UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

BOEHRINGER INGELHEIM PHARMA GmbH & CO. KG, *et al.*,	)	
Plaintiffs,	)	
v.	)	Case No: 1:15-cv-00656
UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,	)	
Defendants.	)	

DEFENDANTS' MOTION TO DISMISS, OR IN THE ALTERNATIVE CROSS-MOTION FOR SUMMARY JUDGMENT, AND OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

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INTRODUCTION

Congress has provided for the extension of a pharmaceutical product's patent to make up for the time that it took the United States Food and Drug Administration ("FDA") to review the product's new drug application ("NDA"). The extension is tied to the date on which an "application [that] was approved" was "initially submitted"; "initially submitted" is a term of art which refers to the date a sufficiently complete and reviewable application is provided to FDA.[1] In this case, FDA refused to file Plaintiffs' first incomplete and insufficient application and refunded 75% of their application fee, and Plaintiffs then provided a sufficiently complete application that was approved. Nonetheless, they now contend that they should receive a longer patent term extension based on the date they provided their first incomplete and insufficient application, rather than the date they provided the further, sufficiently complete application that was ultimately approved.

To obtain this longer patent term extension, Plaintiffs Boehringer Ingelheim Pharma GmbH & CO. KG and Boehringer Ingelheim Pharmaceuticals, Inc. (collectively, "Boehringer") brought this lawsuit challenging FDA's determination of the regulatory review period, because its components are used to calculate the patent-term extension period. The regulatory review period "consists of the sum of the lengths of a testing phase and an approval phase." 21 C.F.R. § 60.22. *See also* 35 U.S.C. § 156(g)(1)(B) (defining "regulatory review period" for new drugs). Subject to certain exceptions not at issue here, the patent term is extended for half the testing-phase time, plus the full duration of the approval phase. 35 U.S.C. § 156(c)(2). This structure gives sponsors an incentive to complete the testing phase promptly, so that the approval phase

[1] Due to the contested term "initially submitted," this brief generally refers to material as being "provided" to FDA, to avoid any confusion or overtones that might be caused by using the word "submitted."

begins sooner. The dispute in this case is about how to categorize the first 125 days after Boehringer provided an incomplete application on December 15, 2009. Boehringer had begun providing data, and FDA had begun reviewing it, months before that date, as early as September 2009. But FDA advised Boehringer on February 12, 2010, 59 days after what Boehringer asserted to be its first, complete, application, that the application did not include sufficient information for review of a full application, and refunded 75% of Boehringer's application fee. Boehringer did not dispute FDA's determination, and did not ask FDA to file the application over protest and review it as filed. Two months later, on April 19, 2010—125 days after its December 15 incomplete application—Boehringer provided a new application with revised data; this is the application that FDA ultimately approved. In response to Boehringer's patent-term extension request, FDA calculated the testing phase as 2,449 days (half of which is excluded from the extension period), and the approval phase as 184 days. Without addressing other elements that the United States Patent and Trademark Office ("USPTO") is charged with calculating, FDA's calculation of these two phases would yield a total patent-term extension of 1,409 days.[2] Boehringer challenges FDA's calculations as arbitrary and capricious, because, in its view, the contested 125 days should be counted as part of the approval phase, rather than the testing phase. Again without addressing other elements that USPTO is charged with calculating, adding 125 days to the approval phase, and subtracting those 125 days from the testing phase, would add 62 days to the patent-term extension, for a total of 1,471 days.[3] Boehringer's argument contravenes

[2] Calculated in accordance with 35 U.S.C. § 156(c), FDA's determinations would yield a total regulatory review period, minus ½ of the testing phase, of 2,633 - 1/2 (2,449) = 1,409 days.

[3] Calculated in accordance with 35 U.S.C. 156(c), the dates Boehringer is currently asserting would yield a total regulatory review period, minus ½ of the testing phase, of 2,633 - 1/2 (2,324) = 1,471 days. These figures come from Boehringer's complaint, Compl. ¶ 53; in its

the statute's meaning and purpose, and must give way to FDA's reasonable interpretation of the governing provision.

For human drugs, the testing phase for a new drug application ("NDA") begins when an exemption to permit clinical investigations becomes effective and continues until the approval phase begins. *See* 35 U.S.C. § 156(g)(1)(B)(i); 21 C.F.R. § 60.22(a)(1). The approval phase for such drugs begins on "the date the application was initially submitted for the approved product" pursuant to 21 U.S.C. § 355(b) and continues until FDA grants permission to market the product. *See* 35 U.S.C. § 156(g)(1)(B)(ii); 21 C.F.R. § 60.22(a)(2). An NDA must include all the sections, or modules, required by 21 U.S.C. § 355(b) and 21 C.F.R. § 314.50, and 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) (emphases added). Here, Boehringer provided an application with sufficient information on April 19, 2010. Therefore, FDA determined that April 19, 2010 was the date Boehringer "initially submitted" the application that was ultimately approved. Although Boehringer provided modules of the application on a rolling basis starting on September 17, 2009, not all required parts were provided and reviewable until it sent in its further application on April 19, 2010.

Generally, priority review shortens the targeted review time[4] for a drug that may provide a significant improvement over marketed therapies. *See* AR 8191 (Guidance for Industry: Fast Track Drug Development Programs–Designation, Development, and Application Review).

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request for extension, it calculated the approval phase as 2,322 days and the approval phase as 308 days. Administrative Record ("AR") 5111.

[4] Under the Prescription Drug User Fee Act ("PDUFA"), the pharmaceutical industry gives FDA funding to help the agency conduct reviews for new products within targeted time frames. *See* AR 8217 (Center for Drug Evaluation and Research, 2011 Novel New Drugs (January 2012)).

Priority review often enables a drug sponsor to market its product sooner than the traditional review process. But there is a trade-off. Priority review usually leads to a shorter patent term extension because a shorter approval phase typically reduces the regulatory review period. Yet here, Boehringer wants it all. In order to obtain an earlier approval, Boehringer requested and enjoyed the benefits of priority and rolling review (and a shorter approval phase); but in order to obtain a longer patent term extension, Boehringer now seeks a longer approval–phase than the statute provides. In an earlier lawsuit, similarly challenging FDA's determination of the date a New Animal Drug Application was "initially submitted" in a case where it had conducted phased review, the Federal Circuit rejected a similar request for an overly generous patent term extension, holding that the statutory term "initial submission" was ambiguous, and that FDA's interpretation was reasonable. *Wyeth Holdings Corp. v. Sebelius*, 603 F.3d 1291, 1297 (Fed. Cir. 2010).[5] The same is true here, and this Court should likewise reject Boehringer's attempt to unduly extend its patent term.

Accordingly, for the reasons set forth more fully below, this Court should grant Defendants' Motion to Dismiss or, in the Alternative, for Summary Judgment and deny Plaintiffs' Motion for Summary Judgment.

STATUTORY AND REGULATORY BACKGROUND

Pharmaceutical companies seeking to market new "innovator" or "pioneer" drugs must file an NDA to obtain FDA approval. 21 U.S.C. § 355(a), (b)(1). The NDA must include

[5] Any appeals from this Court's decision will be made to the Federal Circuit Court of Appeals, and that Court's decisions therefore "provide[] controlling precedent for this case." *Abraxis Bioscience, LLC v. Kappos*, 10 F. Supp. 3d 53, 88 n.14 (D.D.C. 2014) (patent-term adjustment case; citing 28 U.S.C. §§ 1338(a), 1295(a)(1); *Panduit Corp. v. All States Plastic Mfg. Co.*, 744 F.2d 1564, 1573 (Fed. Cir. 1984), *overruled on other grounds by Richardson–Merrell, Inc. v. Koller*, 472 U.S. 424 (1985)), *vacated in part by agreement sub nom. Abraxis Bioscience, LLC v. Lee*, 563 F. App'x 786 (Fed. Cir. 2014).

extensive scientific data demonstrating the safety and effectiveness of the drug. 21 U.S.C. § 355(b). Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), the following specific sections or modules must be included in an application:

> (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in 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 as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, and (G) any assessments required under section 355c of this title.

21 U.S.C. § 355(b)(1); *see also* 21 C.F.R. § 314.50 (specifying requirements). To submit an application that complies with FDA regulations, a new drug sponsor must provide, among other things, a "[c]linical data section." 21 C.F.R. § 314.50(d)(5). This section must include "a description and analysis of each controlled clinical study pertinent to a proposed use of the drug, including the protocol and a description of the statistical analyses used to evaluate the study." 21 C.F.R. § 314.50(d)(5)(ii). Furthermore, "[e]ach technical section is required to contain data and information in sufficient detail to permit the agency to make a knowledgeable judgment about whether to approve the application or whether grounds exist under section 505(d) of the act [21 U.S.C. § 355(d)] to refuse to approve the application." 21 C.F.R. § 314.50(d).

Once it receives an application, FDA has 60 days to determine whether it may be "filed." 21 C.F.R. 314.101(a)(1). FDA's "filing" an application means that "FDA has made a threshold determination that the *application* is *sufficiently complete* to permit a substantive review." *Id*. (emphases added). In other words, the date of "filing" is the date, up to 60 days after an application is provided, that FDA determines that it is sufficiently complete for review—the same criteria that govern whether an application with the required elements was "initially submitted" under 21 U.S.C. § 355(b)(1). *See* 21 C.F.R. § 60.22 (an NDA is "*initially submitted*

on the date it contains *sufficient* information to allow FDA to commence *review* of the *application*.") (emphasis added).

If FDA does accept an application for filing, it notifies the sponsor in writing. 21 C.F.R. 314.101(a)(2). If FDA determines that an application is *not* sufficiently complete to permit substantive review, it sends the sponsor a "Refusal to File" letter, stating the reason for the refusal. 21 C.F.R. § 314.101(a)(2); *see also* AR 5517–23 (New Drug Evaluation Guidance Document: Refusal to File (July 12, 1993)). If FDA refuses to file an application under 21 C.F.R. § 314.101(d), the sponsor may within 30 days request an informal conference; after the informal conference, the sponsor may renew its request for filing, and FDA "will file the application over protest, notify the applicant in writing, and review it as filed." 21 C.F.R. § 314.101(a)(3).

After FDA accepts an application for filing (or files the application over protest) and completes its review, it will approve an application unless one or more of the grounds for refusing to approve an application are present, none of which are at issue here. *See* 21 U.S.C. § 355(c), (d).

FDA's review of an application may use a form of expedited review, such as priority review. FDA "categorizes some new drugs . . . as 'priority drugs' and seeks to accelerate their availability." *Abigail Alliance for Better Access to Dev. Drugs v. von Eschenbach*, 495 F.3d 695, 728 n.4 (D.C. Cir. 2007). New drugs "are eligible for priority review if they provide a significant improvement compared to marketed products in the treatment, diagnosis, or prevention of a disease." AR 8192 (Guidance for Industry: Fast Track Drug Development Programs–Designation, Development, and Application Review). Priority review generally shortens the

target review timeframe from ten to six months. *See* AR 8216 (Center for Drug Evaluation and Research, 2011 Novel New Drugs (January 2012)).

The Drug Price Competition and Patent Term Restoration Act of 1984 (frequently referred to as the "Hatch-Waxman Amendments") provides for an extension of a patent's term to recover some of the time spent in regulatory review. *See* Pub. L. No. 98-417, 98 Stat. 1585 (1984). As explained above, a "regulatory review period" consists of a "testing phase" and an "approval phase." *See* 35 U.S.C. § 156(g)(1)(B); 21 C.F.R. § 60.22(a). For human drugs, the testing phase is "the period beginning on the date an exemption under subsection (i) of section 505 [codified at 21 U.S.C. § 355] . . . became effective for the approved product and ending on the date an application was initially submitted for such drug product under section . . . 505." 35 U.S.C. § 156(g)(1)(B)(i). The approval phase is "the period beginning on the date the application was initially submitted for the approved product under . . . subsection (b) of section 505 [codified at 21 U.S.C. § 355] . . . and ending on the date such application was approved under such section." *Id.* § 156(g)(1)(B)(ii). Patent terms may be extended by half of the testing phase, plus the full length of the approval phase. *See* 35 U.S.C. § 156(c)(2).[6]

USPTO determines patent term extensions, based on certain determinations from FDA. *See Astra v. Lehman*, 71 F.3d 1578, 1580–81 (Fed. Cir. 1995). Specifically, USPTO receives an application for a patent extension, calculates the extension based on the regulatory review period,

[6] Although not implicated here, the statute imposes additional restrictions on any patent term extension. First, the patent term extension must be reduced by the amount of time during the regulatory review period that an applicant "did not act with due diligence." 35 U.S.C. § 156(c)(1). Second, the period of time remaining in the patent term after marketing approval and with the patent term extension may not exceed fourteen years. *Id*. § 156(c)(3). Third, the patent term extension itself "may not exceed five years." *Id*. § 156(g)(6)(A). Fourth, the patent term extension does not include any regulatory review period that occurs before the patent is issued. *Id.* § 156(c).

and issues the certificate of extension. *Id.*; *see also* 35 U.S.C. § 156(d)(1). FDA is charged by statute with determining the actual length of the regulatory review period (including its component parts, the testing phase and the approval phase) and notifying USPTO of such. *Astra*, 71 F.3d at 1580–81; 35 U.S.C. § 156(d)(2)(A).

STATEMENT OF FACTS

Boehringer holds NDA 22-512 for Pradaxa (dabigatran etexilate mesylate), the active ingredient of which is patented in United States Patent Number 6,087,380. FDA granted Boehringer an exemption to begin conducting clinical trials pursuant to 21 U.S.C. § 355(*i*) on August 6, 2003. *See e.g.*, AR 5404 (Letter from Jane A. Axelrad, FDA to Hon. David J. Kappos, USPTO (4/18/2012)).[7] This is when Pradaxa's "testing phase" began for purposes of determining the patent term extension.

At a meeting between Boehringer and FDA on August 17, 2009, Boehringer stated that it was planning to request priority review for the Pradaxa NDA, and the agency explained it was likely Boehringer would receive it. AR 5637 (RE-LY Results Meeting Minutes). The parties also discussed rolling review, meaning the agency might consider reviewing portions of the NDA before the application was complete. *Id*. FDA emphasized that "[a]t the time the last module of the NDA is received, the decision will be made regarding a priority review, and the review clock will start." *Id.*

Months before December 15, 2009, Boehringer began providing information to FDA as part of a rolling review process. Boehringer acknowledged that these were "pre-submission[s],"

[7] Boehringer's patent-extension request mistakenly identified this date as August 7, 2003, which would have shortened the testing phase by a day, to its detriment. AR 5252 (77 Fed. Reg. 26289). FDA observed the error and employed the correct date of August 6, 2003 in its determination to USPTO. *Id*.

and that "[t]he final documents to complete the original new drug application for dabigatran etexilate [Pradaxa]" were still needed. *See* AR 5645–46 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (9/17/2009)). *See also* AR 5682–83 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (9/30/2009)); AR 5685 (Letter from Jessica Collis, Boehringer to Norman Stockbridge, FDA (9/30/2009)); AR 5699 (Letter from Jessica Collis, Boehringer to Norman Stockbridge, FDA (10/13/2009)); AR 5705 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (10/27/2009)); AR 5707 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (11/4/2009)); AR 5711 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (11/9/2009)); AR 5716–17 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (11/13/2009)); AR 5735 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (11/30/2009)); AR 5752 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (12/08/2009)). Boehringer provided additional documents on December 15, 2009, which, it said, completed its application. *See* AR 5769–70 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (12/15/2009)) ("Boehringer . . . is hereby providing the eleventh submission of its 505(b)(1) New Drug Application . . . . This submission completes the New Drug Application for dabigatran etexilate and provides the formal request for priority review.").

In February 2010, however, FDA sent Boehringer a "Refusal to File" letter, informing it that the clinical data it had provided contained too many errors and could not be reviewed. *See* AR 5962 (Letter from Norman Stockbridge, FDA to Michelle Kliewer, Boehringer (2/12/2010)) ("We recognize that that there may be occasional inaccuracies in a large trial database; however, the frequency of errors in the data sets impedes our ability to perform an adequate review, and undermines our confidence in your data."). Boehringer agreed that "[w]hile statistical sampling

of the RE-LY database supported the fact that the overall pre-specified quality standards for the primary and secondary endpoint data were met, the frequency of errors in [a particular] data-set was too high, thereby undermining confidence in the data and impeding FDA's ability to perform an adequate regulatory review of the clinical data." AR 6084 (E-mail from Michelle Kliewer, Boehringer to Alison Blaus, FDA (4/19/2010)). Boehringer also confirmed that it had not provided the datasets used to create a so-called "time to censoring" analysis. AR 5985-86 (February 18, 2010 Meeting Minutes) ("Post Meeting Note: The sponsor acknowledged that the censoring analysis datasets had not been submitted to the NDA. The datasets were submitted to the NDA on 24 February 2010.").[8] Therefore, FDA was not able to sufficiently review all of the modules required in an application. *See also* 21 C.F.R. § 314.50(d)(5). In the "Refusal to File" letter dated February 12, 2010, FDA notified Boehringer that the December 15, 2009 application was "not sufficiently complete to permit a substantive review" and that FDA was therefore "refusing to file this application under 21 CFR 314.101(d)." AR 5961-5962 (Letter from Norman Stockbridge, FDA to Michelle Kliewer, Boehringer).

Boehringer appeared to understand at the time that its initial application of December 15, 2009 was not complete. Boehringer accepted a refund of 75% of the fees paid for the incomplete application. *See e.g.*, AR 5962 (Letter from Norman Stockbridge, FDA to Michelle Kliewer, Boehringer (2/12/2010)); AR 5624–25 (Email from Beverly Friedman, FDA to Marie Casseus, FDA (3/4/2010)); AR 5630–31 (NDA 22-512 Payment and Receipts). Nor did Boehringer ask FDA to "file" its incomplete December 15, 2009 application over protest, as permitted when, as

[8] Time to censoring analysis calculates how long a particular subject was contributing data to the clinical trial. For example, if a subject is randomized in a clinical trial for 5 days and then dies, the subject's data are "censored" at that point and the subject contributed 5 days. The censor point is different for each subject, and this dataset is used in order to analyze the overall trial results.

here, FDA refuses to file an application under 21 C.F.R. § 314.101(d). *See* 21 C.F.R. § 314.101(a)(3) (providing that when FDA refuses to file an application under § 314.101(d) and the sponsor asks FDA to file the application over protest, FDA will indeed file the application as requested—but will then "review it *as filed*") (emphasis added). Moreover, when Boehringer submitted updated data on April 19, 2010, Boehringer stated that "[t]his submission provides the final documents to *complete* the original new drug application for dabigatran etexilate (NDA 22-512) [Pradaxa]." AR 6082 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (4/19/2010)) (emphasis added). Boehringer also sent in another user fee for the application. *See* AR 5629 (Letter from Marilyn Maxwell, Boehringer to FDA (4/13/2010)). By regulation, FDA is required to determine within 60 days whether to "file" an application. 21 C.F.R. § 314.101(a). (This timing requirement is what led to FDA's February 12, 2010 "Refusal to File" letter, following Boehringer's insufficient December 15, 2009 application, 59 days before.) After "complet[ing] [its] filing review," FDA found the April 19, 2010 application (with additional "submissions" "dated April 20, 28, and 30, May 3, 4, 5, 6, 7, 10, 13, 14, 17, 21, 24, 26, 27, and 28, and June 1, 2010") to be "sufficiently complete to permit a substantive review. Therefore this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a)." *See* AR 6247 (Letter from Norman Stockbridge, FDA to Michelle Kliewer, Boehringer (6/10/2010)) ("Priority Review Designation" letter). Thus, there was no complete application to review until April 19, 2010. And that is the "initial submission" date.

On October 19, 2010, FDA approved the application. *See, e.g.*, AR 8148–86 (Letter from Ellis Unger, FDA to Michelle Kliewer, Boehringer (10/19/2010)).

Thereafter, Boehringer submitted a request for a patent term extension, asserting that it was entitled to an extension of 1,469 days (one half of the 2,322-day testing phase it alleged at the time, plus all of the 308-day approval phase it alleged at the time). AR 5001, 5111-5113 (Application for Extension of Patent Term (December 13, 2010)).[9] FDA informed USPTO that Pradaxa had been subject to regulatory review. AR 5248 (Letter from Jane A. Axelrad, FDA to Hon. David J. Kappos, USPTO (4/25/2011). USPTO contacted FDA for its determination of the regulatory review period, AR 5249 (Letter from Mary C. Till, USPTO to Beverly Friedman, FDA (8/1/2011)), and FDA notified USPTO of its determination. AR 5250–51 (Letter from Jane A. Axelrad, FDA to Hon. David J. Kappos, USPTO (4/18/2012)); *see also* 21 C.F.R. § 60.20(b). FDA determined that the regulatory review period was 2,633 days, including 2,449 days during the testing phase and 184 days during the approval phase. AR 5250 (Letter from Jane A. Axelrad, FDA to Hon. David J. Kappos, USPTO (4/18/2012)). This calculation did not exclude one half of the testing phase. FDA also published its determination of the regulatory review period for Pradaxa in the Federal Register. AR 5252–53 (77 Fed. Reg. 26289).

Pursuant to 21 C.F.R. § 60.24(a), "[a]ny person may request a revision of the regulatory review period determination within 60 days after its initial publication in the Federal Register." Boehringer requested a revision by letter dated June 27, 2012. AR 5255–5273 (Letter from David M. Fox, Hogan Lovells to FDA re: Request for Revision of Regulatory Review Period PRADAXA® (6/27/2012)). FDA considered Boehringer's request, but determined that no revision was required. AR 5524–5532 (Letter from Jane A. Axelrad, FDA to David M. Fox, Hogan Lovells (12/24/2014)). In its response, FDA explained that "for the purposes of patent

[9] In the Complaint, ECF No. 1, ¶ 53, Boehringer currently alleges that it is entitled to an extension of 1,471 days (one-half of the 2,324-day testing phase it apparently now alleges, plus all of the 309-day approval phase it now alleges).

term extension, a marketing application is considered to be 'initially submitted' when the Agency has *all* the elements required by statute and regulation to make an approval decision." AR 5527.

Based on FDA's calculations of the testing phase and the approval phase, and without addressing other elements that USPTO is charged with calculating, the difference between the government's position and Boehringer's is 62 days' worth of additional patent term extension, *i.e.*, 1,409 days vs. 1,471 days. *See* page 2 *and* notes 2-3, *supra*.

LEGAL STANDARD

A motion to dismiss under Fed. R. Civ. P. 12(b)(6) challenges the legal sufficiency of a complaint. *Browning v. Clinton*, 292 F.3d 235, 242 (D.C. Cir. 2002). When reviewing a Rule 12(b)(6) motion, a court accepts as true all the plaintiff's well-pled factual allegations; however, courts "accept neither 'inferences drawn by plaintiffs if such inferences are unsupported by the facts set out in the complaint,' nor 'legal conclusions cast in the form of factual allegations.'" *Browning*, 292 F.3d at 242 (citations omitted). Dismissal is appropriate here as Boehringer's complaint is "legally insufficient to state claims upon which relief can be granted." *Trudeau v. FTC*, 456 F.3d 178, 191 (D.C. Cir. 2006).

Additionally, "[t]he district court may . . . examine matters of public record in ruling on a Rule 12(b)(6) motion, and when a district court is reviewing agency action—sitting as an appellate tribunal—the legal questions raised by a 12(b)(6) motion and a motion for summary judgment are the same." *Marshall Cnty. Health Care Auth. v. Shalala*, 988 F.2d 1221, 1222-23 (D.C. Cir. 1993). Moreover, "[t]he entire case on review is a question of law, and only a question of law." *Id.* at 1226. And due to the nature of APA review, the Court can decide this case on a motion to dismiss. *See id.* ("And because a court can fully resolve any purely legal question on a motion to dismiss, there is no inherent barrier to reaching the merits at the 12(b)(6) stage.").

Alternatively, because the facts necessary to resolve this case are not disputed, summary judgment for the government is warranted pursuant to Fed. R. Civ. P. 56(a). A court may grant summary judgment to a party where the "movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). But, the usual summary judgment standard under Fed. R. Civ. P. 56(c) does not apply in cases involving review of final agency action under the APA "because of the limited role of a court in reviewing the administrative record." *Coal. for Common Sense in Gov't Procurement v. United States*, 821 F. Supp. 2d 275, 280 (D.D.C. 2011). In such cases, "the agency resolves factual issues to arrive at a decision that is supported by the administrative record," and "[s]ummary judgment is the mechanism for deciding whether as a matter of law the agency action is supported by the administrative record and is otherwise consistent with the APA standard of review." *Id.*

Here, Boehringer challenges FDA's decision under sections 706(2)(A) and 706(2)(C) of the APA. 5 U.S.C. § 706(2)(A)&(C). Pursuant to 5 U.S.C. § 706(2)(A), an agency's administrative decision may be disturbed only if "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." This standard of review is very deferential to the government as "[t]he scope of review under the 'arbitrary and capricious' standard is narrow and a court is not to substitute its judgment for that of the agency." *Motor Vehicle Mfrs. Ass'n of the United States, Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983); *see also Hi-Tech Pharmacal Co. v. FDA*, 587 F. Supp. 2d 13, 18 (D.D.C. 2008) ("Agency actions are entitled to much deference, and the standard of review is narrow."). An agency action must be upheld if "rational, based on consideration of the relevant factors and within the scope of the authority delegated to the agency by the statute." *Motor Vehicle*, 463 U.S. 29 at 42.

Separately, under 5 U.S.C. § 706(2)(C), an agency action may be set aside if "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right." Courts have adopted a similar deferential standard of review for challenges under this provision. *See Wright v. Foreign Serv. Grievance Bd.*, 503 F. Supp. 2d 163, 172 (D.D.C. 2007) (noting the "deferential standard of review" for an APA case under 5 U.S.C. § 706(2)(C)).

Furthermore, in reviewing an agency's interpretation of a statute it administers, courts apply the familiar two-step analysis articulated in *Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837 (1984). First, a court must determine "whether Congress has directly spoken to the precise question at issue." *Id*. at 842; *see also Gilead Scis., Inc. v. Lee*, 778 F.3d 1341, 1349 (Fed. Cir. 2015). In other words, a court must determine "whether the statute unambiguously forbids the Agency's interpretation," *Barnhart v. Walton*, 535 U.S. 212, 218 (2002), and uses "traditional tools of statutory construction" to do so. *Timex V.I., Inc. v. United States*, 157 F.3d 879, 882 (Fed. Cir. 1998) (quoting *Chevron*, 467 U.S. at 843 n.9).

If the statute "is silent or ambiguous with respect to the specific issue," a court proceeds to the second prong of *Chevron*, under which "the question . . . is whether the agency's answer is based on a permissible construction of the statute." *Id.* at 837-38, 843; *Wilder v. Merit Sys. Prot. Bd.*, 675 F.3d 1319, 1322 (Fed. Cir. 2012); *Cnty. of L.A. v. Shalala*, 192 F.3d 1005, 1012–13 (D.C. Cir. 1999). Importantly, the agency's interpretation need not be the only one it could have adopted or the one a court would have adopted. It need only be permissible. *See Chevron*, 467 U.S. at 843–44 & n.11.

ARGUMENT

I. FDA's statutory interpretations are entitled to deference

A. FDA's interpretation is entitled to *Chevron* deference.

As explained above, at *Chevron* step one, this Court determines whether the statute "unambiguously forecloses the agency's interpretation, and therefore contains no gap for the agency to fill." *Nat'l Cable & Telecomms. Ass'n v. Brand X Internet Servs.*, 545 U.S. 967, 982–83 (2005). Here, as the Federal Circuit has found, the statutory terms are ambiguous: "the plain language does not clearly indicate when an application is initially submitted under 35 U.S.C. § 156(g)." *Wyeth*, 603 F.3d at 1297.

At *Chevron* step two, the Court determines whether FDA's interpretation is reasonable. Here, Congress specifically directed FDA to determine the regulatory review period. *See* 35 U.S.C. § 156(d)(2)(A). Therefore, "[a]t this stage of the *Chevron* analysis, judicial deference to an agency's construction of a statutory scheme is afforded considerable weight." *Gilead Scis.*, 778 F.3d at 1349; *see also Gonzales v. Oregon*, 546 U.S. 243, 244 (2006) (substantial deference applies when "Congress delegated authority to the agency generally to make rules carrying the force of law") (quoting *United States v. Mead Corp.*, 533 U.S. 218, 226–227 (2001)). A court must defer to "an agency's reasonable interpretation of a statute and must not substitute its own judgment for that of the agency even if the court might have preferred another interpretation and even if the agency's interpretation is not the only reasonable one." *Wheatland Tube Co. v. United States*, 495 F.3d 1355, 1360–61 (Fed. Cir. 2007); *see also Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1348 (Fed. Cir. 2003) ("FDA's interpretation of the statute is permissible and . . . therefore must be upheld.").

B. FDA's interpretation is reasonable.

Section 156(g)(B) provides that "the regulatory review period for a new drug" is "the sum of" both the testing phase and the approval phase. 35 U.S.C. § 156(g)(B). The testing phase is "the period beginning on the date an exemption under subsection (i) of section 505 [21 U.S.C. § 355] . . . became effective for the approved product and ending on the date an application was initially submitted for such drug product under section . . . 505." *Id.* § 156(g)(1)(B)(i). The approval phase is "the period beginning on the date the application was initially submitted for the approved product under . . . subsection (b) of section 505 [of the FDCA, codified at 21 U.S.C. § 355(b)] . . . and ending on the date such application was approved under such section." *Id.* § 156(g)(1)(B)(ii). Accordingly, what separates the testing phase from the approval phase is the date that "the [ultimately approved] application" was "initially submitted."

An "application" for purposes of this provision must be "submitted . . . under"—and thus contain the information required by—the cross-referenced subsection of the FDCA, namely, 21 U.S.C. § 355(b). *See also* 21 C.F.R. § 314.50 (providing further detail on required components of an application); 21 C.F.R. § 314.3 (defining "application" as "the application described under § 314.50, including all amendments and supplements to the application."). An application with inadequate sections that cannot be substantively reviewed is not enough. *See* 21 C.F.R. § 314.50(d) ("Each technical section is required to contain data and information in sufficient detail to permit the agency to make a knowledgeable judgment about whether to approve the application or whether grounds exist under section 505(d) of the act [21 U.S.C. § 355(d)] to refuse to approve the application."). In order words, to count as "the application . . . submitted

. . . under subsection (b) of section 505 [of the FDCA, codified at 21 U.S.C. § 355(b)]," "the application" must be sufficiently complete and capable of being reviewed.[10]

The legislative history provides further support for this interpretation:

> [F]or 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. 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."

AR 5562 (H. Rep. No. 98-857, part 1, June 21, 1984) (emphasis added).

Therefore, an "application" is "initially submitted" under 21 U.S.C. § 355(b) when the sponsor has provided FDA with all the elements required by Section 355(b) and the corresponding regulations to make an approval decision. Indeed, the House Report's use of the words "all information necessary" rather than "some information necessary" reflects Congress's intent that the approval phase commence when an application is sufficiently complete to permit FDA's substantive review of all required components of the application.

In *Wyeth Holdings Corp. v. Sebelius*, the Federal Circuit found that the statute is ambiguous: "the plain language does not clearly indicate when an application is initially submitted under 35 U.S.C. § 156(g)." 603 F.3d at 1297. *Wyeth* involved a new animal drug sponsor who requested a patent term extension and disputed FDA's regulatory review period determination. *Id.* at 1295. Because *Wyeth* involved animal drugs, rather than human drugs, the

[10] By sufficiently complete, FDA does not mean that no additional information will be necessary. Rather, sufficiently complete means that the application contains all required components, although minor changes and amendments might still be necessary. AR 5519 (CDER, New Drug Evaluation Guidance Document: Refusal to File (July 12, 1993)) ("Minor defects or omissions that could be repaired after the review commenced and that would not materially interfere with or delay review of the remainder of the application should not lead to RTF [Refusal to File].").

required components of an "application" were spelled out in 21 U.S.C. § 360b, rather than 21 U.S.C. § 355. As in this case, the central issue in *Wyeth* was when the new (animal) drug application was initially submitted (*i.e.*, sufficiently complete). *Wyeth* observed that that the "application," which is not defined in 35 U.S.C. § 156(g), means, for animal drugs, an application that contains all the required components of a new animal drug application under the FDCA (in that case, 21 U.S.C. § 360b(b)). *Id.* at 1293. Similarly, the "application" that is ultimately approved for a human drug must contain the information required by the FDCA (in this case, 21 U.S.C. § 355(b)), and FDA reasonably understands this as "the application" that must be "initially submitted." *See* 35 U.S.C. § 156(g)(1)(B).

Boehringer's attempts to distinguish *Wyeth* are unavailing. *See* Pl.'s Mem., ECF No. 23-1, at 16. As in this case, *Wyeth* involved FDA's reviewing the sections of an application as it received them. Boehringer argues that the dispute in *Wyeth* was the significance of "a single module [provided during] the *investigational* phase," and that the sponsor in that case could not "submit" an actual application until after FDA completed its review of all investigational modules. *Id*. That distinction is irrelevant: for both types of applications, FDA has reasonably concluded that "the application" is not "initially submitted" until it is sufficiently complete (by including the sections required by the FDCA and FDA regulations) and capable of substantive review. *Wyeth* even noted that in the human drug approval context, a complete application is needed to begin the approval phase. *Id.* at 1300. Here, as there, FDA's interpretation "reasonably resolves the ambiguity in applying the relevant statutes to a factual situation not fully foreseen or provided for by the Congress when it enacted the statutes or the FDA when it promulgated regulations." *Id*. (citations omitted).

C. Boehringer's interpretation is not supported by the text, legislative history, or purpose of the Hatch-Waxman Amendments.

Boehringer wrongly focuses on the words "initially submitted" rather than the phrase "the application . . . for the approved product . . . under . . . [21 U.S.C. § 355(b)]" as the critical statutory language in this case. *See* Pl.'s Mem., ECF No. 23-1, at 13 (discussing a dictionary definition of "initial"). The relevant question is *what* must be "initially submitted." Determining the date that "the application . . . for the approved product . . . under . . . [21 U.S.C. § 355(b)]" is "initially submitted" requires knowing what constitutes such an "application." As explained above, such an "application" must contain the information required by 21 U.S.C. § 355(b) and 21 C.F.R. § 314.50. Boehringer did not submit clinical data (which is required by FDA regulations) that was sufficiently reviewable until April 19, 2010. Therefore, Boehringer did not "initially submit[]" a sufficiently complete and reviewable application until April 19, 2010.

Boehringer mischaracterizes the deficiencies in the clinical data it provided with its first application. Although FDA's Refusal to File letter did note "transcription errors, transposition errors, and auditing errors," *see* Pl.'s Mem., ECF No. 23-1, at 6 (not mentioning that FDA found such errors for 5 out of 6 subjects in its initial analysis) (citing AR 5961 (Letter from Norman Stockbridge, FDA to Michelle Kliewer, Boehringer (2/12/2010)), the next page of the Refusal to File letter further explained that "the frequency of errors in the data sets *impedes our ability to perform an adequate review*, and *undermines our confidence* in your data." AR 5962 (Letter from Norman Stockbridge, FDA to Michelle Kliewer, Boehringer (2/12/2010)) (emphases added). Furthermore, Boehringer did not disagree with FDA's conclusions. Boehringer acknowledged that "the frequency of errors in a sample INR data-set was too high, thereby *undermining confidence in the data* and *impeding FDA's ability to perform an adequate regulatory review of the clinical data*." AR 6084 (emphases added). Boehringer did not assert at

the time (as it now does in litigation) that its application was in fact sufficiently complete to be reviewed. *Cf*. AR 6082 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (4/19/2010)) (cover letter for April 19, 2010 application) ("This submission provides the final documents *to complete* the original new drug application for dabigatran etexilate (NDA 22-512) [Pradaxa].") (emphasis added). Boehringer also did not, as it could have, ask FDA to file its December 19, 2009 application over protest, which would have resulted in FDA's reviewing that application "as filed." *See* 21 C.F.R. § 314.101(a)(3).

Boehringer cites to legislative history to argue that the problems with its clinical data and the deficiencies in its December 15, 2009 application were not very significant, merely required "additional information or other changes," and should not have altered the submission date. *See* Pl.'s Mem., ECF No. 23-1, at 14. As discussed above, Congress noted 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.'" AR 5562 (H. Rep. No. 98-857, part 1, June 21, 1984).[11] But the legislative history merely reflects the common understanding that an application would be "initially submitted" when it is sufficiently complete

[11] Priority review and rolling review did not exist when the Hatch-Waxman Amendments were passed. *See* New Drug, Antibiotic, and Biological Drug Product Regulations; Accelerated Approval, 57 Fed. Reg. 58942-01, 58946 (December 11, 1992) (codified at 21 C.F.R. Parts 314 and 601) ("Applications for products for serious or life-threatening illnesses that provide a meaningful therapeutic benefit over existing therapy will receive a priority rating and expedited review, even when not considered under the accelerated approval procedures."). After the Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, 106 Stat. 4491, was enacted, FDA developed a two-tiered system of review—standard and priority review. Thus, the legislative history should be considered in context. Congress did not contemplate a rolling review process. At the time the Hatch-Waxman Amendments were enacted, a sponsor submitted all the required components of an application *before* FDA began its review.

because it contains all required information, and that the initial submission date does not change if later minor amendments or changes are made. In this case, however, FDA's ability to review the clinical data that Boehringer first provided was impeded, and thus the application was missing a required component and not yet complete in December 2009. When Boehringer provided the required component with its new application on April 19, 2010, it was not simply providing "additional information or other changes." In Boehringer's own words, it "provide[d] the final documents to complete the original new drug application for dabigatran etexilate [PRADAXA] for the prevention of stroke and systemic embolism in patients with atrial fibrillation." AR 6082 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (4/19/2010)). And in FDA's "Priority Review Designation" letter of June 10, 2010 (within the 60-day limit to determine whether to "file" the April 19, 2010 application), FDA advised Boehringer that it had "completed [the agency's] filing review and . . . determined that your application is sufficiently complete to permit a substantive review." AR 6247. Boehringer did not avail itself of its right to have its December 15, 2009 application filed over protest and reviewed "as filed"; instead, it submitted a further application, sufficient for substantive review, on April 19, 2010 (with a new fee, after accepting a 75% refund of its original application fee).

The better comparison to this legislative history language is what happened after Boehringer provided the required application component on April 19, 2010. FDA requested, and Boehringer provided, "additional information or other changes to the application" that were relatively minor and did not alter the initial submission date. *See e.g.*, AR 6117–19 (proprietary name request); AR 7195–96 (providing information about drug product specifications).

Boehringer fares no better by pointing out that FDA continued to review its pre-submission materials after the February 12, 2010 Refusal to File letter. *See* Pl.'s Mem., ECF No.

23-1, at 6–7. It is undisputed that FDA reviewed information after Boehringer's first pre-submission in September 2009. *See id.* at 5 ("And as those portions came in, FDA started its review."). Yet, Boehringer makes no claim that the "initially submitted" date should be September 2009, because it makes no claim that it had provided an application sufficiently complete to allow review by that date. *See id*. Therefore, as conceded by Boehringer, FDA's beginning to review its pre-submission *material* did not mean that its *application* had been "initially submitted." Because FDA was already reviewing Boehringer's pre-submissions as part of its rolling review long before even Boehringer's asserted "initial submission" date of December 15, 2009, it would have made little sense for FDA to stop reviewing Boehringer's material (after the February 12, 2010 Refusal to File letter) just because, as in September 2009, Boehringer had yet to provide a sufficiently complete application.

Again, FDA's interpretation is consistent with what Boehringer acknowledged at the time. *See* AR 6082 (Letter from Michelle Kliewer, Boehringer to Norman Stockbridge, FDA (4/19/2010)) ("This submission provides the final documents to *complete* the original new drug application for dabigatran etexilate (NDA 22-512) [Pradaxa].") (emphasis added). Boehringer's attempts to rely on FDA's initial use of December 15, 2009 as the "date of application" and "date of receipt" in some correspondence, *see* Pl.'s Mem., ECF No. 23-1, at 5, before FDA had a chance to determine whether or not the application was sufficiently complete, fall flat.[12] To

[12] Indeed, in the correspondence in which FDA referred to December 15, 2009 as the "date of application" and "date of receipt," FDA stressed that it might notify Boehringer "that the application is not sufficiently complete to permit a substantive review." AR 5794. Furthermore, after Boehringer submitted its April 19, 2010 application, FDA sent Boehringer an "NDA Acknowledgment" letter listing the "date of application" and "date of receipt" as April 19, 2010. *See* AR 6096.

Similarly, Boehringer makes far too much of isolated FDA mentions of the word "submitted" and cognates. *See* Pl.'s Mem., ECF No. 23-1, at 15. An FDA employee's referring

determine the regulatory review period for patent term extension purposes, FDA retrospectively reviews the facts to determine the initially submitted date.

Boehringer makes one more failed attack on FDA's reasonable interpretation. Boehringer asserts that "Congress specifically rejected a standard based on whether a marketing application is 'filed' by FDA." Pl.'s Mem., ECF 23-1, at 3. Boehringer points to a snippet of legislative history: "'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." *Id.* at 14; *see also* AR 5562 (H. Rep. No. 98-857, part 1, June 21, 1984). That same legislative history more specifically defines the actual statutory language "initially submitted" as the point when "the applicant has made a deliberate effort to submit an application containing all information necessary for the agency review to begin." *Id.* Boehringer argues that this is somehow a lesser standard than the "filing" standard in 21 C.F.R. § 314.101(a)(1), and that Boehringer met this standard. Pl.'s Mem., ECF No. 23-1, at 14. Neither argument is correct.

As an initial matter, the legislative history distinguishes the *filing* date (within 60 days of receiving an application, FDA must "determine whether the application may be *filed*," 21 C.F.R. § 314.101(a)(1) (emphasis added)) from the *initially submitted* date. FDA likewise distinguishes these time-markers. As noted above, FDA has determined that the application was *initially submitted* on April 19, 2010, while it was *considered filed* as of 60 days later, on June 18, 2010.

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to December 15, 2009, as the date Boehringer's first, incomplete, application was "submitted," rather than as the date it was "provided," is not an FDA determination that the December 15 application was sufficiently complete to allow review—much less an FDA determination of the date that "the application . . . for the approved product" was "initially submitted" for patent term extension purposes. *See* 21 C.F.R. § 10.85(k) (statements of individual employees do not bind the agency).

"Initially submitted" refers to the date the agency *receives* a sufficiently complete and reviewable application, while "filing" refers to the date of FDA's determination, within 60 days of receipt, that the application *is* sufficiently complete to allow review. *See* 21 C.F.R. §§ 60.22(f), 314.101(a)(1). The fact that FDA makes the "filing" decision after the date an application is received does not mean that Congress contemplated allowing incomplete applications to start the approval phase. Indeed, if an application cannot be filed because it lacks "sufficient information to allow FDA to commence review of the *application*," 21 C.F.R. § 60.22(f) (emphasis added), it cannot be considered "initially submitted."

FDA's interpretation is also consistent with the underlying objectives of the Hatch-Waxman Amendments, and appropriately balances complex policy considerations involving patent term restoration and FDA's expedited review programs. *See Babbitt v. Sweet Home Chapter of Cmtys. for a Great Or.*, 515 U.S. 687, 708 (1995) ("When Congress has entrusted the Secretary with broad discretion, we are especially reluctant to substitute our views of wise policy for his."). The Hatch-Waxman Amendments provide for an extension of a patent's life based on time lost during the regulatory review period. Priority and rolling review, however, generally allow for a shorter and more efficient regulatory review period. When the time spent in regulatory review is reduced, due to priority or rolling review, the patent term extension would be similarly reduced because less time is lost in the regulatory review period.

Boehringer's interpretation would frustrate the purpose of the Hatch-Waxman Amendments, and the balance struck between the interests of innovator and generic drug manufacturers, by allowing sponsors to submit deficient and incomplete applications to prematurely start the approval phase and thus get a longer patent term extension. Boehringer asserts, without basis, that "applicants are unlikely to intentionally submit deficient applications

in the hopes that they will get a jump-start on the approval phase." Pl.'s Mem., ECF No. 23-1, at 18.

By contrast, FDA's long-standing interpretation of 35 U.S.C. § 156(g) advances the provision's legislative purpose while remaining faithful to its language. Here, as in *Wyeth*, FDA's interpretation "reasonably resolves the ambiguity in applying the relevant statutes to a factual situation not fully foreseen or provided for by the Congress," 603 F. 3d at 1300, and should be upheld.

II. FDA's interpretation is consistent with its regulations.

Section 60.22(a)(1) of Title 21 of the Code of Federal Regulations provides that the "[t]he testing phase begins on the date an exemption under section 505(i) of the [FDCA] becomes effective . . . for the approved human drug product and ends on the date a marketing application under . . . section 505 of the [FDCA] is initially submitted to FDA." Section 60.22(a)(2) of Title 21, Code of Federal Regulations, states that "[t]he approval phase begins on the date a marketing application under . . . section 505(b) of the [FDCA] is initially submitted to FDA . . . and ends on the date the application is approved." Additionally, 21 C.F.R. § 60.22(f) provides that a "marketing application" is "*initially submitted* on the date it contains sufficient information to allow FDA to commence review of the application." This regulation, like the statute (35 U.S.C. § 156(g)), refers to the submission of an *application*, not modules or sections of it.

And FDA regulations define an NDA as "the application described under § 314.50." 21 C.F.R. § 314.3. Section 314.50 of Title 21 of the Code of Federal Regulations details the components required to make an application. Therefore, to be an "application," the sponsor must have provided the information required by 21 C.F.R. § 314.50. *See also* 21 C.F.R. § 60.3(b)(12) ("Marketing application means an application for . . . [h]uman drug products submitted under

section 505(b) of the [FDCA].”). As explained above, the regulations also clarify that “[e]ach technical section is required to contain data and information in sufficient detail to permit the agency to make a knowledgeable judgment about whether to approve the application or whether grounds exist under section 505(d) of the act [21 U.S.C. § 355(d)] to refuse to approve the application.” 21 C.F.R. § 314.50(d).

Furthermore, FDA regulations also contemplate review of sections of an application, before the “initial submission” of the application as a whole. *See e.g.*, 21 C.F.R. § 314.50(d)(1)(iv) (“The applicant may, at its option, submit a complete chemistry, manufacturing, and controls section 90 to 120 days before the anticipated submission of the remainder of the application. FDA will review such early submissions as resources permit.”). Here, Boehringer did not provide a sufficiently complete NDA in a form that could be substantively reviewed until April 19, 2010. Although FDA reviewed pre-submissions, the application was not yet sufficiently complete (*i.e.*, the application did not contain sufficient information). Thus, the application was not initially submitted until April 19, 2010. Contrary to Boehringer’s assertions, FDA’s position is entirely consistent with and required by its regulations.

III. FDA’s long-standing and consistently-applied interpretation should be upheld.

FDA’s position in this case is not new. On the contrary, the agency has consistently maintained, for over two decades, that the approval phase begins when FDA receives an application that is sufficiently complete to be reviewed. *See e.g.*, AR 5574 (Letter from Stuart L. Nightingale, FDA to Peter O. Safir and Millicent C. Yim re: Request for Revision of Regulatory Review Period Determination for Lovenox® (7/14/1994)) (“FDA has determined that ‘sufficient information’ means all information and sections specified in 21 C.F.R. § 314.50. The standard

for filing embodies the same concept that an application must contain the information necessary for the agency to commence review of the entire application."); AR 8227 (Letter from Jane A. Axelrad, FDA to Milan M. Vinnola re: Request for Revision of Regulatory Review Period, Kepivance (3/20/2012)) ("Accordingly, we affirm our determination that the date the Kepivance application was 'initially submitted' for purposes of determining the end of the testing phase and the beginning of the approval phase is June 15, 2004, when the marketing application was complete (i.e., when it contained all the information necessary for the Agency to make an approval decision)."); AR 8236 (Letter from Jane A. Axelrad, FDA to Christopher N. Sipes re: Request for Revision of Regulatory Review Period, Zolinza (April 17, 2012)) ("It is FDA's position that, for the purposes of patent term extension, the approval phase begins when the marketing application is complete; in other words, a marketing application is considered to be 'initially submitted' when the Agency has *all* the elements required by statute and regulation to make an approval decision."). FDA's long-standing interpretation is entitled to deference. *See Smiley v. Citibank (South Dakota), N.A.*, 517 U.S. 735, 740 (1996) ("To be sure, agency interpretations that are of long standing come before us with a certain credential of reasonableness, since it is rare that error would long persist.").

FDA did not act arbitrarily and capriciously in its determination of the regulatory review period for Pradaxa, and Boehringer is mistaken to claim that FDA's determination here "is contrary to the agency's past precedent with regard to similarly situated applicants." Pl.'s Mem., ECF No. 23-1, at 21. Boehringer cites to FDA's regulatory review period determination for Tonocard Tablets. *Id.* But this case is readily distinguishable. In the Tonocard Tablet case, the non-approvable decision is not analogous to FDA's refuse-to-file decision for Pradaxa: the Tonocard application was "complete enough" for FDA to commence review and determine that it

was not approvable, *see* AR 5516 (50 Fed. Reg. 19,809), while for Pradaxa, the deficient module in the application meant that it was not yet at that stage.[13] *See* AR 5955 (Letter from Norman Stockbridge, FDA to Michelle Kliewer, Boehringer (2/12/2010)).

As FDA explained in its 1993 guidance, "[r]efusal to file an application must be distinguished from refusal to approve the application after full review (not approvable action). The former is, in general, based on omissions or inadequacies so severe as to render the application incomplete on its face." AR 5518 (New Drug Evaluation Guidance Document: Refusal to File (July 12, 1993)). Here, FDA has explained why Boehringer's submissions before April 19, 2010 did not create an application that was "complete enough" because the clinical data section's inadequacies impeded FDA's review. As a result, FDA could not make an approval decision until the application contained its required components.

Strong policy reasons also support FDA's position. FDA has appropriately balanced competing goals. As FDA explained in its January 27, 1994 response to Fox, Bennet & Turner,

> FDA finds that limited inquiries by the agency regarding information contained in an incomplete application do not constitute substantive review, and hence will not support a claim that an NDA was "initially submitted" for purposes of patent term extension. This decision reflects important policy considerations. Even an application lacking crucial information required by the statute, regulations, or FDA presubmission communications with the applicant, might contain information capable of some preliminary probing by the agency. If the agency's preliminary discussions with an applicant about material submitted prior to the submission of a complete application were determinative of the "initially submitted" date, applicants would have the incentive to submit deficient applications in order to shorten the testing phase of the regulatory review period. In addition, FDA could be forced to choose between doing business less efficiently (i.e., defer all inquiries regarding information in a submission even

[13] The legislative history explains that "[a]s long as the application was complete enough so that Agency *action* could be commenced, it would be considered to be "initially submitted." AR 5562 (H. Rep. No. 98-857, part 1, June 21, 1984) (emphasis added). It is reasonable to interpret this as meaning an application that is "complete enough" to allow a decision about approval.

> when resources are available to make such initial inquiries), or risk affecting patent rights inequitably. Therefore, FDA concludes that it would be a misreading of 21 C.F.R. 60.22(d) to deem an application "initially submitted" whenever the Agency makes limited inquiries regarding certain information in the submission.

AR 5512–13 (Letter from Stuart L. Nightingale, FDA to Terry Coleman and Mark E. Boulding, Fox, Bennett & Turner (1/27/1994)).

Here, Boehringer seeks to benefit from the efficiency of priority and rolling review while greatly expanding the approval phase. Interestingly, Boehringer wants its approval phase to have begun months before it would have begun under traditional review–before its application was sufficiently complete. Boehringer must accept that a shorter approval period is simply "the trade-off for choosing the more fluid review process." *Wyeth*, 603 F.3d at 1299. As "[w]hatever balance may have been struck" by the Hatch-Waxman Amendments between pioneer and generic drug manufacturers' interests "envisioned traditional review . . . " *Id.* at 1300.

Boehringer should not be rewarded for submitting an incomplete application with deficient clinical data in December 2009. Instead, this Court should uphold FDA's determination that "the application . . . for the approved product under . . . [21 U.S.C. § 355(b)]" was "initially submitted" on April 19, 2010.

CONCLUSION

As the Federal Circuit did in *Wyeth*, this Court should reject Boehringer's claims and deny Boehringer an approval date that is tied to an incomplete application that was not sufficient to allow review of all required components. For the foregoing reasons, this Court should grant the government's motion to dismiss, or in the alternative, motion for summary judgment. Plaintiffs' motion for summary judgment should be denied.

Respectfully submitted,

Dated: October 22, 2016

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