IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

BOEHRINGER INGELHEIM PHARMA GmbH & CO. KG, BOEHRINGER INGELHEIM PHARMACEUTICALS, INC., Plaintiffs, v. UNITED STATES FOOD AND DRUG ADMINISTRATION, STEPHEN OSTROFF, in his official capacity as Acting Commissioner, United States Food and Drug Administration, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, SYLVIA MATHEWS BURWELL, in her official capacity as Secretary, United States Department of Health and Human Services, UNITED STATES PATENT AND TRADEMARK OFFICE, and MICHELLE K. LEE, in her official capacity as Undersecretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office, Defendants.	Civil Action No. 15-cv-00656 (CKK)

PLAINTIFFS' MEMORANDUM OF POINTS AND AUTHORITIES
IN SUPPORT OF THEIR MOTION FOR SUMMARY JUDGMENT

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page

CASES:

TABLE OF AUTHORITIES—Continued

Page

STATUTES:

TABLE OF AUTHORITIES—Continued

Page

REGULATIONS:

TABLE OF AUTHORITIES—Continued

Page

LEGISLATIVE MATERIAL:

OTHER AUTHORITIES:

INTRODUCTION

As part of the Hatch-Waxman Act's grand bargain, Congress provided that the patent term of a drug subject to FDA review should be extended to compensate the drug sponsor for the period of time during which the drug was subject to regulatory review. Congress expressly described how that so-called "patent term extension" should be calculated based on the date the drug sponsor "*initially submitted*" its application. 35 U.S.C. § 156(g)(1)(B)(i)-(ii).

When calculating Boehringer's patent term extension for its drug product PRADAXA®, however, FDA did not calculate the extension from the date Boehringer "initially submitted" its application. The agency instead held Boehringer to a later-in-time, "ready for filing" standard that Congress expressly *rejected* in passing the Hatch-Waxman Act. The result was that Boehringer was denied the full patent term extension to which it is entitled. FDA's decision contradicts the statute, violates the agency's own regulations, and is inconsistent with the agency's own past treatment of similarly situated applicants.

For all of these reasons, FDA's conduct violates the APA.

STATEMENT OF FACTS

I. STATUTORY BACKGROUND

The federal Food, Drug and Cosmetic Act (FDCA) requires FDA approval of all new drugs before they can be marketed. 21 U.S.C. § 355(a). Many such new drugs are patented. In theory, a patent entitles the holder to exclusive commercial exploitation of an invention from the time the patent is granted until 20 years after the patent application was filed. 35 U.S.C. § 154(a)(2). But in practice, patents covering products subject to FDA pre-market approval requirements confer much less of a practical benefit. A drug product's "regulatory review period"—the time it takes the sponsor to test the drug and the time it takes for FDA to review the

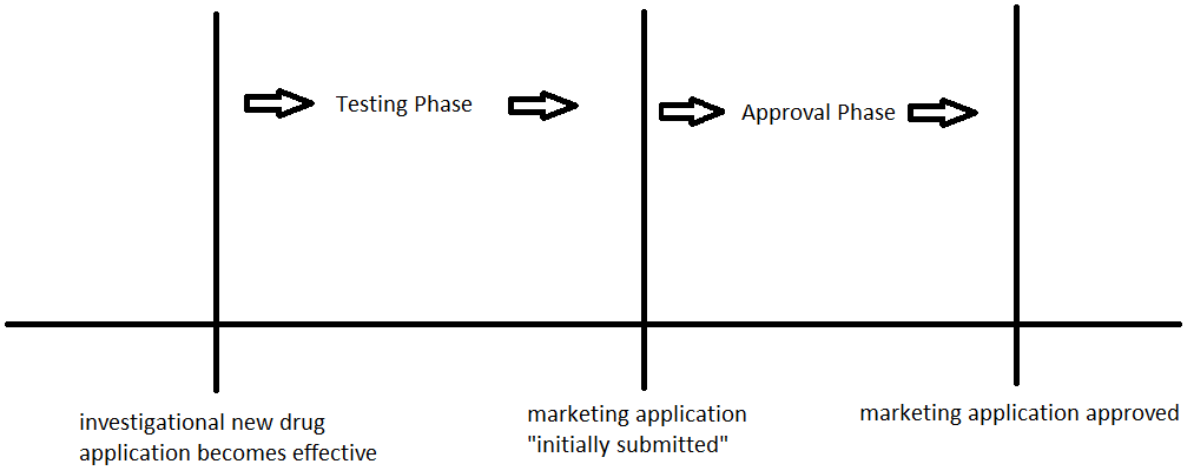
sponsor's application—typically lasts for years. As a result, the regulatory review period can substantially reduce the effective terms of any patents covering the drug.

Congress addressed this problem in the Hatch-Waxman Act. *See* Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984). Title II of the Act provides that the holder of a patent covering a drug subject to FDA's regulatory review is entitled to a patent term extension to compensate for the period of time the agency's pre-market approval requirement barred commercial marketing of the product. 35 U.S.C. § 156(a). The purpose of the statutory provision was "to further encourage new drug research by restoring some of the patent term lost while drug products undergo testing and await FDA pre-market approval." *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 396 (Fed. Cir. 1990).

A drug's regulatory review period is the sum of two parts, known as the "testing phase" and the "approval phase." 35 U.S.C. § 156(g)(1); 21 C.F.R. § 60.22(a). There is a distinction between the two phases, however: the statute gives more significance to the approval phrase in calculating the patent term extension. The regulatory review period is made up of *one-half* of the time the drug was in the testing phase, plus *all* of the time the drug was in the approval phase. 35 U.S.C. § 156(c). FDA determines the length of the regulatory review period, and then notifies the United States Patent and Trademark Office (PTO) in writing of its determination. 21 C.F.R. § 60.20(a)-(b). The PTO is bound by FDA's determination of the regulatory review period in issuing a patent term extension. *See* 37 C.F.R. § 1.775.

The Hatch-Waxman Act expressly defines when the testing and approval phases begin and end. The *testing* phase for human drugs begins on the date an investigational new drug application (IND) "became effective for the approved product"; it ends on the date a marketing

application "was initially submitted for such drug product." 35 U.S.C. § 156(g)(1)(B)(i).[1] The approval phase begins right when the testing phase is complete—that is, "on the date the application was initially submitted for the approved product"—and ends "on the date such application was approved." 35 U.S.C. § 156(g)(1)(B)(ii).



Congress chose the term "initially *submitted*" deliberately. There are two steps to lodging a marketing application with FDA: the sponsor first "submits" an application to FDA, 21 U.S.C. § 355(a), and after reviewing the application and determining that the agency has sufficient information to make a decision, FDA accepts the application for "filing." 21 C.F.R. § 314.101. When it crafted the language pertaining to patent term extensions, Congress specifically rejected a standard based on whether a marketing application is "filed" by FDA:

The term "initially submitted" is used to describe the point in time when the

[1] An Investigational New Drug Application (IND) authorizes a sponsor to administer an investigational new drug to humans. Once the sponsor believes that enough evidence on the drug's safety and effectiveness has been obtained to meet FDA's requirements for marketing approval, the sponsor submits a marketing application to FDA. For innovator drugs, the marketing application is in the form of a new drug application (NDA). An NDA is typically organized into five technical parts, called modules. These include: administrative and prescribing information, summaries and overview, information on product quality, nonclinical study reports, and clinical study reports.

> testing phase is considered to be completed and the agency approval phase to have begun. *This term is used instead of the term "file," because an application is often not considered to be filed, even though agency review has begun, until the agency has determined that no other information is needed and a decision on the application can be made.* For purposes of determining the regulatory review period and its 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 the agency review to begin.* [A.R. 5562 (H.R. Rep. No. 98-857, pt. 1 (1984) (emphasis added)).]

Consistent with Congress's intent, FDA's regulations provide that for "purposes of determining the regulatory review period for any product, a marketing application . . . is initially submitted on the date it contains sufficient information to allow FDA to commence review of the application." 21 C.F.R. § 60.22(f).

II. FACTUAL BACKGROUND

A. The Regulatory Review Period for Boehringer's PRADAXA

Boehringer's drug, PRADAXA, is a prescription blood thinner medicine; it is used to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation.[2] U.S. Patent No. 6,087,380 covers PRADAXA. A.R. 5028. Boehringer is the assignee of the '380 patent and owns rights, title, and interests in and thereto. *Id.* The original expiration date of the '380 patent was February 18, 2018. As the sponsor of an FDA-approved drug that is the subject of a U.S. patent, however, Boehringer is entitled to a patent term extension to restore the time that otherwise would have been lost due to FDA's regulatory review period.

The investigational new drug application (IND) for PRADAXA became effective on August 6, 2003, marking the start of the testing phase. A.R. 5275-76 (77 Fed. Reg. 26,289, 26,290 (May 3, 2012)). After that point—but before Boehringer submitted its marketing application—FDA notified Boehringer that it expected to review the PRADAXA application on

[2] Systemic embolism is a blood clot in an artery. Non-valvular atrial fibrillation is a rapid heartbeat that is not caused by valve disease.

a "priority" basis because the drug represented a significant improvement over existing therapy. A.R. 5637 (Minutes of Aug. 17, 2009 FDA Meeting). As a result, FDA requested that Boehringer submit portions of the application on a rolling basis: "In order for us to complete our review of your NDA in a timely fashion, we request that you submit each module as you complete it." *Id.*

Boehringer complied with FDA's request. Starting in September 2009, Boehringer submitted the first modules of the marketing application for PRADAXA, including the clinical module. A.R. 5633-34, 5645-47, 5682-86. Boehringer continued submitting modules over the next few months as they were completed. And as those portions came in, FDA started its review. A.R. 5729 (E-mail from A. Blaus, FDA Project Manager, to M. Kliewer, Boehringer (Nov. 23, 2009)), 5754-56 (Request for Consultation regarding dissolution method and specification and bioequivalence data (Sept. 20, 2009)).

On December 15, 2009, Boehringer submitted the final elements of the PRADAXA marketing application. A.R. 5769-70. At that point, Boehringer had submitted all modules necessary for a complete marketing application. *See, e.g., id.* ("This submission provides the final documents to complete the original new drug application").

Several weeks later, FDA sent Boehringer an acknowledgment of its receipt of the complete marketing application, listing both the "date of application" and "date of receipt" as December 15, 2009. A.R. 5794 (FDA Acknowledgment Letter (Jan. 5, 2010)). The letter went on to state: "Unless 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 C.F.R. § 314.101(a)." *Id.*

On February 12, 2010, after FDA's review was well underway and one day before the

agency's deadline to determine whether to accept the application for filing, the Division of Cardiovascular and Renal Products sent a "refuse-to-file" (RTF) letter to Boehringer identifying certain "transcription errors, transposition errors, and auditing errors" in one portion of the PRADAXA application, known as the clinical data module. A.R. 5961. In some circumstances, FDA's letter would have halted review of the PRADAXA marketing application. However, as FDA's longstanding guidance makes clear, the agency nevertheless "might review parts of a refused application if it believes that initiating the full review at the earliest possible time will better advance the public health." A.R. 5517-23 (New Drug Evaluation Guidance Document: Refusal to File (July 12, 1993)).

This is exactly what FDA did with respect to the PRADAXA application. In fact, FDA's letter specifically stated that the agency would continue its ongoing review of the marketing application:

> 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.

A.R. 5962. At a meeting with Boehringer a few days later, FDA asked the company to conduct a series of "data quality checks" and to re-organize the application's study results "in a manner that facilitates review." A.R. 5985 (Minutes of Feb. 18, 2010 FDA Meeting). FDA did not request any new testing data, nor did it identify any major omissions from the PRADAXA application. *Id.;* A.R. 5961-63. In fact, FDA acknowledged that occasional inaccuracies are expected to occur in a large trial database. A.R. 5962.

As FDA said it would, the agency continued its review of the PRADAXA application in the meantime. For example:

- On February 16, four days after the RTF letter, FDA's lead Project Manager for the

PRADAXA application sent Boehringer an e-mail posing questions from the agency's liver toxicity experts. The e-mail reiterated FDA's commitment to ongoing review of the application: "As I mentioned on the phone, regardless of the RTF, we are continuing our review of the application." A.R. 5970-71.

- That same day, FDA's Executive Carcinogenicity Assessment Committee met to consider Boehringer's rat and mice carcinogenicity studies. A.R. 5465-68.

- On March 1, Boehringer submitted a plan for the packaging and appearance of PRADAXA capsules in response to comments from FDA's Division of Medication Error Prevention and Analysis. A.R. 6003-05 (E-mail from M. Kliewer, Boehringer to P. Ton, FDA (Mar. 1, 2010)).

- On March 9, the Office of Biostatistics within the Office of Pharmacoepidemiology and Statistical Science submitted its Carcinogenicity Study. A.R. 6012-51.

- On March 15, FDA's Division of Medication Error Prevention and Analysis concurred with the packaging plan Boehringer had submitted on March 1. A.R. 6003-05 (E-mail from N. Ton, FDA to M. Kliewer, Boehringer (Mar. 15, 2010)).

- On March 30, Boehringer submitted a letter with attachments in response to a request from FDA for "additional information to assist in the medical review." A.R. 6069-70.

- Between March 24 and April 15, FDA met with Boehringer to review Boehringer's clinical investigation. A.R. 6852-53 (Letter from T. Purohit-Sheth, FDA to N. Morcos, clinical investigator (July 27, 2010)).

While FDA continued its review of the PRADAXA application, Boehringer worked to address the transcription and formatting concerns the agency raised in the RTF letter. A.R. 5984-5987, 7763 (clinical inspection summary (Oct. 13, 2010)). On April 19, 2010, Boehringer

submitted an updated clinical data module re-affirming the conclusions of the module originally submitted in December. A.R. 6082. In the cover letter accompanying the documents, Boehringer reiterated that "the primary efficacy and safety conclusions of RE-LY[3] remain unchanged." *Id.* On the basis of the April 19, 2010 submission, FDA agreed to file the NDA. A.R. 6095-98 (NDA Acknowledgement Letter (April 27, 2010)).

FDA approved the PRADAXA marketing application a few months later, on October 19, 2010. A.R. 8149.

B. FDA's Calculation of the Patent Term Extension

In December 2010, after FDA approved the PRADAXA application, Boehringer applied to the PTO for a patent term extension. A.R. 5001-12. Its application asserted that the PRADAXA marketing application was "initially submitted" on December 15, 2009, because as of that date the application contained "all information necessary for agency review to begin." A.R. 5092-93. Based on the statutory calculation (one half of the "testing phase" plus all of the "approval phase"), Boehringer determined that the appropriate patent term extension for PRADAXA was 1,469 days, meaning that the revised expiration date of the '380 patent should be February 26, 2022. A.R. 5001.

In April 2012, FDA informed the PTO that the agency had reviewed Boehringer's application and determined the regulatory review period applicable to PRADAXA. A.R. 5250-51 (Letter from J. Axelrad, FDA to D. Kappos, PTO (April 18, 2012); *see also* 5275-76. FDA determined that the *testing* phase began on August 6, 2003, when the investigational new drug

[3] The acronym "RE-LY" describes a long name for a clinical trial: The 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.

application for PRADAXA became effective.[4] But the agency asserted that the date triggering the *approval* phase was *April 19, 2010*—the date on which Boehringer had resubmitted the portion of its application updating the presentation of clinical data. *Id.* In FDA's view, the PRADAXA application could not have been "initially submitted" on December 15, 2009, the date upon which all modules had been submitted by Boehringer, because the agency subsequently issued a letter requesting additional information. *Id.* Instead, FDA determined that the "initially submitted" date did not occur until the application was "completed," thus shortening the patent term extension for PRADAXA by more than two months.

C. FDA Denies Boehringer's Request for Revision.

FDA published formal notice of this decision in the Federal Register in early May. A.R. 5275-76. Boehringer subsequently requested that FDA revise the date upon which the application was deemed "initially submitted" from April 19, 2010, to December 15, 2009. A.R. 5255-73 (Request for Revision of Regulatory Review Period (June 27, 2012)). Boehringer pointed out that FDA's decision was premised on the assertion that a marketing application must be *complete* in order to count as "initially submitted," and that FDA's test for completeness wrongly depended on whether the application met the agency's standard for "filing." But as Boehringer pointed out, Congress expressly *rejected* a "filing" standard in favor of an "initially submitted" standard. *Id.* Boehringer also pointed out that FDA's determination was a departure from its own regulation and from the agency's past practice. *Id.*

FDA issued its response in December 2014, refusing to reconsider its conclusion that the "initially submitted" date should be April 19, 2010. A.R. 5524-32 (Response to Request for Revision (Dec. 24, 2014). FDA again based its decision on a "filing" standard:

[4] Although this date is one day off from Boehringer's initial calculation of August 7, 2003, Boehringer does not challenge FDA's calculation of the August 6 date.

> *If an application can be filed, then it is considered sufficiently complete.* If the application is sufficiently complete, then the end date of the testing phase of the regulatory review period and the beginning of the approval phase can be declared and the initially submitted date is the NDA receipt date. However, if the application cannot be filed (RTF), then it is not sufficiently complete and the approval phase has not yet begun. [A.R. 5527.]

In keeping with its decision to apply a "filing" standard, FDA's response used the term "complete" or "completed" to define the relevant benchmark no less than 25 times, A.R. 5524-32. Applying that standard to the PRADAXA application, FDA contended that the PRADAXA application "was not sufficiently complete for Agency approval action until the complete final module was received April 19, 2010." A.R. 5530. In other words, FDA considers an application to be initially submitted only if it contained all information necessary for the agency to make an *approval decision*, and only if such information was presented in the manner preferred by FDA, regardless of whether the agency had enough information to start *reviewing* the application.

In January 2015, FDA notified the PTO that its regulatory review period determination was "final." A.R. 5254 (Letter from J. Axelrad, FDA to M. Lee, PTO (Jan. 21, 2015)); *see also* 21 C.F.R. § 60.26(a). The PTO is bound by FDA's determination. *See* 37 C.F.R. § 1.775.

ARGUMENT

"[W]hen a party seeks review of agency action under the APA, 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) (internal quotation marks and citation omitted). Summary judgment in a suit under the APA thus "serves as a mechanism for deciding, as a matter of law, whether the administrative record supports the agency action and whether the agency action is consistent with the APA standard of review." *Int'l Swaps & Derivatives Ass'n v. U.S. Commodity Futures Trading Comm'n*, 887 F. Supp. 2d 259, 266 (D.D.C. 2012) (citation omitted). Under the APA, a court must set aside agency action that is "arbitrary, capricious, an

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

Agency action is routinely set aside as unlawful where it violates a statute. *See, e.g.*, *Bennett v. Donovan*, 4 F. Supp. 3d 5, 13 (D.D.C. 2013). An agency also acts arbitrarily and capriciously in violation of the APA when it violates its own regulations. *Brock v. Cathedral Bluffs Shale Oil Co.*, 796 F.2d 533, 536 (D.C. Cir. 1986) ("It is axiomatic that an agency must adhere to its own regulations." (citations omitted)). And agency action is arbitrary and capricious when it treats similarly situated parties differently without adequate explanation, *see Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27 (D.D.C. 1997), or deviates from past precedent without reason, *see Friedman v. Sebelius*, 686 F.3d 813, 828 (D.C. Cir. 2012) (finding agency decision arbitrary and capricious because "it failed to explain its departure from the agency's own precedents").

FDA fails all of these tests here. The agency violated the Hatch-Waxman Act's plain language 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). The agency failed to follow its own patent term extension regulation, which makes clear that the approval phase begins when an applicant initially submits an application sufficiently complete to allow review to *commence*. And the agency abandoned without reason or explanation the previous position that it had applied to other applicants.

I. FDA'S DECISION VIOLATED THE HATCH-WAXMAN ACT.

Congress has spoken directly to the question of when an application is "initially submitted." Because FDA's interpretation violates that statutory command, the agency's action should be vacated.

The two-step analysis under *Chevron* is well known. "First, always, is the question whether Congress has directly spoken to the precise question at issue." *Chevron, U.S.A., Inc. v. Natural Resources Def. Council, Inc.*, 467 U.S. 837, 842 (1984). To determine Congress's intent, a court is charged with "employing traditional tools of statutory construction," including evaluation of a statute's "text, structure, purpose and history." *Hearth, Patio & Barbecue Ass'n v. U.S. Dep't of Energy*, 706 F.3d 499, 503 (D.C. Cir. 2013) (citations omitted). "If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Chevron*, 467 U.S. at 842-43.

Only when the statute is ambiguous or leaves gaps for the agency to fill does a court move on to *Chevron* Step Two, where the question becomes whether the agency's interpretation is "based on a permissible construction of the statute." *Chevron*, 467 U.S. at 843. A court only defers to an agency's permissible interpretation under Step Two "if the agency has offered a reasoned explanation for why it chose that interpretation." *Amarin Pharms. Ireland Ltd. v. F.D.A.*, No. 14-cv-00324 (RDM), --- F. Supp. 3d ---, 2015 WL 3407061, at *17 (D.D.C. May 28, 2015) (citation omitted). "This analysis overlaps substantially with the APA's 'arbitrary and capricious' inquiry," because "[w]hether a statute is unreasonably interpreted is close analytically to the issue whether an agency's actions under a statute are unreasonable." *Id.* (alteration in original) (citations omitted). Even under Step Two, the reasonableness of an agency's construction "depends on the construction's 'fit' within the statutory language as well as its conformity to statutory purposes." *Abbott Labs. v. Young*, 920 F.2d 984, 988 (D.C. Cir. 1990). *See also Council for Urological Interests v. Burwell*, No. 13-5235, --- F.3d ---, 2015 WL 3634632, at *9 (D.C. Cir. June 2, 2015) ("[O]ur deferential analysis under *Chevron* step two is limited to determining whether the regulation is rationally related to the goals" of the relevant

statute) (citation omitted); *Van Hollen v. F.E.C.*, No. 11-0766 (ABJ), --- F. Supp. 3d ---, 2014 WL 6657240, at *5 (D.D.C. Nov. 25, 2014) (under *Chevron* Step Two, challenged interpretation "must also be tested against the policy that [the statute] was intended to advance").

A. FDA's Interpretation Fails Under *Chevron* Step One.

As the agency explained in denying Boehringer's request for revision of the extension period, "[i]t is FDA's position that, for the purposes of patent 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." A.R. 5527. The agency went on: "[i]f an application can be filed, then it is considered sufficiently complete," but "if the application cannot be filed (RTF), then it is not sufficiently complete and the approval phase has not begun." *Id.* FDA's position is flawed: its proposed standard describes when the application is ready for "filing" by the agency, *see* 21 C.F.R. § 314.101, not when it is "initially submitted" by the applicant. *See* 35 U.S.C. § 156(g)(1)(B). Because the text, structure, and purpose of the statute unambiguously compel a different result, FDA's decision should be reversed under *Chevron* Step One.

First, FDA's position is fatally inconsistent with the plain text of the Hatch-Waxman Act itself. The statute does not provide that the approval phase starts when an application is "ready for filing," "accepted for filing," "finally submitted," or "complete." The statute mandates that the approval phase commences when an application is "*initially* submitted." 35 U.S.C. § 156(g)(1)(B). "Initial" means "happening or being at the very beginning: FIRST." Webster's II New College Dictionary (1995). And Congress quite deliberately chose to use the word "*submitted*" rather than "*filed*," making clear that the application need only be submitted by the applicant and need not be cleared for filing by FDA before the review phase starts. By selecting

the words "initially submitted" rather than "ready for filing," Congress chose to end the testing phase and begin the approval phase based on the action of the *sponsor*, not the action of the agency.

Lest there be any doubt, Congress directly addressed the very issue presented in this case during passage of the Hatch-Waxman Act:

> The term "initially submitted" is used to describe the point in time when the testing phase is considered to be completed and the agency approval phase to have begun. *This term is used instead of the term "file," because an application is often not considered to be filed, even though agency review has begun, until the agency has determined that no other information is needed and a decision on the application can be made.* For purposes of determining the regulatory review period and its 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 the agency review to begin.*

A.R. 5562 (emphasis added).

Here, Boehringer plainly "made a deliberate effort to submit an application containing all information necessary for the agency review to begin" by December 19, 2009. *Id.* By that date, Boehringer had submitted all modules necessary for FDA to commence review. *See* A.R. 5794 (NDA Acknowledgement Letter (Jan. 5, 2010)).[5] Yes, FDA subsequently identified some transcription errors and requested that some of the data be re-submitted. A.R. 5961-63. But the Committee of Energy and Commerce (Committee) expressly contemplated this exact scenario:

> The Committee recognizes that the agency receiving the application might decide it needs additional information or other changes to 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."

A.R. 5562. And that is the exact situation that occurred here. FDA cannot seriously dispute that it continued to review the PRADAXA application even after the RTF requesting more

[5] In fact, FDA commenced review even prior to that date, but by December 19, 2009, the agency had all information necessary to commence review on all portions of the application, including the clinical module, and in fact did commence such review.

information from Boehringer. A.R. 5970-71 (confirming that FDA was "*continuing [its] review* of the application"); A.R. 8143 (Memorandum from ONDQA Division Director (Oct. 18, 2010)) ("due to the priority/rolling status of the application, the CMC review remained ongoing after the RTF"); A.R. 6012-51 (In March 2010, Office of Biostatistics within the Office of Pharmacoepidemiology and Statistical Science submitted its Carcinogenicity Study). *See generally* 7-8 *supra*.

In fact, contrary to its current litigation position, FDA referred to the December 2009 submission as Boehringer's "initial submission" multiple times. *See, e.g.*, A.R. 7255 (Office of Surveillance and Epidemiology Memorandum (July 30, 2010)) ("The initial submission of the application . . . was made on 15 December 2009"); A.R. 7019 (Clinical Review cover page)(Submit Dates listed as "December 15, 2009 (Initial)." *See also* A.R. 6247 (Priority Review Designation Letter (June 3, 2010)) ("[Y]our [NDA] originally submitted on December 15, 2009"). There simply can be no dispute that the statute unambiguously requires the "initially submitted" date to be December 15, 2009.

In its response, FDA relied heavily on *Wyeth Holding Corp. v. Sebelius*, 603 F.3d 1291 (Fed. Cir. 2010), but that case bears little relevance here. In *Wyeth*, the Federal Circuit merely found that Section 156(g) of the patent term extension statute did not unambiguously require that a new animal drug application (NADA) be deemed "initially submitted" when the applicant had submitted only a single section of the *investigational* file, not the marketing application, for phased review. But the phased reviews for new animal drugs at issue in *Wyeth* are very different than the rolling reviews for human drugs at issue here. Most principally, for the phased review of new animal drugs, all modules are required to be submitted to the investigational new animal drug (INAD) file before the marketing application is even submitted; this is in contrast to human

drug applications, where the modules are submitted to FDA as part of marketing application itself. *See id.* at 1294 (for animal drugs, "FDA treats technical sections as submissions to the INAD file . . . . When FDA completes its review of a technical section, it sends the sponsor a 'complete letter' for that section. Once the sponsor compiles all of its complete letters, it may submit an administrative NADA.").In other words, the marketing application cannot, by definition, be "initially submitted" until *after* all required modules are submitted during the INAD process and FDA completes its review of the modules. To drive this point home, the time between the sponsor's submission of the NADA and FDA's approval of the NADA in *Wyeth* was only 16 days. It is hardly surprising, then, that the Court found that submission of a single module during the *investigational* phase did not constitute "initial submi[ssion]" of the *marketing* application. But that had nothing to do with the timing of module submission and everything to do with the fact that no marketing application can be submitted during the INAD phase (and, in fact, none was). The *Wyeth* court recognized this and reasoned that "Because the administrative NADA is the first application submitted, it is reasonable to interpret the date that it is submitted as the 'initially submitted' date. Prior to the submission of an administrative NADA, no application has been submitted, initially or otherwise." *Id.* at 1299. That simply bears no relevance to rolling reviews for human drugs, where the marketing application itself contains the modules, nor does it answer the question whether a marketing application that actually *was* submitted should be deemed to be "initially submitted" under the circumstances presented here.

Because FDA's decision does not comport with the statute, it cannot withstand scrutiny under *Chevron* Step One.

B. FDA's Interpretation Fails Even Under *Chevron* Step Two.

FDA's statutory interpretation even fails under the more lenient Step Two. For even under Step Two, the reasonableness of an agency's construction "depends on the construction's 'fit' within the statutory language as well as its conformity to statutory purposes." *Abbott Labs. v. Young*, 920 F.2d 984, 988 (D.C. Cir. 1990); *Prevor v. F.D.A.*, 9 F. Supp. 3d 125, 137-39 (D.D.C. 2014) (finding that FDA's interpretation of an FDCA provision failed under *Chevron* Step Two).

FDA's interpretation is flatly inconsistent with the statute as a whole and its underlying purpose. Congress specifically laid out a detailed mechanism of calculating the patent term extension in order "to further encourage new drug research by restoring some of the patent term lost while drug products undergo testing and await FDA pre-market approval." *Glaxo Operations UK Ltd.*, 894 F.2d 392 at 396. In doing so, Congress made clear that the approval phase—during which FDA reviews the application – is entitled to full credit for each day spent under review. 35 U.S.C. § 156(c); *see also* 5534 ("the extension would be for a period equal to: (1) half of the time required to test the product for safety (and effectiveness in some cases); and (2) *all of the time required for the agency to approve marketing of the product*.") (emphasis added). FDA's decision to deny Boehringer full credit for days where FDA was actively reviewing the PRADAXA application simply does not square with that purpose.

Congress specified that the approval phase starts when a marketing application is "initially submitted." 35 U.S.C. § 156(g)(1). As the Committee on Energy and Commerce explained, "[t]his term 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." A.R. 5562.

And yet this same "filing" standard that Congress *expressly rejected* is precisely the standard that FDA purported to apply here. FDA's interpretation simply cannot be squared with the statutory context.

FDA argues that implementation of statute as Congress drafted it would give applicants an incentive to "submit deficient applications in order to shorten the testing phase of the regulatory review period." A.R. 5530. FDA thus suggests that "limited inquiries" and "preliminary discussions" regarding information contained in an application should not signal the beginning of the approval period. *Id.* But the review undertaken by FDA in this case was not confined to "limited inquiries" of the applicant; rather, the record makes clear that FDA dove deep into the application and commenced an aggressive, substantive review *at least* as of December 19, 2009 (if not earlier).

In any event, applicants are unlikely to intentionally submit deficient applications in the hopes that they will get a jump-start on the approval phase. RTF decisions generally cause substantial delays in the overall approval time. In most cases, RTF decisions cause FDA to halt review entirely; FDA's decision to continue review of the PRADAXA application was a rare occurrence and unlikely to be counted on by other applicants. *See, e.g.*, A.R. 5517-23. Even day-for-day patent term extensions provide only partial compensation for regulatory delays, which postpone launch of the product and undermine sponsors' goals of providing patient populations with much-needed therapies. In any event, even if this concern were legitimate, it is simply not the case here. The record shows that FDA was continuously engaged in a deep and meaningful review of the PRADAXA application throughout the contested months. FDA's ability to undertake this substantive review proves that Boehringer had made "a deliberate effort to submit an application containing all information necessary for the agency review to begin."

A.R. 5562. Indeed, the updated clinical data module that Boehringer submitted at FDA's request reaffirmed the conclusions of the module originally submitted in December.

II. FDA'S DECISION VIOLATED ITS OWN REGULATIONS.

"It is axiomatic that an agency must adhere to its own regulations." *Brock*, 796 F.2d at 536. Administrative agencies "may not violate their own rules and regulations to the prejudice of others." *Battle v. F.A.A.*, 393 F.3d 1330, 1336 (D.C. Cir. 2005) (citation omitted). And yet that is exactly what FDA has done here. FDA's own patent term extension regulations make clear that an application need not be "ready for filing" in order to count as "initially submitted."

First, the agency has defined the term "marketing application" as an application for human drug products, medical devices, food and color additives, or animal drug products "*submitted*" under the applicable laws. 21 C.F.R. § 60.3(b)(12). Nowhere do the regulations define a marketing application as one that FDA has "*filed*." *See id.*

Second, FDA's patent term extension regulations define the phrase "initially submitted" as the date upon which a marketing application "contains sufficient information to allow FDA to *commence* review of the application." 21 C.F.R. § 60.22(f) (emphasis added). The regulation makes no reference to "filing," and its definition is a far cry from the separately-articulated filing standard under 21 C.F.R. § 314.101. By its careful choice of words, the agency has made clear that the "initially submitted" standard is tied to FDA commencing review of the application, not whether the application is ready for filing.

Thus, when given the opportunity to define the statutory terms "application" and "initially submitted" under Section 156(g)(1)(B), the agency declined to incorporate any requirement that the application be deemed ready for "filing." Instead, FDA followed the lead of the statute and based its regulatory framework on the sponsor's act of submitting an application sufficient to permit the agency to "commence" review.

Any FDA interpretation to the contrary should be rejected. Judicial deference to an agency's interpretation of its own regulation is not warranted where the regulation is clear on its face. *Gardebring v. Jenkins*, 485 U.S. 415, 430 (1988) (agency's interpretation receives no deference where an "alternative reading is compelled by the regulation's plain language"); *see also Pfizer, Inc. v. Heckler*, 735 F.2d 1502, 1509 (D.C. Cir. 1984). Nor is it warranted where the interpretation is nonsensical. *Auer v. Robbins*, 519 U.S. 452, 461 (1997).

III. FDA ACTED ARBITRARILY AND CAPRICIOUSLY BY TREATING SIMILARLY SITUATED PARTIES DIFFERENTLY AND DEVIATING FROM AGENCY PRECEDENT WITHOUT REASON.

It is a fundamental rule of administrative law that "an agency must treat similar cases in a similar manner unless it can provide a legitimate reason for failing to do so." *Bracco Diagnostics*, 963 F. Supp. at 27-28 (citations omitted). That is because "[g]overnment is at its most arbitrary when it treats similarly situated people differently." *Id.* (quoting *Etelson v. Office of Personnel Mgmt.*, 684 F.2d 918, 926 (D.C. Cir. 1982)). "The disparate treatment of functionally indistinguishable products is the essence of the meaning of arbitrary and capricious." *Prevor*, 895 F. Supp. 2d at 99. *See also Cnty. Of Los Angeles v. Shalala*, 192 F.3d 1005, 1022 (D.C. Cir. 1999) ("A long line of precedent has established that an agency action is arbitrary when the agency offer[s] insufficient reasons for treating similar situations differently." (internal quotation marks and citations omitted)); *Freeman Eng'g Assocs. Inc. v. F.C.C.*, 103 F.3d 169, 180 (D.C. Cir. 1997) (remanding to agency to remedy inconsistent treatment). In order to justify treating similarly-situated entities differently, an agency must "do more than enumerate factual differences, if any, between [one case] and the other cases; it must explain the relevance of those differences to the purposes of the [underlying law]." *Melody Music, Inc. v. F.C.C.*, 345 F.2d 730, 733 (D.C. Cir. 1965).

Agency action also is arbitrary and capricious where it deviates from agency precedent without reasoned explanation. *See, e.g., Lone Mtn. Processing, Inc. v. Sec'y of Labor*, 709 F.3d 1161, 1164 (D.C. Cir. 2013) (finding action arbitrary and capricious where agency "failed to even mention or discuss, let alone distinguish" prior orders); *Friedman v. Sebelius*, 686 F.3d 813, 828 (D.C. Cir. 2012) (finding agency decision arbitrary and capricious because "it failed to explain its departure from the agency's own precedents"); *Fox v. Clinton*, 684 F.3d 67, 80 (D.C. Cir. 2012) (finding agency's action to be "arbitrary and capricious for want of reasoned decisionmaking"). Although "[a]gencies are free to change course as their expertise and experience may suggest or require, . . . when they do so they must provide a 'reasoned analysis indicating that prior policies and standards are being deliberately changed, not casually ignored.'" *Ramaprakash v. FAA*, 346 F.3d 1121, 1125 (D.C. Cir. 2003). *See also Action for Children's Television v. FCC*, 821 F.2d 741, 745 (D.C. Cir. 1987) ("It is axiomatic that an agency choosing to alter its regulatory course 'must supply a reasoned analysis indicating that its prior policies and standards are being deliberately changed, not casually ignored."). FDA has violated these basic maxims here.

FDA's calculation of PRADAXA's regulatory review period is contrary to the agency's past precedent with regard to similarly situated applicants. Previously, FDA has determined that submission of an application starts the approval phase of the regulatory review period even when the agency later determines that the application is not approvable. *See* A.R. 5514-16 (Determination of Regulatory Review Period for Purposes of Patent Extension; Tonocard Tablets, 50 Fed. Reg. 19,809, 19,810 (May 9, 1985)). The facts in that case are strikingly similar to those presented here: The applicant submitted an application on December 19, 1979. Six months later, FDA declared the initial application to be "nonapprovable." The applicant submitted a different

application a few years later that was eventually approved. The agency found that even though the first application had been declared "nonapprovable" and was replaced by a later application, that fact "did not preclude that application's commencement of the approval phase of the regulatory review period." *Id.* The agency reasoned that while the December application "was not approvable, it was sufficiently complete to permit agency action to begin." *Id.* Accordingly, the applicant received day-for-day credit for the intervening months for patent term extension purposes. *Id.*

FDA has articulated no legitimate basis to justify treating PRADAXA differently than Tonocard Tablets. As a result, FDA should have reached the same result here and included in the approval phase the time it spent reviewing the PRADAXA application between December 2009 and April 2010. *See Friedman v. Sebelius*, 686 F.3d 813, 828 (D.C. Cir. 2012) (finding agency decision arbitrary and capricious because "it failed to explain its departure from the agency's own precedents"); *Bracco Diagnostics*, 963 F. Supp. at 27-28 ("[A]n agency must treat similar cases in a similar manner unless it can provide a legitimate reason for failing to do so." (citations omitted)). Because FDA acted arbitrarily and conspicuously, its decision should be reversed.

CONCLUSION

For all of the foregoing reasons, Plaintiffs' motion for summary judgment should be granted.

Respectfully submitted,

HOGAN LOVELLS US LLP

By: /s/ Catherine E. Stetson

Catherine E. Stetson (DC Bar # 453221)
Susan M. Cook (DC Bar # 462978)
James R. Johnson (DC Bar # 1003740)
555 Thirteenth Street NW
Washington, DC 20004
Telephone: 202-637-5600
Fax: 202-637-5910
cate.stetson@hoganlovells.com
susan.cook@hoganlovells.com
james.johnson@hoganlovells.com

Counsel for Plaintiffs Boehringer Ingelheim Pharma & Co. KG and Boehringer Ingelheim Pharmaceuticals, Inc.

Dated: September 18, 2015