Buchanan Ingersoll & Rooney PC
Attorneys & Government Relations Professionals

Edward John Allera
202 452 7985
edward.allera@bipc.com

1700 K Street, N.W., Suite 300
Washington, DC 20006-3807
T 202 452 7900
F 202 452 7989
www.buchananingersoll.com

March 21, 2014

VIA HAND DELIVERY/RETURN RECEIPT REQUESTED

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs
U.S. Food and Drug Administration
WO Bldg. 1, Rm. 2217
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: Ferring Pharmaceuticals, Inc. Petition for Reconsideration and Petition for Stay of Action of FDA's Determination Regarding Prepopik®

Dear Dr. Hamburg:

On behalf of our client, Ferring Pharmaceuticals, Inc. ("Ferring" or "the Company"), we are filing this Petition for Reconsideration and Petition for Stay of Action (hereinafter "Petition") pursuant to 21 C.F.R. §§ 10.33 and 10.35, respectively.[1] We request that the U.S. Food and Drug Administration ("FDA" or "the Agency") review and reverse its February 21, 2014 determination that Ferring's product, Prepopik®, is not eligible for five-year new chemical entity ("NCE") exclusivity. FDA made this decision despite the Agency's recognition that drug products meeting the definition of a NCE such as Prepopik are eligible for, if not entitled to, five-year exclusivity regardless of whether the drug was first approved in a single-entity drug product or in a fixed-combination with another drug substance that does not meet the definition

[1] Ferring is filing this Petition under both regulatory sections so that FDA can both reconsider its decision to deny Ferring's request for five-year NCE exclusivity for Prepopik, and stay application of the Agency's new statutory interpretation to any pending or newly-filed abbreviated new drug applications ("ANDAs") pending resolution of the issues presented herein. The Petition for Reconsideration and the Petition for Stay of Action are in response to Docket No. FDA-2013-P-0119.

California :: Delaware :: Florida :: New Jersey :: New York :: Pennsylvania :: Virginia :: Washington, DC

of a NCE.[2] We also request, should the Agency finalize its new "Draft Guidance for Industry – New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products"[3] (hereinafter "2014 NCE Exclusivity Draft Guidance") prior to issuing a response to this Petition, that FDA stay the application of its new interpretation in that guidance document until FDA resolves the matters in this Petition.

FDA has reached a conclusion about the applicability of five-year NCE exclusivity to fixed-combination drug products such as Prepopik, but it has failed to apply its decision to Prepopik. Furthermore, it is unclear from either FDA's February 21 decision or the 2014 NCE Exclusivity Draft Guidance when (if ever) the Agency's new position regarding exclusivity for fixed-combination drug products will become effective and to whom it will apply. As a result, the Agency's actions in this case are unreasonable, arbitrary, and capricious. These actions also fail to provide Ferring the due process protections that are afforded to it under the law and are poor public policy. As the current situation stands, Ferring risks irreparable harm should FDA's actions result in premature loss of valuable market exclusivity and approval of a generic version of its Prepopik drug product.[4] Therefore, we respectfully submit this Petition in good faith requesting reconsideration and stay of action. Only a decision recognizing Prepopik's five-year NCE market exclusivity is a reasonable statutory interpretation.

PETITION FOR RECONSIDERATION
PETITION FOR STAY OF ACTION

The undersigned submit this Petition requesting that the Commissioner of Food and Drugs ("Commissioner") reconsider the decision outlined above and stay application of the Agency's new position regarding five-year NCE exclusivity eligibility for fixed-combination

---

[2] *See* Letter from Janet Woodcock to David M. Fox, Theodore M. Sullivan, Edward John Allera, and Joy J. Liu (February 21, 2014) (hereinafter, "FDA Decision") (**Attachment 1**).

[3] Issued February 2014, *available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm121568.htm.

[4] Courts have regularly found irreparable harm, and ordered injunctive relief to block generic drug approval. *See, e.g.,* AstraZeneca LP v. Apotex, Inc., Nos. 09-1381, -1424 (Fed.Cir. 2010).

drug products, as set forth in its new 2014 NCE Exclusivity Draft Guidance, pending resolution of the issues raised in this Petition.

A. DECISION INVOLVED

On February 21, 2014, FDA determined that Ferring's fixed-combination drug product, Prepopik, may not be retroactively granted five-year NCE exclusivity. In its combined Response to Citizen Petitions submitted by Ferring, Gilead Sciences, Inc. ("Gilead"), and Bayer HealthCare Pharmaceuticals ("Bayer") (collectively, "Petitioners" and "Citizen Petitions"), FDA acknowledged that the governing statute and regulations regarding NCE exclusivity were ambiguous and that Petitioners' alternative interpretation of the provisions was reasonable. FDA also acknowledged that the new interpretation proffered by Petitioners would encourage future development of important novel fixed-combination products, and that adoption of this interpretation would therefore be in the interest of the public health. Despite these acknowledgements, however, the Agency declined to recognize five-year exclusivity for Ferring's, Gilead's, and Bayer's products, stating that (1) retroactively applying the new interpretation to the Petitioners' products would not advance the goal of the Drug Price Competition and Patent Term Restoration Act of 1984,[5] ("Hatch-Waxman Amendments") to encourage development of novel drugs because FDA had already approved the products in question; and (2) if the new interpretation were to be applied to products for which ANDAs have already been filed, it could impose a burden on the ANDA sponsors that relied on FDA's existing statutory interpretation when filing the applications.

B. ACTION REQUESTED

Ferring requests that the Commissioner reconsider the determination that its product, Prepopik, may not retroactively be granted five-year NCE exclusivity under the new statutory interpretation of the exclusivity provisions being adopted by FDA. Specifically, Ferring requests that five-year exclusivity be recognized for Prepopik. In addition, Ferring requests that the Agency stay application of its new position, as set forth in the new 2014 NCE Exclusivity Draft

[5] Pub. Law No. 98-417 (September 24, 1984).

Guidance, to any applications pending resolution of the issues in this Petition. Ferring requests these actions based upon the following positions:

- The Commissioner's statutory interpretation of the five-year exclusivity provisions for fixed-combinations with at least one novel drug substance is the only correct interpretation, and must be applied to all relevant applications. No change in the Agency's regulations is required legally or technically.
- The Commissioner failed to adequately consider all points raised in the original Citizen Petitions, including wildly inconsistent exclusivity results under its umbrella policy and the support in the legislative history for five-year exclusivity for fixed-combinations with novel ingredients.
- Due Process and fairness require that five-year exclusivity be recognized for all applicable drug applications with remaining exclusivity, particularly Ferring's Prepopik.
- The Commissioner should adopt Petitioners' statutory interpretation immediately. The Commissioner's decision to implement the interpretation prospectively at some indefinite future date (*i.e.*, through final guidance) is arbitrary and capricious action that cannot be considered reasonable when all relevant factors are considered.

C. STATEMENT OF GROUNDS

I. FACTUAL OVERVIEW

A. Prepopik

The Prepopik new drug application ("NDA") was approved on July 16, 2012[6] for cleansing of the colon as a preparation for colonoscopy in adults. The drug contains sodium picosulfate, a stimulant laxative, in combination with magnesium oxide and anhydrous citric acid. Magnesium oxide and anhydrous citric acid combine in the body to form magnesium citrate, an osmotic laxative. Sodium picosulfate is a novel active ingredient that has never been a component of an approved NDA. Both magnesium oxide and citric acid are prodrugs of the

[6] NDA 202535.

active ingredient magnesium citrate, and both have previously been components of approved NDAs.

FDA granted Ferring a three-year period of exclusivity for Prepopik under the Federal Food, Drug, and Cosmetic Act ("FFDCA" or "the Act") §§ 505(c)(3)(E)(iii) and 505(j)(5)(F)(iii).[7] FDA based this decision on the grounds that the previous approvals for magnesium oxide and citric acid precluded granting five-year exclusivity under FFDCA §§ 505(c)(3)(E)(ii) and 505(j)(5)(F)(ii)[8] for drug products containing novel active ingredients.

B. Citizen Petitions and FDA's Decision

On January 29, 2013, Ferring filed a Citizen Petition with FDA,[9] pursuant to FFDCA § 505[10] as well as 21 C.F.R. §§ 10.20, 10.30, and 314.108, requesting that the Commissioner amend the exclusivity period granted for Ferring's Prepopik. The Company also requested that the Agency stay acceptance of any ANDA or § 505(b)(2) NDA that references Prepopik's NDA and further stay any approval of such drug (should any application be accepted) until this critical question about the exclusivity period was addressed.

Nearly contemporaneously, similar Citizen Petitions were filed on behalf of Gilead[11] and Bayer[12] that also sought five-year NCE exclusivity for those companies' products. The three Citizen Petitions presented similar statutory, regulatory, and policy reasons for FDA to depart from its existing interpretation of the applicability of five-year NCE eligibility including:

---

[7] *Codified at* 21 U.S.C. § 355(c)(3)(e)(iii) and 21 U.S.C. § 355(j)(5)(F)(iii), respectively.

[8] *Codified at* 21 U.S.C. § 355(c)(3)(E)(ii) and 21 U.S.C. § 355(j)(5)(F)(ii), respectively.

[9] Ferring Citizen Petition (January 29, 2013) (**Attachment 2**).

[10] *Codified at* 21 U.S.C. § 355.

[11] Gilead Citizen Petition (January 8, 2013), Docket No. FDA-2013-P-0058 (**Attachment 3**).

[12] Bayer Citizen Petition (April 19, 2013), Docket No. FDA-2013-P-0471 (**Attachment 4**).

- FDA incorrectly interprets the word "drug" in the statute and regulations to mean "drug product" rather than "drug substance";

- The legislative history of the Hatch-Waxman Amendments supports the position that five-year NCE exclusivity should be awarded to all drug substances containing no previously-approved active moiety, whether such drug substance was first approved in a single-entity drug product or in a fixed combination;

- FDA's existing interpretation of the provisions governing five-year NCE exclusivity put undue weight on the order in which a sponsor's applications are approved in determining their eligibility for five-year exclusivity, thereby leading to illogical and arbitrary results for certain fixed combinations; and

- FDA's existing interpretation discourages the development of new active moieties in fixed combinations, which will in turn result in fewer life-saving, innovative drugs in certain therapeutic areas, including HIV, hepatitis C, tuberculosis, and cancer.

On February 21, 2014, the Agency issued the FDA Decision responding to all three Citizen Petitions. In its response, FDA acknowledged that the term "drug" is ambiguously defined, and that the alternative interpretation of the exclusivity statutory provisions presented by Ferring, Gilead, and Bayer was a reasonable and correct reading of the FFDCA.[13] The Agency further concluded that recent changes in drug development, particularly in the field of fixed-combination products, as well as the importance of fixed-combinations to key therapeutic areas (*e.g.*, HIV, cancer, etc.), warranted revisiting FDA's existing policy.[14] FDA admitted that its existing interpretation of the five-year NCE exclusivity statutory provisions may result in suboptimal drug development strategies, and places undue importance on the order in which applications are approved.[15] As a result, given the interest in encouraging development of innovative fixed-combination products for the benefit of the public health, FDA issued the 2014 NCE Exclusivity Draft Guidance proposing to adopt Ferring's, Gilead's, and Bayer's recommended statutory interpretation that would recognize five-year NCE exclusivity for a drug substance that does not contain a previously-approved active moiety, even where such a drug

---

[13] *See* FDA Decision.

[14] FDA Decision, at 14.

[15] FDA Decision, at 15.

substance is approved in a fixed combination with another drug substance that contains at least one previously-approved active moiety.[16]

Despite the fact that the legal arguments resulting in FDA's change in statutory interpretation were championed by Petitioners Ferring, Gilead, and Bayer, FDA declined to apply the new five-year exclusivity interpretation to the Petitioners' products.[17] In explaining its decision to deny five-year exclusivity for these products, FDA stated that (1) retroactively applying the new interpretation to the Petitioners' products would not advance the goal of the Hatch-Waxman Amendments to encourage development of novel drugs because FDA had already approved the products in question; and (2) if the new interpretation were applied to products for which ANDAs have already been filed, it could impose a burden on the ANDA sponsors that relied on FDA's existing statutory interpretation when filing applications.[18] FDA stated that it will apply its new five-year NCE exclusivity policy prospectively[19]; however, it is unclear how FDA will do so in practice, as discussed in greater detail in Section D below.

As described further in the sections below, Ferring has sufficient grounds to request reconsideration and stay of the Agency's actions. FDA's regulations at 21 C.F.R. § 10.33(d) require that the Commissioner grant the Petition for Reconsideration if certain grounds apply:

(1) The petition demonstrates that relevant information or views contained in the administrative record were not previously or not adequately considered.

(2) The petitioner's position is not frivolous and is being pursued in good faith.

(3) The petitioner has demonstrated sound public policy grounds supporting reconsideration.

---

[16] FDA Decision, at 16.

[17] FDA Decision, at 17.

[18] FDA Decision, at 17.

[19] 2014 NCE Exclusivity Draft Guidance, at 1.

(4) Reconsideration is not outweighed by public health or other public interests.

This Petition meets all of these requirements for the following reasons.

First, this Petition includes only information and views that were presented in the original Citizen Petitions filed with FDA, as well arguments that address the information and views raised in the FDA Decision.

Furthermore, the Petition is not frivolous and is being pursued in good faith. The non-frivolous nature of the subject matter of this Petition is clearly evidenced by the fact that FDA was persuaded by the correctness of the legal and policy arguments in the original Citizen Petitions, and the FDA Decision addressed the issue of implementation timing. The arguments below are further evidence of the non-frivolous nature of this Petition.

Finally, the arguments in this Petition put forth clear legal and public policy arguments supporting reconsideration, and the arguments for reconsideration significantly outweigh any other public health or other public interests.

A request for stay under 21 C.F.R. § 10.35(e) requires a similar showing of grounds. In addition to demonstrating that the petition is not frivolous and is being pursued in good faith, that policy grounds support the stay, and that these factors are not outweighed by public health or other interests, the petition must also show that the petitioner will otherwise suffer irreparable injury if the stay is not granted. As explained below in more detail, failure to grant this Petition and stay the implementation of a policy that will limit the market exclusivity for Prepopik to three years will cause Ferring irreparable harm.[20]

---

[20] Courts have long held that early market entry of generic drugs by generic competitors may represent irreparable harm to NDA holders, and have used the equitable remedy of injunction to stay that entry until resolution of various intellectual property and exclusivity matters. *See, e.g.,* Purdue Pharma L.P. v. Boehringer Ingelheim GmbH, 237 F.3d 1359, 1368 (Fed.Cir. 2001) ("Given the testimony of the likelihood of price erosion and loss of market position without corresponding market expansion from the introduction of Roxane's product, we see no deficiency in the district court's finding of irreparable harm.").

II. LEGAL ARGUMENTS

A. FDA's New Statutory Interpretation of the FFDCA's Five-Year Exclusivity Provisions is the Correct Interpretation, and Must be Applied to *All* Relevant Applications

The Hatch-Waxman Amendments created the foundation for the current generic drug approval and proprietary rights enforcement system, balancing the protection of innovator's intellectual property and research investment in new drugs with the need for the timely approval of lower-cost generic drugs. To promote better access to affordable drugs, the Hatch-Waxman Amendments created abbreviated pathways for drug approvals, including ANDAs and § 505(b)(2) NDAs. In order to promote research and development, the Hatch-Waxman Amendments also included provisions that granted various forms of regulatory exclusivity to makers of innovative drug products. Congress recognized that granting periods of exclusivity would incentivize drug manufacturers to engage in the time- and cost-intensive process of researching and developing new drugs. One of Congress' clear intentions in enacting the Hatch-Waxman Amendments was to reward innovators such as Ferring that have developed drug products that contain novel active ingredients.

As previously established by all three Citizen Petitions, FDA's historic interpretation of the FFDCA for fixed-combination drug products, which denied five-year exclusivity to such drug products if any active moiety in the drug product as a whole had previously been approved by the Agency, has not been the subject of any comprehensive formal analysis or discussion by FDA. This historic interpretation is not only out of step with the governing regulation, but is also contrary to (1) clear Congressional intent to support broad applicability of five-year exclusivity to drugs with novel ingredients; (2) clear public interest of rewarding developers of drug products containing novel active ingredients; and (3) prior Agency actions in related statutory interpretation. As acknowledged by FDA's Decision, the Agency's prior interpretation has led to, and will continue to lead to, illogical and arbitrary results for fixed-combination drugs such as Prepopik (particularly where no NDA can be approved for the single ingredient as the sole ingredient). Where FDA's previous interpretation of the FFDCA's five-year NCE

exclusivity provisions perpetuates arbitrary and irrational results, it need not and should not be followed.[21]

Applying FDA's correct new statutory interpretation to Prepopik now – even though the drug product has already been approved – would be entirely in line with established administrative procedures of statutory interpretation. As previously noted,[22] agencies are free to alter their past rulings and practices even in adjudicatory settings. It is only when an agency has provided a definitive interpretation to a regulation on which there has "been substantial and justifiable reliance,"[23] and then later significantly revises that interpretation, that such interpretation may only be implemented with notice and comment rulemaking.[24] No such situation exists here.

In the case of Ferring's Prepopik, neither condition is met. FDA's past interpretation was never "definitive,"[25] as shown by the Citizen Petitions' reviews of the statute, FDA's multiple interpretations, and the multiple petitions filed over the years to seek five-year NCE exclusivity for numerous other combination products.

Nor has it been "substantially relied upon" because, to our knowledge, there have been no ANDAs submitted to FDA which reference Prepopik. We are not aware of any Paragraph IV certifications having been filed to Ferring's product. The more important issue of reliance is the

---

[21] Matter of Brown Transport Truckoad, Inc., 169 B.R. 781 (Bkrtcy.N.D.Ga. 1994) (while agency interpretations normally receive deference, an agency's application of statutory language need not be followed when there are compelling indications of error).

[22] Gilead Citizen Petition (January 8, 2013).

[23] MetWest Inc. v. Secretary of Labor, 560 F.3d 506, 511 (D.C.Cir. 2009).

[24] Honeywell Intern, Inc. v. Nuclear Regulatory Com'n, 628 F.3d 568, 579 (D.C.Cir. 2010).

[25] As previously established by Ferring, Gilead, and Bayer in each of the three Citizen Petitions, the existing interpretation regarding five-year NCE exclusivity is not memorialized in an express, formal and definitive policy or rule, as the FFDCA does not specifically address fixed-combination products. To our knowledge, the most prominent statement of an FDA position on the award of exclusivity to fixed-combination products is contained in an internal Agency housekeeping document, known as the Exclusivity Summary. The Exclusivity Summary, and other Agency documents that recognize the approach taken in the Exclusivity Summary, do not rise to the level of formality and authority needed to bind the Agency, such that notice and comment rulemaking would be needed to establish a new approach.

complexity of showing bioavailability and bioequivalence to Prepopik. These factors are crucial issues and are medically and scientifically complex. Until these issues are resolved, any reliance on market exclusivity is folly. The remaining market exclusivity period is of interest but not critical. FDA's application of the new interpretation is not only required as the only valid interpretation, but would not adversely impact any current ANDA applicants for Prepopik.

B. The Agency Failed to Adequately Consider All Points Raised in Ferring's Original Citizen Petition

In its decision, FDA failed to adequately respond to all points raised in Ferring's Citizen Petition. In particular, the Agency failed to address inconstancies in application of its exclusivity period for combination drug products where some drug substances had been previously approved in single ingredient drug products. Under FDA's umbrella policy, the exclusivity period for the combination drug product depended on the timing of the approval of the single ingredient drug product, rather than the specific facts and circumstances applicable to drug substances in the combination drug product alone.[26] The Agency also failed to adequately address the extensive support in the legislative history of the Hatch-Waxman Amendments for five years of exclusivity for fixed-combination drug products where at least one drug substance had not been previously approved.[27] When these facts are all taken into consideration, recognition of Prepopik's five-year market exclusivity is the only reasonable decision.

1. *Umbrella Policy*

FDA's response acknowledged that under its umbrella policy, "5-year NCE exclusivity, once it attaches . . . protects not only the drug product that is the subject of the application but also subsequently approved drug products that contain the same active moiety."[28] This policy creates a situation where identical drug products may receive different exclusivity periods based simply on timing of approval. In its Citizen Petition, Ferring provided specific examples of fixed-combination drugs that were granted more than three years of market exclusivity based on

[26] Ferring Citizen Petition, at 22-23.

[27] Ferring Citizen Petition, at 8-14.

[28] FDA Decision, at 11.

the prior approval of an entirely different NDA for a product that contained a novel drug ingredient that was subsequently included in the combination drug product. The exclusivity granted was based on the remaining five-year exclusivity term for single ingredient drug products containing the novel active ingredient, and not on any particular legal or factual circumstance with the combination drug product.

In its Citizen Petition, Ferring also noted the arbitrary nature of FDA's rules on grants of exclusivity based on the order of drug approval. Under FDA's existing and incorrect exclusivity interpretation, a combination drug with one novel drug substance is only eligible for three years of exclusivity because it contains previously-approved drug substances. If an NDA containing the exact same novel drug substance is subsequently approved in a single ingredient NDA, then that NDA would also only be eligible for three years of exclusivity on the grounds that the active ingredient had been previously approved in the combination drug NDA. The innovator would never receive five years of exclusivity for its significant investment in drug development. In the reverse situation, where the single ingredient drug is first approved, then both drugs would be protected by the five-year exclusivity for the single ingredient NDA under FDA's umbrella policy. FDA's original interpretation is irrational, and runs counter to both the stated public health goals of the Agency as well as the intent of the Hatch-Waxman Amendments' incentives for innovation.

In the FDA Decision, the Agency stated:

> Although FDA explicitly recognized that reading the term "drug" in the bar clause to also refer to "drug product" would have been the more natural reading, it declined to adopt this reading in the context of the umbrella policy, because such a reading would not preserve the incentive to innovate and improve upon the initially approved product during the exclusivity period [citation omitted].[29]

Inconsistently, FDA recognized the importance of preserving the incentive to innovate, while at the same time creating and defending a policy and interpretation that removed five-year exclusivity from innovative products.

---

[29] FDA Decision, at 11.

FDA recognized the irrational and arbitrary nature of its policy as evidenced by its actions in the recent approvals of NDAs for Takeda Pharmaceuticals U.S.A, Inc. ("Takeda"). On January 25, 2013, Takeda simultaneously received approval for three NDAs: Nesina (alogliptin),[30] Oseni (alogliptin and pioglitazone),[31] and Kazano (alogliptin and metformin).[32] Of particular note in these approvals is a curious statement contained in the electronic signature of the approval letter for Nesina, which states:

> CURTIS J ROSEBRAUGH
>
> 01/25/2013
> I am approving the single-entity alogliptin first, before approving the combination products containing alogliptin.

As a result of this very specific and highly unusual approval language, Nesina will receive five-year NCE exclusivity while the two combination products will also, in effect, reap the benefit of that five-year exclusivity term because no NDA containing alogliptin can be approved during that time period. Although this is not the first instance in which a combination product containing a new active ingredient has benefited from the five-year exclusivity for the single-ingredient product's prior approval,[33] it is nonetheless unusual that the products – ostensibly approved on the same day – were purposefully distinguished by FDA as having been approved in a particular chronological order.

The Takeda situation is a clear example of FDA recognizing the value of original research and development efforts to gain approval of a drug containing a novel active ingredient, and rewarding such efforts with a five-year term of exclusivity. It is clear from the Takeda review documents that a significant amount of the later review was coordinated for all three

---

[30] NDA 22271, submitted December 27, 2007.

[31] NDA 22426, submitted September 19, 2008.

[32] NDA 203414, submitted November 22, 2011.

[33] Ferring Citizen Petition, at 22-23.

products. Timing of the decision and recognition of the five-year exclusivity is critical, as FDA recognizes.

This concocted process also clearly shows the arbitrary nature of FDA's current interpretation of the FFDCA's exclusivity provisions. Based on FDA's current (*i.e.*, pre-Citizen Petition) policy on exclusivity, if either of the combination products had been deemed to have been approved first, none of the products would have been able to obtain five years of exclusivity, regardless of the fact that the same amount of effort would have been involved in the drug development process. These conclusions produce precisely the type of result that courts have feared, whereby exclusivity periods are based on the order of NDA approval rather than any scientific, technical, economic, or other rationale.[34] Interpretation of the statute in a manner that permits such outcomes, when there is an alternate valid interpretation (one which FDA acknowledges in its decision), is arbitrary and capricious in violation of the Administrative Procedures Act ("APA").[35] FDA's approach here highlights the fears raised by the courts about the Agency juggling or manipulating the timing of approvals to accomplish a preconceived goal that affects intellectual property (here, market exclusivity) rights. In fact, it raises those fears by orders of magnitude.

FDA cannot continue to apply its current interpretation pending finalization of a guidance process. The exclusivity interpretation advanced by the Petitioner is the only rational interpretation (*i.e.*, the recognition of Prepopik's five-year NCE exclusivity) and the only one

---

[34] Abbott Laboratories v. Young, 920 F.2d 984 (D.C.Cir. 1990). In calling for a rational interpretation of statutory language that would not depend on the vagaries of drug approval order, the Court stated the following:

> Abbott's interpretation...fails to serve any conceivable statutory purpose. It would mean that if an original drug application has an active ingredient in the form of a salt, a drug company cannot obtain extended protection by merely filing a new application for a drug with an active ingredient in its non-salt form, but if it does the reverse . . . it can. That construction appears to be farfetched because it is not consistent with any legislative goal: Abbot can advance no hypothetical reason why Congress (or indeed any of the interest groups) would have wanted the degree of protection a drug received to turn on this variable sequence. Abbott's reading promotes neither the interests of the research-oriented pharmaceutical industry nor the generic drug industry in a rational way, producing instead a windfall depending on an accident of chemical nomenclature. We have not been offered any scientific, technical, economic or other explanation why Congress would intend the grant of a ten year market exclusivity to depend on the temporal sequence in which [§ 505(b)] applications were approved....

[35] 5 U.S.C § 706(2)(A).

that avoids absurd exclusivity results. FDA does not have the choice between two reasonable interpretations. The Agency's original interpretation is invalid and unreasonable, and the Agency can only implement the reasonable interpretation that permits five-year exclusivity for fixed-combination drugs with novel ingredients regardless of order of approval. Only immediate application of the new policy to at least those drugs with remaining exclusivity and no current generic competitor (such as Prepopik) considers all the relevant factors and is reasonable.

2. Legislative History

FDA's decision failed to address the points raised by Ferring and the other Petitioners regarding clear Congressional understanding of the applicability of three and five year exclusivity terms for new drugs. The Agency states:

> Petitioners also claim that the legislative history of the Hatch-Waxman Amendments supports their position that 5-year NCE exclusivity should be awarded to all drug substances containing no previously approved active moiety, whether such a drug substance was first approved in a single-entity drug product or in a fixed-combination. According to Petitioners, Congress intended to reward the development and approval of new active ingredients (drug substances) with 5-year NCE exclusivity, because they require more time and resources to bring to market compared to those drug products that consist of a previously approved active ingredient. Therefore, Petitioners maintain that the interpretation of "drug" in the definition of "new chemical entity" as "drug substance," not "drug product," is more consistent with Congressional intent [citations omitted].[36]

After acknowledging the points regarding Congressional intent, the Agency fails to address this issue in any meaningful way. The Agency fails to consider or address the Petitioners' position that the clear intent of Congress is for application of five years of exclusivity to any NDA that contains novel drug ingredients, and that the three-year exclusivity was intended for products that were less innovative changes to existing drugs. In making its decision not to apply the five-year exclusivity to Prepopik, FDA failed to consider that its prior interpretation was not valid, as it was inconsistent with clear Congressional intent. Therefore, the proper interpretation – five-year exclusivity for fixed-combination drug products that contain novel drug substances – must be applied immediately, and not after some vague and indefinite guidance document process.

---

[36] FDA Decision, at 13.

Ferring's position regarding Congressional intent was based on multiple clear statements from the legislative history of the Hatch-Waxman Amendments. These statements demonstrated the well-established and accepted goal of the five-year exclusivity period to encourage pharmaceutical innovation by rewarding those sponsors that bring drugs containing novel active ingredients to market. FDA's interpretation requiring all ingredients in a combination drug product to be novel ingredients is not supported by the record, and is contrary to all statements of the purposes of the exclusivity periods. The Agency's interpretation is unreasonable, arbitrary, and capricious.

As discussed in detail in Ferring's Citizen Petition, the three- and five-year exclusivity periods were rewards for drug development, and were distinguished by the degree of that effort and innovation. The periods were not to be determined by vagaries of approval order, artificial timing issues, and whether the drug was a fixed-combination or a single ingredient product. Drugs that included novel ingredients requiring significant clinical development deserved a longer exclusivity period than simple improvements on already approved drugs/ingredients. This point is clear from the record. A number of examples of statements demonstrating this intended approach are provided in the Citizen Petitions, including (among others) these statements explaining the applicability of the longer exclusivity period for innovative drugs with novel ingredients:

> FDA may not make effective the approval of an ANDA for a drug including an active ingredient (including any ester or salt of the active ingredient) which was approved for the first time in an NDA between January 1, 1982 and the date of enactment of this bill until 10 years after the date of approval of the NDA.[37]

And:

> First, the amendment provides a 5-year period of exclusive market life for drugs approved for the first time after enactment of this legislation. This provision

[37] Report accompanying H.R. 3605 (June 12, 1984), at 29. This section of the report refers specifically to the ten-year exclusivity term under FFDCA § 505(j)(5)(F)(i); however, the statutory language of this section is directly analogous to the language of FFDCA § 505(j)(5)(F)(ii).

> gives the drug industry incentives needed to develop new chemical entities whose therapeutic usefulness is discovered late when little or no patent life remains.[38]

Both of these statements (as well as other statements included in the Citizen Petitions) demonstrate that the five-year reward was contingent on the inclusion of novel ingredients, and was not concerned with the presence of other, previously-approved ingredients in the same drug product. In contrast, it is very clear from other statements in the legislative history that the three-year exclusivity was a lesser reward that was intended to apply to drugs that were less innovative, *i.e.,* that contained only non-novel active ingredients:

> First, under this proposal, a drug company whose patent is going to expire could – under some circumstances – conduct short, simple, noninnovative, clinical trials and seek FDA approval for an over-the-counter version of the drug. Under this proposal, even though this change would not affect patent status, the drug company would receive a "reward" of 3 years of marketing exclusivity.[39]

And

> The 3-year protection, in effect, provides that a product that is not a new chemical entity would be protected for 3 years after the FDA approval because there were essential clinical trials submitted to FDA, and only when clinical trials were submitted.[40]

Both of these statements demonstrate the clear Congressional understanding that the three-year exclusivity applied to those drugs that were viewed as including only previously-approved active ingredients, and thus did not require the greater incentive necessary for drugs that include novel ingredients.

---

[38] Statement of Representative Waxman found in the Congressional Record (Cong. Rec. H9113 (September 6, 1984)).

[39] Statement of Representative Kastenmeier found in the Congressional Record (Cong. Rec. H9114 (September 6, 1984)).

[40] Statement of Representative Waxman found in the Congressional Record (Cong. Rec. H9121 (September 6, 1984)).

FDA's own statements in the preambles to the 1989 proposed regulations for implementation of the Hatch-Waxman Amendments demonstrates a clear understanding of the reasons for the exclusivity incentives:

> FDA"s interpretation of the scope of the 5-year exclusivity provision is also consistent with the legislative history, which reveals that Congress was aware of FDA's classification scheme and did not intend to confer significant periods of exclusivity on minor variations of previously approved chemical compounds.[41]

FDA's original interpretation that fixed-combination drugs with both new and previously-approved drug substances is inconsistent with the clear understanding in the legislative record, and cannot be applied to Prepopik. Thus, the statutory interpretation that FDA has now recognized as reasonable *must* be applied to Prepopik, and cannot be applied at some inconclusive future date. Only such immediate application is consistent with the way FDA and the courts have applied analogous statutory interpretation decisions to the Agency's policies in other petition and litigation situations. FDA's failure to apply a statutory interpretation here is inconsistent with past actions and therefore arbitrary and capricious for that reason alone.

C. Due Process and Fairness Require that Five-Year NCE Exclusivity be Applied to all Relevant Drug Products, and Apply to Ferring's Prepopik

Five-year NCE exclusivity, for which Ferring's fixed-combination drug product clearly qualified under the relevant statutory and regulatory authorities (and by FDA's own recent admission), is an intellectual property right that was granted and vested at the time of Prepopik's NDA approval. The fact that FDA has decided to apply its new statutory interpretation prospectively is merely a canard. That alleged prospective interpretation is not only unreasonable but is also arbitrary and capricious. Where, as here, there is only one valid statutory interpretation (and FDA concludes that the interpretation is reasonable), it must be applied to all parties equally. An interpretation that is no longer valid, such as FDA's previously-stated interpretation of the five-year NCE exclusivity provisions, cannot be arbitrarily retained until some indeterminate future point in time. Even in the event that FDA's previous

---

[41] 54 Fed. Reg. 28871, 28898 (July 10, 1989). In support, FDA cites the statement of Representative Waxman found in the Congressional Record (Cong. Rec. H9124 (September 6, 1984)), and statements found in House Report 857 Part I, 98th Cong., 2d Sess. 38 (1984).

interpretation was a valid alternative to the new interpretation, fairness, sound policy, and due process and fairness require FDA to apply the new rule to Ferring's Prepopik.

FDA's decision to deny application of its new five-year exclusivity interpretation to the very Petitioners who requested it is not only invalid, but it can also be considered uniquely punitive to the Petitioners. FDA acknowledges that the interpretation of the relevant exclusivity authorities crafted by Ferring, Gilead, and Bayer is reasonable. The Agency also acknowledges that the interpretation is desirable as a matter of policy, and that the new policy will lead to the development of effective, life-saving fixed-combination products in high risk therapeutic areas (*e.g.,* cancer, HIV, etc.). FDA's decision here denies Petitioners the benefit of the changes, even though those changes are a direct result of the extensive work that the Petitioners did to further FDA's public health policy.

1. *FDA's Approach Weakens Incentives to Petition for Future Improvements to Public Health Policy*

FDA claims that applying the Agency's new interpretation to Ferring's, Gilead's, and Bayer's products would not advance the goals of the Hatch-Waxman Amendments. FDA believes that Hatch-Waxman's goal of incentivizing and rewarding the development and approval of novel drugs would not be achieved here, as the three Petitioners' products have already been developed and approved. This short-sighted view of the situation is not only incorrect, but it will also have potential negative impacts on companies' willingness to effect further improvements to public health policy in the future.

The FDA Decision only addressed one of two incentives that are of concern in the Citizen Petitions. FDA stated:

> Although we recognize that the Hatch-Waxman Amendments contain incentives to reward the development and approval of novel drugs, these particular products already have been developed and approved. Recognizing additional exclusivity in this case is not necessary to encourage the *development* of novel drugs. We believe that changing our interpretation going forward will foster Congress's goal

> of encouraging the development and approval of novel drugs (emphasis in original).[42]

This statement is true to the extent that it states that prospective application of the new interpretation is not necessary to reward development of the Petitioner's drugs because they are already approved. However, FDA's position fails to address how its implementation of the new interpretation at some vague future date once guidance is finalized provides incentives to fixed-combination drug manufacturers. Contrary to its apparent intent, FDA's position on future implementation has created a *dis*incentive to innovation. FDA's development and implementation of guidance is seldom rapid and often indefinite. Drug manufacturers have no incentive to develop fixed-combination drugs that include novel and previously-approved drug substances because there is no certainty whether five-year exclusivity for such drugs will ever be available. Additionally, drug manufacturers may place development of such drug products on hold pending finalization of the guidance, delaying rather than speeding development (and approval) of novel new drugs.

FDA also fails to recognize that its actions create a different sort of *dis*incentive. FDA acknowledges that the Petitioners' position would be in the public interest and help encourage development of new fixed-combination therapies. The Citizen Petitions were the driving force behind this new valuable policy interpretation that will incentivize future drug development. Such change in policy would likely not have occurred but for the efforts of the Petitioners. If the Agency takes the position that it will not apply the results of its new interpretation to the parties largely responsible for the change, it is creating a situation where future potential petitioners will not see the benefit of attempts to improve policy through the petition process. FDA's overly narrow focus on only incentives for *future* drug approval fails to consider the disincentives it is creating for participation in future public process to improve FDA policy.

2. *ANDA Applicants Will Not be Burdened by Application of FDA's New Statutory Interpretation to Ferring's Prepopik*

FDA justified its decision to deny five-year exclusivity to Ferring's, Gilead's, and Bayer's products by stating that "if the new interpretation were to be applied to products for

---

[42] FDA Decision, at 17.

which ANDAs have already been filed, it could impose a burden on the ANDA sponsors, who relied on our existing interpretation in filing their applications."[43] This argument has no merit, particularly in Ferring's specific case, for several reasons.

First, Ferring has not to date received any Paragraph IV certifications referencing Prepopik. Additionally, there is no clinical trial information for a generic Prepopik product currently listed in ClinicalTrials.gov. It is therefore our belief that there have been no ANDAs submitted that reference Prepopik. Thus, no generic manufacturer has relied on either FDA's previous or new statutory exclusivity interpretation regarding Prepopik in filing an application, and no burden would be imposed if the Agency were to apply its new interpretation to Ferring's product. The most critical issue in ANDA development is establishing bioavailability and bioequivalence to the Reference Listed Drug ("RLD"). No bioavailability and bioequivalence guidelines exist for Prepopik. Sodium picolinate cannot be tested alone, and real biopharmaceutics issues exist. For Prepopik, the remaining market exclusivity is not the seminal issue of reliance, even if an ANDA were to be filed as the Agency delays its response to this Petition.

Second, any applicants with pending or future pending ANDAs would have been on notice that the length of exclusivity for Prepopik and the other drugs was uncertain as of the date of the publication of the Citizen Petitions. Any generic applicant that chose to submit an ANDA in this situation would have therefore voluntarily assumed the risk of the uncertain exclusivity period, and would likely have planned for the possibility that exclusivity may continue to run past the stated time period given the uncertainty surrounding the product. Any burdens on such applicant would therefore not be as unforeseen or oppressive as the Agency appears to assume.

Furthermore, delays and burdens for ANDA applicants come from many sources in the approval process and are an expected cost of doing business. It is highly unlikely that any generic company has hinged its business on an expectation that FDA will only award three-year exclusivity to fixed-combination products containing both new and previously-approved active moieties. The generic space is an area that is replete with change. There is a never-ending quest

[43] FDA Decision, at 17.

by companies to increase intellectual property protection for their products, including seeking exclusivity for new indications and pediatric exclusivity, and increasing the length of patents, among other strategies. To suggest that there is a concrete expectation by ANDA applicants regarding when exclusivity for a pioneer drug product will expire, or even when a generic product may be approved, is erroneous and disingenuous. Generic manufacturers are aware of these obstacles, and actively prepare to deal with them. Retroactive application of five-year NCE exclusivity to Ferring's product would be unlikely to create additional hardships for ANDA applicants beyond what is already expected or for which an ANDA applicant has prepared.

In contrast, there is a greater hardship on the pioneer applicant, which has only a limited window to recoup its new drug development costs. Generic competition is now routinely recognized by the courts to cause irreparable harm. FDA estimates that approximately 80% of all drugs dispensed are generic drugs and, among drugs for which a generic version is available, approximately 94% are dispensed as a generic.[44] Pioneer sponsors are therefore increasingly forced to endure price erosion and loss of market position and revenue, which can cause them irreparable harm in the long run.[45] FDA's refusal to grant five-year exclusivity to Ferring's Prepopik, despite the Company's significant efforts in assisting the Agency in reaching its new public health-promoting exclusivity policy, would therefore unfairly cause the Company to suffer irreparable harm. It is our belief that, in the interests of fairness and the public health, five-year exclusivity should be recognized when there are no ANDAs filed as of the date of the Citizen Petition (or, alternatively, FDA's response), as with Prepopik.

---

[44] 78 Fed. Reg. 67985, 67988 (November 13, 2013).

[45] *See, e.g.,* Purdue Pharma L.P. v. Boehringer Ingelheim GmbH, 237 F.3d 1359, 1368 (Fed.Cir. 2001) (likelihood of price erosion and loss of market position are evidence of irreparable harm); Bio–Technology Gen. Corp. v. Genentech, Inc., 80 F.3d 1553, 1566 (Fed.Cir. 1996) (loss of revenue, goodwill, and research and development support constitute irreparable harm); Polymer Technologies, Inc. v. Bridwell, 103 F.3d 970, 975–76 (Fed.Cir. 1996) (loss of market opportunities cannot be quantified or adequately compensated, and is evidence of irreparable harm).

D. Due Process and Fairness Require FDA to Apply the New Statutory Interpretation to Ferring's Prepopik

FDA decided to adopt the Petitioners' statutory interpretation of the FFDCA exclusivity provisions but to implement that interpretation at some undefined and unforeseeable point in the future by choosing to issue Level 1 draft guidance for public comment. This decision to issue draft guidance for public comment was legally incorrect because draft guidance is not binding, does not create or confer rights, is intended to help *industry* carry out its obligations, and may be deviated from in appropriate circumstances. FDA's change in statutory interpretation here is in fact binding, does create rights, is meant to help FDA (not industry) carry out an obligation, and cannot be departed from lest individual FDA reviewers decide to award exclusivity however they see fit. Guidance is therefore not the appropriate legal means to implement FDA's change in statutory interpretation with respect to NCE exclusivity for fixed-combination drug products.

FDA's decision to issue a draft guidance document and to implement a final guidance at some point in the future creates even more of the regulatory uncertainty that the Agency was trying to avoid. Draft guidance documents never have to be finalized but, even if they are, there is no proscribed statutory or regulatory timeline for doing so. FDA's decision recognizes the statutory rights for the regulated industry, but the choice of issuing the 2014 NCE Exclusivity Draft Guidance for public comment means that the Agency never has to actually implement its decision. Current and future applicants have no way of knowing if and when FDA will finalize the guidance document. Furthermore, industry has no way of anticipating how the new interpretation will be applied to applicants who have submitted applications that have not yet been received for filing or that are already in the review queue. FDA's 2014 NCE Exclusivity Draft Guidance is entirely silent on this point, merely noting that it will be applied prospectively.

The Agency's decision here represents an arbitrary and capricious application of the new policy. As the courts have repeatedly noted in the FFDCA approval area, timing and approval of applications is critical (*e.g.*, timing of filing Paragraph IV petitions, 180-day market exclusivity decisions), and the exclusivity periods have been implemented immediately. These statutory interpretation decisions immediately recognize the intellectual property rights of the applicants.

As is FDA's normal practice with statutory interpretation, the Agency should have implemented its decision immediately by regulating directly from the FFDCA. FDA has historically implemented statutory changes directly on parties, especially in the area of Hatch-Waxman exclusivity. In many of those cases FDA did not issue guidance, but implemented its decisions immediately based upon statutory interpretation. FDA's approach here is therefore a departure from its normal course of action when implementing a new statutory interpretation, particularly in matters of exclusivity conclusions.

We believe that FDA's decision to issue Level 1 draft guidance for public comment in this case was legally inappropriate and that the Agency should have instead regulated directly from the statute. However, if FDA determines that issuing Level 1 draft guidance was legally correct, then we argue in the alternative that the guidance should have been implemented immediately as a Level 1 guidance document that does not require prior public comment and should have been applied to Ferring's Prepopik. Level 1 guidance that is implemented immediately is the appropriate course of action when "prior public participation is not feasible or appropriate." In this case, FDA has reinterpreted the FFDCA provisions governing the award of five-year NCE exclusivity for fixed-combination drug products. FDA had two choices: either five-year exclusivity is appropriate in certain cases for these drug products, or it is not. FDA has made its decision. The decision for Prepopik's five-year market exclusivity is not a decision that is appropriate for public comments, because it is the Agency's jurisdiction to interpret and implement its governing statute. The Agency reassessed its earlier interpretation and has stated that there are significant public policy reasons for making this change. If these public policy reasons are legitimate, then there is no reason to seek the public's prior comment on the legitimacy of those matters.

1. *FDA's Decision to Issue Draft Guidance was Legally Incorrect*

a. Purpose and Legal Status of Guidance

Historically, FDA has used a variety of means to interpret Agency regulations and policies;[46] however, recognizing the need for consistency, FDA announced the availability of its good guidance practices ("GGPs") document in 1997.[47] Congress subsequently used this GGP document when it amended the FFDCA to include a statutory provision on the development of informal Agency statements.[48] After this change in the Act, FDA issued proposed[49] and final[50] regulations that conformed to the new statutory mandate and largely tracked the pre-statutory GGP document.

The GGP regulations define a "guidance document" as an FDA-prepared document for FDA staff, industry, and the public that describes FDA's interpretation of or policy on a regulatory issue.[51] There are two "levels" of guidance documents. Level 1 guidance documents can be used to establish an initial interpretation of the statute or regulations; establish more than minor changes in policy or interpretation; address complex scientific issues; or deal with very controversial issues. Level 1 guidance documents may be issued for public comment, or they may be issued and implemented immediately when "prior public participation is not feasible or appropriate."[52] Level 2 guidance documents are documents outlining existing practices or minor policy or interpretation changes, and include all guidance that is not considered to be Level 1.[53]

---

[46] For example, trade correspondence, formal and informal policy statements, and compliance policy guides, among others.

[47] 62 Fed. Reg. 8961 (February 27, 1997).

[48] Food and Drug Administration Modernization Act of 1997 ("FDAMA"), Pub. Law No. 105-115 (November 21, 1997), at § 405; FFDCA § 701(h), *codified at* 21 U.S.C. § 371(h).

[49] 65 Fed. Reg. 7321 (February 14, 2000).

[50] 65 Fed. Reg. 56468 (September 19, 2000).

[51] 21 C.F.R. § 10.115(b)(1).

[52] 21 C.F.R. § 10.115(c)(1).

The most important features of guidance documents are that they can survive in draft form indefinitely without being finalized; they are non-binding on all parties and do not create or confer any rights (whether in draft or final form); they are intended to help industry carry out its legal obligations under the Act and the implementing regulations; and FDA can deviate in cases where there is appropriate justification and supervisory concurrence. Each of these features is critical, because they illustrate why guidance was the wrong choice in the case at hand.

First, there is no legal requirement that draft guidance must be finalized. Level 1 guidance documents are often, but not always, released for public comment prior to implementation.[54] However, nowhere does the statute or regulations indicate that a draft guidance document *must* be finalized. In fact, CDER has draft guidance documents dating back to 1997, the year that FDA issued its GGP document,[55] and 23 draft guidance documents remaining for 1998 and 1999 combined.[56] This lack of action for 15 or more years means that FDA has decided that these documents should not be finalized and implemented. There is, therefore, no assurance that any draft guidance document, including the 2014 NCE Exclusivity Draft Guidance, will ever be finalized and implemented.

Second, all guidance documents in both draft and final form are non-binding documents. This was FDA's position when it issued its GGP document in 1997,[57] Congress' position when it

---

[53] 21 C.F.R. § 10.115(c)(2).

[54] FFDCA § 701(h)(1)(C)(i), *codified at* 21 U.S.C. § 371(h)(1)(C)(i); 21 C.F.R. § 10.115(g)(1)(ii)(c).

[55] *See, e.g.,* FDA, "Draft Guidance for Industry – Evaluating Clinical Studies of Antimicrobials in the Division of Anti-Infective Drug Products" (February 1997), *available at* http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/guidances/ucm064980.htm.

[56] FDA, "Center for Drug Evaluation and Research List of Guidance Documents" (January 2, 2014), *available at* www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm079645.pdf.

[57] 61 Fed. Reg. 9181, 9182 (March 7, 1996) (notice and request for comments on GGP document) ("The agency explicitly states that guidance is not binding in many of its guidance documents."); 62 Fed. Reg. 8961, 8962-8963 (February 27, 1997) (notice announcing GGP document) ("The only binding requirements are those set forth in the statute and FDA's regulations.").

enacted FDAMA to amend the FFDCA to include GGP provisions,[58] and FDA's position in the proposed[59] and final[60] rules implementing the GGP regulations and in other Agency explanatory materials.[61]

Third, guidance documents help industry carry out its obligations under the FFDCA and regulations. Guidance provides "the kind of specific detail that often is not included in the relevant statutes and regulations." They also "reduce uncertainty" because "their absence would disadvantage the industry."[62] Indeed, guidance documents typically address issues such as manufacturing, labeling, promotion, and testing of products; inspection and enforcement issues; and the content of applications.[63] Each of these issues is amenable to Agency guidance because they provide information to help *industry* comply with its obligations under the Act and regulations.

Finally, although guidance documents reflect FDA's current position on a regulatory matter, FDA staff may deviate from draft or final guidance documents if there is "appropriate justification and supervisory concurrence."[64] Therefore, there is no actual certainty that FDA's position as stated in a guidance document will be implemented fairly or consistently across the Agency.

---

[58] FFDCA § 701(h)(1)(B), *codified at* 21 U.S.C. § 371(h)(1)(B) ("Although guidance documents shall not be binding on the Secretary....").

[59] 65 Fed. Reg. 7321, 7323 (February 14, 2000) ("Consistent with [the Act], proposed § 10.115(d) describes the nonbinding effect of guidance documents.").

[60] 65 Fed. Reg. 56468 (September 19, 2000) (implementing 21 C.F.R. § 10.115).

[61] *See, e.g.,* FDA, Manual of Policies and Procedures ("MAPP"), "Developing and Issuing Guidance" (MAPP 4000.2) (revised September 13, 2005), *available at* www.fda.gov/downloads/aboutfda/centersoffices/cder/manualofpolicesprocedures/ucm073004.pdf , at 4 ("Guidance documents are ***not legally binding*** or enforceable" (emphasis in original)).

[62] 61 Fed. Reg. 9181, 9182 (March 7, 1996).

[63] 21 C.F.R. § 10.115(b)(2); MAPP 4000.2 at 4.

[64] 21 C.F.R. § 10.115(d)(3).

The Agency succinctly summarized the legal status of guidance documents in the GGP final rule: "[b]ecause a guidance document represents the agency's current thinking on a subject but it is *not ever binding* on FDA or outside parties, *you should not rely on any guidance document*, draft or final" (emphasis added).[65] As explained below, each of these characteristics of Agency guidance documents illustrates why FDA should not have issued draft guidance for public comment to implement its new statutory interpretation of the relevant exclusivity provisions.

b. FDA's New Statutory Interpretation is Not Suitable for Draft Guidance

Contrary to the purpose and features of guidance documents as discussed above, FDA's change in statutory interpretation here is in fact binding, does create rights, is meant to help FDA – not industry – carry out an obligation, and cannot be departed from lest FDA decide to award exclusivity however it sees fit. For each of these reasons, the issuance of draft guidance was not the legally appropriate means of implementing this change in FDA's statutory interpretation.

FDA's response to the Petitioners acknowledges that the word "drug" is ambiguous in the five-year NCE statutory provision.[66] FDA has nonetheless concluded that Petitioners' position – that the word "drug" means drug *substance* – is supported by the Agency's policies and initiatives to encourage fixed-combination drug product development. As a result, FDA's historical interpretation of "drug" to mean "drug product" "may result in drug development strategies that are suboptimal from a public health perspective." FDA has therefore acknowledged that a change in interpretation is legally correct.[67]

This new interpretation of the existing statutory language is in fact binding and does create or confer rights on certain applicants that existed in the past but that FDA did not

---

[65] 65 Fed. Reg. 56468, 56471 (September 19, 2000).

[66] As presented elsewhere in this Petition, Ferring believes that the term is clear, and that it means "drug substance" for purposes of fixed-combination exclusivity.

[67] FDA Decision, at 14-16.

recognize until it issued its decision on the Citizen Petitions. These rights to five-year exclusivity for certain fixed-combination drug products will be critical to companies' drug development programs, as FDA recognized.[68] If the award of NCE exclusivity is a statutory right based on FDA's interpretation of the Act, but guidance documents do not create or confer rights, then the Agency should not have issued a guidance document for prior public comment on this issue.

Furthermore, FDA's draft guidance in this case does not address how industry is supposed to comply with a statutory or regulatory provision. Rather, the new draft guidance is directed entirely at how *FDA* will carry out *FDA's* new statutory interpretation of the exclusivity provisions in particular cases. This area is, therefore, beyond the subject matter that is appropriate for communication through guidance. The fact that the Agency has previously issued guidance to communicate policy issues related to exclusivity is irrelevant to the legal standard, and such approaches have been or should have been rejected where such interpretations confer or create rights.

Finally, the interpretation of how FDA awards exclusivity is not open to the discretion of each individual within the Agency. The interpretation of these statutory provisions must be applied consistently. FDA has acknowledged that the statute and regulations are ambiguous, and FDA has therefore communicated its intent about how the Agency will apply these provisions. These FFDCA provisions can have different meanings, but FDA has decided which interpretation is legally correct. As a result, no alternative interpretation can be justified by individual FDA staff. To permit deviation by individual FDA reviewers would strip away a statutory right that is contrary to the law. Issuing guidance on this matter that permits such deviation is therefore legally inappropriate.

For all of these reasons, the issuance of Level 1 draft guidance for prior public comments is not the legally correct way to implement a decision on the meaning of the governing statute. Because this decision involves statutory interpretation of the five-year NCE exclusivity provision, FDA should not have issued draft guidance for public comment.

---

[68] FDA Decision, at 15-16.

c. Draft Guidance Leaves the Public with no Regulatory Certainty

FDA acknowledges that the Petitioners' reading of the Act is legally appropriate and is "desirable as a matter of policy"[69] in light of the Agency's recent efforts to promote the development of fixed-combination drug products. In spite of this decision, FDA states that "*[i]f at the conclusion* of the comment period we are convinced that our *proposed new interpretation is appropriate*, we will issue a final guidance adopting the new interpretation" (emphasis added).[70] FDA goes on to state that "*[i]f the new interpretation is adopted*, the Agency intends to apply the new interpretation *prospectively*" (emphasis added).[71]

Despite the fact that FDA's decision is a critical interpretation of its own implementing statute regarding the award of NCE exclusivity in particular cases – and is therefore a binding interpretation of the Act – FDA has not provided industry with any certainty at all that it will actually implement this change, when it would do so, and how it would do so. This "maybe, maybe not" approach that is inherent in guidance document development is inappropriate for a matter as critical as the statutory award of NCE exclusivity pursuant to the Act. The decision demands immediate implementation that is applicable to all parties based on the direct application of the Act. To do otherwise by issuing draft guidance for prior public comment only creates regulatory uncertainty for all parties involved. Moreover, there are several serious legal problems associated with this approach.

First: When will FDA implement its new interpretation? As already discussed, draft guidance documents do not have to be finalized. Indeed, there are still 24 CDER draft guidance documents from the 1990s (1997-1999) and 79 CDER draft guidance documents from the 2000s (2000-2009).[72] With so many draft guidance documents existing for years, there is absolutely no

---

[69] FDA Decision, at 17.

[70] FDA Decision, at 16.

[71] FDA Decision, at 18.

[72] FDA, "Center for Drug Evaluation and Research List of Guidance Documents" (January 2, 2014), *available at* www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm079645.pdf.

assurance that the Agency will ever finalize the 2014 NCE Exclusivity Draft Guidance, especially as Agency priorities shift in unpredictable ways. FDA has accepted the Petitioners' statutory interpretation, but ironically FDA may never recognize its effect in practice.

Second: How will FDA apply this new interpretation prospectively? FDA states that if it adopts this new interpretation after reviewing public comments, then the guidance "does not apply to fixed-combination drug products that were approved *prior to adopting the new interpretation*"[73] (emphasis added). FDA has not stated whether this means that it will apply the new interpretation to applications that are already in the review queue, to applications that have been submitted but not yet accepted for filing, or to applications submitted only after the adoption of the interpretation.

Finally: How will FDA's draft guidance approach eliminate regulatory uncertainty? The FDA Decision states that the Agency is concerned about the burdens on industry of new statutory interpretations, noting that "we wish to avoid any unnecessary disruption to regulated industry."[74] However, the issuance of this draft guidance for prior public comment creates the same ambiguity and unfairness that FDA claims would have existed had it applied the FDA Decision retroactively to cover the Petitioners' products. Furthermore, by FDA's own acknowledgement, the Agency's ability to receive and approve ANDAs or § 505(b)(2) NDAs depends upon whether three-year or five-year exclusivity is at stake.[75] As a result, FDA's prospective application creates regulatory uncertainty for companies that are in the process of developing or plan to develop fixed-combination drug products that may be affected by any final FDA decision about how or when to implement this change.

For all of these reasons, FDA's issuance of draft guidance for public comment was legally inappropriate. Because the decision involved the Agency's interpretation of its governing

---

[73] 2014 NCE Exclusivity Draft Guidance, at 1.

[74] FDA Decision, at 17.

[75] FDA Decision, at 6.

statute, FDA should instead implement its decision immediately by regulating directly from the FFDCA, as the Agency has done in similar cases in the past.

2. *FDA Should Implement its Decision Immediately by Regulating Directly from the FFDCA*

a. FDA has Regulated Directly from the FFDCA for Other Exclusivity Issues

FDA should have immediately implemented its decision regarding the statutory interpretation of five-year NCE exclusivity for fixed-combination drug products by regulating directly from the FFDCA – regardless of whether FDA later decides to amend its exclusivity regulations at 21 C.F.R. § 314.108. FDA has taken this approach numerous times in the past, particularly with respect to exclusivity matters, when it was critical to implement a statutory interpretation to eliminate industry confusion without waiting for the promulgation or revision of regulations. FDA should therefore have implemented this change immediately here as well.

For example, FDA regulated directly from the Act with respect to multiple first-to-file applicants sharing 180-day exclusivity. FDA had initially limited the availability of 180-day exclusivity to an ANDA applicant that was the first to challenge a patent and win that patent litigation. Several circuit courts, however, disagreed with FDA's interpretation,[76] determining that the first ANDA applicant to challenge a patent – whether or not it was successful in patent litigation – would receive 180-day exclusivity. As a result, several applicants could in theory share the statutory 180-day exclusivity available to first Paragraph IV first filers.

FDA issued guidance in 1998 stating that it would remove the "successful defense" requirement from the regulations in the future; until that time, "*FDA will regulate directly from the statute*, and will make decisions on 180-day generic drug exclusivity on a case-by-case basis" (emphasis added).[77] FDA issued a proposed rule[78] but later withdrew it[79] for reasons unrelated to

[76] Mova Pharmaceuticals, Inc. v. Shalala, 140 F.3d 1060 (D.C.Cir. 1998); Granutec v. Shalala, 46 U.S.P.Q.2d 1398 (4th Cir. 1998).

[77] FDA, "Guidance for Industry – 180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act" (June 1998), at 4.

the merit of the proposal. FDA's notice withdrawing the proposed rule similarly stated that "FDA will *continue to regulate directly from the statute* and applicable regulations and make regulatory decisions on an issue-by-issue basis" (emphasis added).[80] This position was reiterated in subsequent guidance.[81]

FDA has also regulated directly from the Act in the case of forfeiture of 180-day exclusivity. In response to a letter from Teva regarding the application and forfeiture of 180-day exclusivity to granisetron hydrochloride,[82] the Agency noted that the ANDA at issue was submitted after enactment of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA").[83] Because FDA had not yet at that time promulgated regulations implementing the new statutory provisions, "*[FDA] will regulate directly from the statute* in determining whether ANDA applicants are entitled to exclusivity" (emphasis added),[84] as "[i]t is FDA's practice to make decisions on eligibility for 180-day exclusivity only in the context of specific ANDAs that are otherwise eligible for approval."[85] The Agency took this same approach later that same year when it issued a "Dear ANDA Applicant" letter regarding 180-day exclusivity and forfeiture issues relative to ANDAs for dorzolamide hydrochloride/timolol

---

[78] 64 Fed. Reg. 42873 (August 6, 1999).

[79] 67 Fed. Reg. 66593 (November 1, 2002).

[80] 67 Fed. Reg. 66593, 66593 (November 1, 2002).

[81] FDA, "Guidance for Industry – 180-Day Exclusivity When Multiple ANDAs are Submitted on the Same Day" (July 2003), *available at* www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm072851.pdf (hereinafter "180-Day Exclusivity Guidance").

[82] Letter from Gary Buehler, FDA, to Marc Goshko, Teva Parenteral Medicines (January 17, 2008), *available at* http://www.fda.gov/downloads/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/abbreviatednewdrugapplicationandagenerics/ucm151237.pdf (hereinafter "FDA Response to Teva").

[83] Pub. Law No. 108-173 (December 8, 2003).

[84] FDA Response to Teva, at 1.

[85] FDA Response to Teva, at 1, fn. 1.

maleate. FDA similarly stated that it had not yet promulgated regulations under the MMA and would, therefore, "regulate directly from the statute."[86]

Finally, FDA has applied this approach to the interpretation of "court" in the 180-day exclusivity provision. After losing several court challenges to FDA's interpretation of the meaning of "court decision,"[87] FDA determined that it would not apply the regulatory definition of "court" and would remove the salient provisions of the regulation.[88] The Agency also noted that "[t]he new definition of *court* will apply to certain ANDAs submitted after the publication of this guidance" (emphasis in original).[89] Because the guidance was therefore considered to be implemented immediately, and the amendment of the regulations would require notice and comment rulemaking, FDA's actions there meant that it would necessarily have to regulate directly from the statute.

In each of these examples – all of which involved statutory interpretation of exclusivity provisions – FDA chose to immediately implement a change in interpretation, pending further regulatory actions. In the case at hand, whether or not FDA later decides to amend the regulations to make its new statutory interpretation clear, the Agency should, in the interim, regulate directly from the statute as it has done in each of these other cases.[90]

---

[86] Letter from Gary Buehler, FDA, to "Dear ANDA Applicant," Docket No. FDA-2008-N-0483 (October 28, 2008), *available at* www.regulations.gov.

[87] TorPharm v. Shalala, 1997 WL 33472411 (D.D.C. 1997); Mylan Pharmaceuticals, Inc. v. Shalala, 81 F.Supp.2d 30 (D.D.C. 2000), *cited in* FDA, "Guidance for Industry – Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act" (March 2000), *available at* www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm072868.pdf (hereinafter "Court Decision Guidance").

[88] Court Decision Guidance, at 3.

[89] Court Decision Guidance, at 4.

[90] We do not believe that formal rulemaking changes to 21 C.F.R. § 314.108 are necessary here, for the reasons explained in the Gilead Citizen Petition, at 30-43.

b. FDA Can Implement Exclusivity Decisions Immediately without the Need for New Guidance

Although FDA issued guidance in the above examples, FDA often makes decisions about exclusivity matters without issuing new draft guidance. These decisions are usually implemented immediately and do not rely on prior public comment on FDA's decision.

For example, on the same day that the Agency issued its decision in the Petitioners' case, FDA also issued an exclusivity determination to Amarin Pharmaceuticals Ireland Limited/Amarin Pharma Inc. ("Amarin") that rejected the companies' request for five-year NCE exclusivity for Vascepa® Capsules.[91] Eicosapentaenoic acid ("EPA") is the only active moiety in Vascepa. However, FDA had previously approved Lovaza®, a drug containing omega-3 acid ethyl esters as the active ingredient. Omega-3 acid ethyl esters are a mixture containing several different esters obtained from fish oil, one of which was EPA. FDA considered this mixture to be a "naturally derived mixture."

The Agency's response to Amarin analyzed the same five-year NCE exclusivity statutory provision that was at issue in the case of fixed dose combination drug products. FDA reviewed the relevant definitions, and concluded that EPA is an active moiety in the earlier-approved Lovaza. Because Vascepa includes EPA as the sole active moiety, the Agency determined that Vascepa does not qualify for five-year NCE exclusivity.[92]

In its response, FDA also reviewed its prior decisions involving exclusivity determinations for naturally derived mixtures, including racemic mixtures and enantiomers; pancrelipase and hyaluronidase; podophyllum resin; conjugated estrogens; beractant; and menotropins.[93] The Agency concluded that, based on its past decisions, "FDA has not had a

---

[91] FDA response to Amarin Pharmaceuticals Ireland Limited/Amarin Pharma Inc. (February 21, 2004), Exhibit 1 to Complaint for Declaratory and Injunctive Relief in Amarin Pharmaceuticals Ireland Limited v. FDA, No 1:14-cv-0324 (D.D.C. 2014) (hereinafter "FDA Response to Amarin").

[92] FDA Response to Amarin, at 17.

[93] FDA Response to Amarin, at 8-16.

fully consistent practice in this regard."[94] FDA's response to Amarin "provides the best approach for identifying the active moiety or moieties of such [naturally derived] mixtures"[95] and was intended to provide a new, cohesive interpretation and application of the NCE exclusivity provisions to naturally derived mixtures. Despite the criticality of this conclusion, the Agency chose there to implement it immediately. FDA did not issue draft or final guidance.

This decision – which analyzed the same statutory authorities used to render a decision on Petitioners' fixed-combinations – similarly addressed the applicability of statutory exclusivity to a drug that had already been approved[96] and that contained more than one active moiety. There is, therefore, little difference between the Amarin decision and the fixed-combination decision. Despite this fact, FDA chose to implement the Amarin exclusivity determination immediately and based on statutory interpretation but, in the case of the Petitioners, chose to issue draft guidance seeking prior public comment for some possible future implementation. These disparate outcomes are evidence that the decision to issue draft guidance for fixed-combination drug product NCE exclusivity cannot legally stand.

3. *In the Alternative, FDA should have Issued Class 1 Guidance with an Immediate Implementation Date that Applied to Ferring's Prepopik*

Even if the Agency determines that issuing Class 1 guidance to implement the FDA Decision was appropriate, the Agency should have implemented it immediately without prior public comment. FDA has used this approach in the past with respect to exclusivity issues, namely when the Agency issued guidance regarding multiple 180-day exclusivity periods. In that guidance document, FDA noted its immediate implementation "given the need for public guidance on this pressing issue...."[97] The new guidance document in this case merits the same immediate implementation.

---

[94] FDA Response to Amarin, at 19.

[95] FDA Response to Amarin, at 6.

[96] Vascepa (NDA 202057) was approved on July 26, 2012.

[97] 180-Day Exclusivity Guidance, at 6; *see also* 68 Fed. Reg. 45252, 45255 (August 1, 2003) (announcing availability of the 180-Day Exclusivity Guidance).

The FDA Decision states that the Agency "shall ensure public participation" when the Level 1 guidance document establishes an initial interpretation of a statute or regulation or changes in interpretation or policy that are more than minor in nature.[98] FDA quotes the FFDCA for this authority.[99] However, FDA ignores the second half of that same statutory provision, which states that FDA *does not* have to seek public participation in Level 1 guidance development when the Agency "determines that such prior public participation is not feasible or appropriate." In those cases, FDA "shall provide for public comment upon implementation and take such comment into account."[100] FDA's decision to reinterpret the statutory exclusivity provisions in this case clearly makes this a case where public participation is not "appropriate."

FDA has previously stated that it would not seek public comment for Level 1 guidance when, among other cases, "there is a statutory requirement, executive order, or court order that requires immediate implementation." As noted in the proposed rule implementing the GGP regulations, FDA would continue to apply this exception (as well as others) to seeking public comment on Level 1 guidance.[101] Level 1 guidance documents that are immediately implemented without public comments will, nonetheless, be posted for public comment. The Agency will review any comments it receives and will revise the guidance when appropriate.[102] Over the years, FDA has issued Level 1 guidance for immediate implementation in numerous cases, both when there are serious health hazards at stake[103] and in routine cases of enforcement

---

[98] FDA Decision, at 16.

[99] FFDCA § 701(h)(1)(C), *codified at* 21 U.S.C. § 371(h)(1)(C).

[100] FFDCA § 701(h)(1)(C), *codified at* 21 U.S.C. § 371(h)(1)(C).

[101] 65 Fed. Reg. 7321, 7324 (February 14, 2000).

[102] 21 C.F.R. § 10.115(g)(3).

[103] *See, e.g.,* 66 Fed. Reg. 18257 (April 6, 2001) (announcing a guidance for hospitals, nursing homes, and health care facilities for immediate implementation regarding potentially fatal hazards associated with handling and mixups of medical gases); 72 Fed. Reg. 24316 (May 2, 2007) (announcing a guidance for industry regarding testing of glycerin for diethylene glycol for immediate implementation "because of the potential for a serious public health impact if DEG-contaminated glycerin were to enter the domestic market."); 74 Fed. Reg. 39704 (August 7, 2009) (announcing a guidance for industry on pharmaceutical components at risk for melamine contamination for immediate implementation "because of the potential for a serious public health impact if melamine-contaminated pharmaceuticals were to enter the domestic market.").

discretion, drug development issues, and others.[104] Based upon the wide-ranging topics in these documents that were immediately implemented, there is little apparent consistency regarding which topics are appropriate for prior public comment and which are not. In those cases where FDA has considered public comment and made revisions to guidance documents, the subject matter did not involve statutory interpretation, contrary to the situation here.[105]

Here, FDA has made a decision that it is in the best interest of the public health to encourage the development of new fixed dose combination drug products and to award the applicants with five-year NCE exclusivity as appropriate. Further, it is Ferring's position that such decision is mandatory and not discretionary. This decision is simply not one that is amenable to public comment. If the majority of commenters respond that they disagree with FDA's new interpretation, FDA could not reverse course and conclude that encouraging the development of fixed-combination drug products was poor policy, and should not be awarded five years of exclusivity. FDA has already recognized the legal correctness of the Petitioners' decision as a matter of both law and public policy. FDA cannot abdicate its responsibility for the public health nor implement an invalid interpretation of the FFDCA by allowing the public to make a decision about the correctness of a policy direction and a related statutory right. Such decisions are within the purview of FDA, as limited by the statute. This issue is certainly more

---

[104] *See, e.g.,* 66 Fed. Reg. 65977 (December 21, 2001) (announcing a guidance for industry on major, minor, and telephone amendments to ANDAs for immediate implementation "[b]ecause it lessens the burden on industry"); 74 Fed. Reg. 34025 (July 14, 2009) (announcing a guidance for institutional review boards on frequently asked questions about registration because "[p]rior public participation is not feasible and FDA believes the guidance is necessary to help IRBs better understand their responsibilities under the new rule."); 73 Fed. Reg. 77724 (December 19, 2008) (announcing a guidance for industry on diabetes mellitus and cardiovascular risk for immediate implementation "because of the need to immediately notify sponsors with ongoing development programs of the need to address cardiovascular risk in ongoing drug development programs."); 68 Fed. Reg. 33164 (June 3, 2003) (announcing a guidance for industry on labeling enforcement policy for particular drug products with no explanation why it was being implemented without public comment).

[105] *See, e.g.,* 78 Fed. Reg. 55261 (September 10, 2013) (revising the Generic Drug User Fee Amendments questions and answers guidance to address user fees; self-identification; generic drug submission reviews; and inspections/compliance); 77 Fed. Reg. 12311 (February 29, 2012) (issuing the final guidance on bead size in drugs labeled for sprinkle, before which "[a] number of comments were received from the public, all of which the Agency considered carefully as it finalized the guidance and made appropriate changes"); 77 Fed. Reg. 9946 (February 21, 2012) (revising the draft guidance on drug interaction studies after receiving and considering comments during the revision process); 77 Fed. Reg. 48989 (August 15, 2012) (revising the draft guidance regarding suicidal ideation and behavior in clinical trialsafter receiving and considering comments on the draft guidance).

important than others for which FDA issued guidance for immediate implementation without public comment.[106]

For these reasons, if FDA concludes that Level 1 draft guidance was the correct course of action (although we disagree for all of the reasons stated herein), then the guidance should have been implemented immediately without prior public comment and should have been applied immediately to Ferring's Prepopik.

E. Conclusion

For all of the reasons set forth herein, the undersigned respectfully request that the Commissioner review and reverse FDA's February 21, 2014 determination that Ferring's Prepopik is not eligible for five-year NCE exclusivity. FDA made this decision despite the Agency's recognition that drug products meeting the definition of a NCE, including Prepopik, are eligible for (if not entitled to) five-year exclusivity regardless of whether the drug was first approved in a single-entity drug product or in a fixed-combination with another drug substance that does not meet the definition of a NCE. We also request, should FDA finalize the 2014 NCE Exclusivity Draft Guidance prior to issuing a response to this Petition, that FDA stay the application of its new interpretation in that guidance document until FDA resolves the matters in this Petition.

Despite reaching a conclusion about the applicability of five-year NCE exclusivity to fixed-combination drug products such as Prepopik, the Agency has failed to apply its decision to Prepopik. Furthermore, FDA's decision to issue draft guidance leaves it unclear when – if ever- FDA's new statutory interpretation regarding exclusivity for these types of products will become effective, and to whom it will apply. As a result, the Agency's actions here are unreasonable, arbitrary and capricious, and deny Ferring the due process protections that are afforded to it under the law. FDA's actions deny Ferring the five-year exclusivity property right to which it is

[106] For example, the guidance on major, minor, and telephone amendments to ANDAs; the guidance on 180-day exclusivity; and the guidance on frequently asked questions about IRB registration.

entitled. As it stands, Ferring risks irreparable harm if FDA's actions result in the premature loss of valuable market exclusivity through the approval of a generic version of Prepopik.

This Petition meets all of the regulatory requirements for petitions for reconsideration and petitions for stay of action. It demonstrates that the information and views in the administrative record here were not adequately considered; Ferring's position is not frivolous and is being pursued in good faith; there are sound public policy grounds that support the reconsideration; reconsideration is not outweighed by public health or other public interests; and Ferring will suffer irreparable harm if the stay is not granted. Therefore, for all of the reasons cited herein, we respectfully request that FDA grant this Petition for Reconsideration/Petition for Stay of Action.

F. Certification

While Ferring does not believe that a certification under FFDCA § 505(q) is required for this petition under 21 C.F.R. §§ 10.33 and 10.35, the Company is including the certification in the event that the Agency disagrees.

I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: February 21, 2014. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: Ferring Pharmaceuticals, Inc. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.

Edward John Allera
(202) 452-7985
edward.allera@bipc.com
Buchanan Ingersoll & Rooney PC
1700 K Street NW, Suite 300
Washington, DC 20006

Theodore M. Sullivan
(202) 452-7992
theodore.sullivan@bipc.com
Buchanan Ingersoll & Rooney PC
1700 K Street NW, Suite 300
Washington, DC 20006

Barbara A. Binzak Blumenfeld
(202) 452-7906
barbara.binzak@bipc.com
Buchanan Ingersoll & Rooney PC
1700 K Street NW, Suite 300
Washington, DC 20006

Tina Hu-Rodgers
(202) 452-7308
tina.hu@bipc.com
Buchanan Ingersoll & Rooney PC
1700 K Street NW, Suite 300
Washington, DC 20006

cc (via hand delivery):

FDA Division of Dockets Management

cc (via UPS):

Elizabeth Dickinson, J.D.
Chief Counsel, FDA

Janet Woodcock, M.D.
Director, Center for Drug Evaluation and Research

cc (via www.regulations.gov):

Docket FDA-2013-P-0119

Docket FDA-2013-P-0058

Docket FDA-2013-P-0471

Attachments (as stated)

Buchanan Ingersoll & Rooney PC
Attorneys & Government Relations Professionals

Edward John Allera
202 452 7985
edward.allera@bipc.com

1700 K Street, N.W., Suite 300
Washington, DC 20006-3807
T 202 452 7900
F 202 452 7989
www.buchananingersoll.com

Ferring Pharmaceuticals, Inc.
Petition for Reconsideration and Petition for Stay of Action
of FDA's Determination Regarding Prepopik®

Attachments

1. Letter from Janet Woodcock to David M. Fox, Theodore M. Sullivan, Edward John Allera, and Joy J. Liu (February 21, 2014).

2. Ferring Citizen Petition (January 29, 2013).

3. Gilead Citizen Petition (January 8, 2013).

4. Bayer Citizen Petition (April 19, 2013).