UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

BOEHRINGER INGELHEIM PHARMA GMBH & CO. KG, *et al.*,
Plaintiffs

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,
Defendants

Civil Action No. 15-656 (CKK)

MEMORANDUM OPINION
(July 6, 2016)

In this challenge to an action of the United States Food and Drug Administration ("FDA") under the Administrative Procedure Act, the underlying facts are complex, the related science even more so. But the legal issue before this Court is relatively narrow: the legal sufficiency of the FDA's interpretation of the statutory reference to "the date an application was initially submitted for such [approved] drug product" and the agency's implementation of that interpretation.[1] Before the Court are Plaintiffs' [23] Motion for Summary Judgment, and Defendants' [26] Motion to Dismiss, or in the Alternative Cross-Motion for Summary Judgment. Plaintiffs argue that the FDA's action violated the relevant statutory provisions, that the action violated the agency's own regulations, and the FDA acted arbitrarily and capriciously because this action was inconsistent with prior agency practice. Defendants respond that the agency's interpretation of the relevant statutory language is due deference, that its interpretation of that language was reasonable, that its action in this case was consistent with its regulations and the statutory language, and that it did not act arbitrarily or capriciously.

[1] In practical terms, what is at stake is approximately 62 additional days of a patent term extension.

Upon consideration of the pleadings,[2] the relevant legal authorities, and the record for purposes of this motion, the Court GRANTS Defendants' [26] Motion for Summary Judgment, DENIES Plaintiffs' [23] Motion for Summary Judgment, and DENIES AS MOOT Defendants' [26] Motion to Dismiss.[3] The Court concludes the agency's interpretation of the statutory language is due deference in the *Chevron* framework, that the interpretation is reasonable, that the agency reasonably applied that interpretation, and that the agency did not act arbitrarily or capriciously. The Court also concludes that Plaintiffs have identified no other legal shortcomings with the agency's application of that interpretation in this case. This case is dismissed in its entirety.

I. BACKGROUND

A. Statutory and Regulatory Framework

Under the Food, Drug, and Cosmetic Act, approval of the Food and Drug Administration ("FDA") is required before a new drug can be distributed in interstate commerce. *See AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1045 (Fed. Cir. 2010) (citing 21 U.S.C. § 355(a)). "To obtain approval for a new drug, an applicant may file a New Drug Application … that

[2] The Court's consideration has focused on the following documents:

- Pls.' Mot. for Summary Judgment ("Pls.' Mot."), ECF No. 23;
- Defs.' Mot. to Dismiss, or in the Alt. Cross-Mot. for Summary Judgment and Opp'n to Pls.' Mot. ("Defs.' Mot."), ECF No. 26;
- Pls.' Comb. Opp'n to Defs.' Mot. & Reply ("Pls.' Opp'n"), ECF No. 28; and
- Defs.' Reply in Support of their Mot. ("Defs.' Reply"), ECF No. 30.

The Court refers throughout this Memorandum Opinion only to materials in the redacted version of the Joint Appendix. In an exercise of its discretion, the Court finds that holding oral argument in this action would not be of assistance in rendering a decision. *See* LCvR 7(f).

[3] The Court concludes that it is best to resolve the issues presented under the framework of the cross-motions for summary judgment on the full record before the Court rather than on the basis of Defendants' motion to dismiss, presented in the alternative to its motion for summary judgment.

includes examples of the proposed label for the drug and clinical data demonstrating that the drug is safe and effective for use." *Id.* (citing 21 U.S.C. § 355(b)(1)(A), (b)(1)(F)). The statute requires that certain informational components be included in an application:

> Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe 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).

To compensate patent holders for time lost regarding the use of their patents while a drug is undergoing FDA review, Congress has provided for certain extensions of patent duration associated with the FDA approval process. Congress promulgated these provisions in 1984 through what are often described as the Hatch-Waxman Amendments or the Hatch-Waxman Act. *See* Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. 98-417, 98 Stat. 1585 (1984). The Hatch-Waxman Amendments provide for an extension of a patent's term to account for a portion of the time consumed by regulatory review before the FDA. *See id.* Under the statute, the "regulatory review period" for a new drug such as the one whose approval is at the center of this case consists of

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

35 U.S.C. § 156(g)(1)(B); *see Astra v. Lehman*, 71 F.3d 1578, 1579 (Fed. Cir. 1995). Only drug products submitted under section 505, codified at 21 U.S.C. § 355, are relevant to this case. In other words, the first phase of the "regulatory review period," which is commonly referred to as the testing phase, ends when "an application was initially submitted for such drug product"; the second phase of the "regulatory review period," known as the approval phase, begins on this same date and ends when the application is approved. For the reasons explained below, it is only the proper calculation of the "initially submitted date"—and thus the boundary between the testing and the approval phases—that is at issue in this case.

Subject to other exceptions not relevant here, the patent term extension is equal to *half* of the length of the testing period *plus* the *entire* length of the approval period. *See* 35 U.S.C. § 156(c) (explaining that the extension equals the regulatory review period with a reduction for half of the length of the period under section 156(g)(1)(B)(i), the testing period applicable in this case).[4] Under regulations promulgated by the FDA regarding the determination of a patent term extension, an application "is initially submitted on the date it contains sufficient information to allow FDA to commence review of the application." 21 C.F.R. § 60.22. Plaintiffs agree that this definition is consistent with Congress's intent in passing the Hatch-Waxman Amendments. Pls.' Mot. at 4.

To receive a patent term extension, a patent holder must submit a timely application to the Director of the United States Patent and Trademark Office. 35 U.S.C. § 156(d)(1); *see also*

[4] To understand how this formula is applied, take an example of a regulatory review period of 100 days. If the period is evenly divided with 50 days in a testing phase and 50 days in the approval phase, the patent term extension would be 75 days: half of the 50 testing days (25 days) plus 50 approval days. Similarly, a testing phase of 52 days and an approval phase of 48 days yields a patent term extension of 74 days: half of 52 days (26 days) plus 48 approval days. In other words, for each day shifted from the approval phase to the testing phase, the patent term extension is reduced by half a day.

Astra, 71 F.3d at 1580. For drugs such as the one at issue in this case, the Director of the Patent and Trademark Office refers the application to the Secretary of Health and Human Services who "determine[s] the applicable regulatory review period." 35 U.S.C. § 156(d)(2)(A)). The Secretary of Health and Human Services has the sole authority to determine the length of the regulatory review period and, concomitantly, the patent term extension. *Astra*, 73 F.3d at 1581. The Secretary of Health and Human Services must then communicate this information to the Patent and Trademark Office. 35 U.S.C. § 156(d)(2)(A). Under the applicable regulations, these responsibilities of the Secretary of Health and Human Services are delegated to the FDA. *See* 21 C.F.R. § 60.20; Patent Term Restoration Regulations, 53 Fed. Reg. 7,298, 7,298 (Mar. 7, 1988).

After the FDA determines the regulatory review period, it publishes that determination in the Federal Register. 21 C.F.R. § 60.20(c). "Any person may request a revision of the regulatory review period determination within 60 days after its initial publication in the Federal Register." *Id.* § 60.24(a). The FDA then considers such a request and makes a definitive determination of the regulatory review period.

B. Factual Background

Plaintiff Boehringer holds all rights in U.S. Patent No. 6,087,380 ("the '380 patent"), which covers the active ingredient in Pradaxa. On August 6, 2003, the FDA granted Boehringer an exemption under 21 U.S.C. § 355(i) to begin clinical trials on Pradaxa. *See* AR 5404; *see also* Determination of Regulatory Review Period for Purposes of Patent Extension; PRADAXA, 77 Fed. Reg. 26,289, 26,289 (May 3, 2012). There is no dispute that this date—August 6, 2003—marks the beginning of the testing phase in this case.

On August 17, 2009, the FDA officials participated in a meeting with representatives of Boehringer regarding the development of Pradaxa. AR 5636. Certain proposed drugs are eligible

for priority review by the FDA.[5] AR 8192. For drugs under priority review, the agency sets a target of approving a drug within six months rather than within 10 months. AR 8192. At the August 2009 meeting, Boehringer indicated that it intended to request priority review for the drug in development. AR 5637. In response, the FDA representatives indicated that they "believe[d] it likely" the application for Pradaxa would receive priority review if Boehringer requested one. *Id.* The FDA further indicated that its "ability to complete [its] review within six months is critically dependent on the quality of your application." *Id.* The agency further indicated that "[i]n order for us to complete our review of your [New Drug Application] in a timely fashion, we request that you submit each module as you complete it." *Id.* Finally, the agency indicated that, "[a]t the time the last module of the [New Drug Application] is received, the decision will be made regarding a priority review, and the review clock will start." *Id.*

In the aftermath of that meeting, Boehringer submitted portions of its applications on a rolling basis throughout the Fall of 2009, as agreed, with the first submission on September 17, AR 5645-46; the second and third submissions on September 30, AR 5682-83, 5685-86; the fourth submission on October 13, AR 5699-5700; the fifth on October 27, AR 5705-06; the sixth on November 4 and November 9, AR 5707-08[6], 5711-12; the seventh on November 13, AR 5716-17; the ninth on November 30, AR 5735-46; and the tenth on December 8, AR 5752-53. On December 15, 2009, Boehringer submitted its eleventh submission. AR 5770. In the letter

[5] *See* AR 8192 ("Products regulated by [the Center for Biologics Evaluation and Research] are eligible for priority review if they provide a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious or life-threatening disease."); *see also Abigail Alliance for Better Access to Dev. Drugs v. von Eschenbach*, 495 F.3d 695, 699 n.4 (D.C. Cir. 2007) ("The FDA categorizes some new drugs, including nearly all cancer drugs, as 'priority drugs' and seeks to accelerate their availability.").

[6] It appears that the seventh submission was mistakenly labeled as the sixth, resulting in two submissions labeled sixth, and that the eighth was mistakenly labeled as the seventh. These differences are immaterial to the issues presented in this case.

accompanying the eleventh submission, Boehringer represented that "[t]his submission provides the final documents to complete the original new drug application for dabigatran etexilate (NDA 22-512) for the prevention of stroke and systemic embolism in patients with atrial fibrillation." AR 5769. Through that letter, Boehringer also requested priority designation for its application. *Id.* On January 5, 2010, the FDA sent Boehringer a letter in response, acknowledging that it had received the application denominated as NDA 22-512 on December 15, 2009, and that the application was dated December 15, 2009.[7] AR 5794-96. That letter noted that, "[u]nless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on February 13, 2010 in accordance with 21 CFR 314.101(a)."[8] AR 5694.

On February 12, 2010, the agency sent Boehringer a follow-up letter stating that, "[a]fter a preliminary review, we find that your application is not sufficiently complete to *permit a substantive review*." AR 5961 (emphasis added). Therefore, the agency refused to file the application. *Id.* (citing 21 C.F.R. 314.101(d)). The agency explained why it deemed the application insufficient as follows:

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[7] Contrary to Plaintiff's position, the Court does not read any legal significance into the fact that the agency's letter noted that the application that was received on December 15, 2009, was dated that same day.

[8] The relevant regulations provide as follows:

> Within 60 days after FDA receives an application, the agency will determine whether the application may be filed. The filing of an application means that FDA has made a threshold determination that the application is sufficiently complete to permit a substantive review.

21 C.F.R. § 314.101(a)(1) (2009). If the agency does not "refuse to file" the application, the "date of filing will be the date 60 days after the date FDA received the application." *Id.* § 314.101(a)(2).

> In support of the proposed indication, you conducted a single phase 3 trial titled "Randomized Evaluation of Long term anticoagulant therapy comparing the efficacy and safety of two blinded doses of dabigatran etexilate with open label warfarin for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation: prospective, multi-centre, parallel-group, non-inferiority trial (RE-LY)." The primary objective of RE-LY was to demonstrate the efficacy and safety of dabigatran etexilate in subjects with non-valvular atrial fibrillation for the prevention of stroke and systemic embolism.
>
> We note that you claim an overall data error rate of 0.1% or less for primary outcome data and 0.25% or less for all other data. However, we found data errors in five out of six subjects in our initial analysis of your INR.xpt data. These errors are described in Tables 1 and 2. These errors include transcription errors, transposition errors, and auditing errors.
>
> [Data tables omitted]
>
> We note that you closed site 6; therefore, we do not comment on problems evident in the data from that site.
>
> 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.
>
> In recognition of the importance of this priority application, we proposed a rolling review. We will, of course, continue our review of parts of your application that are complete and reviewable, such as the chemistry and pharmacology toxicology sections. In addition, the clinical reviewers will work with you to evaluate further data integrity issues and to provide comment on your plans to respond to these issues. Please note that the above comments are only a partial listing of deficiencies, and that there may be additional deficiencies with your submission that are not included in this letter.

AR 5961-62. The letter also noted that the agency would refund 75% of the total user fee associated with the application. AR 5962. Finally, the letter informed Boehringer of its ability to seek review of the agency's "refusal to file" decision. *Id.*

After the "refusal to file" decision, Boehringer and the FDA continued to exchange emails regarding the materials that had already been submitted. AR 5970-71, 5982-83. In addition, agency representatives met with Boehringer representatives regarding steps for moving

forward on February 18, 2010. AR 5984-86. The internal meeting notes from that meeting summarized the shortcomings with Boehringer's application as follows:

> Preliminary review revealed a number of errors in the blood transfusion dataset and the INR dataset. These errors included transcription errors, transposition errors, and auditing errors. Though the Agency recognizes that that there will be some errors in the datasets of large trials, the errors found by relatively unsophisticated means in clinically important datasets during preliminary review *called into question the overall quality of those datasets*.

AR 5985 (emphasis added). The agency and company representatives discussed the issues with the data and the other materials submitted and set out a roadmap to resolve those issues. AR 5985-5986. Boehringer did not seek to have the agency file its December 15, 2009, application over protest. *See* 21 C.F.R. § 314.101(a)(3) ("If, following the informal conference, the applicant requests that FDA file the application (with or without amendments to correct the deficiencies), the agency will file the application over protest … , notify the applicant in writing, and review it as filed."). Accordingly, Boehringer accepted the refund of 75% of the filing fees that it had paid for the earlier filings. *See* AR 5624-5632, 5962.

Following the February, 2010, meeting between Boehringer and the agency, Boehringer provided additional materials on February 19, 2010, which had been requested by the agency. AR 5988-90 ("Reference is made to the communication from the Division to the Sponsor on February 16, 2010 requesting the 85 case report forms (CRFs) from RE-LY that have been identified in review of the transfusion page … . This submission provides the 7 additional [case report forms] that have not been previously submitted."). That same day, by a separate submission, Boehringer provided additional information that responded to the agency's request for information in light of the deficiencies in the materials previously submitted. AR 5998-6000 ("Reference is made to the communication from the Division to the Sponsor on February 16, 2010 requesting documentation on what would trigger the investigator to complete the RE-LY

[case report form] 122. The medical reviewer has requested details surrounding what the investigators were told and how they were told to fill this out. Additionally, it was requested that this documentation be provided for all the outcome events."). One week later, on February 26, 2010, Boehringer provided additional materials again responding to deficiencies in its earlier submissions. AR 5998-99 ("Reference is made to the February 23, 2010 telephone conversation from Sharon Gershon (Division of Scientific Investigations) identifying Site 0006 – Patrick Simpson, M.D. and Site 0351 – Initially Melvin Tonkon, M.D. replaced by Charles Morcos, M.D. as for cause inspections and requesting the following documents to be provided on 2 CDs per site for the inspectors …. This submission provides the documents as outlined in the table below."). A month later, Boehringer provided yet another set of materials responding to the agency's "requesting additional information to assist in the medical review." AR 6069.

More than two months after the "refusal to file" decision, Boehringer provided another submission on April 19, 2010, and represented that *that* submission "provides the final documents to the complete the original new drug application" for the drug in question. AR 6082 (emphasis added); *see also id.* ("Included in this submission are [case report forms] (CRFs), narratives, updated CRF datasets, analysis datasets, PK/PD datasets, SAS programs for review and executable SAS programs with a data Reviewer's Guide (provided in the Module 5.3.5.1 tabulations folder) to re-create the efficacy analysis dataset."). Boehringer explained how the new submitted information resolved deficiencies previously identified by the agency regarding the materials that had been submitted through December 15, 2009. *See* AR 6082-83 ("We have completed the additional data quality checks agreed to during the February 18, 2010 meeting with the Agency. To the extent possible, the deficiencies noted during the initial FDA review and those identified by the quality checks have been corrected. Based on re-analyses of the update

data, the primary efficacy and safety conclusions of RE-LY remain unchanged."). Boehringer once again requested priority designation for the application submitted on April 19, 2010, as it had done with respect to the application materials submitted on December 15, 2009. AR 6083. Several days in advance of the April 19, 2010, filing, Boehringer paid the filling fee for that application. AR 5629 (Letter dated April 13, 2010, including check with filing fee).

Boehringer continued to provide additional materials after the April 19, 2010, submission, including materials submitted on April 20, 28 and 30; May 3-7, 10, 13-14, 17, 21, 24, and 26-28; and June 1, 2010. AR 6247. On June 3, 2010, the agency sent a letter to Boehringer indicating that the application as "originally submitted on December 15, 2009 and resubmitted on April 19, 2010," together with the materials submitted in April, May, and June of that year, was "sufficiently complete to permit a substantive review." *Id.*; *see* AR 6248. Therefore, the agency considered the application filed 60 days after the application was received (April 19, 2010). *Id.* The agency also determined that the review classification for the application was "priority," as requested by Boehringer, and it set a goal of completing the approval process by October 19, 2010. *See id.* Boehringer continued to provide additional material amending the application through October 19, 2010. AR 8149. On October 19, 2010, the application, as amended, was approved by the FDA. AR 8148-49.

On December 10, 2010, Boehringer applied for a patent term extension of patent '380 in connection with the FDA review and approval of Pradaxa. AR 5001-5012. Boehringer sought an extension of 1,469 days—in light of its claim of a 2,322-day testing phase, beginning on August 7, 2003, and ending on December 15, 2009, and its claim of a 308-day approval phase, beginning on December 15, 2009, and ending on October 19, 2010. AR 5111-5113. The FDA determined that the regulatory review period was 2,633 days—2,449 days during the testing phase

(beginning on August 6, 2003, and ending on April 19, 2010), and 184 days in the approval phase (beginning on April 19, 2010, and ending on October 19, 2010). AR 5250. In the FDA's letter to the Patent and Trademark Office notifying it of the length of the regulatory review period, the FDA explained why it determined that April 19, 2010, was the date for the transition from the testing phase to the approval phase:

> The applicant claims December 15, 2009, as the date the new drug application (NDA) for PRADAXA (NDA 22-512) was initially submitted. However, FDA records indicate that NDA 22-512, received December 15, 2009, was incomplete. FDA refused to file this application and notified the applicant of this fact by letter dated Februa1y 12, 2010. The completed NDA was then submitted on April 19, 2010, which is considered to be the NOA initially submitted date.

AR 5250. This determination was published in the Federal Register as required by law, and the FDA presented there the same explanation regarding the lengths of the testing and approval phases. *See* 77 Fed. Reg. at 26,290.

Under the applicable regulatory provision, "[a]ny person may request a revision of the regulatory review period determination within 60 days after its initial publication in the Federal Register." 21 C.F.R. § 60.24(a). Boehringer did so on June 27, 2012, requesting that date dividing the testing and approval phases be shifted earlier to December 15, 2009, the date that it first claimed it had submitted all materials necessary for FDA review. AR 5255-5273; *see also* AR 5769. The FDA denied Boehringer's request with a lengthy explanation of why it determined that the beginning of the approval phase was April 19, 2010. *See* AR 5524-5532.

Boehringer brings this civil action challenging the FDA's determination of the regulatory review period. Specifically, Boehringer continues to argue, as it did in its initial patent term extension request, that the approval phase ought to be considered to begin on December 15, 2009, rather than on April 19, 2010, and that the agency's contrary conclusion is legally flawed.

II. LEGAL STANDARD

Under Rule 56(a) of the Federal Rules of Civil Procedure, "[t]he court shall grant summary judgment if 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." However, "when a party seeks review of agency action under the APA [before a district court], the district judge sits as an appellate tribunal. The 'entire case' on review is a question of law." *Am. Bioscience, Inc. v. Thompson,* 269 F.3d 1077, 1083 (D.C. Cir. 2001). Accordingly, "the standard set forth in Rule 56[ ] does not apply because of the limited role of a court in reviewing the administrative record.... Summary 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." *Southeast Conference v. Vilsack,* 684 F. Supp. 2d 135, 142 (D.D.C. 2010).

The APA "sets forth the full extent of judicial authority to review executive agency action for procedural correctness." *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 513 (2009). It requires courts to "hold unlawful and set aside agency action, findings, and conclusions" that are "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). "This is a 'narrow' standard of review as courts defer to the agency's expertise." *Ctr. for Food Safety v. Salazar,* 898 F. Supp. 2d 130, 138 (D.D.C. 2012) (quoting *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.,* 463 U.S. 29, 43 (1983)). An agency is required to "examine the relevant data and articulate a satisfactory explanation for its action including a rational connection between the facts found and the choice made." *Motor Vehicle Mfrs. Ass'n*, 463 U.S. at 43 (internal quotation omitted). "Moreover, an agency cannot 'fail[ ] to consider an important aspect of the problem' or 'offer[ ] an explanation for its decision that runs counter to the evidence' before it." *Dist. Hosp. Partners,*

L.P. v. Burwell, 786 F.3d 46, 57 (D.C. Cir. 2015) (quoting *Motor Vehicle Mfrs. Ass'n*, 463 U.S. at 43). The reviewing court "is not to substitute its judgment for that of the agency." *Id.* Nevertheless, a decision that is not fully explained may be upheld "if the agency's path may reasonably be discerned." *Bowman Transp., Inc. v. Arkansas–Best Freight Sys., Inc.*, 419 U.S. 281, 286 (1974).

III. DISCUSSION

Plaintiffs argue that the FDA's determination of the patent term extension—specifically the agency's determination of the date of the beginning of the approval phase—contradicts the terms of the statute, violates the agency's own regulations, and is inconsistent with the agency's own past treatment of similarly situated applicants. In response, Defendants argue that the agency's action is consistent with the statute, consistent with its regulations, and consistent with its past treatment of other applications. With respect to the statute, Defendants argue that, under the familiar two-step *Chevron* analysis, the statute is ambiguous and that Defendants' determination was based on a reasonable interpretation of the statute. The Court agrees with Defendants with respect to each issue presented.

Before proceeding to evaluate the parties' arguments on the several issues presented to the Court, the Court emphasizes the fundamental principles of this Court's review of agency actions such as the one at issue in this case. To evaluate Plaintiffs' claim that the agency's determination is inconsistent with the language of the Food, Drug, and Cosmetic Act, as amended, the Court applies the framework established in *Chevron U.S.A., Inc. v. NRDC*, 467 U.S. 837 (1984). The Court first asks "whether Congress has directly spoken to the precise question at issue, in which case we must give effect to the unambiguously expressed intent of Congress." *Deppenbrook v. Pension Benefit Guar. Corp*, 778 F.3d 166, 172 (D.C. Cir. 2015)

(citation omitted). “If the statute is silent or ambiguous with respect to the specific issue, however, we move to the second step and defer to the agency's interpretation as long as it is based on a permissible construction of the statute.” *Id.* “To trigger deference,” an agency must show that Congress has “ ‘delegated authority to the agency generally to make rules carrying the force of law’ ” and that “ ‘the agency interpretation claiming deference was promulgated in the exercise of that authority.’ ” *Fogo De Chao (Holdings) Inc. v. U.S. Dep’t of Homeland Sec.*, 769 F.3d 1127, 1136 (D.C. Cir. 2014) (quoting *United States v. Mead Corp.*, 533 U.S. 218, 226–27 (2001)). Moreover, with respect to the agency’s interpretation of its own regulations, it is a fundamental principle of administrative law that the Court reviews the agency’s “interpretation of its own regulations with ‘substantial deference,’ allowing that interpretation to control unless ‘plainly erroneous or inconsistent with the regulation.’ ” *U.S. Postal Serv. v. Postal Regulatory Comm’n*, 785 F.3d 740, 750 (D.C. Cir. 2015) (quoting *Thomas Jefferson University v. Shalala*, 512 U.S. 504, 512, 514 (1994)).

Ultimately, the question before the Court is narrow: whether the agency’s determination of the date on which the approval phase begins is lawful under the Food, Drug, and Cosmetic Act, as amended, not whether Congress has chosen the *best* statutory scheme or whether the agency has implemented that scheme through the *best* set of regulations. *See Ark Initiative v. Tidwell*, 816 F.3d 119, 126-27 (D.C. Cir. 2016) (“The question before us is of a type ubiquitous to administrative law: Whether the Colorado rule is permissible under federal law, not whether we believe as a matter of environmental policy it is the best rule, or even a good one.”). With that in mind, the Court turns first to the question of consistency with the statute raised by Plaintiffs.

A. Consistency with the Statute

As noted above, Plaintiffs first argue that the agency's determination of the start date of the approval phase of the FDA's regulatory review period is inconsistent with the statute. The Court addresses that argument through the framework of *Chevron*'s two steps and, ultimately, concludes that the agency's determination is consistent with the statute.

a. *Chevron* Step One

"Under step one, the court must determine 'whether Congress has directly spoken to the precise question at issue.' " *W. Minnesota Mun. Power Agency v. Fed. Energy Regulatory Comm'n*, 806 F.3d 588, 591 (D.C. Cir. 2015) (quoting *Chevron*, 467 U.S. at 842). "If so, then the court and the agency must 'give effect to the unambiguously expressed intent of Congress.' " *Id.* (quoting *Chevron*, 467 U.S. at 842–43). "In addressing a question of statutory interpretation, the court begins with the text." *Id*. As presented above, the statute delineates the "approval phase" of the regulatory review period as follows:

> the period beginning on the date the application was initially submitted for the approved product under [21 U.S.C. § 355] and ending on the date such application was approved under such section.

35 U.S.C. § 156(g)(1)(B)(ii). In addition, section 355 requires the following components for 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) (paragraph breaks added).

Plaintiffs argue that the phrase "the date an application was initially submitted" is unambiguous. Defendants respond that the phrase is ambiguous because the statute does not specify exactly what must be "submitted" to satisfy that requirement. The Court agrees with Defendants. Plaintiffs emphasize the use of the word "initially" in the phrase "initially submitted," suggesting talismanic importance to the use of that word. But the fact that the statute refers to the *initial* submission—as opposed to a *later* or *final* submission—does not resolve the question at hand. Notwithstanding Plaintiffs' arguments to the contrary, the Court concludes that the statute simply does not specify *what* must be submitted initially to satisfy the statutory requirements. It is clear that the application must include several components—enumerated immediately above. *See* 21 U.S.C. § 355(b)(1). But it is not clear from the statutory language what must actually be submitted to qualify. That is, the statute is ambiguous as to whether a deficient application qualifies as an application that was "initially submitted" or whether materials submitted must be sufficient for substantive review in order to qualify as an application that was "initially submitted."

Plaintiffs suggest in their reply, for the first time, that "the applicant's intent is what matters." Pls.' Reply at 6. But surely the language of the statute does not *unambiguously* mean that the applicant's intent governs agency's determination as to whether sufficient information has been submitted in order to satisfy the statute's requirements. Nor does the legislative history to which Plaintiffs refer unambiguously indicate that such subjective intent is the proper standard for determining whether the statutory requirements had been satisfied. *See id.* (citing AR 5562). And it is difficult to imagine, absent more explicit direction from Congress, that the statutory

language means that Congress intended for the agency—and in turn this Court—to embark into an inquiry into an applicant's subjective state of mind in order to apply the statutory requirements in the first instance.

In short, the Court is presented with a classic case of statutory ambiguity. The statute states that the approval phase begins on "the date the application was initially submitted for the approved product." 35 U.S.C. § 156(g)(1)(B)(ii). The statute further enumerates certain components that must be included in the application. *See* 21 U.S.C. § 355(b)(1). But the statute includes no more details. It remains ambiguous, therefore, as to exactly what materials must be submitted in order to satisfy these requirements and whether the application must be sufficient for substantive review in order to be considered "initially submitted." Having fully considered the parties' arguments regarding the statute, the Court concludes that, as the agency argues, Congress has not spoken to the question at issue. Therefore, the Court proceeds to analyze the statutory provisions under *Chevron* Step Two.[9]

b. *Chevron* Step Two

Under *Chevron* Step Two, the question for the Court is "whether the agency's answer is based on a permissible construction of the statute." *Chevron*, 467 U.S. at 843.

"*Chevron* deference is appropriate 'when it appears that Congress delegated authority to the agency generally to make rules carrying the force of law, and that the agency interpretation claiming deference was promulgated in the exercise of that authority.' " *Mayo Found. for Med. Educ. & Research v. United States*, 562 U.S. 44, 57 (2011) (quoting *Mead Corp.*, 533 U.S. at

[9] This Court's conclusion that the statutory provision is ambiguous is bolstered by the decision of the United States Court of Appeals for the Federal Circuit regarding a distinct but analogous patent term extension provision in *Wyeth Holdings Corp. v. Sebelius*, 603 F.3d 1291, 1298 (Fed. Cir. 2010).

226–27). "An interpretation is permissible if it is a 'reasonable explanation of how an agency's interpretation serves the statute's objectives.' " *Council for Urological Interests v. Burwell*, 790 F.3d 212, 219 (D.C. Cir. 2015) (citing *Northpoint Tech., Ltd. v. FCC*, 412 F.3d 145, 151 (D.C. Cir. 2005)).

Under regulations promulgated by the FDA, for the purpose of determining a patent term extension, an application "is initially submitted on the date *it contains sufficient information to allow FDA to commence review of the application*." 21 C.F.R. § 60.22 (emphasis added). In other words, the application is not considered "initially submitted" if the materials provided by the applicant are insufficient for the commencement of the FDA's substantive review. Notably, Plaintiffs agree that this definition is consistent with Congress's intent in passing the Hatch-Waxman Amendments. Pls.' Mot. at 4. Accordingly, the Court concludes that, insofar that there is any contrary suggestion by Plaintiffs that the regulatory language is inconsistent with the statute's text or purpose, such an argument is waived as a result of Plaintiffs' explicit concession to the contrary.

Moreover, even absent any waiver or forfeiture by Plaintiffs, the agency's interpretation of the statutory language, as stated in the regulations, warrants deference and is reasonable. As a regulation duly promulgated with notice and comment there is no dispute such an interpretation is the sort of agency pronouncement that warrants deference. Similarly, this interpretation is plainly reasonable. The agency determined that, in order to qualify as "initially submitted," an application must have sufficient information to allow the agency to commence a substantive review. This is sensible. The purpose of the agency's review process is for the agency to be able to review the application to determine whether the proposed product satisfies the several complex statutory criteria. Any application that would not allow the FDA to begin a substantive

review would not fulfill the purpose of the substantive review process. Therefore, it is proper not to consider any such *deficient* application to have been "initially submitted."

Furthermore, the agency's approach minimizes the risk of applicants strategically filing applications before they are fully ready for review for the express purpose of obtaining longer patent term extensions. Plaintiffs protest that no reasonable applicant would submit a purposefully deficient application in order to obtain a longer patent term extension. However, the Court concludes that it is reasonable for the agency, in light of its long experience in administering this complex statute, to arrive at a contrary assessment and to conclude that there is a risk of parties filing applications prematurely for strategic reasons. Moreover, even if Plaintiffs were correct that strategic filing behavior is unlikely or infrequent, it is reasonable for the agency to interpret the statutory framework to encourage applicants to carefully ensure that their applications are complete and ready for substantive review prior to submitting them. For that reason as well, it is reasonable for the agency to consider an application to be "initially submitted" only when the application is ready for substantive review. In short, the FDA's interpretation of the statutory requirements is reasonable.

The Court also concludes that the agency's implementation of the statutory scheme, as interpreted through the agency's regulations, is reasonable as well. As an initial matter, the Court notes that the Court reviews the agency's "interpretation of its own regulations with 'substantial deference,' allowing that interpretation to control unless 'plainly erroneous or inconsistent with the regulation.' " *U.S. Postal Serv.*, 785 F.3d at 750 (citation omitted). The agency here determined that the materials submitted on December 15, 2009, were not sufficient to permit the agency to commence its substantive review. It is true that the agency began *some* review shortly thereafter in order to determine whether the application was sufficiently complete to begin its

substantive review. *See* AR 5794-96 (letter acknowledging receipt of application and indicating that the agency would assess the materials submitted in order to determine whether the application was sufficiently complete for the substantive review to begin). The agency determined that the mere assessment of the application for completeness is not tantamount to the agency's substantive review of the application, and the Court concludes that this determination is reasonable. Indeed, a contrary conclusion would vitiate the standard promulgated through the agency's regulations. That is, even a deficient application must be assessed to determine its completeness. How else could the agency determine that it was deficient in order to inform the applicant of the deficiency and of the necessity of submitting additional materials in order to move forward in the review process? In other words, such an initial review does not constitute the "commencement" of the agency's substantive review and the fact of such review does not mean that the agency had received an application that was sufficient to permit the commencement of its substantive review.

In this case, the agency determined that the application as delivered on December 15, 2009—when the applicant claimed it was complete—was woefully deficient. The agency later summarized the deficiency as follows:

> Preliminary review revealed a number of errors in the blood transfusion dataset and the INR dataset. These errors included transcription errors, transposition errors, and auditing errors. Though the Agency recognizes that that there will be some errors in the datasets of large trials, the errors found by relatively unsophisticated means in clinically important datasets during preliminary review *called into question the overall quality of those datasets*.

AR 5985 (emphasis added). The Court need not review once again the lengthy set of reasons that justified the agency's refusal to file the application as of December 15, 2009, reproduced in full above, because it is clear that the issues were not simply minor issues that could be resolved as the substantive review process proceeded. As the agency noted, the errors discovered "called into

question the overall quality of these datasets." *Id.* Plaintiffs' attempt to whitewash these data quality issues, *see, e.g.*, Pls.' Mot. at 6, Pls.' Reply at 8, cannot hide the serious and significant deficiencies that the agency found with the materials submitted.

Notably, Boehringer did not exercise its right to have its December 15, 2009, application filed over protest. *See* 21 C.F.R. § 314.101(a)(3) ("If, following the informal conference, the applicant requests that FDA file the application (with or without amendments to correct the deficiencies), the agency will file the application over protest … , notify the applicant in writing, and review it as filed."). Instead, it accepted the refund of 75% of the filing fees that it had paid for its earlier filings, *see* AR 5624-5632, 5962, and proceeded to provide, incrementally, the additional information required by the agency in order to remedy the deficiencies in the submissions to that point. Boehringer provided several supplementary submissions with additional information before stating, with its April 19, 2010, submission that "[t]his submission provides the final documents to complete the original new drug application for dabigatran etexilate (NDA 22-512) for the prevention of stroke and systemic embolism in patients with atrial fibrillation." AR 5769; *see* AR 5988-90 (first February 19, 2010, submission); AR 5998-6000 (second February 19, 2010, submission); AR 5998-99 (February 26, 2010, submission); AR 6069-70 (March 30, 2010, submission). Boehringer only then paid the filing fee on April 13, 2010, shortly in advance of the April 19, 2010, submission. AR 5629. In short, after the agency identified various deficiencies with the submissions provided through December 15, 2009, it was necessary for Boehringer to submit substantial new data and other material before even Boehringer *itself* claimed that it had provided the documents necessary to "complete" the application. It was therefore reasonable for the agency to conclude that the application was

sufficient to permit a substantive review *only* as of the April 19, 2010, submission and not as of the December 15, 2009, submission.

In any event, the determination of whether a submission is sufficient to permit the agency's statutorily-mandated substantive review is precisely the sort of issue that warrants agency deference. It is not for this Court to second-guess the determination of the expert agency that the data was insufficient for the agency's subject matter experts to begin their substantive review of the product. Therefore, the Court defers to the agency's interpretation of its regulations and its implementation of those regulations in this case, and it concludes that the agency's determinations were reasonable in that light. Having considered all of parties' arguments, the Court concludes that none of Plaintiffs' arguments to the contrary are persuasive, and the Court finds no need to address them any further.[10] In short, the agency's implementation of the statutory and regulatory scheme in this case was reasonable.[11]

B. Consistency with the Agency's Regulations

Plaintiffs also argue that the agency's action was inconsistent with its own regulations, specifically with the requirement that the approval phase begins "on the date [the application] contains sufficient information to allow FDA to commence review of the application." 21 C.F.R. § 60.22. This argument largely parallels the parties' arguments regarding consistency with the statute. Indeed, because it was necessary under *Chevron* to analyze the question of statutory

[10] Plaintiffs emphasize that the date an application is "initially submitted" must be different from the filing date. *See* Pls.' Mot. at 4 (discussing legislative history). But pursuant to the agency's determination, the date of initial submission is different than the filing date. The former was April 19, 2010, whereas the filing date was deemed to be June 19, 2010.

[11] Although this case does not pertain to the same precise provision as the one considered by the Federal Circuit in *Wyeth*, this Court's conclusion that the FDA's determination is reasonable is consistent with and bolstered by the Federal Circuit's similar conclusion in that case. *See Wyeth*, 603 F.3d at 1300.

consistency through the lens of the agency's regulations, the analysis presented above resolves this argument as well in Defendants' favor. As explained above, the Court is bound to defer to the agency's interpretation of its own regulation in this case given that the interpretation is neither plainly erroneous nor inconsistent with the statute. Accordingly, for the reasons stated at length above regarding consistency with the statute, the Court concludes that agency's determination is consistent with its regulations, as well. Specifically, the Court concludes that it was reasonable for the agency to determine that the materials provided to the agency as of December 15, 2009, did not "contain[] sufficient information to allow FDA to commence review of the application" because they were fatally deficient and would not allow a full substantive review of the proposed product. For that reason, the Court rejects Plaintiffs' argument regarding consistent with the agency's own regulations, as well.

C. Consistent Treatment with Other Applicants

Finally, Plaintiffs argue that the agency's determination was arbitrary and capricious because it was inconsistent with a single determination regarding a patent term extension dating from 1985. As an initial matter, it is far from clear that any putative consistency in comparison to a *single* determination dating from over 30 years ago would be enough, standing on its own, to mark the agency's Pradaxa determination as arbitrary and capricious. In any event, the agency has shown—and Plaintiffs have not rebutted—that the agency's determination in this case is consistent with numerous similar determinations made in other cases. *See* Defs.' Mot. at 27-28 (citing other determinations). In addition, the agency has persuasively explained the differences between this case and the 1985 Tonocard Tablet case, which is the sole case on which Plaintiffs rely for this argument. The Court is persuaded by the differences highlighted by the agency. *See id.* at 28-30. Ultimately, the question comes down to whether, in each *individual* case, the

applicant has provided sufficient information for the agency to commence its substantive review. As noted above, this question is particularly appropriate for deference to an expert agency. The expert agency is well-suited to determine whether, in a particular set of circumstances, the data provided by an applicant is sufficient for the agency's substantive review to commence. Fundamental principles of administrative law indicate that it is not for this Court to substitute its view for that of the agency. This Court's review is therefore appropriately limited to whether, on the basis of the record before the Court, the agency's determination is arbitrary and capricious. Having reviewed the record and all of the parties' arguments, the Court concludes that the agency's determination was not arbitrary and capricious.

* * *

In short, this is the type of case for which deference to the expert agency is particularly appropriate. The Court concludes that the relevant statutory provisions are ambiguous, that the agency's interpretation warrants deference and is reasonable, and that the agency's application of that interpretation in this case is reasonable. None of the Plaintiffs' arguments to the contrary—ranging from their linguistic arguments to their reliance on snippets of legislative history to their comparison with a single case from more than three decades ago—are persuasive. Accordingly, the Court concludes that the agency's determination of the patent term extension for Pradaxa survives this Court's deferential review under the Administrative Procedure Act.

IV. CONCLUSION

For the foregoing reasons, the Court GRANTS Defendants' [26] Motion for Summary Judgment and DENIES Plaintiffs' [23] Motion for Summary Judgment. The Court also DENIES Defendants' [26] Motion to Dismiss as MOOT. This case is dismissed in its entirety.

An appropriate Order accompanies this Memorandum Opinion.

Dated: July 6, 2016

/s/
COLLEEN KOLLAR-KOTELLY
United States District Judge