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.

REPLY BRIEF FOR APPELLANTS

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December 9, 2009

CERTIFICATE OF INTEREST

Counsel for Appellants Wyeth Holdings Corporation and Wyeth LLC certifies the following:

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

Wyeth Holdings Corporation and Wyeth LLC

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 is a wholly owned subsidiary of AC Acquisition Holding Company, which is a wholly owned subsidiary of Appellant Wyeth LLC.

Appellant Wyeth LLC, in turn, is a wholly owned subsidiary of Pfizer LLC, which is a wholly owned subsidiary of Pfizer, Inc.

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: December 9, 2009

Randolph D. Moss
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INTRODUCTION

To restore valuable patent rights that would otherwise be lost due to the time taken for premarket review by the FDA, Congress granted the holder of a patent covering a new animal drug a day-for-day extension of its patent term equal to the period of agency review. That period is measured from the day the new animal drug application ("NADA") is "initially submitted." The FDA, however, has taken the position that an application submitted under its phased-review program is not "initially submitted"—and thus the review period does not start—until the applicant has submitted all of the relevant information, the FDA has reviewed and approved those submissions, and the applicant has then effectively *re*submitted the information in a ministerial "Administrative NADA" incorporating its earlier filings by reference. This counterintuitive interpretation—which does not start the period of review until FDA review is nearly finished—cannot be reconciled with the statutory text, the relevant legislative history, or the FDA's own regulations.

Under the proper reading of 35 U.S.C. § 156(g)(4)(B), an application is "initially submitted" as soon as the first phased-review "technical section" is filed. The text and legislative history of the statute, as well as the FDA's own regulation, indicate that an application is "initially submitted" when the applicant has provided enough information to allow FDA review *to begin*—not, as the FDA maintains, at the point when the application is complete and the process of FDA review is nearly

finished. And it is undisputed that the FDA starts to review the technical sections that comprise a phased-review application as soon as the first one is submitted. The FDA asserts that its review of technical sections does not constitute review of an "application" because "application" means "complete application." In fact, however, the only plausible reading of the text, the legislative history, and the FDA's own regulation is that an application can be "*initially* submitted" even if it is not complete.

Moreover, the FDA offers virtually no defense of the agency's position that an application is not even "initially submitted" once an applicant has submitted all of the required technical sections. The bulk of the FDA's opposition is devoted to arguing that an application is not "initially submitted" when the *first* technical section is submitted. In so arguing, the FDA places great emphasis on the definition of an application contained in 21 U.S.C. § 360b(b) and 21 C.F.R. § 514.1(b). But when it comes to arguing that an application is not "initially submitted" even after the *last* technical section has been submitted, the FDA has very little to say. *See* FDA Br. 33-35.

This is perhaps because the FDA does not—and could not—dispute that an applicant is required to have submitted all of the information set forth in § 360b(b) and § 514.1(b) by the time the applicant files the *last* technical section. The agency's own guidance documents make this clear. Indeed, the FDA has never—

not during administrative proceedings, and certainly not before this Court—identified any required element of an application that is submitted for the first time in an "Administrative NADA."

The FDA's only response is to argue that a "single submission" cross-referencing the prior materials is required. But it provides no basis for adhering to this empty formalism. It also is unable to reconcile this required *re*submission of the contents of an application with the key statutory standard—that an application be "*initially* submitted." Moreover, the FDA's interpretation is contrary to the purposes of the Hatch-Waxman Act. After weighing the competing interests at stake, Congress crafted a detailed formula that allows applicants to recover half of the time spent in the testing phase but all of the time in the review phase. *See* 35 U.S.C. § 156(c). By refusing to recognize that review has even begun until it is almost over, the FDA upsets that careful balance. Accordingly, the submission of the *final* technical section marks the latest point at which an application can even arguably be said to be "initially submitted."

Finally, the FDA action under review must be set aside because the agency failed to explain its differing interpretation of "initially submitted" in the context of the "fast track" review program for certain human drugs. The FDA insists that in both contexts it deems an application "initially submitted" only when it is complete. But the FDA's own decisions reveal that it considers a "fast track"

application to be complete—and thus initially submitted—as soon as the applicant submits the last module for review. FDA's failure even to acknowledge this inconsistency requires vacatur.

ARGUMENT

I. A PHASED-REVIEW APPLICATION IS "INITIALLY SUBMITTED" WHEN THE APPLICANT SUBMITS ITS *FIRST* TECHNICAL SECTION

A. An "Application" Is "Initially Submitted" As Soon As It Is Sufficiently Complete To Allow FDA Review To Begin

In its opposition, the FDA assumes that 35 U.S.C. § 156(g)(4)(B)'s reference to an "application" necessarily refers to a *complete* application. *See* FDA Br. 27. It then repeatedly invokes that premise to dismiss any suggestion that an "application" might be "initially submitted" before it is complete. *See id.* at 27-31. But the FDA's position is contrary to basic principles of statutory interpretation, which show that "the date the application was initially submitted" is not the date the application was complete, but rather the date that the application contained sufficient information to allow FDA review to begin.

First, the phrase "initially submitted" by definition contemplates future submissions. Accordingly, an application must be "initially submitted" at some point before it contains all of the information required for FDA approval; a contrary interpretation would read the word "initially" out of the statute. Wyeth Br. 30-32. Even the FDA appears to concede this much. FDA Br. 36-37. The

FDA argues that only "the minor amendments, corrections, or additions that FDA often requires applicants to provide" can qualify as these further submissions. *Id.*; *see also id.* at 30-31. But the phrase "the date the application was initially submitted" contemplates further submissions *of the application*. And this reveals a contradiction in the FDA's interpretation.

On one hand, if the "amendments, corrections, or additions" that the agency requires after an application has been "initially submitted" are not part of the application, then they cannot be the further submissions *of the application* contemplated by the statute—and thus the agency's interpretation gives no effect to the word "initially." On the other hand, however, if the required supplemental submissions *are* part of the application, then that necessarily means that the original application was incomplete—and thus, under the FDA's interpretation, that it was not "initially submitted" until after the applicant filed the amendments or additions necessary to complete it. Accordingly, under the plain language of the statute, it is not tenable to assert that an application is not initially submitted until a complete application is filed.

Second, the legislative history makes clear that Congress intended "the date on which the application was initially submitted" to be interpreted to mean the date on which the applicant had submitted enough information to allow FDA review to begin rather than the date on which the application was complete:

> [A]n 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 agency action could be commenced*, it would be considered to be "initially submitted."

H.R. Rep. No. 98-857, pt. 1, at 44 (1984) (emphases added).

The FDA does not deny that the quoted passage reflects congressional intent on the meaning of "initially submitted."[1] But the agency contends that "[i]n referring to a submission that is 'complete enough' to allow 'agency action,'" Congress actually meant "'complete enough' to allow 'approval.'" FDA Br. 28-29. This interpretation is wholly implausible. For one thing, it contradicts the very passage it purports to interpret. Although the third sentence of the quoted passage refers to the point at which "the application was complete enough so that agency action could be commenced," the first sentence makes clear that the "agency action" in question is "review," not approval. Additionally, it would make no sense to ask when the final and discrete FDA act of approving a drug could "be commenced." Approval does not "commence"; it occurs.

[1] It could scarcely do so. In promulgating its regulation interpreting § 156(g), the FDA explained that its "interpretation of the term 'initially submitted' is derived from the legislative history of the statute" and then quoted this same language from the House Report. 53 Fed. Reg. 7,298, 7,301 (1988).

The FDA also entirely ignores the legislative history explaining that Congress deliberately chose the phrase "initially submitted" rather than the term "filed" because "an application is often not considered to be filed … until the agency has determined that no other information is needed." H.R. Rep. No. 98-857, pt. 1, at 44. Congress thus rejected precisely the sort of completeness standard that the FDA now urges.[2] And although the district court concluded that the meaning of "initially submitted" is ambiguous for purposes of *Chevron* step one, the Supreme Court has admonished that a court should find that Congress has left a "gap" for an agency to fill only after applying all of the "traditional tools of statutory interpretation." *Chevron U.S.A. Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 843 n.9 (1984). As this Court has recognized, "those 'tools' include the statute's structure, canons of statutory construction *and legislative history*." *Timex V.I., Inc. v. United States*, 157 F.3d 879, 882 (Fed. Cir. 1998) (emphasis added); *see also, e.g., California Indus. Prods., Inc. v. United States*, 436 F.3d 1341, 1355-1357 & n.15 (Fed. Cir. 2006). Here, the House Report removes any ambiguity and makes clear that an application is "initially submitted" when it is complete enough "for agency review to begin."

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[2] *See* D. Beers, *Generic and Innovator Drugs: A Guide to FDA Approval Requirements* § 4.04[D] (6th ed. 2004) ("It is noteworthy … that the date of 'submission' has been chosen rather than the date of 'filing,' as FDA and the courts have interpreted 'filing' of an application to occur only at a point at which *the agency has found the application complete*." (emphasis added)).

Third, the FDA's own regulation strongly supports Wyeth's interpretation. It reads: "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). In promulgating this rule, the FDA specifically explained that it meant that an application could be "initially submitted" even "[i]f the agency requires additional information after beginning its review." 53 Fed. Reg. 7,298, 7,302 (1988). Furthermore, because this regulation expressed the FDA's published interpretation of the phrase "initially submitted" in the human drug context when Congress adopted the same language in extending the Hatch-Waxman Act to cover animal drugs, it not only binds the agency but also sheds light on congressional intent.[3]

B. The FDA's Review Of A Phased-Review Application Begins When The Applicant Submits The First Technical Section

For the foregoing reasons, it is clear that an application is "initially submitted" as soon as it contains enough information to allow FDA review to begin. The FDA concedes that the technical sections submitted during phased review are parts of the application. FDA Br. 27. It also does not deny that it

[3] *See Forest Grove Sch. Dist. v. T.A.*, 129 S. Ct. 2484, 2492 (2009) ("Congress is presumed to be aware of an administrative or judicial interpretation of a statute and to adopt that interpretation when it re-enacts a statute without change." (internal quotation marks omitted)).

begins review of those technical sections as soon as the first one is submitted. Nonetheless, the FDA maintains that this does not constitute review of an "application" because an "application" is "a document containing or referencing all the information required by statute and regulation." *Id.* at 38; *see id.* at 28.

This argument cannot be reconciled with the text and legislative history. As explained above, the word "initially" necessarily implies that an application can be "initially submitted" before it is complete. Moreover, Congress specifically rejected a standard that would have equated the date on which an application was "initially submitted" with the date it was "complete." The House Report's use of terms like "sufficient information" and "complete enough" also make it abundantly clear that Congress understood that it is possible to begin review of an application before the application includes all required information. In the face of these contrary authorities, the FDA's reliance on the meaning of the word "application" considered in isolation is unpersuasive.[4]

Similarly, the FDA's present interpretation cannot be reconciled with its own regulation. If, as the FDA now contends, the term "application" necessarily means "complete application, containing all required information," then § 60.22(f)

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[4] *See Dolan v. USPS*, 546 U.S. 481, 486 (2006) ("Interpretation of a word or phrase depends on reading the whole statutory text, considering the purpose and context of the statute, and consulting any precedents or authorities that inform the analysis.").

must be understood as follows: "[A] marketing application … is initially submitted on the date it contains sufficient information to allow FDA to commence review of the complete application, including all required information." But if that were right, then the reference to "sufficient information to allow FDA to commence review" would have been unnecessary.[5]

C. The FDA's Remaining Arguments Are Unpersuasive

In defense of its position, the FDA offers several additional arguments—all of which lack merit.

First, the FDA contends that Wyeth's interpretation leads to inconsistent treatment of traditional and phased applications because "a sponsor proceeding under phased review could trigger the approval phase with a partial submission … whereas a traditional-review sponsor must submit the [full] application." FDA Br. 32. But this alleged inconsistency is a result of the statute itself: Congress intended an application to be deemed "initially submitted" when the FDA can

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[5] A reviewing court must reject an agency's interpretation of its own regulation if "an alternative reading is compelled by the regulation's plain language or by other indications of the [agency's] intent at the time of the regulation's promulgation." *Thomas Jefferson Univ. v. Shalala*, 512 U.S. 504, 512 (1994) (internal quotation marks omitted). Here, both the language of the regulation and the FDA's contemporaneous explanation, *see* 53 Fed. Reg. at 7,301-7,302, demonstrate that an application need not be "complete" to be "initially submitted."

begin its review, and under Wyeth's interpretation both phased and traditional applications are "initially submitted" at the point when FDA review begins.[6]

Second, the FDA attempts to defend its interpretation on policy grounds. It first contends that its restrictive interpretation of the patent term extension provision is justified because phased-review applicants benefit from more efficient review. FDA Br. 33. By seeking a full patent term extension as well, the FDA claims, Wyeth is trying to "have it both ways." *Id.* at 41-43. Moreover, the FDA warns that if this Court adopts Wyeth's position, sponsors will be able to abuse the system by "submit[ting] virtually any amount of testing data to FDA and then claim[ing] that the submission of that data triggered the beginning of the approval phase." *Id.* at 43. Both of these policy arguments are meritless.[7]

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[6] In any event, the FDA's consistency argument actually supports Wyeth's alternative argument that an application is initially submitted as soon as the applicant submits its *last* technical section. That is the point at which a sponsor proceeding under phased review has submitted the same content as a traditional-review applicant that has submitted its application. *See infra* Section II.

[7] The FDA's policy views are not entitled to any special deference. To the contrary, the case on which the agency relied found such deference appropriate only because "Congress ha[d] entrusted [the agency] with broad discretion." *Babbitt v. Sweet Home Chapter of Cmtys. for a Great Or.*, 515 U.S. 687, 708 (1995); *see* FDA Br. 41. Here, in contrast, Congress itself has made the relevant policy decision by specifying that the approval phase begins as soon as an application is "initially submitted." The FDA is left with the much narrower task of applying that term. Indeed, the FDA itself has explained that its task in a patent term extension proceeding is "a purely ministerial function." 67 Fed. Reg. 65,358, 65,359 (2002).

As to the claim that Wyeth is seeking to have its cake and eat it too, the FDA is certainly right that a shorter regulatory delay should result in a shorter patent term extension. But as Wyeth explained in its opening brief, Congress established a precise formula that *automatically* reduces the available extension whenever the regulatory review period is shortened. Under any interpretation, then, phased-review applicants will have their patent term extensions reduced to the extent that they receive FDA approval faster. Wyeth Br. 49-50 & n.18. But the FDA's position goes even further: It not only reduces the available patent term extension by an amount corresponding to the reduction in total regulatory delay, but also shifts nearly all of the time that the agency spends reviewing the application from the approval phase (which provides day-for-day compensation) to the testing phase (which provides only half as much). *Id.* at 49-50. The FDA does not explain how this additional reduction furthers congressional intent or any related policy interest.

The FDA's concern that sponsors will abuse the system by rushing to submit incomplete information is similarly misplaced. The FDA bases this argument on the mistaken premise that Wyeth's position is that "'an application' is 'initially submitted' when the first document containing *any* of the information required by Section 360b(b)(1) is submitted." FDA Br. 18; *see also id.* at 27, 43. In fact, however, Wyeth's position is that only the submission of a technical section—a substantial package of information specifically defined by the FDA's guidance

documents, *see* JA62-67, 210-214—and the initiation of FDA review trigger the start of the approval phase. *See, e.g.*, Wyeth Br. 22.[8] Moreover, Wyeth's opening brief explained why there is little risk of the sort of abuse that the FDA fears. Most obviously, the FDA will refuse to accept an incomplete technical section in the first place and can also reduce the available patent term extension to account for any period in which the applicant failed to act with diligence. *Id.* at 47-48. Finally, Wyeth also explained that the FDA's asserted policy concerns are not even arguably implicated by Wyeth's alternative interpretation, which would hold that an application is "initially submitted" when the sponsor submits the *last* technical section. Wyeth Br. 48. The FDA failed to respond to these arguments.[9]

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[8] If Wyeth actually took the extreme position described by the FDA, it would be contending that its application was "initially submitted" long before the submission of the first technical section on August 8, 1995. Wyeth submitted substantial information about Cydectin to the FDA between 1990 and 1995, including information required to be included in an "application" under § 360b(b). *See, e.g.*, JA136 (noting the August 12, 1992 submission of "preliminary target animal safety data for [FDA] evaluation").

[9] Wyeth's opening brief also contended that this Court should decline to consider the FDA's policy arguments because the agency failed to articulate them during administrative proceedings. Wyeth Br. 46-47. In response, the FDA points to its reconsideration decision, which in turn quoted the agency's 2002 draft guidance document (published well after Wyeth received FDA approval to market Cydectin and submitted its application for a patent term extension in 1998). FDA Br. 43-44. But that document offers no policy rationale for the FDA's interpretation—it simply states, as a descriptive matter, that under the FDA's interpretation, "a new animal drug that was the subject of an Administrative NADA is likely, in most cases, to receive a shorter patent term extension than it would have received had it been the subject of a traditional NADA." JA161.

Third, the FDA claims that its interpretation is entitled to special deference because it is "long-standing." FDA Br. 45-46 (citing *Smiley v. Citibank (S.D.), N.A.*, 517 U.S. 735, 740 (1996)). But the FDA points to only three prior decisions applying its interpretation, the earliest of which was issued in 1998. *See id.* at 46.[10] Moreover, none of those decisions expressly articulated the agency's statutory interpretation, and they do not appear to have been challenged in court. In contrast to the situation contemplated in *Smiley*, there is little reason to think that a decade-old interpretation applied a handful of times has any special "credential of reasonableness" due to its longevity. 517 U.S. at 740.[11]

II. AT THE LATEST, A PHASED-REVIEW APPLICATION IS "INITIALLY SUBMITTED" WHEN THE APPLICANT SUBMITS ITS *LAST* TECHNICAL SECTION

The FDA provides no colorable basis for contesting the proposition that, at the very latest, an application is "initially submitted" when the *last* technical section is submitted. Most of the FDA's brief is devoted to arguing that an

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[10] The FDA also claims that it set forth its interpretation in its 1995 guidance document. *See* FDA Br. 45-46. But the references to the meaning of an "application" in that document were made in the context of the FDA's administrative procedures—the FDA did not even mention patent term extensions, let alone cite or quote the statutory language it now claims to have been interpreting. *See* JA48-84.

[11] *Cf. United States v. Cleveland Indians Baseball Co.*, 532 U.S. 200, 219 (2001) (deferring to an interpretation in a "61-year-old regulation implementing a 62-year-old statute"); *Rosete v. OPM*, 48 F.3d 514, 518-519 (Fed. Cir. 1995) (deferring to an interpretation in regulations that had been in force for more than 50 years).

application is not "initially submitted" upon the filing of the *first* technical section. In that respect, the FDA argues that the first technical section does not constitute a "complete" application—as defined in 21 U.S.C. § 360b(b) and 21 C.F.R. § 514.1. *See* FDA Br. 24-32. But the FDA does not dispute that all of the information it contends is required in an application must be submitted in the technical sections. It is therefore left to argue empty formalisms—that a single piece of paper using the label "Administrative NADA" must be filed—and that in the particular circumstances of this case, all of the required information was not submitted with the technical sections. Neither contention supports its position.

A. The FDA Cannot Identify Any Element Of An Application That Is Submitted For The First Time In The "Administrative NADA"

The FDA's position is that a phased-review application is not complete until the applicant submits its "Administrative NADA." JA232. But, as Wyeth's opening brief explained, the "application" referenced in § 156(g)(4)(B) is an "application … under subsection (b) of section 512" of the Federal Food, Drug, and Cosmetic Act—*i.e.*, under 21 U.S.C. § 360b(b). And the FDA's own guidance documents make clear that a phased-review applicant must submit all of the information required by § 360b(b) in its technical sections, long before it files its "Administrative NADA." Wyeth Br. 27-29 & n.11. Indeed, those guidance documents reveal that an "Administrative NADA" is a purely ministerial filing that does not contain any new information at all. *Id.* at 29. The FDA does not dispute

these points. Indeed, its brief does not identify a single piece of information listed in § 360b(b) that is not contained in the technical sections.

The FDA does argue that its regulation implementing § 360b(b)—21 C.F.R. § 514.1—expands the information that must be included in an "application." *See* FDA Br. 26 n.11. But the agency's guidance documents make clear that all of the information required by *both* the statute *and* the regulation must be included in the technical sections and that nothing new is added by the "Administrative NADA." *See* JA156 (stating that an "Administrative NADA" is "submitted after all of the technical sections that fulfill the requirements for the approval of the new animal drug under 21 CFR 514.1 have been reviewed"); *see also* JA71 (the technical sections must "contain all appropriate information and declarations"). And the FDA's brief likewise fails to identify any category of information required by § 514.1 that is not included in the technical sections but rather submitted for the first time in the "Administrative NADA."[12]

[12] Portions of the FDA's brief might be read to suggest that the term "application" in § 156(g)(4)(B) includes additional required elements beyond those specified in § 360b(b) and § 514.1. *See, e.g.*, FDA Br. 18. But the agency never explains what those additional requirements might be, let alone demonstrates that an applicant submits them for the first time in an "Administrative NADA." In fact, the agency's regulation makes clear that its list of required elements is exhaustive. *See* 21 C.F.R. § 514.1(a) ("Applications to be filed under [§ 360b(b)] shall be submitted in the form described in paragraph (b) of this section.").

Finally, the FDA appears to have abandoned the argument, advanced during administrative proceedings, that the missing elements of an application supplied by the "Administrative NADA" are the "technical section complete" letters issued by the agency itself. In its decision denying Wyeth's request for reconsideration, the FDA asserted 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 emphasis added). But as Wyeth pointed out in its opening brief, these letters "are the FDA's *responses* to an application, not parts of that application." Wyeth Br. 30. The FDA's brief disputes Wyeth's claim that the "complete" letters are responses to an "application," FDA Br. 34, but does not—and could not—claim that those letters are required elements of an application under either § 360b(b) or § 514.1(b).

B. Nothing In The Statute Supports The FDA's Assertion That An "Application" Must Be Contained In A Single Submission

Instead of arguing that an "Administrative NADA" supplies some necessary element of an application, the FDA's brief advances a new theory: Even if an applicant submits all of the required elements of an application in its technical sections, it still does not submit an "application" until it files its "Administrative NADA" because an application must be "a *single submission*." FDA Br. 19 (emphasis added); *see also id.* at 33-34. The FDA does not take the position that a single submission *containing* all of the information required to be part of an

application is necessary; it admits that an "Administrative NADA" merely "incorporate[s] by reference [the] technical section[s] the sponsor has previously submitted." *Id.* at 6. Thus, the FDA is left to argue that an application is not "initially submitted" until the applicant files a piece of paper merely "*referencing* all the required information" that it has previously submitted. *Id.* at 19 (emphasis added); *see also id.* at 33.

The FDA provides no support for this highly formalistic contention.[13] The FDA does not explain why an applicant that submits the information required by § 360b(b) and § 514.1(b) in a single document should be treated differently than one who submits precisely the same information in several documents rather than one. It certainly provides no reason to think Congress intended to differentiate between applicants depending upon whether they filed a piece of paper that simply *incorporates by reference* previous filings. To the contrary, the statutory text shows that Congress intended no such thing. Congress granted a day-for-day patent term extension beginning on the day that the patent holder's application was "*initially* submitted." As Wyeth's opening brief explained, the use of the word

[13] In denying Wyeth's request for reconsideration, the FDA had similarly exalted form over substance. It argued that the technical sections are not an "application" because the agency places them in an "investigation" file rather than an "application" file. JA232. But as Wyeth's opening brief explained, if the technical sections satisfy the statutory definition of an "application," then the FDA cannot change that result by calling them something else. Wyeth Br. 39-40. The FDA's brief abandons this argument.

"initially" must refer, at the very least, to the first submission of the relevant material. Wyeth Br. 30-32. But the FDA's "single submission" requirement would mean that an applicant has not "initially submitted" its application until it has submitted all of the relevant materials (in its technical sections) and then *re*submitted those same materials (by incorporating them by reference into its "Administrative NADA"). This interpretation cannot be reconciled with the plain meaning of "initially." And even if the text standing alone were ambiguous, the relevant legislative history makes clear that Congress intended for an application to be deemed "initially submitted" as soon as the sponsor has provided "all information necessary for agency review to begin." H.R. Rep. No. 98-857, pt. 1, at 44. This forecloses any claim that a sponsor that has already submitted *all* required information has not "initially submitted" its application until it collects that information into a single submission.

The arbitrariness of the FDA's position is only further highlighted by its observation that Wyeth could have avoided the loss of its patent rights by "submit[ting] a traditional NADA … at any time during the phased review process." FDA Br. 35 (citing JA66-67). The guidance document that the FDA cites explains that a sponsor that initially proceeds under the phased-review program can switch to traditional review by filing an NADA that "incorporate[s] … by reference" the technical sections the sponsor has already submitted. JA67.

In other words, the FDA contends that on the date it is prepared to submit its last technical section, a phased-review applicant may instead submit a document containing exactly the same substantive information but styled as a "traditional NADA" incorporating the applicant's earlier-filed technical sections by reference. The agency would apparently treat such an application as having been "initially submitted" as soon as it is received, whereas an applicant who filed precisely the same substantive information without the cross-references would not be deemed to have "initially submitted" its application until the filing of its "Administrative NADA"—which cannot occur until after the FDA completes months or years of review.

The FDA gives no reason to think that Congress intended for valuable patent rights to turn on whether a sponsor invoked a particular label in its submissions to the FDA. To the contrary, Congress 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. But all of the period between submission of the last technical section and submission of an "Administrative NADA" is spent "awaiting" the FDA's approval. In fact, in this respect a phased-review applicant that has submitted its last technical section is in exactly the same position as a traditional-review applicant that has submitted its application. By depriving phased-review applicants of full compensation for

subsequent delays, the FDA's "single submission" requirement improperly frustrates congressional purpose and must be set aside. *See Shays v. FEC*, 528 F.3d 914, 925 (D.C. Cir. 2008); *see also* Wyeth Br. 40.[14]

Given the evident flaws in the FDA's "single submission" argument, it is perhaps unsurprising that this position was never articulated during the administrative proceedings. *See* JA166-170 (initial decision); JA228-232 (decision denying reconsideration). But this failure provides yet another reason to reject this argument. It is well settled that "an agency's action must be upheld, if at all, on the basis articulated by the agency itself" and that a court thus "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).

C. If Necessary, This Court Should Remand To The FDA To Allow The Agency To Apply The Correct Interpretation Of The Statute In The First Instance

For the foregoing reasons, the last date on which an application can plausibly be deemed "initially submitted" is the date on which the applicant

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[14] The FDA asserts that it is "[i]mportant[]" that "Wyeth was always aware that it could have submitted a traditional NADA … at any time during the phased review process." FDA Br. 35. But Wyeth had no reason to believe that the failure to take this otherwise pointless step would result in a dramatic loss of its patent rights. As explained above, *see supra* p.14 & n.10, the FDA had not even hinted at its eventual interpretation of the phrase "initially submitted" when Wyeth submitted the filings at issue here.

submits the final required element of an application as defined by § 360b(b) and § 514.1(b). Furthermore, the agency's own guidance documents make clear that a phased-review applicant must submit the final required element when it submits its last technical section for review. *See supra* pp.14-16.

The FDA suggests, however, that in this case it did not have "all the information required by statute and regulation" when Wyeth filed its last technical section. FDA Br. 34. The agency's only support for this claim is its observation that Wyeth continued to submit additional information until shortly before it filed its "Administrative NADA." *Id.* at 34-35. But the FDA never actually identifies any of these submissions as containing elements of an application required by § 360b(b) or § 514.1(b) that should have been submitted with Wyeth's technical sections. To the contrary, the only submission that the FDA discusses in any detail—the January 9, 1998 submission of a "protocol pertaining to [a] residue depletion study in pre-ruminating calves," *id.* at 34—was not relevant to Wyeth's application at all, much less required by the statute or regulation.[15]

[15] In the application at issue here, Wyeth sought—and the FDA granted—permission to market Cydectin for use in beef and non-lactating dairy cattle, but *not* for use in "pre-ruminating calves" (*i.e.*, veal calves). *See* 21 C.F.R. § 524.1451 (1999) (FDA listing providing that "[a] withdrawal period has not been established for [Cydectin] on preruminating calves" and stating that Cydectin was not for "use on calves to be processed for veal"); *see also* 63 Fed. Reg. 14,035 (1998) (FDA notice of the approval of NADA 141-099). The planned study described in the protocol cited by the FDA would thus have supported a future request for

Moreover, the mere fact that Wyeth continued to supplement and amend its application after the date on which it filed its last technical section does not establish that the application was not "initially submitted" on that date. To the contrary, the FDA's own brief elsewhere concedes that "minor amendments or changes to an application that has been 'initially submitted' to the agency do not 'reset' the clock for the beginning of the approval phase," even if those amendments or supplements are prerequisites for approval. FDA Br. 40.

The FDA implies that a "major" amendment would result in an application being deemed "initially submitted" on the date of the amendment rather than the original submission. *See* FDA Br. 31 (citing JA59). But the FDA never argues that any of Wyeth's post-filing submissions qualified as this sort of "major" amendment. More fundamentally, the FDA's proposed major/minor distinction is both novel and contrary to the statute. It is not clear that the FDA has ever before suggested that a major amendment prevents an application from being "initially submitted" within the meaning of § 156(g) at an earlier date. To the contrary, in one case, the agency found a marketing application for a medical device to be "initially submitted" for patent-term-extension purposes even though the agency "later determined that additional studies were required and issued a major

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permission to market Cydectin for use in pre-ruminating calves, not the application that the FDA approved just days after the protocol was submitted.

deficiency letter," prompting the sponsor to resubmit an amended application. 65 Fed. Reg. 31,010 (2000). Similarly, in another case, the FDA found a marketing application for a human drug "initially submitted" even though the agency "declared [that application] nonapprovable" and the applicant then submitted a new application. 50 Fed. Reg. 19,809 (1985).[16]

The approach reflected in these decisions is correct. The FDA will accept a traditional application or technical section for review only if it first determines that the submission contains all required elements. JA59, 66. The decisions cited above demonstrate that if a traditional application passes this initial screen, it is deemed "initially submitted" even if the FDA later finds that major changes are necessary. This is the only result consistent with the legislative history: In explaining that an application is "initially submitted" even if the FDA later "decide[s] it needs additional information or other changes in the application," H.R. Rep. No. 98-857, pt. 1, at 44, the House Report gave no indication that only "minor" additions and changes were permitted.

[16] The guidance document on which the FDA relies suggests that the major/minor distinction relates not to the date on which an application is deemed "initially submitted" for patent-term-extension purposes, but rather to the date on which the application is deemed to be submitted for purposes of the FDA's obligation to respond to an application within 180 days after filing pursuant to 21 U.S.C. § 360b(c)(2)(C). *See* JA59.

Because the FDA requires phased-review applicants to include all of the necessary components of an application in their technical sections, and because it generally will not accept a technical section for review unless it addresses all required elements, JA65, a phased-review application should likewise be deemed "initially submitted" as soon as the applicant submits (and the agency accepts) the last technical section. Therefore, Wyeth's subsequent submissions to the FDA are relevant only to the extent that they shed light on the date that Wyeth submitted its last technical section for agency review.

The FDA's brief does not address this issue at all. But while reviewing its submissions in the course of preparing this reply, Wyeth determined that its final technical section, Environmental Safety, was submitted in three modules pursuant to a special arrangement negotiated with the FDA. In light of these circumstances, it would be appropriate for this Court to remand to the FDA to allow the agency to consider whether Wyeth's Environmental Safety technical section was submitted on June 13, 1997—the date on which Wyeth submitted the last module—rather than on August 14, 1996, as has previously been understood in this litigation. This issue should be addressed on remand because the relevant facts are outside the administrative record filed in the district court.

* * *

For the foregoing reasons, this Court should hold that, at the very latest, an application is "initially submitted" on the date that the applicant submits its last technical section. In this case, however, if the Court accepts this interpretation of the statute, it is appropriate to remand to the FDA to allow the agency to apply the proper legal standard in the first instance.

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 because the agency has failed to provide an adequate explanation for its differing interpretation of identical statutory language in the context of rolling review of certain human drugs, known as "fast track" approval. Wyeth Br. 52-55. The FDA does not dispute that such unexplained inconsistency would be arbitrary and capricious. Instead, it denies that there is any inconsistency to explain. But that contention cannot withstand scrutiny.

Wyeth's opening brief demonstrated that the FDA deems a fast-track application "initially submitted" as soon as "the final module of the marketing application [i]s submitted," 71 Fed. Reg. 54,996, 54,997 (2006)—a point parallel to the date on which a phased-review applicant submits its last technical section. Wyeth Br. 32-33, 52-53. In response, the FDA asserts that Wyeth is mistaken: According to the FDA, the agency "does not begin the approval phase … until the

sponsor has informed FDA that the application is complete."[17] The FDA maintains that this is consistent with its treatment of phased review of animal drug applications because "the sponsor's notice that the application is complete serves as the equivalent of an administrative NADA" in the phased-review context. FDA Br. 49.

The FDA's actual regulatory review period determinations for fast-track drugs, however, make clear that the agency has consistently considered the "initially submitted date" to be the date on which "the final module of the marketing application was submitted." 71 Fed. Reg. 57,546, 57,547 (2006); *see also, e.g.*, 73 Fed. Reg. 27,838 (2008) (same); 71 Fed. Reg. 54,998 (2006) (same); 71 Fed. Reg. 54,996 (2006) (same). These determinations do not even mention the "complete notice" that the FDA's brief now claims marks the date on which a fast-track application is "initially submitted."

Moreover, even if fast track applicants do submit such a notice along with the final module of their marketing applications, that notice is not analogous to an "Administrative NADA." A phased-review applicant does not submit its "Administrative NADA"—and thus, on the FDA's view, its approval phase cannot

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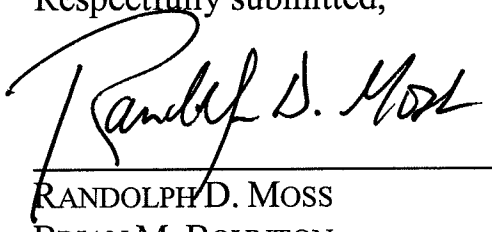
[17] FDA Br. 49 (citing FDA, *Guidance for Industry: Fast Track Drug Development Programs—Designation, Development, and Application Review* 13 (2006), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079736.pdf).

begin—until after the FDA has reviewed all of the modules of its application. Even in its brief, the agency gives no justification for its differing treatment of fast-track applicants, who can apparently submit their complete notices as soon as they file the last modules of their applications. This still-unexplained inconsistency renders the FDA's decision arbitrary and capricious.

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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CERTIFICATE OF SERVICE

I hereby certify that on this 9th day of December, 2009, I caused two copies of the foregoing Reply Brief for Appellants to be served via overnight courier on:

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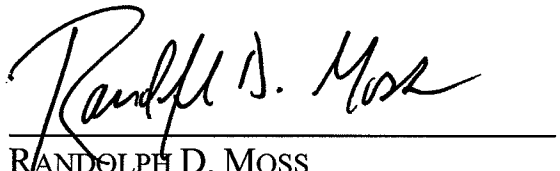

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Pursuant to Federal Rule of Appellate Procedure 32(a)(7)(C), the undersigned hereby certifies that this brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B)(ii).

1. Exclusive of the exempted portions of the brief, as provided in Federal Rule of Appellate Procedure 32(a)(7)(B), the brief contains 6,977 words.

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