IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

EISAI INC.,	)	
Plaintiff,	)	
v.	)	No. 1:14-CV-01346-RCL
UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,	)	
Defendants.	)	

EISAI INC.'S MEMORANDUM OF POINTS AND AUTHORITIES
IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT

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INTRODUCTION

When a pharmaceutical company secures approval from the Food and Drug Administration (FDA) of a drug with an active ingredient not previously approved in the United States (called a New Chemical Entity, or NCE), the company is awarded five years of market exclusivity—meaning that the company is entitled to market its drug for five years while no other company can market the same drug during that period. In keeping with this arrangement, Eisai, the Plaintiff here, was awarded five years of market exclusivity for two of its drugs, BELVIQ® and FYCOMPA®, both of which represented NCEs to treat important medical conditions. But that period was arbitrarily cut short. FDA prohibited Eisai from marketing the drugs until the Drug Enforcement Administration (DEA) had "scheduled" them under the Controlled Substances Act (CSA) and the products' labeling incorporated the scheduling information—which did not occur for months and months after FDA issued approval letters for the products. Yet FDA insisted that Eisai's market exclusivity period for both drugs began to run from the date of FDA's approval letters, not from the much later date when Eisai was finally permitted to market its drugs. As a result, instead of having five years of market exclusivity, Eisai will be limited to a little over four years of such exclusivity for BELVIQ®, and less than four years for FYCOMPA®.

FDA got it wrong. The Congressionally mandated exclusivity periods for BELVIQ® and FYCOMPA® should have been triggered only when those products could be legally marketed. FDA's determination that the exclusivity periods were triggered at an earlier date, when the products could not be marketed, is arbitrary, capricious, contrary to the law, and contrary to the agency's prior practice. The Court should grant Eisai's motion and prevent Defendants from depriving Eisai of its full, five-year exclusivity periods for BELVIQ® and FYCOMPA®.

STATEMENT OF LEGAL AND FACTUAL BACKGROUND

A. FIVE-YEAR MARKET EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

1. The Hatch-Waxman Act

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585. Commonly known as the "Hatch-Waxman Act," the law amended the Federal Food, Drug, and Cosmetic Act (FDCA) to put in place incentives designed to expedite approval of generic drugs without undermining the development of innovative drugs. *See generally Actavis Elizabeth LLC v. U.S. Food & Drug Admin.*, 625 F.3d 760, 765 (D.C. Cir. 2010).

At the same time the Hatch-Waxman Act made it significantly easier for generic drugs to receive FDA approval, Congress recognized that developers of NCEs invest substantial sums on research and development, with no guarantee that their efforts will bear fruit. Indeed, the development of NCEs is resource-intensive and fraught with failure. It has been estimated that it takes about twelve years and hundreds of millions of dollars to bring a new drug to market—and few drugs ever make it that far. AR 45. Accordingly, the Hatch-Waxman Act amended the FDCA to grant successful developers of certain new drug substances a limited period of protection from generic competition. *See* AR 161-263, H.R. Rep. No. 98-857 (1984).

One of the ways Congress implemented that protection was through a five-year market exclusivity period for NCEs. *See* 21 U.S.C. §§ 355(c)(3)(E), (j)(5)(F). During that five-year exclusivity period, generic drug sponsors are generally precluded from seeking FDA approval through the abbreviated procedures ordinarily available for generic versions of approved new

drug products.[1] *See id*.

2. The "Trigger Date" For Five-Year Market Exclusivity

FDA defines the trigger date for the start of a market exclusivity period as:

> the date on the letter from FDA stating that the new drug application is approved, whether or not final printed labeling or other materials must yet be submitted *as long as approval of such labeling or materials is not expressly required*. "Date of approval" refers only to a final approval and not a tentative approval that may become effective at a later date.

21 C.F.R. § 314.108(a) (emphasis added). The governing FDA regulation thus makes clear that, while typically the date of a drug's FDA approval letter is the "trigger date" for exclusivity, there are exceptions. And the preamble to the final rule promulgating the above regulation made clear that such exceptions involved situations where, even though an approval letter was issued, additional labeling was required before the drug could be "legally marketed." AR 282, 54 Fed. Reg. 28,872, 28,898 (July 10, 1989) ("labeling or other material that might delay the actual initiation of marketing of the product is not relevant to a determination of the date of approval, *so long as the product could be legally marketed*.") (emphasis added). Simply put, if further labeling is required to legally market the drug, the approval letter would not trigger the exclusivity period.[2]

True to the regulation, FDA previously has applied 21 C.F.R. § 314.108(a) to assign the

[1] Under the FDCA, when an NCE is entitled to five-year market exclusivity, a generic drug application may not be submitted to FDA "before the expiration of five years from the date of the approval of the [NCE] application." 21 U.S.C. §§ 355(c)(3)(E), (j)(5)(F). A generic application may be submitted after the expiration of four years from the date of the approval if it contains a certification of patent invalidity or noninfringement. *See id.* FDA's regulation—21 C.F.R. § 314.108(a)—defines the "date of approval" for purposes of triggering a market exclusivity period.

[2] References throughout this brief to the date on which Eisai could "market" or "legally market" the drug refer to the date on which Eisai could legally launch the drug in interstate commerce.

trigger date for exclusivity to when a drug could be marketed, not when the approval letter was issued. *See* AR 17 n.92. For the drug RAZADYNE® ER, for example, FDA issued an approval letter in December 2004. *See* Dkt. 1-1, 1-2, 1-3, Compl. Exs. A, B, C. But FDA later changed the date triggering the drug's exclusivity period to April 1, 2005, because the agency concluded that was the earliest date that RAZADYNE® ER could have been marketed.[3] *See* Dkt. 1-4, 1-5, 1-6, Compl. Exs. D, E, F.

B. CSA SCHEDULING OF FDA-APPROVED DRUGS

The CSA requires the United States Department of Health and Human Services (HHS) to notify DEA when it appears that a New Drug Application (NDA) involves a drug that has "abuse potential." 21 U.S.C. § 811. In those instances, FDA analyzes the drug's potential for abuse and prepares a recommendation as to how that drug should be scheduled, which HHS must forward to DEA "within a reasonable time." *Id.* § 811(b). After analyzing the recommendation and assessing the drug's abuse potential, DEA initiates notice-and-comment rulemaking for the drug's "scheduling"—meaning its placement of a drug substance into a controlled-substance category, or "schedule."[4] *Id.* § 811(a); 21 C.F.R. pt. 1308. Once DEA has reviewed comments to its proposed rule scheduling the drug, it publishes a notice in the Federal Register finalizing the drug's scheduling and setting the effective date for its action. *See* 21 C.F.R. § 1308.45. In

[3] RAZADYNE® ER (known at the time of its approval as galantamine hydrobromide extended release capsules) was approved on December 22, 2004 without a trade name, but the drug's sponsor agreed to not market the drug until a trade name was adopted. *See* Dkt. 1-1, Compl. Ex. A at 2. The drug's sponsor and FDA agreed to the trade name "Razadyne" on April 1, 2005. *See* Dkt. 1-4, Compl. Ex. D. Thereafter, FDA moved the trigger date for exclusivity to April 1, 2005—the earliest date RAZADYNE® ER could be marketed. *See* Dkt. 1-3, 1-4, 1-5, Compl. Exs. D, E, F.

[4] There are five schedules, indicated by Roman numerals I through V. Schedule I drugs have no acceptable medical use. Schedule V drugs have a very low abuse potential. Schedules II through IV occupy the spectrum in between. *See* 21 U.S.C. § 812.

accordance with both FDA and DEA regulations, the final scheduling information must then be incorporated into the drug's labeling. *See* 21 C.F.R. §§ 201.57(a)(2), 201.57(c)(10)(i), 1302.04.

A pharmaceutical company cannot legally market a product subject to CSA scheduling until this process has run its course. To begin with, as a precondition to its review of an NDA, FDA requires that a company certify that it "agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision." AR 88, 91; *see also* 21 C.F.R. §§ 314.50, 314.101(d); Revised Form FDA 356h, Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use, 62 Fed. Reg. 36,558, 36,560 (July 8, 1997). FDA concedes that "FDA will not file an NDA unless the NDA holder has completed and signed the Form FDA 356h." AR 9. Failure to comply with the certification could result in criminal penalties. AR 88, 91. FDA's regulations also expressly require that FDA approve the labeling with the CSA symbol. *See* 21 C.F.R. §§ 314.70(b)(2)(v)(C), 201.57(a)(2).

C. FDA SHORTENS THE MARKET EXCLUSIVITY PERIODS OF EISAI'S NEW CHEMICAL ENITIES

1. BELVIQ®

Eisai holds the NDA for BELVIQ®, an NCE statutorily entitled to a five-year period of market exclusivity. BELVIQ® is an innovative weight-management treatment designed to treat obesity; it is the first drug in over thirteen years deemed safe and effective for that purpose. AR 22-23. It took fourteen years and cost over $300 million to develop BELVIQ®. AR 22. Under a marketing and supply agreement with Arena Pharmaceuticals GmbH (Arena) for BELVIQ®, Eisai is responsible for the marketing and distribution of BELVIQ® in the United States. AR 23.

On June 27, 2012, FDA issued a letter approving BELVIQ® as safe and effective. But the letter stated that Eisai could not yet legally market the drug:

The final scheduling of this product under the Controlled Substances Act

> is currently proceeding, but not yet complete as of the date of this letter. We remind you that . . . you agreed not to market this drug until the Drug Enforcement Administration has made a final scheduling decision. We further note that, when the scheduling is finalized, you will need to make appropriate revisions to the package insert, the patient package insert and the carton and immediate-container labels through supplementation of your NDA. This would include the statements detailing the scheduling of Belviq in the labeling, as required under 21 CFR 201.57(a)(2) and (c)(10)(i).

AR 67-68. After issuing the letter, FDA included BELVIQ® in its publication *Approved Drug Products With Therapeutic Equivalence Evaluations*, commonly known as "the *Orange Book*." In so doing, FDA determined that BELVIQ®'s five-year market exclusivity period began on June 27, 2012—the date of FDA's approval letter. AR 97.

At that time, however, DEA had not even begun its scheduling process. On June 25, 2012, just two days before FDA approved BELVIQ® as safe and effective, DEA received HHS's scheduling recommendation for the drug. AR 421-23, 77 Fed. Reg. 75,075, 75,077 (Dec. 19, 2012). DEA's notice-and-comment rulemaking process to schedule BELVIQ® did not begin until six months later. *Id.* DEA finalized BELVIQ®'s scheduling under the CSA as a Schedule IV drug effective June 7, 2013. *See* AR 452, 78 Fed. Reg. 26,701 (May 8, 2013). Only then—nearly a year after FDA's approval letter and FDA's improper triggering of the market exclusivity period—was Eisai able to incorporate the final schedule into the BELVIQ® labeling and legally market the drug.

2. FYCOMPA®

Eisai also holds the NDA for FYCOMPA®, another NCE statutorily entitled to a five-year period of market exclusivity. FYCOMPA® is a groundbreaking treatment for uncontrolled partial-onset seizures, which can occur in a patient with epilepsy. AR 24-25. Eisai developed FYCOMPA® by targeting certain brain receptors that had never before been targeted by a drug

proven safe and effective. *Id.* That exhaustive research effort took years and a substantial investment of resources, resulting in 1,410,750 pages of data submitted as part of FYCOMPA®'s FDA approval process. *See* Dkt. 1, Compl. ¶ 46. Because of FYCOMPA®'s "unique mechanism of action," FDA has recognized the drug as "First-in-Class" for treating partial-onset seizures. AR 25.

On October 22, 2012, FDA issued a letter approving FYCOMPA® as safe and effective. In the letter, FDA restated the same prohibition it had for BELVIQ®:

> The final scheduling of this product under the Controlled Substances Act is currently proceeding, but not yet complete as of the date of this letter. We remind you that . . . you agreed not to market this drug until the Drug Enforcement Administration has made a final scheduling decision. We further note that, when the scheduling is finalized, you will need to make appropriate revisions to the package insert, the patient package insert and the carton and immediate-container labels through supplementation of your NDA. This would include the statements detailing the scheduling of Fycompa in the labeling, as required under 21 CFR 201.57(a)(2) and (c)(10)(i).

AR 76-77. Indeed, the labeling itself that accompanied FDA's letter for FYCOMPA® states:

> **9.1 Controlled Substance**
>
> FYCOMPA contains perampanel. **(Schedule to be determined after DEA review).**

See Ex. 1, FDA Approved Labeling Text, NDA 202834; *see also* AR 34 n.20. After issuing the letter, FDA included FYCOMPA® in the *Orange Book*, determining that FYCOMPA®'s five-year market exclusivity period began on October 22, 2012. AR 101-02.

When FDA issued the letter approving FYCOMPA® as safe and effective, however, DEA had not even received FDA's scheduling recommendation. That happened three months later on January 22, 2013. AR 465-66, 78 Fed. Reg. 62,500, 62,501 (Oct. 22, 2013). The start of FYCOMPA®'s scheduling process was then delayed for another nine months. *Id.* Final scheduling of FYCOMPA® as a Schedule III drug under the CSA did not become effective until

January 2, 2014—more than fourteen months after FDA's approval letter. *See* 78 Fed. Reg. 72,013 (Dec. 2, 2013). Again, only then—more than fourteen months after FDA's approval letter and FDA's improper triggering of the market exclusivity period—was Eisai able to incorporate the final schedule into the FYCOMPA® labeling and legally market the drug.

D. FDA DENIES EISAI'S CITIZEN PETITION

In July 2013, Eisai filed Citizen Petition No. 2013-P-0884 to address FDA's premature commencement of the market exclusivity periods for BELVIQ® and FYCOMPA®. *See* AR 20-143. The Petition requested that the Commissioner determine that the trigger date that starts the five-year exclusivity period for BELVIQ® is June 7, 2013, the date Eisai could launch BELVIQ® in interstate commerce; and that the Commissioner determine that the trigger date that starts the five-year exclusivity period for FYCOMPA® is the date Eisai could launch the product in interstate commerce. (That date turned out to be January 2, 2014.)

FDA did not respond to the Petition until late April 2014. FDA acknowledged that Eisai had "lost valuable marketing time during the 5-year NCE exclusivity period" and stated that it understood Eisai's "equitable arguments." AR 18. Although FDA explained that it was "actively considering whether it should change its approach going forward," it denied the Petition. *Id.*

In denying the Petition, FDA conceded that 21 C.F.R. § 314.108(a) provides both a "general rule" that market exclusivity is triggered on the date of FDA's approval letter and an "exception to the general rule" when exclusivity is triggered at a later date, i.e., when approval of further labeling or materials is expressly required. AR 17-18. Nonetheless, FDA refused to apply the § 314.108(a) "exception" to BELVIQ® and FYCOMPA®, contending that "the approval letters for the drugs at issue here do not 'expressly require' approval of labeling or other

materials," nor do the letters "impliedly require such approval." AR 17. FDA's decision constitutes a final agency action. *See* 21 C.F.R. § 10.45(d).

STANDARD OF REVIEW

Summary judgment is appropriate when "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). "[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).

SUMMARY OF ARGUMENT

The Congressionally mandated exclusivity periods for BELVIQ® and FYCOMPA® should have been triggered only when those products could be legally marketed. But FDA erroneously triggered the five-year market exclusivity periods for BELVIQ® and FYCOMPA® long before FDA allowed Eisai to legally market the products. As a consequence, BELVIQ® lost almost one year and FYCOMPA® lost *more* than one year of their respective five-year market exclusivity periods. In foreshortening those exclusivity periods, FDA violated its own controlling regulation, departed from past agency practice, treated BELVIQ® and FYCOMPA®

differently than similarly situated products, and provided no reasonable basis for any of these actions. For any one of these reasons, Defendants' actions violate the APA. Eisai is entitled to summary judgment.

ARGUMENT

I. FDA VIOLATED THE APA BY TRIGGERING BELVIQ® AND FYCOMPA®'S FIVE-YEAR MARKET EXCLUSIVITY PERIODS BEFORE THE PRODUCTS COULD BE LEGALLY MARKETED.

FDA's determination that the five-year market exclusivity periods for BELVIQ® and FYCOMPA® commenced well before those products could be legally marketed is contrary to its own controlling regulations and past agency practice. FDA has failed to proffer any reasonable justification for its decision, and no case law supports its actions.

A. FDA Violated Its Own Regulation Governing the Five-Year Market Exclusivity Trigger Date.

FDA has violated one of the core axioms of administrative law: "that an agency must adhere to its own regulations." *Brock v. Cathedral Bluffs Shale Oil Co.*, 796 F.2d 533, 536 (D.C. Cir. 1986) (citations omitted). Administrative agencies "may not violate their own rules and regulations to the prejudice of others." *Battle v. Fed. Aviation Admin.*, 393 F.3d 1330, 1336 (D.C. Cir. 2005) (citation omitted). Yet that is precisely what FDA has done here, and that error alone warrants this Court invalidating FDA's actions regarding BELVIQ® and FYCOMPA®'s five-year market exclusivity periods.

FDA's regulation, 21 C.F.R. § 314.108(a), specifically defines the market exclusivity trigger date as:

> the date on the letter from FDA stating that the new drug application is approved, whether or not final printed labeling or other materials must yet be submitted *as long as approval of such labeling or materials is not expressly required*. "Date of approval" refers only to a final approval and not a tentative approval that may

become effective at a later date. (Emphasis added.)

As § 314.108(a) makes clear, the date of FDA's approval letter is not necessarily the trigger date for market exclusivity. The regulation provides for what FDA has called an "exception," AR 17 n.92, applicable when approval of further "labeling or other materials" is required. *Id.* Because a drug cannot be legally marketed without its required labeling, *see* 21 U.S.C. §§ 331(a), (k), and 352; 21 C.F.R. pt. 201, this exception in effect ensures that the exclusivity trigger is tied to the date that the drug can be legally marketed.

This is precisely how FDA has applied 21 C.F.R. § 314.108(a) in the past. *See infra* at 14-15. For example, FDA candidly admitted in denying Eisai's Petition that it previously had "applied" the § 314.108(a) "exception" to the drug RAZADYNE® ER, and in doing so had changed the date triggering RAZADYNE® ER's exclusivity period from the date of FDA's approval letter to the date that the drug could have been marketed. *See* AR 17-18 n.92; Dkt. 1-1 - 1-6, Compl. Exs. A - F.

Tying the market-exclusivity trigger to the date on which a drug can be legally marketed is also consistent with other provisions of the FDCA and FDA regulations. Under the FDCA, for instance, a drug cannot be legally marketed in interstate commerce until approval is *effective*—not just announced. The statute states:

> No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of [a new drug] application . . . *is effective* with respect to such drug.

21 U.S.C. § 355(a) (emphasis added). The corresponding regulation also expressly makes clear that approval is only effective when a company is able to legally market the drug: 21 C.F.R. § 314.105(a) provides that "[a] new drug product . . . may not be marketed until an approval is effective."

It is entirely logical that five-year market exclusivity should hinge on when the drug could actually be commercially launched. It would have been odd indeed if Congress granted an NCE sponsor five years of exclusivity to market the product only to allow FDA to shorten that time frame by hinging the exclusivity period on a trigger *other* than when FDA allows the sponsor to legally market the product.[5] In the preamble to the final rule promulgating 21 C.F.R. § 314.108(a), FDA recognized as much. It noted that the key to determining when the exclusivity period begins is when the product could be "legally marketed": "labeling or other material that might delay the actual initiation of marketing of the product is not relevant to a determination of the date of approval, *so long as the product could be legally marketed*." *See* AR 282, 54 Fed. Reg. 28,872, 28,898 (July 10, 1989) (emphasis added).

In this case, Eisai could not legally market BELVIQ® and FYCOMPA® until the products' labeling incorporated final CSA scheduling symbols. For one thing, FDA's Form FDA 356h expressly required that Eisai refrain from launching BELVIQ® and FYCOMPA® into the marketplace prior to CSA scheduling. And once CSA scheduling was complete, FDA regulations expressly required that labeling incorporate the CSA symbol *before the products could be legally marketed.* See 21 C.F.R. §§ 201.57(a)(2), 201.57(c)(10)(i), 1302.04.[6] FDA's

[5] " 'FDA may not . . . change the incentive structure adopted by the Congress, for the agency is bound not only by the ultimate purposes Congress has selected, but by the means it has deemed appropriate, and prescribed, for the pursuit of those purposes.' " *Teva Pharm. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1316 (D.C. Cir. 2010) (quoting *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120, 121-122 (D.C. Cir. 2006)). FDA cannot arrogate for itself the power to deprive an NCE sponsor of its "earned exclusivity." *Id.* at 1317 (citing *Ranbaxy Labs.*, 469 F.3d at 125).

[6] FDA's letters approving BELVIQ® and FYCOMPA® as safe and effective further support this conclusion. FDA's letters make clear that the products' labeling would need to be revised once CSA scheduling was complete. *See supra* at 5-7. Indeed, the labeling itself that accompanied FDA's letter for FYCOMPA® states:

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regulations, moreover, expressly required that FDA approve BELVIQ® and FYCOMPA®'s labeling with the CSA symbol. *See* 21 C.F.R. §§ 314.70(b)(2)(v)(C), 201.57(a)(2).

Pursuant to 21 C.F.R. § 314.108(a), then, the date of FDA's approval letters for BELVIQ® and FYCOMPA® cannot be considered the triggering date for market exclusivity purposes. Rather, BELVIQ®'s market exclusivity should not have begun to run until June 7, 2013—the date on which the drug's labeling incorporating the assigned CSA symbol permitted the product to be first legally marketed. FYCOMPA®'s market exclusivity period should not have begun to run until January 2, 2014—the date on which the drug's labeling incorporating the assigned CSA symbol permitted the product to be first legally marketed. FDA's failure to follow the plain language of its own regulations violated the APA. *See, e.g.*, *Mine Reclamation Corp. v. Fed. Energy Regulatory Comm'n*, 30 F.3d 1519, 1524 (D.C. Cir. 1994) ("On its way to decision, however, the agency must follow its own regulations; '[i]t is a well-settled rule that an agency's failure to follow its own regulations is fatal to the deviant action.' ") (internal quotation marks and citation omitted); *Fuller v. Winter*, 538 F. Supp. 2d 179, 186 (D.D.C. 2008) ("It is a fundamental principle of administrative law that an agency is bound to adhere to its own regulations. Indeed, failure to do so can lead to arbitrary and capricious decision-making in violation of the APA.") (citations omitted).

B. FDA Departed from Past Agency Practice.

FDA's error in failing to adhere to its own controlling regulations is all the more glaring because it is contrary to the agency's prior practice.

FYCOMPA contains perampanel. **(Schedule to be determined after DEA review).**

See supra at 7. Thus, after CSA scheduling, a revision to the labeling was required before the product could be legally marketed.

FDA has previously applied 21 C.F.R. § 314.108(a) to ensure that the date triggering a drug's exclusivity period was the date the drug could be marketed rather than the approval letter date. *See* AR 17 n.92. On December 22, 2004, FDA issued an approval letter for RAZADYNE® ER. *See* Dkt. 1-1, Compl. Ex. A. The approval letter unambiguously stated that the drug was "approved, effective [December 22, 2004], for use as recommended in the attached agreed-upon labeling text." *Id.* Thereafter, the drug's sponsor issued a press release confirming that RAZADYNE® ER was "[a]pproved by the U.S. Food and Drug Administration (FDA) in December 2004." *See* Dkt. 1-2, Compl. Ex. B. As of the date of this lawsuit, FDA's public database of approved drug products still listed RAZADYNE® ER's approval date as December 22, 2004. *See* Dkt. 1-3, Compl. Ex. C.

On June 13, 2006, however, well after RAZADYNE® ER was commercially launched, FDA decided to reach back and move the date triggering the drug's exclusivity period to April 1, 2005, because that was the earliest date on which RAZADYNE® ER could have been marketed.[7] *See* Dkt. 1-4, Compl. Ex. D. FDA then officially changed the trigger date for RAZADYNE® ER's market exclusivity period from December 22, 2004 to April 1, 2005 in the *Orange Book*. *Compare* Dkt. 1-5, Compl. Ex. E *with* Dkt. 1-6, Compl. Ex. F.

As the RAZADYNE® ER example makes clear, FDA has relied on 21 C.F.R. § 314.108(a) to retroactively amended the date triggering a drug's exclusivity period from the

[7] RAZADYNE® ER was approved without a trade name, and the drug's sponsor agreed to not market the drug until a trade name was adopted. *See supra* at 4 n.3; Dkt. 1-1, Compl. Ex. A at 2. The decision by the drug's sponsor to not market the drug before a trade name was adopted was voluntary; a trade name is not required to legally market an approved drug. *See* 21 U.S.C. § 352 (requiring an established or non-proprietary name on the label of a drug product but not requiring a proprietary or trade name). Thus, if FDA was willing to alter RAZADYNE® ER's exclusivity-trigger date when the decision to not market the drug was a voluntary agreement between the sponsor and FDA, the agency certainly should have done so for BELVIQ® and FYCOMPA® when the ability to market those products was actually prohibited by FDA itself.

approval letter date to the date the drug could be marketed. *See* AR 17 n.92. And in the case of RAZADYNE® ER, FDA did so long after the drug was approved and commercially launched. Despite this clear agency precedent, FDA has refused to change the market exclusivity triggers for BELVIQ® and FYCOMPA®. Such "an administrative about-face" requires searching judicial review, *Greater Yellowstone Coal. v. Kempthorne*, 577 F. Supp. 2d 183, 189 (D.D.C. 2008), because an "unexplained reversal" from past practice is "the height of arbitrary and capricious decision making." *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 884 (D.C. Cir. 2004). FDA also has failed to provide any basis—let alone the required reasonable basis—for treating BELVIQ® and FYCOMPA® differently. AR 1-19. Indeed, the Administrative Record indisputably confirms that FDA made no attempt to consider why BELVIQ® and FYCOMPA® should be treated differently than RAZADYNE® ER. AR 1-538.

Because FDA "has failed to provide a reasoned explanation," and "the record belies the agency's conclusion," the Court should "undo its action." *Cnty. of Los Angeles v. Shalala*, 192 F.3d 1005, 1021 (D.C. Cir. 1999) (internal quotation marks and citation omitted); *see also PREVOR v. Food & Drug Admin.*, 895 F. Supp. 2d 90 (D.D.C. 2012) (vacating FDA's decision because, among other things, FDA failed to provide a reasoned basis for its change in course).

C. FDA Provided No Justifiable Basis for Determining that BELVIQ® and FYCOMPA® Do Not Qualify for the 21 C.F.R. § 314.108(a) "Exception."

FDA has provided no justifiable basis for determining that BELVIQ® and FYCOMPA® do not qualify for the 21 C.F.R. § 314.108(a) "exception." AR 1-19. In its response to Eisai's Petition, FDA articulated only one rationale: "the approval letters for the drugs at issue here do not 'expressly require' approval of labeling or other materials" nor do the letters "impliedly require such approval." AR 17. But the agency erroneously read into the 21 C.F.R. § 314.108(a) "exception" a requirement that the "approval letters for the drugs" must *themselves* expressly

require approval of further labeling. There is no such requirement under the clear language of the regulation. And the RAZADYNE® ER approval letter makes no mention of an express requirement for the "approval of labeling or other materials." *See* Dkt. 1-1, Compl. Ex. A.

FDA's rationale is also flawed for the reasons we have explained above. The agency ignored the fact that FDA's Form FDA 356h expressly required final CSA scheduling before BELVIQ® and FYCOMPA® could be legally marketed; once CSA scheduling was complete, FDA and DEA regulations expressly required labeling that incorporated the CSA symbol before the products could be legally marketed, *see* 21 C.F.R. §§ 201.57(a)(2), 201.57(c)(10)(i), 1302.04; and FDA regulations expressly required that FDA approve the labeling with the CSA symbol, *see* 21 C.F.R. §§ 314.70(b)(2)(v)(C), 201.57(a)(2). It also ignored the fact that both the BELVIQ® and FYCOMPA® approval letters expressly required that the drugs' labeling incorporate CSA scheduling information through supplementation of their respective NDAs before the products could be marketed,[8] and as already discussed, FDA's regulations expressly require that FDA approve the labeling with the CSA symbol. And it ignored the very standard the agency applied to RAZADYNE® ER. *See* AR 17-18 n.92. If RAZADYNE® ER meets the 21 C.F.R. § 314.108(a) "exception" standard—because the agency and sponsor voluntarily agreed that the drug would not be marketed until a trade name was adopted—surely so must BELVIQ® and FYCOMPA®.

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[8] The BELVIQ® and FYCOMPA® approval letters both expressly stated that:

> when the scheduling is finalized, you will need to make appropriate revisions to the package insert, the patient package insert and the carton and immediate-container labels through supplementation of your NDA. This would include the statements detailing the scheduling of [the drug] in the labeling, as required under 21 CFR 201.57(a)(2) and (c)(10)(i).

AR 67-68, 76-77.

II. FDA VIOLATED THE APA BY TREATING BELVIQ® AND FYCOMPA® DIFFERENTLY THAN OTHER NCES AND SIMILARLY SITUATED PRODUCTS.

The arbitrariness of FDA's actions depriving BELVIQ® and FYCOMPA® of full five-year market exclusivity periods is also plain when comparing its treatment of BELVIQ® and FYCOMPA® to its treatment of other NCEs. " 'An agency must treat similar cases in a similar manner unless it can provide a legitimate reason for doing so.' " *PREVOR*, 895 F. Supp. 2d at 99 (quoting *Indep. Petroleum Ass'n of Am. v. Babbitt*, 92 F.3d 1248, 1258 (D.C. Cir. 1996)). Yet FDA has treated BELVIQ® and FYCOMPA® differently from other similarly situated products with absolutely no justification. That "is the essence of the meaning of arbitrary and capricious." *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 28 (D.D.C. 1997) (citations omitted).

A. Disparate Treatment of NCEs that Do Not Require CSA Scheduling.

FDA's refusal to tie the market exclusivity trigger for BELVIQ® and FYCOMPA® to the date on which Eisai could legally market those products unfairly penalizes Eisai for developing NCEs that require CSA scheduling. Under FDA's flawed application of the law, sponsors of NCEs that do *not* require CSA scheduling—and thus can legally market their products immediately after receiving NDA approval—enjoy full five-year market exclusivity periods. For example, the FDA approved MYRBETRIQ® (mirabegron) on June 28, 2012 and XELJANZ® (tofacitinib) on November 6, 2012—roughly the same time as it approved BELVIQ® and FYCOMPA®, respectively. AR 125-31, 133-41. In contrast to Eisai's products, however, MYRBETRIQ® and XELJANZ® were not subject to CSA scheduling. They accordingly will enjoy full five-year market exclusivity periods, free from the vagaries of DEA's scheduling process. FDA failed to articulate any legitimate explanation for this disparity in response to

Eisai's Petition or in the administrative record more generally.[9]

B. Disparate Treatment of NCEs that Require CSA Scheduling.

FDA's erroneous view of the trigger for market exclusivity not only results in products that require CSA scheduling being treated differently from those that do not, but it also results in various CSA scheduled products being treated differently from one another. *See, e.g.*, AR 143 (historical data detailing CSA scheduled products being treated differently from one another). The time it takes FDA to provide DEA with scheduling recommendations for drugs with "abuse potential" varies dramatically and does not correspond to the date FDA issues approval letters. This results in similarly situated products having exclusivity periods of fluctuating and arbitrary lengths.

For PROVIGIL® (modafinil), for instance, FDA submitted its recommendation to DEA 367 days *before* issuing the drug's approval letter.[10] AR 143; *see also* 64 Fed. Reg. 4050, 4051 (Jan. 27, 1999). As a result, the sponsor of PROVIGIL® lost only 34 days of its five-year market exclusivity period. *Id.* But for BELVIQ®, FDA submitted its scheduling recommendation a mere two days before issuing the approval letter, and Eisai subsequently lost 345 days of market exclusivity for the product. AR 38-39, 143. That is a difference of 313 days compared to the period of market exclusivity enjoyed by the sponsor of PROVIGIL®.

FDA's arbitrary and capricious conduct is even more glaring in light of FDA's handling of the drug BELSOMRA® (suvorexant). BELSOMRA® was scheduled directly after FYCOMPA®. But that is where the likenesses end. For FYCOMPA®, FDA submitted its

[9] Eisai raised this issue in its Petition. AR 38. FDA ignored it. FDA's denial of the Petition and the Administrative Record are both devoid of any consideration of FDA's disparate treatment of NCEs that do not require CSA scheduling. AR 1-538.

[10] FDA issued the PROVIGIL® approval letter on December 24, 1998. *See* http://www.accessdata.fda.gov/drugsatfda_docs/nda/98/020717A_Provigil_appltr.pdf.

scheduling recommendation 92 days *after* issuing the approval letter, and as a result, Eisai lost 437 days of its market exclusivity period. *See supra* at 7; AR 143. In contrast, for BELSOMRA®, FDA submitted its scheduling recommendation 412 days *before* issuing the approval letter, and as a result, the sponsor lost only 47 days of its market exclusivity period.[11] *See* 79 Fed. Reg. 51,243 (Aug. 28, 2014).

FDA has again failed to proffer any rationale for such discrepancies. Its denial of the Petition and the Administrative Record are both devoid of any consideration of FDA's disparate treatment of NCEs that require CSA scheduling.[12]

* * *

The five-year exclusivity period is a valuable statutory right. The FDA has acknowledged as much, stating that "such exclusivity provides a critical incentive for drug development that advances FDA's goal of protecting and promoting public health." AR 64, Defendant's Motion for Stay Pending Appeal, *Tummino v. Hamburg*, No. 12-CV-763 (ERK/VVP), Dkt. 91-1 at 16 (E.D.N.Y. May 1, 2013). Depriving Eisai full exclusivity "would stifle rather than encourage innovation, to the detriment of the public." *Id.* The Court should correct FDA's error. Defendants' actions violate the FDCA, its implementing regulations, and the APA. Accordingly, declaratory and injunctive relief is needed to remedy Defendants' unlawful acts and to obtain for BELVIQ® and FYCOMPA® the full five-year market exclusivity period to which each product is statutorily entitled.

[11] FDA issued the BELSOMRA® approval letter on August 13, 2014. *See* http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/204569Orig1s000Approv.pdf.

[12] Eisai also raised this issue in its Petition, AR 38-39, and again FDA ignored it. AR 1-538.

CONCLUSION

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

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Respectfully submitted,

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