Eisai Inc.
100 Tice Blvd., Woodcliff Lake, NJ 07677
Phone: 201-692-1100

hhe
human health care

July 25, 2013

2458 13 JUL 25 P1:56

HAND DELIVERY

Dockets Management Branch (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

Eisai Inc. (Eisai) submits this petition under 21 USC 355(c) and (j); 21 CFR 314.107; and 21 CFR 10.30, among other provisions of law, to request that the Food and Drug Administration (FDA) ensure that Eisai receives the full statutory exclusivity period mandated by Congress for New Chemical Entities (NCEs). Congress provided NCEs with five years of market exclusivity to provide an incentive for drug development and to allow companies to recoup at least some of their initial investment. Contrary to the law and Congressional intent, FDA started the NCE exclusivity periods for two of Eisai's products before Eisai can commercially market the products.[1] Specifically, as a consequence of the FDA's own requirements of sponsors, Eisai's products could not be commercially marketed – that is, introduced into interstate commerce – until the U.S. Drug Enforcement Administration (DEA) finalizes the schedules for the drugs under the Controlled Substances Act (CSA).

Although the drug scheduling process and the dates Eisai can market its products are outside of Eisai's control, FDA has started Eisai's market exclusivity periods. Indeed, unless the relief requested is granted, one of Eisai's products, BELVIQ®, will lose approximately one year – or 20% – of exclusivity due to FDA-required delays. Eisai respectfully requests that FDA ensure that Eisai's products receive the full statutory exclusivity period as Congress intended.

[1] The two products at issue are BELVIQ® (lorcaserin hydrochloride) and FYCOMPA™ (perampanel). Eisai has a marketing and supply agreement with Arena Pharmaceuticals GmbH (Arena) for BELVIQ®.

2013-6053

CP

FDA-2013-P-0884

FDA can do so by determining that the NCE market exclusivity periods for Eisai's products begin after DEA completes the drug scheduling process.

ACTIONS REQUESTED

The undersigned respectfully requests that the Commissioner take the following actions:

1. Determine that the date of approval that starts the five-year NCE exclusivity period for BELVIQ® is June 7, 2013, the date that Eisai could commercially market BELVIQ® in interstate commerce.
2. Determine that the date of approval that starts the five-year NCE exclusivity period for FYCOMPA™ is the date that Eisai can commercially market the product in interstate commerce.
3. Provide a substantive response to this petition before FYCOMPA™'s CSA scheduling is finalized, or within five months from the date this petition is submitted to FDA, whichever date is earliest.

STATEMENT OF GROUNDS

I. BACKGROUND

Eisai holds the New Drug Applications (NDAs) for BELVIQ® and FYCOMPA™, which are important new therapies that contain NCEs as active ingredients. FDA issued letters stating that both products are approved, but did not allow commercial marketing of the products until the products' CSA scheduling is completed. Although the drug scheduling process and the dates Eisai can market its products are outside of Eisai's control, FDA erroneously triggered Eisai's market exclusivity periods long before commercial marketing could occur. This deprives Eisai of its *full* five-year NCE exclusivity period for each product.

As FDA well knows, the five-year NCE exclusivity period is a valuable statutory right. FDA has acknowledged the significant interests implicated by diluting the period of exclusivity.

Just this year, FDA publicly advocated against shortening the congressionally-mandated exclusivity period because it would "cause irreparable harm to the regulatory process by undermining the benefits to the public and to FDA of the marketing exclusivity that the [Federal Food Drug and Cosmetic Act (FDCA)] affords to drug sponsors."[2] FDA further stated, "such exclusivity provides a critical incentive for drug development that advances FDA's goal of protecting and promoting public health" and depriving a company, such as Eisai, of its entitled exclusivity period "would stifle rather than encourage innovation, to the detriment of the public."[3] Yet, contrary to those assertions, FDA would deprive Eisai of its full statutory five-year exclusivity periods in these instances.

A. BELVIQ® Is an Important Weight Management Treatment

Americans spend billions of dollars fighting obesity on weight-loss programs, special foods, appetite suppressants, gym memberships, diet books, exercise videos, and even medical surgeries. However, the pharmaceutical industry had not made meaningful progress in combating obesity and had been hampered by diet drugs that proved dangerous, like fen-phen in the 1990s. Determined to overcome this problem, Arena, founded in 1997, recognized early on that obesity is a life-threatening disease for which there was a substantial unmet global medical need for an effective therapeutic treatment.

Arena began its search for a viable therapy for obesity in 1999. Fourteen years later, after an investment of over $300 million, Arena developed BELVIQ® (lorcaserin hydrochloride) for chronic weight management. Arena identified lorcaserin hydrochloride after synthesizing a variety of novel chemical compounds that were subsequently subjected to a serotonin receptor agonist screening program. Critical to the success of this program was Arena's hypothesis that selective serotonin 2C receptor agonists would provide weight-loss benefits without the

[2] Defendant's Motion for Stay Pending Appeal, *Tummino v. Hamburg*, No. 12-CV-763 (ERK/VVP), at 15-16 (E.D.N.Y. May 1, 2013) [Attachment A].

[3] *Id.* at 16.

unacceptable side effects shown by prior drugs. BELVIQ® is believed to work by activating the serotonin 2C receptor in the brain, which may help a person eat less and feel full after eating smaller amounts of food. Beginning in 2002, Arena filed a series of patent applications in order to protect its invention.

Arena had faith in the concept and took a chance to transform the fledgling company into a clinical stage pharmaceutical company. After identification of the molecule, Arena commenced Phase I clinical testing in 2004. Five years would pass before completion of Phase III clinical testing, allowing Arena to begin the FDA approval process. To maintain the financial wherewithal to move forward with its first NDA, Arena was forced to cut costs and reduce its workforce. But despite many ups and downs throughout the years, Arena persisted to bring BELVIQ® to the marketplace.

Eisai has a marketing and supply agreement with Arena with respect to BELVIQ® and has worked with Arena during the NDA review and approval process. Under the agreement with Arena, Eisai is responsible for the marketing and distribution of BELVIQ®, as well as the completion of the required postmarketing studies and trial.

BELVIQ® is an important innovation from a public health perspective. Obesity is the third leading cause of preventable death, and obesity-related medical care is projected to increase annual health care costs in the U.S. by $28 billion/per year through 2020. Given that about one-third of American adults are obese and another one-third are overweight, treating obesity and obesity-related diseases makes up nine percent of all health care spending in this country. Physician and patient access to FDA-approved treatment options has become critical. BELVIQ® was the first drug deemed by the FDA to be safe and effective for this indication in over thirteen years.

B. FYCOMPA™ Is an Important New Therapeutic Option for Epilepsy

Similar to BELVIQ®, FYCOMPA™ is the result of years of development and a significant investment of resources. FYCOMPA™ contains perampanel as its active ingredient and is used to treat patients with epilepsy. Generally, epilepsy is difficult to treat, and FYCOMPA™ represents an important new treatment option. Perampanel acts as a selective, non-competitive a-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor antagonist. The AMPA receptor is present in almost all excitatory neurons and is believed to play a role in a large number of central nervous system diseases. Eisai invested substantially in the identification of the AMPA receptor as a promising target for drug development and the subsequent development of perampanel. The resulting drug product, FYCOMPA™, is the outcome of an exhaustive research effort aimed at discovering and developing an AMPA antagonist compound with a favorable pharmacokinetic and safety profile.

FYCOMPA™ is indicated for use as an adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy aged 12 years and older. Because DEA is still in the process of scheduling perampanel, Eisai is currently not able to commercially market FYCOMPA™ in interstate commerce, despite the fact that it has been 9 months since FDA initiated its five-year NCE exclusivity period.

Epilepsy imposes an immense burden on patients, families, and society. According to the Institute of Medicine's 2012 report "Epilepsy Across the Spectrum: Promoting Health and Understanding," approximately 2.2 million people in the United States have epilepsy. Additionally, 150,000 new cases are diagnosed annually. Partial-onset seizures are the most common type of seizure seen in people with epilepsy. Many patients with partial-onset seizures are uncontrolled and continue to experience seizures with currently available treatments. To address this health concern, it is critical that physicians and their patients have access to additional treatment options that have been FDA-approved for the safe and effective management of these seizures.

FDA noted the need for different treatment options in a press release regarding FYCOMPA™. Dr. Russell Katz, then the director of the Division of Neurology Products in the FDA's Center for Drug Evaluation and Research, stated that "[s]ome people with epilepsy do not achieve satisfactory seizure control from treatments they are currently using." Dr. Katz noted that "[i]t is important to have a variety of treatment options available for patients with epilepsy." FDA also identified FYCOMPA™ as "First-in-Class," because of perampanel's "new and unique mechanism of action for treating a medical condition." FYCOMPA™ is indicated for use as adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy aged 12 years and older. FYCOMPA™ was made available to physicians and patients in Europe in June 2012, and was made available to physicians and patients in Canada in April 2013.

C. Eisai Could Not Commercially Market BELVIQ® and FYCOMPA™ Until Their CSA Scheduling is Complete

FDA has issued letters regarding both BELVIQ® and FYCOMPA™ stating that their NDAs are approved but, at the same time, that the products could not be commercially marketed. Specifically, on June 27, 2012, FDA issued a letter stating that FDA had reviewed the application for BELVIQ® and that the application is approved effective on the date of the letter. However, FDA's letter also "reminds" Eisai that it cannot market BELVIQ® because drug scheduling and related product labeling are not complete. As FDA explained, after the drug scheduling is finalized, the labeling must be revised to incorporate the scheduling information. FDA issued a similar letter regarding FYCOMPA™ on October 22, 2012. Specifically, FDA's letters for BELVIQ® and FYCOMPA™ include the following language:

> We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTROLLED SUBSTANCE SCHEDULING

> 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 on . . . 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/Fycompa] in the labeling, as required under 21 C.F.R. § 201.57(a)(2) and (c)(10)(i).

BELVIQ® and FYCOMPA™ Letters, page 1-2, Attachments B and C.

FDA's marketing prohibition is grounded in the agency's drug application form. FDA required Eisai and Arena, like it has all NDA sponsors for almost 30 years, to sign Form FDA 356h to submit its applications for BELVIQ® and FYCOMPA™.[4] See Attachments D and E. Form FDA 356h includes the following statement prepared by FDA:

> If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

Without signing the Form FDA 356h certification with its prohibition on marketing, FDA would not have filed the new drug applications for BELVIQ® and FYCOMPA™.[5]

---

[4] Arena signed the Form FDA 356h for the initial submission of the BELVIQ® application, however, Eisai, as a subsequent NDA holder, is responsible for the obligations of the initial NDA holder.

[5] *See* 21 CFR 314.101(d); *see also* Revised Form FDA 356h, Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use, 62 FR 36558, 365560 (July 8, 1997). ("Applicants submitting an NDA, ANDA, or AADA may begin to use the new Form FDA 356h immediately. However, such applicants will be required to use the new Form FDA 356h beginning January 8, 1998.").

Following issuance of the letters, FDA included BELVIQ® and FYCOMPA™ in FDA's list of approved drug products. As the products contain NCEs, FDA also indicated that the products had earned NCE exclusivity. The FDCA provides five years of exclusivity for NCEs.[6] The exclusivity prohibits the submission of an Abbreviated New Drug Application (ANDA) or 505(b)(2) application that references the product with exclusivity before the expiration of five years from the "date of approval" of the application with exclusivity.[7] Using the dates from the letters as the "date of approval" for NCE exclusivity purposes, FDA concluded that the NCE exclusivity for BELVIQ® started on June 27, 2012,[8] and the NCE exclusivity for FYCOMPA™ started on October 22, 2012.[9]

FDA made its determination that the exclusivity periods had started even though Eisai could not launch its products into interstate commerce because drug scheduling was not complete. As described below, this is arbitrary, capricious, and contrary to the law, as the timing of the drug scheduling and commercial launch of the products is controlled by FDA and DEA, and not Eisai.

D. Drug Scheduling Is Outside Of Eisai's Control

Under the CSA, FDA-approved drugs with abuse potential, such as lorcaserin (BELVIQ®) and perampanel (FYCOMPA™), are assigned to a schedule (schedules II-V) and regulated as controlled substances. The scheduling of controlled substances is a coordinated effort involving FDA, the Department of Health and Human Services (HHS), and DEA. The

---

[6] *See* 21 USC 355(c)(3)(E) and (j)(5)(F).

[7] If the ANDA or 505(b)(2) application includes a patent challenge, then the application can be submitted after four years from the date of approval of the application with exclusivity.

[8] *See* Attachment F, relevant portion of the *Approved Drug Products With Therapeutic Equivalence Evaluations* (commonly referred to as "the *Orange Book*").

[9] *See* Attachment G, relevant portion of the *Orange Book*.

statute requires FDA to inform DEA at the time an application is submitted for a drug that may have abuse potential. Subsequently, FDA prepares a medical and scientific analysis of the data and information regarding the substance's potential for abuse, and a recommendation for scheduling based on eight factors set out in the CSA. HHS, of which FDA is a part, provides the recommendation to DEA. Based on DEA's review of this analysis, DEA publishes a notice of proposed rulemaking in the Federal Register regarding the proposed scheduling. After reviewing comments to the proposed rule, DEA publishes another Federal Register notice finalizing the scheduling action and establishing a date on which the scheduling action is effective.

With respect to BELVIQ®, HHS's analysis and scheduling recommendation was provided to DEA on June 25, 2012, two days before FDA issued its letter stating that BELVIQ® was approved as safe and effective. It took DEA six months, until December 19, 2013, to publish the proposed rulemaking for lorcaserin in the Federal Register. *See* 77 FR 75075-75079 (December 19, 2012). Although the comment period for the proposed rulemaking ended on January 18, 2013, DEA did not publish a final rule placing lorcaserin into Schedule IV of the CSA until May 8, 2013. *See* 78 FR 26701 (May 8, 2013). The scheduling for lorcaserin was not completed until June 7, 2013, almost a year *after* FDA issued its letter stating that BELVIQ® was approved as safe and effective. *Id.*

With respect to FYCOMPA™, DEA received HHS's analysis and scheduling recommendation around January 28, 2013, which is about three months *after* FDA issued its letter stating that the drug was approved as safe and effective. Although DEA has had the recommendation for almost six months, DEA has yet to publish a proposed rule to schedule perampanel.

Congress provided FDA and DEA with ample lead-time during the review of an NDA to address scheduling issues.[10] It appears that sections 201(b) and (f) of the CSA contemplate that

[10] *See* 21 USC 811(a)-(c).

FDA will make submissions to DEA in a manner that would permit DEA to schedule new drugs by the time FDA completes its review of an NDA. Section 201(f) requires that FDA inform DEA when it receives a new drug application for a drug that may have an abuse potential.[11] Further, HHS must submit its analysis and scheduling recommendation to DEA "within a reasonable time."[12] Accordingly, new controlled substances could be, and should be, scheduled at the time FDA approves the drugs as safe and effective.

In the past, new controlled substances had been scheduled shortly after the time FDA sent a letter approving the drugs as safe and effective. For reasons not transparent to sponsors, the lag between scheduling and NDA approval has grown longer and longer. As with BELVIQ® and FYCOMPA™, drugs are now often determined by FDA to be safe and effective long before they are scheduled and able to be marketed.

Current delays in DEA scheduling are particularly unreasonable because, with the benefit of HHS's recommendation and given the lack of actual use data for new chemical entities like BELVIQ® and FYCOMPA™, DEA's role in scheduling new chemical entities is much narrower than it is for other scheduling decisions and should be carried out more expeditiously than it is currently being conducted. Such an approach is consistent with the CSA provision that the HHS recommendation is binding on DEA as to scientific and medical matters.[13] In fact, a review of past scheduling actions for FDA approved new chemical entities scheduled over the past 15 years shows DEA has not deviated from the HHS recommended schedule in the proposed or final scheduling orders.

Scheduling delays persist, however. Consequently, beginning the data exclusivity clock before scheduling is complete deprives sponsors of what Congress intended they receive – five

[11] 21 USC 811(f).

[12] 21 USC 811(b).

[13] *Id.*

years of time actually selling the drug in the marketplace without the threat of generic competition to recoup part of their investment. Yet, as noted above, because of the government's delay in scheduling BELVIQ® and FYCOMPA™, Eisai is not getting that congressionally-mandated opportunity. As detailed below, Eisai should not be so penalized.

II. ARGUMENT

Although Eisai could not commercially market BELVIQ® until June 7, 2013, and currently cannot commercially market FYCOMPA™, FDA has erroneously determined that the market exclusivity periods for these products started long ago. Specifically, FDA concluded that BELVIQ®'s NCE exclusivity period started on June 27, 2012,[14] and FYCOMPA™'s started on October 22, 2012.[15] These determinations are in error because they are contrary to the statute and do not follow FDA's own regulations. As described below, FDA's regulation governing the date of approval for market exclusivity purposes makes clear that exclusivity should not begin so long as additional labeling must be submitted for FDA approval before the sponsor can commercially launch the product. This is true even when the drug is already approved as safe and effective. Thus, the date of approval for purposes of BELVIQ® and FYCOMPA™'s market exclusivity periods is not the date FDA determined they were approved as safe and effective, but rather the date that FDA permits commercial marketing of the products.[16]

Implementation of the NCE exclusivity provision to allow FDA to deprive a company of its statutory five-year exclusivity period based on drug scheduling delays is arbitrary and capricious, unreasonable, and not in accordance with the law. Further, the agency itself has

---

[14] *See* Attachment F, relevant portion of the *Orange Book*.

[15] *See* Attachment G, relevant portion of the *Orange Book*.

[16] There is a similar issue regarding the date of approval for patent-term extension (PTE) purposes for BELVIQ® and FYCOMPA™ under 35 USC 156. This petition does not address the date of approval for PTE purposes. If needed, Eisai and Arena will address that issue through the regulatory process for patent term restoration set out in 21 CFR Part 60.

recognized the significant interests implicated by diluting the period of exclusivity. As mentioned above, FDA recently told a Court that shortening the congressionally-mandated exclusivity period "will cause irreparable harm to the regulatory process by undermining the benefits to the public and to FDA of the marketing exclusivity that the FDCA affords to drug sponsors."[17] FDA's treatment of BELVIQ® and FYCOMPA™ in a different manner from other NCEs is also arbitrary and capricious. Eisai recognizes that FDA has incorrectly applied its interpretation of the date of approval for exclusivity purposes to other drugs subject to CSA scheduling in the past, but Eisai believes that the position advanced in this petition is legally correct. Moreover, as described below, Eisai believes that FDA has the authority to grant the requested actions without going through notice-and-comment rulemaking. Accordingly, Eisai respectfully requests that FDA take the action requested in this petition.

A. The Effective Approval Date for NCE Exclusivity Purposes is the Date the Drug Can Be Commercially Marketed (When CSA Scheduling is Finalized and FDA-Approved Labeling Incorporates the CSA Scheduling Information)

The FDCA provides five years of market exclusivity for NCEs. Under the statute, an ANDA or 505(b)(2) application may not be submitted to FDA "before the expiration of five years from the date of the approval of the [NCE] application under subsection (b) [of 21 USC 355]. . . ." 21 USC 355(j)(5)(F)(ii). FDA regulations define "date of approval" for exclusivity purposes 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.

[17] Defendant's Motion for Stay Pending Appeal, *Tummino v. Hamburg*, No. 12-CV-763 (ERK/VVP), at 15-16 (E.D.N.Y. May 1, 2013) [Attachment A].

21 CFR 314.108(a) (emphasis added). As the regulation makes clear, the *date of the approval letter* is not necessarily the *date of approval for exclusivity*. For example, if further labeling must be submitted for approval, the approval letter would not trigger the exclusivity period. Rather, the regulation is written to ensure that the *effective* approval date for purposes of exclusivity is tied to the date that the drug can actually be commercially marketed.

This approach makes sense. Under the statute, *effective* "approval" occurs when the approved drug can be marketed in interstate commerce.[18] Specifically, 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. (Emphasis added.)

21 USC 355(a). The related regulation also expressly contemplates that effective approval confers the authority to commercially market the drug. Specifically, 21 CFR 314.105(a) states, "[a] new drug product . . . may not be marketed until an approval ***is effective***." (Emphasis added.).

That marketing exclusivity should hinge on when the drug could actually be commercially marketed is entirely logical. It would have been odd, indeed, if Congress granted the NCE sponsor five years of exclusivity to market the product; only to allow FDA to shorten that timeframe by hinging the exclusivity period on some trigger other than when it allows the sponsor to commercially market the product. And, in the preamble to 21 CFR 314.108(a) – the regulation governing NCE exclusivity – FDA appeared to recognize as much. It noted that the key to determining when the exclusivity period begins is when the product could be "legally marketed." FDA wrote: "[a] requirement in the approval letter for submission (but not for approval) of final printed labeling or other material that may delay the actual initiation of

[18] 21 USC 355(a).

marketing of the product is not relevant to a determination of the date of approval, ***so long as the product could be legally marketed***."[19]

Here, FDA has made clear to Eisai that it could not legally market its product until the labeling, incorporating final scheduling, was approved:

- FDA's Form FDA 356h requires that Eisai refrain from commercial marketing of BELVIQ® or FYCOMPA™ prior to CSA scheduling.
- Once CSA scheduling is complete, FDA regulations *expressly require* labeling that incorporates the CSA symbol before the products can be commercially marketed. *See* 21 CFR 201.57(a)(2), 201.57(c)(10)(i), and 1302.04.
- FDA's regulation then mandates that incorporating the CSA symbol into labeling requires FDA approval. 21 CFR 314.70(b)(2)(v)(C); 201.57(a)(2).

Because Eisai could not commercially market its products until CSA scheduling is complete and FDA-approved labeling incorporates the CSA symbol, there could be no "effective" approval for purposes of NCE exclusivity until such conditions are met. As discussed, "effective" approval under the statute occurs only when Eisai can "introduce or deliver for introduction into interstate commerce [the] new drug . . . ." 21 USC 355(a). Accordingly, the *effective* approval date for exclusivity purposes under 21 CFR 314.108(a) must be the date that the products can be commercially marketed.

Therefore, consistent with FDA's regulation and governing statute, the agency should conclude that NCE exclusivity for BELVIQ® and FYCOMPA™ is triggered only when FDA-approved labeling incorporating the final schedule permits commercial marketing of the products. FDA's letters approving the products as safe and effective reinforce this requirement, stating "when the scheduling is finalized, you will need to make appropriate revisions to the

[19] 54 FR 28872, 28898 (July 10, 1989) (emphasis supplied).

package insert, the patient package insert and the carton and the immediate-container labels through supplementation of your NDA."[20]

The label of a product – such as BELVIQ® or FYCOMPA™ – that undergoes CSA scheduling is routinely approved to include the CSA symbol through a changes-being-effected (CBE) supplement after a determination by the review division that a prior-approval supplement is not necessary. If a CBE supplement is used, the day the CBE supplement is submitted with the necessary label changes is the day the sponsor can commercially market the product, and accordingly, should be the date for triggering the NCE exclusivity period.[21] For BELVIQ®, Eisai submitted the CBE supplement adding the CSA symbol to the BELVIQ® label on June 7, 2013.

Alternatively, FDA could determine that the date for triggering the NCE exclusivity period is the date the DEA scheduling order becomes effective as this is the date when a CBE supplement *could be* submitted to permit the sponsor to commercially market the product. As discussed above, FDA's Form FDA 356h and regulatory correspondence make clear that this would be the first possible date that FDA would permit Eisai to commercially market its

---

[20] FDA's letters approving the products as safe and effective make clear that the products' labeling would need further revisions once CSA scheduling is complete. For example, the labeling that accompanied FDA's letter for FYCOMPA™ states:

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

Thus, after CSA scheduling, the labeling would require an FDA-approved revision prior to marketing the product. Therefore, the date of the letters cannot be considered the "date of approval" for exclusivity purposes.

[21] For example, Eisai requested a waiver to submit a CBE supplement for BELVIQ® on August 2, 2012, which FDA granted on October 1, 2012. *See* Letter from Stacie P. O'Sullivan to Mary Parks (Aug. 2, 2012) [Attachment H]; Letter from Julie Marchick to Stacie P. O'Sullivan (Oct. 1, 2012) [Attachment I]. The letter granting the waiver expressly stated that the "[CBE] supplement may not be submitted until the effective date of any final Federal Register notice scheduling the product." Letter from Julie Marchick to Stacie P. O'Sullivan (Oct. 1, 2012) [Attachment I].

products using labeling that incorporates final CSA scheduling. Using the date the DEA scheduling becomes effective provides a consistent point for triggering the NCE exclusivity period regardless of when a sponsor decides to take the necessary steps to incorporate the final CSA scheduling into the labeling. For BELVIQ®, this date would still be June 7, 2013, because Eisai submitted the CBE supplement adding the CSA symbol to the BELVIQ® label on the same day that lorcaserin's CSA scheduling was finalized.

The case law also supports the conclusion that the date of approval for NCE exclusivity purposes must reflect the sponsor's ability to market the product without further agency action. In *Norwich Eaton Pharmaceuticals, Inc. v. Bowen*, 808 F.2d 486 (6th Cir. 1987), the court considered whether the date of NDA approval should be the date for triggering the exclusivity period. In that case, the drug that was already scheduled as a controlled substance, but was subject to a rescheduling procedure, when the FDA approval letter issued. Contrary to the letters involving Eisai, that letter explicitly stated that the rescheduling "in no way impairs your approval to market [the drug] in its current controlled substances schedule."[22] Despite the explicit statement that marketing was permissible, the company decided not to market its product until the rescheduling was complete. FDA concluded that the date of approval relevant for exclusivity purposes was the date of the approval letter, even though the rescheduling was pending. In upholding FDA's determination, the court stated that the company "could have marketed the drug at the time of the 1981 approval as a Schedule II drug. Its decision not to do so was a marketing decision, not a result compelled by law."[23] In contrast to *Norwich*, Eisai could not commercially market its products even though FDA has issued letters approving the drugs as safe and effective. Eisai has not made a strategic business decision not to market its products, but rather is compelled by FDA's Form FDA 356h, as well as the agency's regulations

[22] 808 F.2d at 488.

[23] *Id.* at 492

at 21 CFR 201.57(a) and 314.70(b)(2)(v)(C), to refrain from commercially marketing BELVIQ® and FYCOMPA™.

Similarly, the court in *Mead Johnson Pharmaceutical Group v. Bowen*, 838 F.2d 1332 (D.C. Cir. 1988), also considered whether the date of NDA approval triggered the exclusivity period. *Mead* involved a situation where final labeling was submitted after FDA's approval letter, but there was no requirement that the labeling be FDA-approved before the company could market its product. Specifically, FDA issued an approval letter that requested that the company submit minor labeling changes that were already agreed to by the company, but did not otherwise preclude the company from commercially marketing the product.[24] The company submitted the revised labeling to FDA, which processed it as a supplemental NDA, although FDA had not requested a supplement. FDA concluded that the approval date was the date of the initial approval letter and not the date FDA approved the supplement. In particular, FDA stated that the company could have simply submitted the final labeling and marketed its product.[25] The court agreed with FDA and noted that the company did not argue that, after FDA's initial approval letter, "further action by the FDA was required before it could legally market the drug."[26]

In contrast, Eisai is not its own barrier to marketing. FDA's Form FDA 356h prohibits commercial marketing prior to CSA scheduling and FDA's regulations mandate that incorporating the final CSA symbol into labeling requires FDA approval. *See* 21 CFR 201.57(a) and 314.70(b)(2)(v)(C).

---

[24] 838 F.2d at 1334.

[25] *Id.* at 1334-35.

[26] 838 F.2d at 1336.

It should be noted that *Norwich* and *Mead*, while the only authority bearing directly on this issue,[27] are further distinguishable from the present case because FDA's Form FDA 356h – requiring sponsors to certify that they would not commercially market an approved drug product prior to CSA scheduling – was not applicable at the time of those applications. *See* Attachments J and K. They also involved a different regulation than the one at issue in the present case. These cases occurred before FDA promulgated 21 CFR 314.108(a); indeed, it appears that the cases prompted FDA to promulgate section 314.108(a), in which the FDA specifically recognized that the trigger for exclusivity would ***not*** be the date on the FDA letter stating that the NDA is approved if FDA *expressly required* ***"approval of [additional] labeling or materials."*** The language of 21 CFR 314.108(a), thus, makes clear that when additional labeling is required before commercial marketing can commence, as it is here, the date of approval for exclusivity purposes cannot be the date on the letter from FDA stating that the NDA is approved.

The five-year exclusivity period is a valuable statutory right. FDA has stated, "such exclusivity provides a critical incentive for drug development that advances FDA's goal of protecting and promoting public health" and depriving a company, such as Eisai, of its entitled exclusivity period "would stifle rather than encourage innovation, to the detriment of the public."[28] Accordingly, Eisai requests that the FDA correct the error it has committed in substantially reducing the marketing exclusivity to which Eisai is entitled.

---

[27] Although not directly on point, the Federal Circuit in *Unimed Inc. v. Quigg*, 888 F.2d 826 (Fed Cir. 1989), addressed the issue of the trigger for filing a patent-term-extension application in a situation where the drug was subject to DEA scheduling. The Court cited *Norwich* and *Mead*, but similar to those cases, the NDA sponsor in *Unimed* was not subject to the legal barrier subsequently posed by FDA's Form FDA 356h, requiring sponsors to certify that they would not commercially market an approved drug product prior to CSA scheduling. See Attachment L. Unlike the sponsors in *Norwich*, *Mead*, and *Unimed*, Eisai is faced with an FDA governmental barrier to commercial marketing in the form of the Form FDA 356h certification requirement.

[28] Defendant's Motion for Stay Pending Appeal, *Tummino v. Hamburg*, No. 12-CV-763 (ERK/VVP), at 16 (E.D.N.Y. May 1, 2013) [Attachment A].

B. FDA's Treatment of BELVIQ® and FYCOMPA™ Differently Than Other NCEs is Arbitrary and Capricious

FDA's actions depriving BELVIQ® and FYCOMPA™ of *full* five-year NCE exclusivity periods are arbitrary and capricious. FDA is unfairly penalizing Eisai and Arena for developing and seeking to commercialize NCEs recommended for CSA scheduling. While BELVIQ® and FYCOMPA™ will be deprived their *full* five-year market exclusivity periods, sponsors of NCEs that do not require CSA scheduling continually enjoy *full* five-year NCE exclusivity periods.

For example, Myrbetriq (mirabegron), approved on June 28, 2012, and Xeljanz (tofacitinib), approved on November 6, 2012, were NCEs approved roughly the same time as BELVIQ® and FYCOMPA™, respectively. *See* Attachments M and N. In contrast to Eisai's products, however, Myrbetriq and Xeljanz will enjoy *full* five-year market exclusivity periods because they were not subject to CSA scheduling. FDA's disparate treatment of NDAs entitled to five-year NCE exclusivity – with no explanation and with no sound policy rationale – highlights the arbitrary and capricious nature of FDA's actions with respect to BELVIQ® and FYCOMPA™. *See Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20 (D.D.C. 1997) (holding that the disparate treatment of similarly situated products is arbitrary and capricious).

FDA's actions have also resulted in the disparate treatment among sponsors of CSA scheduled products themselves. For example, an examination of twelve NCEs that FDA recommended for scheduling demonstrates that FDA submitted its recommendation to DEA anywhere from 367 days *prior to* issuing an approval letter (PROVIGIL®) to as many as ninety-four days *after* issuing an approval letter (LYRICA®).[29] FDA has offered no explanation and no sound policy rationale for this disparate treatment, even though FDA's wildly-varying timeframe for providing DEA with scheduling recommendations can substantially degrade an NCE's five-year marketing exclusivity period. For example, FDA submitted its scheduling recommendation for BELVIQ® to DEA two days prior to issuing a letter approving the drug as safe and effective, and Eisai is currently set to lose nearly one year – 345 days – of marketing exclusivity for

[29] *See* Attachment O, CSA Product Approval Timelines.

BELVIQ®. On the other hand, the sponsor of PROVIGIL® only lost thirty-four days of marketing exclusivity due, at least in part, to FDA providing its scheduling recommendation to DEA 367 days prior to issuing the PROVIGIL® approval letter. FDA's determination of marketing exclusivity for two similarly-situated NDA sponsors – resulting in a 313-day disparity – is the epitome of arbitrary and capricious behavior.

C. FDA Has Authority To Grant The Requested Actions Without Notice-And-Comment Rulemaking

Marketing delays attributed to CSA scheduling continue to lengthen, which prevents innovative new medicines from reaching patients in need. Eisai believes that the law supports its position, and FDA can grant the actions requested in the petition immediately without the need for a change to the agency's regulations or the need for notice-and-comment proceedings. It is settled law that "an agency is free to alter its past rulings and practices even in an adjudicatory setting." *Airmark Corp. v. FAA,* 758 F.2d 685, 691-692 (D.C. Cir. 1985) (citation omitted); *see also, e.g., SEC v. Chenery Corp. (II),* 332 U.S. 194, 202-203 (1947).

Of course, "[w]hen an agency has given its regulation a definitive interpretation," on which there has been "substantial and justifiable reliance," and the agency "later significantly revises that interpretation, the agency has in effect amended its rule, something it may not accomplish without notice and comment." *Honeywell Int'l, Inc. v. NRC,* 628 F.3d 568, 579 (D.C. Cir. 2010) (quoting *Alaska Prof'l Hunters Ass'n v. FAA,* 177 F.3d 1030, 1034 (D.C. Cir. 1999); *MetWest Inc. v. Sec'y of Labor,* 560 F.3d 506, 509-10 (D.C. Cir. 2009)). Neither condition is met in this case because the agency's past interpretation was neither "definitive" nor has it been substantially and justifiably relied upon, particularly for newly approved products such as BELVIQ® and FYCOMPA™.

1. FDA Has Not Provided A Definitive Interpretation Of Five-Year Exclusivity For Products Pending CSA Scheduling

A "definitive" agency interpretation means an "express, direct, and uniform interpretation" of the regulation at issue. *Association of Am. R.Rs. v. DOT,* 198 F.3d 944, 949

(D.C. Cir. 1999). It must be "a definitive and binding statement on behalf of the agency" that "come[s] from a source with the authority to bind the agency." *Devon Energy Corp. v. Kempthorne,* 551 F.3d 1030, 1040 (D.C. Cir. 2008). A definitive agency interpretation also must have "the force of law" in that it "'mark[s] the consummation of the agency's decisionmaking process . . . .'" *Id.* at 1039 (quoting *Bennett v. Spear,* 520 U.S. 154, 177-78 (1997)). An interpretation that "does not cabin agency discretion" is not likely to be definitive. *Hudson v. FAA,* 192 F.3d 1031, 1035 (D.C. Cir. 1999). "'The language actually used by the agency' is often central to making such determinations." *Wilderness Society v. Norton,* 434 F.3d 584, 595 (D.C. Cir. 2006) (quoting *Community Nutrition Inst. v. Young,* 818 F.2d 943, 946 (D.C. Cir. 1987)). Even where the agency "uses mandatory language" in a document, the court will view "the document as a whole" to determine whether it "read[s] as a set of rules." *Id.* If it "lacks precision in its directives," then the document is likely just "a statement of policy, not a codification of binding rules." *Id.*

Courts have made clear that the "express, direct, and uniform" standard is a high one. Indeed, even where an agency's interpretation may be inferred from its actions, that inference does not qualify as a definitive interpretation. For example, the court in *Hudson,* 192 F.3d 1031, rejected such a reading of *Alaska Professional Hunters,* the seminal case from which the rule requiring notice-and-comment rulemaking for changes to certain agency regulatory interpretations arises:

> Although petitioners argue that *Alaska Professional Hunters* is pertinent because it, like this case, involved a long-term agency practice which constituted an implicit interpretation or application of the relevant regulation, that is not so. In that case, a formal adjudication by an associate agency had adopted an interpretation of the regulation in accord with the informal practice. *See Alaska Professional Hunters,* 177 F.3d at 1031.

Hudson, 192 F.3d at 1036; *see also Devon Energy Corp.,* 551 F.3d at 1041 (explaining that a guidance document is "plainly distinguishable" from "the disputed agency advice" in *Alaska*

Professional Hunters, which "had been upheld in a formal adjudication by the Civil Aeronautics Board, FAA's predecessor agency.").

With respect to BELVIQ® and FYCOMPA™, no definitive prior interpretation binds FDA because the agency has not expressly and directly addressed when the five-year exclusivity period is triggered for products that have received an FDA letter that determines them safe and effective, but where FDA prohibits them from being commercially marketed because the drugs still have not completed CSA scheduling. Nor does past agency practice provide the necessary authoritative and definitive agency interpretation.

To the best of our knowledge, there are no publicly available decisions that explain FDA's reasoning in arriving at the start date for five-year data exclusivity for drugs like BELVIQ® and FYCOMPA™. The most that can be said about prior determinations is that there exists some "implicit" interpretation that led the agency to recognize the start of the five-year exclusivity period as the date on the letter from FDA stating that the NDA was approved as safe and effective even though FDA prohibited commercial marketing of the product until after CSA was completed. But as the court of appeals explained in *Hudson,* 192 F.3d at 1036, an "implicit interpretation" is not enough to constitute a definitive interpretation. And as further demonstrated by *Honeywell,* 628 F.3d at 579, the court will not infer a binding regulatory interpretation from agency decisions absent some express statement from the agency.

So even if one could infer a uniform agency practice based on the FDA's prior exclusivity decisions, the publicly available information does not provide an "express" or "direct" interpretation of the regulation, *Association of Am. R.Rs.,* 198 F.3d at 949, and certainly not one that reflects "a definitive and binding statement on behalf of the agency," *Devon Energy Corp.,* 551 F.3d at 1040. This makes these circumstances quite unlike those present in *Alaska Professional Hunters,* where the court concluded that the agency was bound by "administrative common law." *See* 177 F.3d at 1035. For as the D.C. Circuit later clarified in *Hudson,* the dispositive fact in *Alaska Professional Hunters* was that "a formal adjudication by an associate

agency had adopted an interpretation of the regulation in accord with the informal practice." *Hudson,* 192 F.3d at 1036 (citing *Alaska Prof'l Hunters,* 177 F.3d at 1031); *accord Devon Energy Corp.,* 551 F.3d at 1041. There has been no such formal adjudication here.

In sum, FDA has not yet provided an express and direct interpretation of the specific question posed here.[30] Therefore, the agency has not yet issued a "definitive interpretation" of 21 CFR 314.108 as it applies to NCEs requiring or pending CSA scheduling. The agency is thus "free to adopt the interpretation at issue in this case without providing an opportunity for notice and comment." *Devon Energy Corp.,* 551 F.3d at 1041.

2. Even If There Had Been A Definitive Interpretation, There Has Been No Substantial And Justifiable Reliance

Moreover, even if there had been a definitive prior interpretation – which there was not – and even if the requested action would constitute a substantial departure from that prior interpretation – which it would not – notice-and-comment rulemaking is not required if there has been no "substantial and justifiable reliance on a well-established agency interpretation." *MetWest Inc.,* 560 F.3d at 511; *accord Honeywell Int'l, Inc.,* 628 F.3d at 579-80. As the court explained in *MetWest,* the "substantial and justifiable reliance" requirement "is a crucial part of the analysis." 560 F.3d at 511 n.4. "To ignore it is to misunderstand *Alaska Professional Hunters* to mean that an agency's initial interpretation, 'once informally adopted, freezes the state of agency law, which cannot subsequently be altered without notice and comment rulemaking.'" *Id.* (quoting Peter L. Strauss, *Publication Rules in the Rulemaking Spectrum: Assuring Proper Respect for an Essential Element,* 53 Admin. L. Rev. 803, 844 (2001)).

An agency is not bound by a prior interpretation just because there has been *some* reliance on that interpretation; rather, the reliance must be both "substantial" and "justifiable."

---

[30] In fact, over the past several months, Eisai has attempted to obtain from FDA the Agency's interpretation of this question. To date, FDA has been unwilling or unable to provide Eisai with such an interpretation.

So, for instance, in *Alaska Professional Hunters,* the court recognized that "[p]eople in the lower 48 states had pulled up stakes and moved to Alaska. They and others within Alaska had opened hunting and fishing 'lodges and built up businesses dependent on aircraft, believing their flights were [not] subject to' certain commercial flight regulations." *MetWest Inc.,* 560 F.3d at 511 (quoting *Alaska Prof'l Hunters,* 177 F.3d at 1035). "Their reliance on the FAA's advice was, as we said, 'justifiable.'" *Id.* at 511 n.5 (quoting *Alaska Prof'l Hunters,* 177 F.3d at 1034). It was also substantial: "Forcing guide pilots to comply with regulations developed for commercial airlines would have driven Alaska's hunting and fishing tourism operations out of business." *Id.* at 511.[31]

There has been no similar reliance on any prior agency interpretation of 21 CFR 314.108 with respect to NCEs subject to CSA scheduling, such as BELVIQ® and FYCOMPA™. *See, e.g., Association of Am. R.Rs.,* 198 F.3d at 950. There is no evidence that innovator sponsors – who may have staged their applications based on FDA's position – nor generic sponsors – who may wish to develop a generic to a product subject to CSA scheduling – have substantially and justifiably relied on FDA's historical position. There is no evidence that these companies built their businesses around the understanding of FDA's start date for exclusivity for this small class of products, as in *Alaska Professional Hunters.* But even if companies had in fact modeled their business operations on producing generic copies of products such as BELVIQ® and FYCOMPA™, they may continue that practice subject to already existing regulatory and patent law restraints.

Plainly, no generic sponsor has built its business around an expectation that FDA will effectively award less than five years of exclusivity to BELVIQ®, FYCOMPA™, and similar

[31] "Furthermore, during this 30-year span, the 'guide pilots and lodge operators had no opportunity to participate in the development of the ... regulations' that the FAA had abruptly decided to apply to them. As a result, they were deprived of any opportunity to request changes or exceptions to accommodate the unique circumstances of Alaskan air travel." *MetWest, Inc.,* 560 F.3d at 511 (quoting *Alaska Prof'l Hunters,* 177 F.3d at 1035-36).

CSA products, particularly as the timing of the drug scheduling process varies considerably. Exclusivity determinations under 21 CFR 314.108 are prospective in effect, making it unlikely in the extreme that *any* competitor could "rely" on hypothetical, forward-looking exclusivity determinations. Exclusivity operates on *future* new drug applications, usually ANDAs for generic drugs, and determines when the agency may accept for filing applications that refer to the active moiety in a previously approved drug product. Thus, the reliance interests in any given case are quite limited, if they exist at all.

If BELVIQ® or FYCOMPA™ are determined to have five-year exclusivity starting after CSA scheduling, a generic drug manufacturer may not submit an application until the end of that five-year period. The timing of the application and approval might change, but the resources that the generic manufacturer would have to expend to submit its application would not change. And the "feasibility" of manufacturers delaying their applications for years "is clear." *MetWest Inc.*, 560 F.3d at 511. Unlike the guiding and hunting industry described in *Alaska Professional Hunters,* the generic industry is in no way founded on FDA's treatment of drugs requiring the scheduling described in this petition.

3. Policy Considerations Support Eisai's Petition

Because there has been no definitive agency interpretation of the regulation with respect to products requiring CSA scheduling, and certainly not one on which there has been substantial and justifiable reliance, the agency may apply a "new" interpretation of the regulation in this proceeding. All that is required is that "the agency . . . acknowledge and provide an adequate explanation for its departure from established precedent." *Dillmon v. NTSB,* 588 F.3d 1085, 1089-90 (D.C. Cir. 2009). No heightened standard applies. *Id.* at 1089 (citing *FCC v. Fox Television Stations, Inc.,* 556 U.S. 502, 514-516 (2009)). A petition response from FDA, after consideration of views submitted to the public docket, would be sufficient.

An agency practice that interprets the statute and 21 CFR 314.108 to grant a full five-year exclusivity period starting once CSA scheduling is complete is the correct practice under the law,

under the regulations, and as a matter of public health policy. Applying this interpretation will preclude the arbitrary shortening of exclusivity due to drug scheduling delays and will reasonably base the exclusivity determination on the true date the sponsor receives authorization to introduce the product into interstate commerce. It also will eliminate the disparate treatment between products that are not subject to CSA scheduling and benefit from the full five-year period of exclusivity, and products that need to be scheduled and thus end up with a reduced period of exclusivity. Additionally, it will protect the incentives for companies to invest the resources necessary to bring NCEs to market.

Congress enacted the NCE exclusivity period to provide an incentive for drug development by ensuring a period during which a company could recoup at least some of the initial investment in bringing an NCE to market. The development of NCEs is resource intensive and fraught with failure. Drugs, such as BELVIQ® and FYCOMPA™, are demonstrated safe and effective through substantial clinical trials. Few developmental drugs ever make it to the market, and it has been estimated that it takes about twelve years and more than $800 million to $1 billion to bring a new drug to market.[32]

Furthermore, the NCE exclusivity period was an important part of the balance that Congress struck to establish the abbreviated approval process for generic drugs. The Hatch-Waxman Act, which included the NCE exclusivity provisions, also created an abbreviated approval pathway for generic drugs. In contrast to NCEs, the abbreviated approval process for generic drugs does not require clinical safety and effectiveness trials. Rather, the generic drug simply relies on the finding of safety and effectiveness for the new drug. Thus, generic drug development avoids the significant risk and cost associated with the development of NCEs and allows the generic to be sold at a lower cost compared to the new drug. Once a generic drug is approved and enters the market, the new drug's market can be significantly eroded. To balance

[32] *See* Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 Managerial & Decision Econ. 469 , 475 (2007); Joseph A. DiMasi *et al., The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. Health Econ. 151 , 166 (2003).

the abbreviated approval process, Congress provided the five-year exclusivity period for NCEs to allow the innovator company to recoup at least some of its investment.

Not only does FDA's current interpretation deprive companies of the value of their exclusivity, it also seriously undercuts the policy considerations that Congress used to establish the ANDA process. Accordingly, FDA should grant Eisai's petition.

III. FDA SHOULD PROVIDE A RESPONSE BEFORE FINAL CSA SCHEDULING FOR FYCOMPA™, AND NO LATER THAN FIVE MONTHS FROM THE DATE OF THIS PETITION

Eisai also requests that FDA make a substantive decision on this petition before final CSA scheduling for FYCOMPA™, or within five months of the date the petition is submitted to FDA, whichever date is earliest. In 2012, Congress required FDA to respond to a citizen petition that could delay an ANDA or 505(b)(2) application within five months. Although there are no pending ANDAs or 505(b)(2) applications for BELVIQ® or FYCOMPA™, the same policy reasons for the five month timeline apply to Eisai's petition. Further, if FDA denies the petition, then Eisai should have sufficient time to seek all available remedies and a final resolution before its current exclusivity periods expire. Ultimately, FDA should be transparent regarding the regulatory framework governing Eisai's products.

IV. CONCLUSION

For all of the reasons stated above, Eisai respectfully requests that FDA grant the requested action.

ENVIRONMENTAL IMPACT

The actions requested in this petition are not within any of the categories for which an environmental assessment is required pursuant to 21 CFR 25.22.

ECONOMIC IMPACT

Information on the economic impact of this proposal will be submitted if requested by the Commissioner.

CERTIFICATION

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.[33]

Respectfully submitted,

Allen Waxman

Allen Waxman
Senior Vice President and General Counsel
Law & Government Affairs
Eisai Inc.
100 Tice Boulevard
Woodcliff Lake, NJ 07677
201-746-2750

Attachments: A – O

cc: Elizabeth H. Dickinson, Chief Counsel, Office of the Chief Counsel
Maryll W. Toufanian, Associate Chief Counsel, Office of the Chief Counsel
Douglas C. Throckmorton, MD, Deputy Director for Regulatory Programs, CDER
Eric P. Bastings, MD, Acting Director, Division of Neurology Products, CDER

[33] Eisai did not provide a certification under 21 USC 505(q) because 505(q) applies only when there is a pending ANDA or 505(b)(2) application, and there cannot be any pending ANDA or 505(b)(2) application due to Eisai's NCE exclusivity.