FDA has completed its review of the sponsor's submissions.

Second, the district court also embraced the FDA's argument that because Phased Review "create[s] greater efficiencies in the approval process for new drugs [and] thereby allow[s] them to enter the market faster," applicants should receive shorter patent term extensions as a "trade-off." JA11 n.7. But the fact that FDA approval is more efficient is no justification for refusing to compensate a patent holder for the (shorter) period of delay. Suppose, for example, that the FDA had not adopted Phased Review but instead had doubled its staff and thereby halved the time required to review each NADA. The agency could not reasonably declare that in light of the resulting efficiency, patent holders would henceforth receive only one day's extension for every two days during the approval phase as a "trade-off." The FDA's claim that the efficiency of the Phased Review process justifies a reduced patent term extension is equally arbitrary.

To be sure, if the Phased Review process results in a shorter period of regulatory review, then the available patent term extension should be reduced accordingly. But under the scheme crafted by Congress, that reduction happens *automatically* because the available patent term extension is determined by the length of the regulatory review period. To the extent that Phased Review results in faster overall approvals and shorter regulatory review periods, it therefore also

results in shorter patent term extensions.[18] By going a step farther, and denying applicants the benefit of a day-for-day extension during the period of FDA review, the agency overstepped its bounds and impermissibly altered the balance struck by Congress. *See Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 396 (Fed. Cir. 1990) (the PTO's views regarding "how to best accommodate the conflicting objectives" of § 156 cannot displace the "the plain meaning of that section"); *see also FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 125 (2000) ("Regardless of how serious the problem an administrative agency seeks to address, … it may not exercise its authority in a manner that is inconsistent with the administrative structure that Congress enacted into law." (internal quotation marks omitted)).

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For all of the foregoing reasons, the FDA's interpretation cannot be reconciled with the text, legislative history, or purpose of the statute. The FDA's interpretation thus fails at both *Chevron* step one and *Chevron* step two and must

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[18] In this case, for example, if Wyeth had waited to submit its application until all of its technical sections were ready in August 1996 (after 2,324 - 6 = 2,318 days of testing, *see supra* p. 18) and the FDA had then reviewed the entire application in the same length of time it took to review the technical section that was pending the longest (855 days, *see* JA129), Wyeth would have been entitled to a patent term extension of 2,014 days before the application of the 5- and 14-year caps (855 + (2,318 / 2) = 2,014). That is substantially longer than the extension due under Wyeth's interpretation of the statute, which is only 1,878 days (again, before the application of the 5- and 14-year caps).

be rejected. Instead, this Court should hold that an NADA submitted via Phased Review is "initially submitted" as soon as the sponsor files the *first* technical section—in this case, on August 8, 1995—because Congress intended day-for-day compensation to start as soon as FDA review begins. This interpretation of the statute would yield a patent term extension of 1,754 days—an increase of more than ten months over the 1,434-day extension that resulted from the FDA's erroneous interpretation. *See supra* pp. 17-18, 20.

In the alternative, this Court should hold that, at the very latest, an NADA submitted via Phased Review is "initially submitted" as soon as the sponsor submits the *last* technical section—in this case, on August 14, 1996. At that point, the agency has all of the information that would have been contained in a traditional NADA and the sponsor has unquestionably submitted an "application" within the meaning of § 360b(b). This interpretation of the statute would yield a patent term extension of 1,692 days, or roughly eight months more than the FDA's reading. *See supra* p. 18. In any event, the interpretation of the statute proffered by the FDA is untenable and should be rejected.[19]

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[19] If this Court determines that the statute's text, legislative history, and purpose show that Congress intended either of the two interpretations advanced by Wyeth, then it should adopt that interpretation at *Chevron* step one. *See Chevron*, 467 U.S. at 843 n.9 ("If a court, employing the traditional tools of statutory construction, ascertains that the Congress had an intention on the precise question at issue, the intention is the law and must be given effect."). But even if this Court determines that the traditional tools of statutory construction support *both* of

III. IN THE ALTERNATIVE, THE FDA'S INTERPRETATION MUST BE SET ASIDE AS ARBITRARY AND CAPRICIOUS

The FDA's decision also must be set aside as arbitrary and capricious because the agency has not adequately explained the contradiction between its interpretation of "initially submitted" in the animal drug context and its interpretation of identical language in the fast-track human drug context.[20] As explained above, *see supra* pp. 32-33, human drugs are subject to substantially the same patent term extension rules as animal drugs, and the fast track program for certain human drugs is materially indistinguishable from Phased Review for patent

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Wyeth's interpretations, that ambiguity cannot save the FDA's construction of the statute, which Congress clearly foreclosed. *See Cuomo v. Clearinghouse Ass'n*, 129 S. Ct. 2710, 2715 (2009) (explaining that "the presence of some uncertainty does not expand *Chevron* deference to cover virtually any interpretation of the [statute]" and rejecting an administrative interpretation because the Court could "discern the outer limits of the [statutory] term"). Instead, if this Court cannot decide between Wyeth's two interpretations, then it should reject the agency's impermissible construction and remand to allow the FDA to choose between the two reasonable alternatives. *See Abbott Labs. v. Young*, 920 F.2d 984, 989 (D.C. Cir. 1990) (when a court "reject[s] [an] agency's interpretation of [a] statute as unreasonable," it should remand to the agency if it identifies more than one "possible reasonable construction[]").

[20] This failure would require a remand even if this Court were to hold that the FDA's interpretation of the statue is otherwise reasonable. *See GHS Health Maint. Org.*, 536 F.3d at 1301 ("Separate and apart from our finding that the regulation conflicts with the statute, we also conclude that [it] is arbitrary and capricious. This is an independent basis for invalidating the regulation."); *see also Shays v. FEC*, 414 F.3d 76, 97 (D.C. Cir. 2005) ("[W]e need not decide whether these three rules represent altogether impermissible interpretations of [the statutes at issue]—the *Chevron* step two inquiry—because in any event the FEC has given no rational justification for them, as required by the APA's arbitrary and capricious standard.").

term extension purposes. Specifically, the fast track program—like Phased Review—permits a sponsor to submit the modules of an application on a rolling basis and to have the FDA review each module as it is submitted. *See Fast Track Guidance* 12-13.

To be consistent with its interpretation of § 156(g)(4)(B), the FDA would have to treat a fast track application as "initially submitted" under the identically worded § 156(g)(1)(B) only after the agency completed its review of all of the modules. In fact, however, the FDA takes the position that a fast track application is "initially submitted" as soon as the "final module of the marketing application was submitted," 71 Fed. Reg. at 54,997—*i.e.*, a point analogous to the submission of the last technical section in a Phased Review.

Where Congress repeats the same term in a single statute, however, courts presume that it intended for agencies to "define [the term] consistently." *SKF USA Inc. v. United States*, 263 F.3d 1369, 1382 (Fed. Cir. 2001). Accordingly, this Court has consistently held that an agency may not adopt inconsistent definitions of the same statutory language unless it offers "an explanation sufficient to rebut this presumption." *Id.*; *see also NSK Ltd. v. United States*, 390 F.3d 1352, 1357-1358 (Fed. Cir. 2004); *National Org. of Veterans' Advocates, Inc. v. Secretary of Veterans Affairs*, 260 F.3d 1365, 1379-1380 (Fed. Cir. 2001).

In this case, the FDA's attempt to explain its inconsistency was plainly insufficient. The agency addressed the issue in a single sentence, asserting that its interpretation of "initially submitted" in the animal-drug context "correlates to the 'fast track' and 'rolling review' of human drug applications in that applications submitted under those programs are not considered initially submitted until all required technical information is addressed and available for FDA decision making to commence." JA232. But this statement is simply inaccurate. For a human drug, the FDA deems an application under fast track review as initially submitted as soon as the applicant submits the last module—presumably because at that point the agency has "all required technical information." But the FDA likewise has "all required technical information" when an animal drug applicant using Phased Review submits its last technical section. Yet the FDA has taken the position that a Phased Review application is not "initially submitted" until much later, after the FDA has completed its *review* of all of the technical sections.

The district court did not grapple with this failure, addressing Wyeth's argument in two sentences in a footnote: "The FDA counters that there is no merit to this allegation [of inconsistency] because Phased Review is not available for human drugs. The court agrees with the FDA." JA12 n.9. But the FDA's argument to the district court relied on a distinction without a difference. It is certainly true that "'Phased Review' is not available for human drugs"; in the

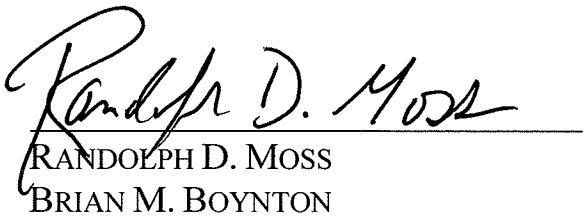
human-drug context, the FDA calls its phased submission program "fast track" review and limits it to certain high-priority new drugs. But like Phased Review, the fast track program involves the rolling submission and review of the components of an application. And the FDA has never even attempted to explain why a fast track application is "initially submitted" when the sponsor submits the last component while a Phased Review application is not.

The FDA has thus failed even to acknowledge its inconsistent interpretations of "initially submitted"—much less to offer an explanation sufficient to overcome the strong presumption that identical statutory terms must be given the same meaning. At a minimum, then, the FDA's interpretation must be set aside and remanded to allow the agency to reconsider the matter and attempt to explain its inconsistency.

CONCLUSION

The district court's judgment should be reversed, the FDA's determination of the regulatory review period should be set aside, and the case should be remanded to the PTO for correction of the certificate of patent term extension it issued in reliance on the FDA's erroneous determination.

Respectfully submitted,



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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

WYETH HOLDINGS CORP., et al., **Plaintiffs,** **v.** **UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, et al.,** **Defendants.**	**Civil Action 08-00981 (HHK)**

MEMORANDUM OPINION

Wyeth Holdings Corporation and Wyeth ("Wyeth") bring this action against defendants U.S. Department of Health and Human Services, U.S. Food and Drug Administration, and others (together, "FDA") under the Administrative Procedure Act, 5 U.S.C. § 551 *et seq*. ("APA") seeking a longer patent term extension for their animal drug product ("Cydectin") than that which the FDA has provided. Before the court are the FDA's motion to dismiss or alternatively for summary judgment [#22], and Wyeth's cross-motion for summary judgment [#32]. Upon consideration of the cross-motions, the oppositions thereto, and the record of this case, the court concludes that the FDA's motion to dismiss or alternatively for summary judgment must be granted and that Wyeth's motion for summary judgment must be denied.

I. BACKGROUND

Before a new animal drug may be marketed its sponsor must submit, and the FDA must approve, a New Animal Drug Application ("NADA"). The NADA process proceeds in two phases. First, the applicant must conduct testing and an investigation concerning the drug

("Testing Phase") with respect to seven "technical sections" and submit its findings to the FDA.[1] Second, the FDA must evaluate and approve the technical sections ("Approval Phase"), and thereby approve the drug. The sponsor may submit the technical sections together (triggering "Traditional Review") or in stages (triggering "Phased Review"). In Traditional Review, the Testing Phase ends and the Approval Phase begins when the sponsor completes its investigation and submits all of the technical sections as its final NADA. In Phased Review, the sponsor submits the technical sections on a rolling basis into an Investigational New Animal Drug file ("INAD File"). The FDA then evaluates the sections on a rolling basis, issuing a "Complete Letter" as to each one. Once the FDA has approved all the technical sections, the sponsor may submit the final NADA, known as the Administrative NADA.[2] In a Phased Review, it is less clear when the Testing Phase ends and the Approval Phase begins. It is this uncertainty that presents the question that underlies this action. It is a pivotal question because certain animal drug patents, such as the one in this case, are eligible for a patent term extension if patent life was lost while the drug was under regulatory review. The extension length is half of the Testing Phase, 35 U.S.C. §§ 156(c)(2) and (g)(4)(B)(i), plus all of the Approval Phase, not exceeding five years, *see* 35 U.S.C. § 156(g)(4)(B)(ii).

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[1] The seven technical sections are: Chemistry; Manufacturing and Controls; Effectiveness; Target Animal Safety; Human Food Safety; Environmental Impact; Labeling; Freedom of Information Summary; and All Other Information.

[2] "An 'Administrative NADA' is a new animal drug application that is submitted after all of the technical sections that fulfill the requirements for the approval of the new animal drug under 21 C.F.R. § 514.1 have been reviewed by the Center for Veterinary Medicine and the CVM has issued a technical section complete letter for each of those technical sections." U.S. Dept. of Health and Human Services, Food and Drug Administration, Center for Veterinary Medicine (CVM), *The Administrative New Animal Drug Application Process: Guidance for Industry*, FDA000107-14, FDA000109 (Nov. 6, 2002) ("Guidance #132").

In March 1990, Wyeth asked the FDA to establish an INAD File for Cydectin, a drug designed to treat and control parasites in beef and dairy cattle. In April 1990, the FDA established the INAD File, which initiated the Administrative NADA process for Cydectin as a Phased Review. Wyeth submitted the first technical section (Chemistry) for Cydectin in August 1995. The FDA issued a Complete Letter for this section in December 1997. Thereafter, Wyeth submitted each technical section. For the duration of the Phased Review, there was no time when a technical section was not pending; thus, there was no lag in the submission of technical sections. (*See* Pl. Mot. for Summ. J. [#32], at 15.) In August 1996, Wyeth submitted the final technical section (Environmental Impact), and the FDA issued a Complete Letter for it in December 1997. At that time, however, at least one other section (Public Safety) was still pending, and the FDA requested supplemental information from Wyeth. By January 1998, Wyeth had submitted all the necessary technical information, and the FDA issued the final Complete Letter on January 13, 1998. Wyeth submitted the Administrative NADA for Cydectin that same day. On or about January 28, 1998, the FDA issued the marketing approval letter for Cydectin.

The dispute in this case arises in connection with Wyeth's application for a patent term extension based on the regulatory review process for Cydectin. The FDA determined that the Testing Phase began on April 5, 1990, (the date the FDA established the INAD file), and that the Approval Phase began on January 13, 1998, (the date Wyeth submitted the Administrative NADA). The FDA thus determined the Testing Phase was 2,841 days, and the Approval Phase was 16 days. Based on these determinations, the U.S. Patent and Trademark Office ("PTO") extended the Cydectin patent from April 10, 2007, to March 14, 2011 — an extension of nearly

four years. Wyeth disputed the FDA's determinations and thus the length of its patent term extension. Accordingly, Wyeth filed a Request for Revision of the Regulatory Review Period with the FDA. Specifically, Wyeth contended that the Approval Phase began upon submission of the first technical section in August 1995, and that the Cydectin patent should be extended from April 10, 2007, until January 28, 2012 — approximately ten months longer than Wyeth's current extension. Alternatively, Wyeth contended that the Approval Phase began no later than upon submission of its final technical section in August 1996, which would extend the patent until November 26, 2011 — approximately eight months longer than Wyeth's current extension. The FDA denied Wyeth's request. Wyeth now seeks a court order that would set aside the FDA's final determination of the regulatory review period for Cydectin.

II. ANALYSIS

The sole question before the court is the following question of law: whether the FDA rightly decided that the Approval Phase began upon submission of the Administrative NADA for Cydectin. Because the court must review this question under the APA, the court only will set aside the FDA's decision if it finds that decision to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law." 5 U.S.C. § 706(2)(A). Applying this standard, the court turns to the following statutory provisions, which establish when the Approval Phase for Cydectin began, and thus determine the appropriate length of the patent term extension for Cydectin:

> (g) For the purposes of this section, the term regulatory review period has the following meanings:
>
> ***

> (4)(A) In the case of a product which is a new animal drug, the term means the period described in subparagraph (B) to which the limitation in paragraph (6) applies:
>
> (B) The regulatory review period for a new animal drug product is the sum of –
>
> > (i) [Testing Phase] 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) [Approval Phase] 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) (emphasis added).[3]

The parties and the court agree that in reviewing this question of statutory interpretation, the court must follow the two-step inquiry set forth in *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 842-43 (1984). Under *Chevron*, the court first inquires as

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[3] As discussed in Section I, *supra*, any patent term extension would include all of the Approval Phase but only half of the Testing Phase:

> (c) The term of a patent eligible for extension under subsection (a) shall be extended by the time equal to the regulatory review period for the approved product which period occurs after the date the patent is issued, except that--
>
> (2) after any reduction required by paragraph (1), the period of extension shall include only one-half of the time remaining in the periods described in paragraphs (1)(B)(i), (2)(B)(i), (3)(B)(i), (4)(B)(i), and (5)(B)(i) of subsection (g); . . .

35 U.S.C. § 156(c)(2).

to "whether Congress has directly spoken to the precise question at issue." *Id*. at 842. "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." *Id*. at 842-43. Second, "[if] the court determines [that] Congress has not directly addressed the precise question at issue, the court does not simply impose its own construction on the statute . . . ." *Id*. at 843. "Rather, if the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the [FDA's interpretation] is based on a permissible construction of the statute." *Id*. If the FDA's interpretation "fills a gap or defines a term in a way that is reasonable in light of the legislature's revealed design, [the court gives] the FDA's judgment 'controlling weight.'" *NationsBank of N.C. v. Variable Annuity Life Ins. Co.*, 513 U.S. 251, 257 (1995) (quoting *Chevron,* 467 U.S. at 844).

A. *Chevron* Step One

The FDA determined that the Approval Phase for Cydectin began on January 13, 1998, the date on which Wyeth submitted the Administrative NADA. The FDA contends that this interpretation follows from the unambiguous language of 35 U.S.C. § 156(g)(4)(B)(ii). Specifically, the FDA emphasizes that the Approval Phase does not commence until "the *application* [i]s initially submitted . . . for the approved animal drug product under subsection (b) of section 512 [of the Food, Drug, and Cosmetic Act ("FDCA")." *Id.* (emphasis added). According to the FDA, an application does not constitute an "application" within the meaning of section 512 of the FDCA, 21 U.S.C. § 360b(b), unless it contains all of the information, samples,

and specimens that are required for FDA approval.[4] *See* 21 U.S.C. § 360b(b); *see also* 21 C.F.R. § 514.1(b) (describing application as consisting of all required technical sections). Accordingly, the FDA contends that an "application" is not "initially submitted" under the Phased Review process until the FDA confirms all technical sections are complete and the applicant submits an Administrative NADA.

Wyeth counters that the Approval Phase corresponds to the entire period of time that the FDA actually spends performing its substantive review of an application, not just the amount of time required to review an Administrative NADA. According to Wyeth, this interpretation follows from the unambiguous language of 35 U.S.C. § 156(g)(4)(B)(ii). Specifically, Wyeth

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[4] Section 512(b) of the FDCA provides:

> (1) Any person may file with the Secretary an application with respect to any intended use or uses of a new animal drug. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe and effective for use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof, of any animal feed for use in or on which such drug is intended, and of the edible portions or products (before or after slaughter) of animals to which such drug (directly or in or on animal feed) is intended to be administered, as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, or in case such drug is intended for use in animal feed, proposed labeling appropriate for such use, and specimens of the labeling for the drug to be manufactured, packed, or distributed by the applicant; (G) a description of practicable methods for determining the quantity, if any, of such drug in or on food, and any substance formed in or on food, because of its use; and (H) the proposed tolerance or withdrawal period or other use restrictions for such drug if any tolerance or withdrawal period or other use restrictions are required in order to assure that the proposed use of such drug will be safe . . . .

21 U.S.C. § 360b(b).

emphasizes that the Approval Phase does not commence until "the application [i]s *initially submitted* . . . for the approved animal drug product under subsection (b) of section 512 [of the FDCA]." 35 U.S.C. § 156(g)(4)(B)(ii) (emphasis added). According to Wyeth, Congress has explained that an application is *initially submitted* when an applicant submits sufficient information to allow the FDA to *commence* its substantive review:

> [The term "initially submitted"] is used instead of the term "filed" because an application is often not considered to be filed, even though agency review has begun, until the agency has determined that no other information is needed and a decision on the application can be made. For purposes of determining the regulatory review period and its components 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. 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 the agency action could be commenced, it would be considered to be "initially submitted."

H.R. Rep. No. 98-857, pt. 1, at 44 (1984). Wyeth also points out that the review of an Administrative NADA does not require the FDA to perform a substantive review at all because an applicant only may submit an Administrative NADA after the FDA already has approved all the technical sections. Thus, according to Wyeth, the FDA's interpretation effectively would read the word "initially" out of the statutory text thereby instituting a "filing" requirement rather than an "initially submitted" requirement, which Wyeth contends is contrary to Congress's intent.

Pointing to the same Report, the FDA argues that the legislative history supports its reading that an application is not an "application" unless all technical sections are complete:

> 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.

H.R. Rep. No. 98-857, pt. 1, at 44 (1984) (emphasis added). The FDA asks the court to interpret this section as evidencing Congress's intent that the submission of partial information to an INAD File, such as one technical section, could not begin the Approval Phase because the Approval Phase cannot begin until an "application contain[s] all information necessary for agency review to begin." *Id*. This argument notwithstanding, the FDA also contends that Wyeth's reliance on H.R. Rep. No. 98-857 is misplaced because the House Report was issued in 1984 and pertains only to Traditional Review considering that Phased Review was not instituted until five years later in 1989.

Although the parties agree that the Approval Phase commences when "the application [i]s initially submitted for the approved animal drug product under [21 U.S.C. § 360b(b)]," 35 U.S.C. § 156(g)(4)(B)(ii), they disagree as to the proper interpretation of this statutory provision and emphasize different text therein in support of their positions: the FDA contends that there was no "application" until Wyeth submitted its Administrative NADA; and Wyeth contends that the application was "initially submitted" upon its submission of the first technical section.[5] Because the court finds that both parties have advanced plausible readings of the statute at issue, the court holds that the statute is ambiguous.

The court begins by looking to the plain text of the provision at issue — 35 U.S.C. § 156(g)(4)(B)(ii). *See U.S. Dep't of Treasury v. Fabe*, 508 U.S. 491, 500 (1993); *Stewart v. Nat'l Shopmen Pension Fund*, 730 F.2d 1552, 1561 (D.C. Cir. 1984). There, the court finds no clear

[5] Wyeth seeks to allay any concerns that, under its interpretation, nearly any filing would trigger the approval process by noting that the FDA may reject a deficient technical section, (see FDA000004; FDA000019), and that only those periods during which an applicant is acting with reasonable diligence are included in a patent term extension, *see* 35 U.S.C. § 156(c)(1).

indication of congressional intent because the statute defines neither "application" nor "initially submitted." Looking to 21 U.S.C. § 360b(b), the court acknowledges the FDA's position that this section sets forth the required "part[s] of the application," but this section does not define "application" nor does it speak to the issue of when an "application" is "initially submitted." Indeed, the words "initially submitted" suggest that something less than a complete or final application may be sufficient to trigger the Approval Phase. Yet, the statute does not plainly state that it must be so.

Because the court cannot discern the meaning of the provision at issue from its plain text, the court must look beyond the text to "examine the meaning of certain words or phrases in context and also 'exhaust the traditional tools of statutory construction, including examining the statute's legislative history to shed new light on congressional intent'[.]" *Sierra Club v. E.P.A.*, 551 F.3d 1019, 1027 (D.C. Cir. 2008) (quoting *Am. Bankers Ass'n v. Nat'l Credit Union Admin.,* 271 F.3d 262, 267 (D.C. Cir. 2001)). Considering the context and legislative history of the statutory provision at issue, however, provides little clarity. As the parties have shown, the court may read H.R. Rep. No. 98-857, pt. 1, at 44 (1984) to support either of their interpretations. Accordingly, the court holds that 35 U.S.C. § 156(g)(4)(B)(ii) is ambiguous based on its text, context, and legislative history.[6]

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[6] Wyeth also relies on certain regulations in support of its contentions with respect to *Chevron* step one. (Pl. Mot. Summ. J. [#32], at 23-29 (citing 21 C.F.R. §§ 60.22(f) and 514.1(a).) Wyeth does not explain, however, how FDA regulations that were promulgated after the enactment of 35 U.S.C. § 156(g)(4)(B)(ii) should bear on the court's interpretation of that statute under *Chevron* step one. Nevertheless, the court has examined these regulatory provisions and determined that they, like the statutory provisions at issue, are sufficiently ambiguous to allow the FDA's interpretation that the Approval Phase commences upon submission of an Administrative NADA. The court reaches this conclusion having given due consideration to the significant deference that courts must afford to an agency's interpretation of

B. *Chevron* Step Two

The FDA contends that even if the court were to find that 35 U.S.C. § 156(g)(4)(B)(ii) is ambiguous, the court should defer to the FDA's reasonable interpretation of the statute. In addition to reiterating its arguments with respect to *Chevron* Step One, the FDA advances numerous policy arguments,[7] and it contends that its interpretation reflects long-standing practice and precedent.[8] Wyeth argues that even if the court finds that § 156(g)(4)(B)(ii) is ambiguous, the court must find the FDA's interpretation to be unreasonable and thus unworthy of deference. In addition to reiterating its arguments with respect to *Chevron* Step One, Wyeth argues that it is

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its own regulation. *Capital Network Sys., Inc. v. FCC*, 28 F.3d 201, 206 (D.C. Cir. 1994) (observing that the deference afforded to an agency's interpretation of its own regulation may be greater than the deference afforded to an agency's interpretation of a statute it is entrusted to administer).

[7] Specifically, the FDA contends that its interpretation is entitled to deference because the FDA reasonably balanced the complex policy considerations of patent term restoration and Phased Review. The FDA contends that the purpose of Phased Review is to create greater efficiencies in the approval process for new drugs thereby allowing them to enter the market faster. The trade-off, according to the FDA, is that drugs which in the Phased Review process generally receive a shorter patent term extension because the Approval Phase for an Administrative NADA is far shorter than the Approval Phase for a traditional NADA. The FDA argues that accepting Wyeth's interpretation would frustrate the policy balance by allowing Phased Review applicants not only to bring their drugs to market faster but also to increase their patent term extension by a disproportionally-long Approval Period. Wyeth discounts these policy objectives and accuses the FDA of supporting its interpretation with non-existent distinctions between the Traditional and Phased Review processes. The court cannot sustain Wyeth's efforts to undercut the FDA's policy arguments because it finds that the FDA's construction of 35 U.S.C. § 156(g)(4)(B)(ii) does not "frustrate the policy that Congress sought to implement." *Shays v. Fed. Election Comm'n*, 528 F.3d 914, 919 (D.C. Cir. 2008) (quoting *Cont'l Air Lines, Inc. v. Dep't of Transp.*, 843 F.2d 1444, 1453 (D.C. Cir. 1988)).

[8] The FDA points out that it has consistently determined that the Approval Phase begins upon submission of the Administrative NADA, and that such determinations have produced similarly short Approval Phases: Neutersol (34 days); Anipryl (54 days); Ivomec (17 days). (Defs.' Mot. to Dismiss [#22], at 8.)

inconsistent for the FDA to admit it is engaging in substantive review by issuing a Complete Letter while maintaining that the Approval Phase has not yet begun. Such an interpretation, according to Wyeth, effectively carves out the entire period of substantive review from the Approval Phase and runs contrary to congressional intent to credit the entire substantive review period toward patent term restoration.[9] The FDA rejoins that Wyeth's interpretation conflates the Approval Phase with the Testing Phase. In particular, the FDA points out that Wyeth cannot deny that while it submitted a technical section as early as 1995, Wyeth continued its investigation and testing with respect to other sections through 1998. Thus, according to the FDA, Wyeth's interpretation would have the court declare that the Testing Phase ended at a time when the bulk of the requisite testing still remained to be done.

Under *Chevron* step two, Wyeth bears the burden of showing that the FDA's interpretation is unreasonable. *See Sweet Home Chapter of Communities for a Great Oregon v. Babbitt*, 17 F.3d 1463, 1473 (D.C. Cir. 1994), *rev'd on other grounds*, 515 U.S. 687 (1995). Wyeth has not met its burden here because the court finds the FDA's arguments to be more persuasive than those made by Wyeth. 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." *NationsBank*, 513 U.S. at 257. 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. *See Chevron,* 467 U.S. at 843; 5 U.S.C. § 706(2)(A).

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[9] Wyeth also contends that the FDA's treatment of animal drugs is inconsistent with its treatment of human drugs, which is contrary to Congressional intent that they be treated similarly. The FDA counters that there is no merit to this allegation because Phased Review is not available for human drugs. The court agrees with the FDA.

III. CONCLUSION

For the foregoing reasons, FDA's motion to dismiss or alternatively for summary judgment [#22] is GRANTED and Wyeth's cross-motion for summary judgment [#32] is DENIED.

An appropriate order accompanies this Memorandum Opinion.

Henry H. Kennedy, Jr.
United States District Judge

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

WYETH HOLDINGS CORP., et al., **Plaintiffs,** **v.** **UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, et al.,** **Defendants.**	**Civil Action 08-00981 (HHK)**

JUDGMENT

Pursuant to Fed. R. Civ. P. 58 and for the reasons stated by the court in its Memorandum Opinion docketed this same day, it is this 23rd day of March 2009, hereby

ORDERED and **ADJUDGED** that judgment is entered in favor of the defendants.

Henry H. Kennedy, Jr.
United States District Court

ADDENDUM 2: STATUTES AND REGULATIONS

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21 U.S.C. § 360b(b)—Filing application for uses of new animal drug; contents; patent information; abbreviated application; presubmission conference

(1) Any person may file with the Secretary an application with respect to any intended use or uses of a new animal drug. Such person shall submit to the Secretary as a part of the application

(A) full reports of investigations which have been made to show whether or not such drug is safe and effective for use;

(B) a full list of the articles used as components of such drug;

(C) a full statement of the composition of such drug;

(D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;

(E) such samples of such drug and of the articles used as components thereof, of any animal feed for use in or on which such drug is intended, and of the edible portions or products (before or after slaughter) of animals to which such drug (directly or in or on animal feed) is intended to be administered, as the Secretary may require;

(F) specimens of the labeling proposed to be used for such drug, or in case such drug is intended for use in animal feed, proposed labeling appropriate for such use, and specimens of the labeling for the drug to be manufactured, packed, or distributed by the applicant;

(G) a description of practicable methods for determining the quantity, if any, of such drug in or on food, and any substance formed in or on food, because of its use; and

(H) the proposed tolerance or withdrawal period or other use restrictions for such drug if any tolerance or withdrawal period or other use restrictions are required in order to assure that the proposed use of such drug will be safe.

The applicant shall file with the application the patent number and the expiration date of any patent which claims the new animal drug for which the applicant filed the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences.

(2) Any person may file with the Secretary an abbreviated application for the approval of a new animal drug. An abbreviated application shall contain the information required by subsection (n) of this section.

(3) Any person intending to file an application under paragraph (1), section 360ccc of this title, or a request for an investigational exemption under subsection (j) of this section shall be entitled to one or more conferences prior to such submission to reach an agreement acceptable to the Secretary establishing a submission or an investigational requirement, which may include a requirement for a field investigation. A decision establishing a submission or an investigational requirement shall bind the Secretary and the applicant or requestor unless (A) the Secretary and the applicant or requestor mutually agree to modify the requirement, or (B) the Secretary by written order determines that a substantiated scientific requirement essential to the determination of safety or effectiveness of the animal drug involved has appeared after the conference. No later than 25 calendar days after each such conference, the Secretary shall provide a written order setting forth a scientific justification specific to the animal drug and intended uses under consideration if the agreement referred to in the first sentence requires more than one field investigation as being essential to provide substantial evidence of effectiveness for the intended uses of the drug. Nothing in this paragraph shall be construed as compelling the Secretary to require a field investigation.

35 U.S.C. § 156—Extension of patent term

(a) The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent, which shall include any patent term adjustment granted under section 154(b), if—

(1) the term of the patent has not expired before an application is submitted under subsection (d)(1) for its extension;

(2) the term of the patent has never been extended under subsection (e)(1) of this section;

(3) an application for extension is submitted by the owner of record of the patent or its agent and in accordance with the requirements of paragraphs (1) through (4) of subsection (d);

(4) the product has been subject to a regulatory review period before its commercial marketing or use;

(5) (A) except as provided in subparagraph (B) or (C), the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred;

(B) in the case of a patent which claims a method of manufacturing the product which primarily uses recombinant DNA technology in the manufacture of the product, the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of a product manufactured under the process claimed in the patent; or

(C) for purposes of subparagraph (A), in the case of a patent which—

(i) claims a new animal drug or a veterinary biological product which (I) is not covered by the claims in any other patent which has been extended, and (II) has received permission for the commercial marketing or use in non-food-producing animals and in food-producing animals, and

(ii) was not extended on the basis of the regulatory review period for use in non-food-producing animals,

the permission for the commercial marketing or use of the drug or product after the regulatory review period for use in food-producing animals is the first permitted commercial marketing or use of the drug or product for administration to a food-producing animal.

The product referred to in paragraphs (4) and (5) is hereinafter in this section referred to as the "approved product."

(b) Except as provided in subsection (d)(5)(F), the rights derived from any patent the term of which is extended under this section shall during the period during which the term of the patent is extended—

(1) in the case of a patent which claims a product, be limited to any use approved for the product—

(A) before the expiration of the term of the patent—

(i) under the provision of law under which the applicable regulatory review occurred, or

(ii) under the provision of law under which any regulatory review described in paragraph (1), (4), or (5) of subsection (g) occurred, and

(B) on or after the expiration of the regulatory review period upon which the extension of the patent was based;

(2) in the case of a patent which claims a method of using a product, be limited to any use claimed by the patent and approved for the product—

(A) before the expiration of the term of the patent—

(i) under any provision of law under which an applicable regulatory review occurred, and

(ii) under the provision of law under which any regulatory review described in paragraph (1), (4), or (5) of subsection (g) occurred, and

(B) on or after the expiration of the regulatory review period upon which the extension of the patent was based; and

(3) in the case of a patent which claims a method of manufacturing a product, be limited to the method of manufacturing as used to make—

(A) the approved product, or

(B) the product if it has been subject to a regulatory review period described in paragraph (1), (4), or (5) of subsection (g).

As used in this subsection, the term "product" includes an approved product.

(c) The term of a patent eligible for extension under subsection (a) shall be extended by the time equal to the regulatory review period for the approved product which period occurs after the date the patent is issued, except that—

(1) each period of the regulatory review period shall be reduced by any period determined under subsection (d)(2)(B) during which the applicant for the patent extension did not act with due diligence during such period of the regulatory review period;

(2) after any reduction required by paragraph (1), the period of extension shall include only one-half of the time remaining in the periods described in paragraphs (1)(B)(i), (2)(B)(i), (3)(B)(i), (4)(B)(i), and (5)(B)(i) of subsection (g);

(3) if the period remaining in the term of a patent after the date of the approval of the approved product under the provision of law under which such regulatory review occurred when added to the regulatory review period as revised under paragraphs (1) and (2) exceeds fourteen years, the period of extension shall be reduced so that the total of both such periods does not exceed fourteen years; and

(4) in no event shall more than one patent be extended under subsection (e)(1) for the same regulatory review period for any product.

(d) (1) To obtain an extension of the term of a patent under this section, the owner of record of the patent or its agent shall submit an application to the Director. Except as provided in paragraph (5), such an application may only be submitted within the sixty-day period beginning on the date the product received permission

under the provision of law under which the applicable regulatory review period occurred for commercial marketing or use. The application shall contain—

(A) the identity of the approved product and the Federal statute under which regulatory review occurred;

(B) the identity of the patent for which an extension is being sought and the identity of each claim of such patent which claims the approved product or a method of using or manufacturing the approved product;

(C) information to enable the Director to determine under subsections (a) and (b) the eligibility of a patent for extension and the rights that will be derived from the extension and information to enable the Director and the Secretary of Health and Human Services or the Secretary of Agriculture to determine the period of the extension under subsection (g);

(D) a brief description of the activities undertaken by the applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities; and

(E) such patent or other information as the Director may require.

(2) (A) Within 60 days of the submittal of an application for extension of the term of a patent under paragraph (1), the Director shall notify—

(i) the Secretary of Agriculture if the patent claims a drug product or a method of using or manufacturing a drug product and the drug product is subject to the Virus-Serum-Toxin Act, and

(ii) the Secretary of Health and Human Services if the patent claims any other drug product, a medical device, or a food additive or color additive or a method of using or manufacturing such a product, device, or additive and if the product, device, and additive are subject to the Federal Food, Drug, and Cosmetic Act,

of the extension application and shall submit to the Secretary who is so notified a copy of the application. Not later than 30 days after the receipt of an application from the Director, the Secretary receiving the application shall review the dates contained in the application pursuant to paragraph (1)(C) and determine the applicable regulatory review period, shall notify the Director of the determination, and shall publish in the Federal Register a notice of such determination.

(B) (i) If a petition is submitted to the Secretary making the determination under subparagraph (A), not later than 180 days after the publication of the determination under subparagraph (A), upon which it may reasonably be determined that the applicant did not act with due diligence during the applicable regulatory review

period, the Secretary making the determination shall, in accordance with regulations promulgated by such Secretary, determine if the applicant acted with due diligence during the applicable regulatory review period. The Secretary making the determination shall make such determination not later than 90 days after the receipt of such a petition. For a drug product, device, or additive subject to the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act, the Secretary may not delegate the authority to make the determination prescribed by this clause to an office below the Office of the Director of Food and Drugs. For a product subject to the Virus-Serum-Toxin Act, the Secretary of Agriculture may not delegate the authority to make the determination prescribed by this clause to an office below the Office of the Assistant Secretary for Marketing and Inspection Services.

(ii) The Secretary making a determination under clause (i) shall notify the Director of the determination and shall publish in the Federal Register a notice of such determination together with the factual and legal basis for such determination. Any interested person may request, within the 60-day period beginning on the publication of a determination, the Secretary making the determination to hold an informal hearing on the determination. If such a request is made within such period, such Secretary shall hold such hearing not later than 30 days after the date of the request, or at the request of the person making the request, not later than 60 days after such date. The Secretary who is holding the hearing shall provide notice of the hearing to the owner of the patent involved and to any interested person and provide the owner and any interested person an opportunity to participate in the hearing. Within 30 days after the completion of the hearing, such Secretary shall affirm or revise the determination which was the subject of the hearing and shall notify the Director of any revision of the determination and shall publish any such revision in the Federal Register.

(3) For the purposes of paragraph (2)(B), the term “due diligence” means that degree of attention, continuous directed effort, and timeliness as may reasonably be expected from, and are ordinarily exercised by, a person during a regulatory review period.

(4) An application for the extension of the term of a patent is subject to the disclosure requirements prescribed by the Director.

(5) (A) If the owner of record of the patent or its agent reasonably expects that the applicable regulatory review period described in paragraph (1)(B)(ii), (2)(B)(ii), (3)(B)(ii), (4)(B)(ii), or (5)(B)(ii) of subsection (g) that began for a product that is the subject of such patent may extend beyond the

expiration of the patent term in effect, the owner or its agent may submit an application to the Director for an interim extension during the period beginning 6 months, and ending 15 days, before such term is due to expire. The application shall contain—

(i) the identity of the product subject to regulatory review and the Federal statute under which such review is occurring;

(ii) the identity of the patent for which interim extension is being sought and the identity of each claim of such patent which claims the product under regulatory review or a method of using or manufacturing the product;

(iii) information to enable the Director to determine under subsection (a)(1), (2), and (3) the eligibility of a patent for extension;

(iv) a brief description of the activities undertaken by the applicant during the applicable regulatory review period to date with respect to the product under review and the significant dates applicable to such activities; and

(v) such patent or other information as the Director may require.

(B) If the Director determines that, except for permission to market or use the product commercially, the patent would be eligible for an extension of the patent term under this section, the Director shall publish in the Federal Register a notice of such determination, including the identity of the product under regulatory review, and shall issue to the applicant a certificate of interim extension for a period of not more than 1 year.

(C) The owner of record of a patent, or its agent, for which an interim extension has been granted under subparagraph (B), may apply for not more than 4 subsequent interim extensions under this paragraph, except that, in the case of a patent subject to subsection (g)(6)(C), the owner of record of the patent, or its agent, may apply for only 1 subsequent interim extension under this paragraph. Each such subsequent application shall be made during the period beginning 60 days before, and ending 30 days before, the expiration of the preceding interim extension.

(D) Each certificate of interim extension under this paragraph shall be recorded in the official file of the patent and shall be considered part of the original patent.

(E) Any interim extension granted under this paragraph shall terminate at the end of the 60-day period beginning on the date on which the product involved receives permission for commercial marketing or use, except that, if within that 60-day period the applicant notifies the Director of such

permission and submits any additional information under paragraph (1) of this subsection not previously contained in the application for interim extension, the patent shall be further extended, in accordance with the provisions of this section—

(i) for not to exceed 5 years from the date of expiration of the original patent term; or

(ii) if the patent is subject to subsection (g)(6)(C), from the date on which the product involved receives approval for commercial marketing or use.

(F) The rights derived from any patent the term of which is extended under this paragraph shall, during the period of interim extension—

(i) in the case of a patent which claims a product, be limited to any use then under regulatory review;

(ii) in the case of a patent which claims a method of using a product, be limited to any use claimed by the patent then under regulatory review; and

(iii) in the case of a patent which claims a method of manufacturing a product, be limited to the method of manufacturing as used to make the product then under regulatory review.

(e) (1) a determination that a patent is eligible for extension may be made by the Director solely on the basis of the representations contained in the application for the extension. If the Director determines that a patent is eligible for extension under subsection (a) and that the requirements of paragraphs (1) through (4) of subsection (d) have been complied with, the Director shall issue to the applicant for the extension of the term of the patent a certificate of extension, under seal, for the period prescribed by subsection (c). Such certificate shall be recorded in the official file of the patent and shall be considered as part of the original patent.

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

(f) For purposes of this section:

(1) The term “product” means:

(A) A drug product.

(B) Any medical device, food additive, or color additive subject to regulation under the Federal Food, Drug, and Cosmetic Act.

(2) The term "drug product" means the active ingredient of—

(A) a new drug, antibiotic drug, or human biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act), or

(B) a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Virus-Serum-Toxin Act) which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques,

including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient.

(3) The term "major health or environmental effects test" means a test which is reasonably related to the evaluation of the health or environmental effects of a product, which requires at least six months to conduct, and the data from which is submitted to receive permission for commercial marketing or use. Periods of analysis or evaluation of test results are not to be included in determining if the conduct of a test required at least six months.

(4) (A) Any reference to section 351 is a reference to section 351 of the Public Health Service Act.

(B) Any reference to section 503, 505, 512, or 515 is a reference to section 503, 505, 512, or 515 of the Federal Food, Drug, and Cosmetic Act.

(C) Any reference to the Virus-Serum-Toxin Act is a reference to the Act of March 4, 1913 (21 U.S.C. 151-158).

(5) The term "informal hearing" has the meaning prescribed for such term by section 201(y) of the Federal Food, Drug, and Cosmetic Act.

(6) The term "patent" means a patent issued by the United States Patent and Trademark Office.

(7) The term "date of enactment" as used in this section means September 24, 1984, for a human drug product, a medical device, food additive, or color additive.

(8) The term "date of enactment" as used in this section means the date of enactment of the Generic Animal Drug and Patent Term Restoration Act for an animal drug or a veterinary biological product.

(g) For purposes of this section, the term "regulatory review period" has the following meanings:

(1) (A) In the case of a product which is a new drug, antibiotic drug, or human biological product, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory review period for a new drug, antibiotic drug, or human biological product is the sum of—

(i) the period beginning on the date an exemption under subsection (i) of section 505 or subsection (d) of section 507 became effective for the approved product and ending on the date an application was initially submitted for such drug product under section 351, 505, or 507, and

(ii) the period beginning on the date the application was initially submitted for the approved product under section 351, subsection (b) of section 505, or section 507 and ending on the date such application was approved under such section.

(2) (A) In the case of a product which is a food additive or color additive, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory review period for a food or color additive is the sum of—

(i) the period beginning on the date a major health or environmental effects test on the additive was initiated and ending on the date a petition was initially submitted with respect to the product under the Federal Food, Drug, and Cosmetic Act requesting the issuance of a regulation for use of the product, and

(ii) the period beginning on the date a petition was initially submitted with respect to the product under the Federal Food, Drug, and Cosmetic Act requesting the issuance of a regulation for use of the product, and ending on the date such regulation became effective or, if objections were filed to such regulation, ending on the date such objections were resolved and commercial marketing was permitted or, if commercial marketing was permitted and later revoked pending further proceedings as a result of such objections, ending on the date such proceedings were finally resolved and commercial marketing was permitted.

(3) (A) In the case of a product which is a medical device, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory review period for a medical device is the sum of—

(i) the period beginning on the date a clinical investigation on humans involving the device was begun and ending on the date an application was initially submitted with respect to the device under section 515, and

(ii) the period beginning on the date an application was initially submitted with respect to the device under section 515 and ending on the date such application was approved under such Act or the period beginning on the date a notice of completion of a product development protocol was initially submitted under section 515(f)(5) and ending on the date the protocol was declared completed under section 515(f)(6).

(4) (A) In the case of a product which is a new animal drug, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory review period for a new animal drug product is the sum 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.

(5) (A) In the case of a product which is a veterinary biological product, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory period for a veterinary biological product is the sum of—

(i) the period beginning on the date the authority to prepare an experimental biological product under the Virus-Serum-Toxin Act

became effective and ending on the date an application for a license was submitted under the Virus-Serum-Toxin Act, and

(ii) the period beginning on the date an application for a license was initially submitted for approval under the Virus-Serum-Toxin Act and ending on the date such license was issued.

(6) A period determined under any of the preceding paragraphs is subject to the following limitations:

(A) If the patent involved was issued after the date of the enactment of this section, the period of extension determined on the basis of the regulatory review period determined under any such paragraph may not exceed five years.

(B) If the patent involved was issued before the date of the enactment of this section and—

(i) no request for an exemption described in paragraph (1)(B) or (4)(B) was submitted and no request for the authority described in paragraph (5)(B) was submitted,

(ii) no major health or environmental effects test described in paragraph (2)(B) or (4)(B) was initiated and no petition for a regulation or application for registration described in such paragraph was submitted, or

(iii) no clinical investigation described in paragraph (3) was begun or product development, protocol described in such paragraph was submitted,

before such date for the approved product the period of extension determined on the basis of the regulatory review period determined under any such paragraph may not exceed five years.

(C) If the patent involved was issued before the date of the enactment of this section and if an action described in subparagraph (B) was taken before the date of the enactment of this section with respect to the approved product and the commercial marketing or use of the product has not been approved before such date, the period of extension determined on the basis of the regulatory review period determined under such paragraph may not exceed two years or in the case of an approved product which is a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act or the Virus-Serum-Toxin Act), three years.

(h) The Director may establish such fees as the Director determines appropriate to cover the costs to the Office of receiving and acting upon applications under this section.

21 C.F.R. § 60.22—Regulatory review period determinations

In determining a product's regulatory review period, which consists of the sum of the lengths of a testing phase and an approval phase, FDA will review the information in each application using the following definitions of the testing phase and the approval phase for that class of products.

(a) For human drugs:

(1) The testing phase begins on the date an exemption under section 505(i) of the Act becomes effective (or the date an exemption under former section 507(d) of the Act became effective) for the approved human drug product and ends on the date a marketing application under section 351 of the Public Health Service Act or section 505 of the act is initially submitted to FDA (or was initially submitted to FDA under former section 507 of the Act), and

(2) The approval phase begins on the date a marketing application under section 351 of the Public Health Service Act or section 505(b) of the Act is initially submitted to FDA (or was initially submitted under former section 507 of the Act) and ends on the date the application is approved.

(b) For food and color additives:

(1) The testing phase begins on the date a major health or environmental effects test is begun and ends on the date a petition relying on the test and requesting the issuance of a regulation for use of the additive under section 409 or 721 of the Act is initially submitted to FDA.

(2) The approval phase begins on the date a petition requesting the issuance of a regulation for use of the additive under section 409 or 721 of the Act is initially submitted to FDA and ends upon whichever of the following occurs last:

(i) The regulation for the additive becomes effective; or

(ii) Objections filed against the regulation that result in a stay of effectiveness are resolved and commercial marketing is permitted; or

(iii) Proceedings resulting from objections to the regulation, after commercial marketing has been permitted and later stayed pending resolution of the proceedings, are finally resolved and commercial marketing is permitted.

(c) For medical devices:

(1) The testing phase begins on the date a clinical investigation on humans is begun and ends on the date an application for premarket approval of the device or a notice of completion of a product development protocol is initially submitted under section 515 of the Act. For purposes of this part, a clinical investigation is considered to begin on whichever of the following dates applies:

(i) If an investigational device exemption (IDE) under section 520(g) of the Act is required, the effective date of the exemption.

(ii) If an IDE is not required, but institutional review board (IRB) approval under section 520(g)(3) of the Act is required, the IRB approval date.

(iii) If neither an IDE nor IRB approval is required, the date on which the device is first used with human subjects as part of a clinical investigation to be filed with FDA to secure premarket approval of the device.

(2) The approval phase either:

(i) Begins on the date an application for premarket approval of the device is initially submitted under section 515 of the Act and ends on the date the application is approved; or

(ii) Begins on the date a notice of completion of a product development protocol is initially submitted under section 515 of the Act and ends on the date the protocol is declared to be completed.

(d) For animal drugs:

(1) The testing phase begins on the date a major health or environmental effects test is begun or the date on which the agency acknowledges the filing of a notice of claimed investigational exemption for a new animal drug, whichever is earlier, and ends on the date a marketing application under section 512 of the Act is initially submitted to FDA.

(2) The approval phase begins on the date a marketing application under section 512 of the Act is initially submitted to FDA and ends on the date the application is approved.

(e) For purposes of this section, a “major health or environmental effects test” may be any test which:

(1) Is reasonably related to the evaluation of the product’s health or environmental effects, or both:

(2) Produces data necessary for marketing approval; and

(3) Is conducted over a period of no less than 6 months duration, excluding time required to analyze or evaluate test results.

(f) For purposes of determining the regulatory review period for any product, a marketing application, a notice of completion of a product development protocol, or a petition is initially submitted on the date it contains sufficient information to allow FDA to commence review of the application. A marketing application, a notice of completion of a product development protocol, or a petition is approved on the date FDA sends the

applicant a letter informing it of the approval or, by order declares a product development protocol to be completed, or, in the case of food and color additives, on the effective date of the final rule listing the additive for use as published in the Federal Register or, in the case of a new animal drug in a Category II Type A medicated article, on the date of publication in the Federal Register of the notice of approval pursuant to section 512(i) of the Act. For purposes of this section, the regulatory review period for an animal drug shall mean either the regulatory review period relating the drug's approval for use in nonfood-producing animals or the regulatory review period relating to the drug's approval for use in food-producing animals, whichever is applicable.

21 C.F.R. § 514.1—Applications

(a) Applications to be filed under section 512(b) of the act shall be submitted in the form described in paragraph (b) of this section. If any part of the application is in a foreign language, an accurate and complete English translation shall be appended to such part. Translations of literature printed in a foreign language shall be accompanied by copies of the original publication. The application must be signed by the applicant or by an authorized attorney, agent, or official. If the applicant or such authorized representative does not reside or have a place of business within the United States, the application must also furnish the name and post office address of, and must be countersigned by, an authorized attorney, agent, or official residing or maintaining a place of business within the United States. Pertinent information may be incorporated in, and will be considered as part of, an application on the basis of specific reference to such information, including information submitted under the provisions of § 511.1 of this chapter, in the files of the Food and Drug Administration; however, the reference must be specific in identifying the information. Any reference to information furnished by a person other than the applicant may not be considered unless its use is authorized in a written statement signed by the person who submitted it.

(b) Applications for new animal drugs shall be submitted in triplicate and assembled in the manner prescribed by paragraph (b)(15) of this section, and shall include the following information:

(1) Identification. Whether the submission is an original or supplemental application; the name and the address of the applicant; the date of the application; the trade name(s) (if one has been proposed) and chemical name(s) of the new animal drug. Upon receipt, the application will be assigned a number NADA _____, which shall be used for all correspondence with respect to the application.

(2) Table of contents and summary. The application shall be organized in a cohesive fashion, shall contain a table of contents which identifies the data and other material submitted, and shall contain a well-organized summary and evaluation of the data in the following form:

(i) Chemistry:

(a) Chemical structural formula or description for any new animal drug substance.

(b) Relationship to other chemically or pharmacologically related drugs.

(c) Description of dosage form and quantitative composition.

(ii) Scientific rationale and purpose the new animal drug is to serve:

(a) Clinical purpose.

(b) Highlights of laboratory studies: The reasons why certain types of studies were done or omitted as related to the proposed conditions of use and to information already known about this class of compounds. Emphasize any unusual or particularly significant pharmacological effects or toxicological findings.

(c) Highlights of clinical studies: The rationale of the clinical study plan showing why types of studies were done, amended, or omitted as related to laboratory studies and prior clinical experience.

(d) Conclusions: A short statement of conclusions combining the major points of effectiveness and safety as they relate to the use of the new animal drug.

(3) Labeling. Three copies of each piece of all labeling to be used for the article (total of 9).

(i) All labeling should be identified to show its position on, or the manner in which it is to accompany the market package.

(ii) Labeling for nonprescription new animal drugs should include adequate directions for use by the layman under all conditions of use for which the new animal drug is intended, recommended, or suggested in any of the labeling or advertising sponsored by the applicant.

(iii) Labeling for prescription veterinary drugs should bear adequate information for use under which veterinarians can use the new animal drug safely and for the purposes for which it is intended, including those purposes for which it is to be advertised or represented, in accord with § 201.105 of this chapter.

(iv) All labeling for prescription or nonprescription new animal drugs shall be submitted with any necessary use restrictions prominently and conspicuously displayed.

(v) Labeling for new animal drugs intended for use in the manufacture of medicated feeds shall include:

(a) Specimens of labeling to be used for such new animal drug with adequate directions for the manufacture and use of finished feeds for all conditions for which the new animal drug is intended, recommended, or suggested in any of the labeling, including advertising, sponsored by the applicant. Ingredient labeling may utilize collective names as provided in § 501.110 of this chapter.

(b) Representative labeling proposed to be used for Type B and Type C medicated feeds containing the new animal drug.

(vi) Draft labeling may be submitted for preliminary consideration of an application. Final printed labeling will ordinarily be required prior to approval of an application. Proposed advertising for veterinary prescription drugs may be submitted for comment or approval.

(4) Components and composition. A complete list of all articles used for production of the new animal drug including a full list of the composition of each article:

(i) A full list of the articles used as components of the new animal drug. This list should include all substances used in the synthesis, extraction, or other method of preparation of any new animal drug and in the preparation of the finished dosage form, regardless of whether they undergo chemical change or are removed in the process. Each component should be identified by its established name, if any, or complete chemical name, using structural formulas when necessary for specific identification. If any proprietary name is used, it should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed component may be specified.

(ii) A full statement of the composition of the new animal drug. The statement shall set forth the name and amount of each ingredient, whether active or not, contained in a stated quantity of the new animal drug in the form in which it is to be distributed (for example, amount per tablet or milliliter) and a batch formula representative of that to be employed for the manufacture of the finished dosage form. All components should be included in the batch formula regardless of whether they appear in the finished product. Any calculated excess of an ingredient over the label declaration should be designated as such and percent excess shown. Reasonable variation may be specified.

(iii) If it is a new animal drug produced by fermentation:

(a) Source and type of microorganism used to produce the new animal drug.

(b) Composition of media used to produce the new animal drug.

(c) Type of precursor used, if any, to guide or enhance production of the antibiotic during fermentation.

(d) Name and composition of preservative, if any, used in the broth.

(e) A complete description of the extraction and purification processes including the names and compositions of the solvents, precipitants, ion exchange resins, emulsifiers, and all other agents used.

(f) If the new animal drug is produced by a catalytic hydrogenation process (such as tetracycline from chlortetracycline), a complete description of each chemical reaction with graphic formulas used to produce the new animal drug, including the names of the catalyst used, how it is removed, and how the new animal drug is extracted and purified.

(5) Manufacturing methods, facilities, and controls. A full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the new animal drug. This description should include full information with respect to any new animal drug in sufficient detail to permit evaluation of the adequacy of the described methods of manufacture, processing, and packing, and the described facilities and controls to determine and preserve the identity, strength, quality, and purity of the new animal drug, and the following:

(i) If the applicant does not himself perform all the manufacturing, processing, packaging, labeling, and control operations for any new animal drug, he shall: Identify each person who will perform any part of such operations and designate the part; and provide a signed statement from each such person fully describing, directly or by reference, the methods, facilities, and controls he will use in his part of the operation. The statement shall include a commitment that no changes will be made without prior approval by the Food and Drug Administration, unless permitted under § 514.8.

(ii) A description of the qualifications, including educational background and experience, of the technical and professional personnel who are responsible for assuring that the new animal drug has the identity, strength, quality, and purity it purports or is represented to possess, and a statement of their responsibilities.

(iii) A description of the physical facilities including building and equipment used in manufacturing, processing, packaging, labeling, storage, and control operations.

(iv) The methods used in the synthesis, extraction, isolation, or purification of any new animal drug. When the specifications and controls applied to such new animal drugs are inadequate in themselves to determine its identity, strength, quality, and purity, the methods should be described in sufficient detail, including quantities used, times, temperature, pH, solvents, etc., to determine these characteristics. Alternative methods or variations in methods within reasonable limits that do not affect such characteristics of the new animal drug may be specified. A flow sheet and indicated equations should be submitted when needed to explain the process.

(v) Precautions to insure proper identity, strength, quality, and purity of the raw materials, whether active or not, including:

(a) The specifications for acceptance and methods of testing for each lot of raw material.

(b) A statement as to whether or not each lot of raw materials is given a serial number to identify it, and the use made of such numbers in subsequent plant operations.

(vi) The instructions used in the manufacturing, processing, packaging, and labeling of each dosage form of the new animal drug, including:

(a) The method of preparation of the master formula records and individual batch records and the manner in which these records are used.

(b) The number of individuals checking weight or volume of each individual ingredient entering into each batch of the new animal drug.

(c) A statement as to whether or not the total weight or volume of each batch is determined at any stage of the manufacturing process subsequent to making up a batch according to the formula card and, if so, at what stage and by whom it is done.

(d) The precautions used in checking the actual package yield produced from a batch of the new animal drug with the theoretical yield. This should include a description of the accounting for such items as discards, breakage, etc., and the criteria used in accepting or rejecting batches of drugs in the event of an unexplained discrepancy.

(e) The precautions used to assure that each lot of the new animal drug is packaged with the proper label and labeling, including provisions for labeling storage and inventory control.

(f) Any special precautions used in the operations.

(vii) The analytical controls used during the various stages of the manufacturing, processing, packaging, and labeling of the new animal drug, including a detailed description of the collection of samples and the analytical procedures to which they are subjected. The analytical procedures should be capable of determining the active components within a reasonable degree of accuracy and of assuring the identity of such components.

(a) A description of practicable methods of analysis of adequate sensitivity to determine the amount of the new animal drug in the final dosage form should be included. The dosage form may be a finished pharmaceutical product, a Type A medicated article, a Type B or a Type C medicated feed, or a product for use in animal drinking water. Where two or more active ingredients are included, methods should be quantitative and specific for each active ingredient.

(b) If the article is one that is represented to be sterile, the same information with regard to the manufacturing, processing, packaging, and the collection of samples of the drug should be given for sterility controls. Include the standards used for acceptance of each lot of the finished drug.

(viii) An explanation of the exact significance of any batch control numbers used in the manufacturing, processing, packaging, and labeling of the new animal drug, including such control numbers that may appear on the label of the finished article. State whether these numbers enable determination of the complete manufacturing history of the product. Describe any methods used to permit determination of the distribution of any batch if its recall is required.

(ix) Adequate information with respect to the characteristics of and the test methods employed for the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

(x) A complete description of, and data derived from, studies of the stability of the new animal drug in the final dosage form, including information showing the suitability of the analytical methods used. A description of any additional stability studies underway or planned. Stability data for the finished dosage form of the new animal drug in the container in which it is to be marketed, including any proposed multiple dose container, and, if it is to be put into solution at the time of dispensing, for the solution prepared as directed. If the new animal drug is intended for use in the manufacture of Type C medicated feed as defined in § 558.3 of this chapter, stability data derived from studies in which representative

formulations of the medicated feed articles are used. Similar data may be required for Type B medicated feeds as determined by the Food and Drug Administration on a case-by-case basis. Expiration dates shall be proposed for finished pharmaceutical dosage forms and Type A medicated articles. If the data indicate that an expiration date is needed for Type B or Type C medicated feeds, the applicant shall propose such expiration date. If no expiration date is proposed for Type B or Type C medicated feeds, the applicant shall justify its absence with data.

(xi) Additional procedures employed which are designed to prevent contamination and otherwise assure proper control of the product. An application may be refused unless it includes adequate information showing that the methods used in, and the facilities and controls used for, the manufacturing, processing, and packaging of the new animal drug are adequate to preserve its identity, strength, quality, and purity in conformity with good manufacturing practice and identifies each establishment, showing the location of the plant conducting these operations.

(6) Samples. Samples of the new animal drug and articles used as components and information concerning them may be requested by the Center for Veterinary Medicine as follows:

(i) Each sample shall consist of four identical, separately packaged subdivisions, each containing at least three times the amount required to perform the laboratory test procedures described in the application to determine compliance with its control specifications for identity and assays. Each of the samples submitted shall be appropriately packaged and labeled to preserve its characteristics, to identify the material and the quantity in each subdivision of the sample, and to identify each subdivision with the name of the applicant and the new animal drug application to which it relates. Included are:

(a) A sample or samples of any reference standard and blank used in the procedures described in the application for assaying each new animal drug and other assayed components of the finished new animal drug.

(b) A representative sample or samples of each strength of the finished dosage form proposed in the application and employed in the clinical investigations and a representative sample or samples of each new animal drug from the batch(es) employed in the production of such dosage form.

(c) A representative sample or samples of finished market packages of each strength of the dosage form of the new animal drug prepared for initial marketing and, if any such sample is not

from a representative commercial-scale production batch, such a sample from a representative commercial-scale production batch, and a representative sample or samples of each new animal drug from the batch(es) employed in the production of such dosage form, provided that in the case of new animal drugs marketed in large packages the sample should contain only three times a sufficient quantity of the new animal drug to allow for performing the control tests for drug identity and assays.

(ii) The following information shall be included for the samples when requested:

(a) For each sample submitted, full information regarding its identity and the origin of any new animal drug contained therein (including a statement whether it was produced on a laboratory, pilot-plant, or full-production scale) and detailed results of all laboratory tests made to determine the identity, strength, quality, and purity of the batch represented by the sample, including assays.

(b) For any reference standard submitted, a complete description of its preparation and the results of all laboratory tests on it. If the test methods used differed from those described in the application, full details of the methods employed in obtaining the reporting results.

(7) Analytical methods for residues. Applications shall include a description of practicable methods for determining the quantity, if any, of the new animal 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 to ensure that the proposed use of this drug will be safe. When data or other adequate information establish that it is not reasonable to expect the new animal drug to become a component of food at concentrations considered unsafe, a regulatory method is not required.

(i) The kind of information required by this subdivision may include: Complete experimental protocols for determining drug residue levels in the edible products, and the length of time required for residues to be eliminated from such products following the drug's use; residue studies conducted under appropriate (consistent with the proposed usage) conditions of dosage, time, and route of administration to show levels, if any, of the drug and/or its metabolites in test animals during and upon cessation of treatment and at intervals thereafter in order to establish a disappearance curve; if the drug is to be used in combination with other drugs, possible effects of interaction demonstrated by the appropriate disappearance curve or depletion patterns after drug withdrawal under appropriate (consistent with the proposed usage) conditions of dosage,

time, and route of administration; if the drug is given in the feed or water, appropriate consumption records of the medicated feed or water and appropriate performance data in the treated animal; if the drug is to be used in more than one species, drug residue studies or appropriate metabolic studies conducted for each species that is food-producing. To provide these data, a sufficient number of birds or animals should be used at each sample interval. Appropriate use of labeled compounds (e.g. radioactive tracers), may be utilized to establish metabolism and depletion curves. Drug residue levels ordinarily should be determined in muscle, liver, kidney, and fat and where applicable, in skin, milk, and eggs (yolk and egg white). As a part of the metabolic studies, levels of the drug or metabolite should be determined in blood where feasible. Samples may be combined where necessary. Where residues are suspected or known to be present in litter from treated animals, it may be necessary to include data with respect to such residues becoming components of other agricultural commodities because of use of litter from treated animals.

(ii) A new animal drug that has the potential to contaminate human food with residues whose consumption could present a risk of cancer to people must satisfy the requirements of Subpart E of Part 500 of this chapter.

(8) Evidence to establish safety and effectiveness.

(i) An application may be refused unless it contains full reports of adequate tests by all methods reasonably applicable to show whether or not the new animal drug is safe and effective for use as suggested in the proposed labeling.

(ii) An application may be refused unless it includes substantial evidence of the effectiveness of the new animal drug as defined in § 514.4.

(iii) An application may be refused unless it contains detailed reports of the investigations, including studies made on laboratory animals, in which the purpose, methods, and results obtained are clearly set forth of acute, subacute, and chronic toxicity, and unless it contains appropriate clinical laboratory results related to safety and efficacy. Such information should include identification of the person who conducted each investigation, a statement of where the investigations were conducted, and where the raw data are available in the application.

(iv) All information pertinent to an evaluation of the safety and effectiveness of the new animal drug received or otherwise obtained by the applicant from any source, including information derived from other investigations or commercial marketing (for example, outside the United States), or reports in the scientific literature, both favorable and unfavorable, involving the new animal drug that is the subject of the application and related new animal drugs shall be submitted. An adequate

summary may be acceptable in lieu of a reprint of a published report that only supports other data submitted. Include any evaluation of the safety or effectiveness of the new animal drug that has been made by the applicant's veterinary or medical department, expert committee, or consultants.

(v) If the new animal drug is a combination of active ingredients or animal drugs, an application may be refused unless it includes substantial evidence of the effectiveness of the combination new animal drug as required in § 514.4.

(vi) An application shall include a complete list of the names and post office addresses of all investigators who received the new animal drug. This may be incorporated in whole or in part by reference to information submitted under the provisions of § 511.1 of this chapter.

(vii) Explain any omission of reports from any investigator to whom the investigational new animal drug has been made available. The unexplained omission of any reports of investigations made with the new animal drug by the applicant or submitted to him by an investigator or the unexplained omission of any pertinent reports of investigations or clinical experience received or otherwise obtained by the applicant from published literature or other sources that would bias an evaluation of the safety of the new animal drug or its effectiveness in use, constitutes grounds for the refusal or withdrawal of the approval of an application.

(viii) If a sponsor has transferred any obligations for the conduct of any clinical study to a contract research organization, the application is required to include a statement containing the name and address of the contract research organization, identifying the clinical study, and listing the obligations transferred. If all obligations governing the conduct of the study have been transferred, a general statement of this transfer—in lieu of a listing of the specific obligations transferred—may be submitted.

(ix) If original subject records were audited or reviewed by the sponsor in the course of monitoring any clinical study to verify the accuracy of the case reports submitted to the sponsor, a list identifying each clinical study so audited or reviewed.

(9) Veterinary feed directive. Three copies of a veterinary feed directive (VFD) must be submitted in the format described under § 558.6(a)(4) of this chapter.

(10) Supplemental applications. If it is a supplemental application, full information shall be submitted on each proposed change concerning any statement made in the approved application.

(11) Applicant's commitment. It is understood that the labeling and advertising for the new animal drug will prescribe, recommend, or suggest its use only under the conditions stated in the labeling which is part of this application and if the

article is a prescription new animal drug, it is understood that any labeling which furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for use of the new animal drug will also contain, in the same language and emphasis, information for its use including indications, effects, dosages, routes, methods, and frequency and duration of administration, any relevant hazards, contraindications, side effects, and precautions contained in the labeling which is part of this application. It is understood that all representations in this application apply to the drug produced until changes are made in conformity with § 514.8.

(12) Additional commitments.

(i) New animal drugs as defined in § 510.3 of this chapter, intended for use in the manufacture of animal feeds in any State will be shipped only to persons who may receive such drugs in accordance with § 510.7 of this chapter.

(ii) The methods, facilities, and controls described under item 5 of this application conform to the current good manufacturing practice regulations in Subchapter C of this chapter.

(iii) With respect to each nonclinical laboratory study contained in the application, either a statement that the study was conducted in compliance with the good laboratory practice regulations set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance.

(13) [Reserved]

(14) Environmental assessment. The applicant is required to submit either a claim for categorical exclusion under § 25.30 or § 25.33 of this chapter or an environmental assessment under § 25.40 of this chapter.

(15) Assembling and binding the application. Assemble and bind an original and two copies of the application as follows:

(i) Bind the original or ribbon copy of the application as copy No. 1.

(ii) Bind two identical copies as copy No. 2 and copy No. 3.

(iii) Identify each front cover with the name of the applicant, new animal drug, and the copy number.

(iv) Number each page of the application sequentially in the upper right hand corner or in another location so that the page numbers remain legible after the application has been bound, and organize the application consistent with paragraphs (b)(1) through (14) of this section. Each copy

should bear the same page numbering, whether sequential in each volume or continuous and sequential throughout the application.

(v) Include complete labeling in each of the copies. It is suggested that labeling be identified by date of printing or date of preparation.

(vi) Submit separate applications for each different dosage form of the drug proposed. Repeating basic information pertinent to all dosage forms in each application is unnecessary if reference is made to the application containing such information. Include in each application information applicable to the specific dosage form, such as labeling, composition, stability data, and method of manufacture.

(vii) Submit in folders amendments, supplements, and other correspondence sent after submission of an original application. The front cover of these submissions should be identified with the name of the applicant, new animal drug, copy number, and the new animal drug application number, if known.

(c) When a new animal drug application is submitted for a new animal drug which has a stimulant, depressant, or hallucinogenic effect on the central nervous system, if it appears that the drug has a potential for abuse, the Commissioner shall forward that information to the Attorney General of the United States.

(d) [Reserved]

CERTIFICATE OF SERVICE

I hereby certify that on this 27th day of August, 2009, I caused two copies of the foregoing Brief for Appellants Wyeth Holdings Corporation and Wyeth to be served by first-class U.S. mail, postage prepaid, on:

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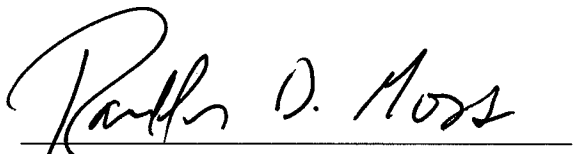

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CERTIFICATE OF COMPLIANCE

Pursuant to Federal Rule of Appellate Procedure 32(a)(7)(C), the undersigned hereby certifies that this brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B)(i).

1. Exclusive of the exempted portions of the brief, as provided in Federal Rule of Appellate Procedure 32(a)(7)(B), the brief contains 13,529 words.

2. The brief has been prepared in proportionally spaced typeface using Microsoft Word 2000 in 14-point Times New Roman font. As permitted by Federal Rule of Appellate Procedure 32(a)(7)(B), the undersigned has relied upon the word count feature of this word processing system in preparing this certificate.

August 27, 2009

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