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Room 1061 (HFA-305)
5630 Fishers Lane
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REFERENCE: Docket No. 2007N-0382

Dear Mr. Buehler:

Barr Laboratories, Inc. submits these comments in Docket No. 2007N-0382, which relates to the 180-day generic exclusivity period provided for in 21 U.S.C. § 355(j)(5)(B)(iv).

I. Introduction

Congress already has considered and enacted legislation that addresses the precise issue of what happens when the first paragraph IV filer and the brand company reach an agreement. Using plain language, Congress concluded that only those agreements found, in a final and unappealable court order, to violate the federal antitrust laws result in the forfeiture of generic exclusivity. As Barr understands it, no such finding has been made with respect to the agreement involving Cobalt and ramipril. For this reason, and the other reasons Barr discusses in this letter, FDA cannot lawfully take away Cobalt's statutory right to 180 days of generic marketing exclusivity.

II. Statutory and Regulatory Background

Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act (FFDCA), an NDA applicant must submit information for each patent that claims the drug or method of using the drug that is the subject of the NDA and for which "a claim of patent infringement could reasonably be asserted if a person not licensed by the patent owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1); *see also id.* § 355(c)(2). FDA publishes patent information submitted by an NDA-holder in the *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the "Orange Book").

An ANDA must include a "certification" to any properly listed Orange Book patent. Specifically, using clear language, Congress provided four certification options:

2007N-0382 C 4

> (vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section--
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> (I) that such patent information has not been filed [a so-called "paragraph I certification"],
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> (II) that such patent has expired [a so-called "paragraph II certification"],
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> (III) of the date on which such patent will expire [a so-called "paragraph III certification"], or
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> (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted [a so-called "paragraph IV certification"]; . . . .

21 U.S.C. § 355(j)(2)(A)(vii).[1] FDA's regulations mirror this unambiguous statutory language. *See* 21 C.F.R. § 314.94(a)(12)(i)(A). Thus, when the NDA holder has submitted patent information, an ANDA applicant has three certification options: a paragraph II, III, or IV certification. An ANDA applicant seeking FDA approval prior to patent expiration has one, and only one, option: file a paragraph IV certification. The statute does not provide any other option. Neither do FDA's regulations.

Submitting a paragraph IV certification has two significant consequences. First, it constitutes a statutory act of patent infringement sufficient to vest the courts with subject matter jurisdiction over an infringement suit prior to product launch. *See* 35 U.S.C. § 271(e). When an ANDA applicant submits a paragraph IV certification, it must notify the patentee and NDA-holder of the factual and legal bases for that certification. *See* 21 U.S.C. § 355(j)(2)(B). If the brand company brings suit within 45 days of receiving the notice letter, FDA cannot approve the ANDA for 30 months, absent a court order otherwise. *See id.* § 355(j)(5)(B)(iii).

Second, the first company to submit an ANDA containing a paragraph IV certification to a listed patent obtains 180 days of generic marketing exclusivity. *See* 21 U.S.C. § 355(j)(5)(B)(iv). Congress created the 180-day generic marketing exclusivity period by

[1] Hatch-Waxman provides only one circumstance in which an ANDA applicant need not certify to a listed patent: "if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection," the applicant can submit "a statement that the method of use patent does not claim such a use." 21 U.S.C. § 355(j)(2)(A)(viii); *see also* 21 C.F.R. § 314.94(a)(12)(iv). FDA's regulations provide one other instance in which an ANDA applicant can avoid certifying to a listed patent. Specifically, an ANDA applicant with an application on file need not certify to any patent submitted for listing more than 30 days after issuance. *See* 21 C.F.R. § 314.94(a)(12)(vi).

preventing FDA from approving competing generic products until 180 days after the earlier of two so-called "triggering" events:

> (iv) If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing [*sic*] such a certification, the application shall be made effective not earlier than one hundred and eighty days after—
>
> > (I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or
> >
> > (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed,
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> whichever is earlier.

Id.[2] Thus, the start of the 180-day exclusivity can be triggered by either of two and only two events: (1) the first paragraph IV applicant's commercial marketing ("the commercial marketing trigger") or (2) a final, unappealable court decision that the patent is invalid or not infringed ("the court decision trigger"), whichever is earlier. *Id.* FDA has concluded that a stipulation entered into by the parties, even if signed by a court and containing an express agreement by the parties regarding non-infringement, is not a "decision of a court." (*See* FDA 11/3/06 Letter regarding Ondansetron Exclusivity at 14 (submitted in Case No. 06-1890 (D.D.C.))). The Agency also does not recognize a dismissal for lack of subject matter jurisdiction as a "decision of a court," even when the dismissal precludes the patentee from bringing a later infringement action. *See Apotex Inc. v. FDA*, 449 F.3d 1249 (D.C. Cir. 2006), *aff'g*, No. 06-627, 2006 WL 1030151 (D.D.C. Apr. 19, 2006).

Significantly, in 2003 Congress enacted a statutory provision under which generic exclusivity is not just triggered, but entirely forfeited. While many provisions of the 2003 MMA apply only to ANDAs filed after its enactment, Congress made this forfeiture event applicable to ***all ANDAs*** – including Cobalt's first-filed paragraph IV ANDA for ramipril. *See* MMA § 1102(b)(2); *see also Guidance for Industry: Listed Drugs, 30-Month Stays, and Approval of ANDAs and 505(b)(2) Applications Under Hatch-Waxman, as Amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003* at 11 & n.32 (Oct. 2004) (recognizing that "[w]ith two exceptions, the new provisions relating to 180-day exclusivity

[2] Because Cobalt apparently submitted its paragraph IV ANDA before December 8, 2003, the quoted language governs with respect to exclusivity for generic ramipril ANDAs. *See* Medicare Prescription Drug, Improvement, and Modernization Act of 2003 § 1102(b)(1), Pub. L. No. 108-173, 117 Stat. 2066 (2003) (codified as amended at 21 U.S.C. § 355 and 35 U.S.C. § 271) ("the MMA").

govern only ANDAs filed after the date of the MMA's enactment (December 8, 2003) that reference a listed drug for which no paragraph IV certification was made in any ANDA before that date. . . . [T]he exception relating to forfeiture based on a first ANDA applicant's entry into an anti-competitive agreement applies if conditions specified in the MMA are met, regardless of when the first ANDA paragraph IV certification for the listed drug was made (see MMA Title XI section 1102(b)(2)).").

More specifically, Congress revisited the 1984 Hatch-Waxman Amendments in 2003. One issue that Congress expressly considered is what, if anything, should happen to the generic exclusivity period when the first company to file a paragraph IV ANDA (the first-applicant) enters into a settlement agreement with the owner of the patents listed in the Orange Book. After fully and carefully considering this issue, Congress enacted a forfeiture provision – *i.e.*, a provision under which the first-applicant would lose its exclusivity entirely. Congress obviously could have enacted legislation under which generic exclusivity is immediately forfeit any time the first-applicant enters into any type of agreement with the brand company. But, as FDA knows, Congress did not do so. Instead, Congress enacted a forfeiture provision under which the law strips the first-applicant of its exclusivity *if, but only if,* there is a final, unappealable order finding that the agreement violates the antitrust laws:

> (i) DEFINITION OF FORFEITURE EVENT.—In this subparagraph, the term "forfeiture event", with respect to an application under this subsection, means the occurrence of any of the following:
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> * * *
>
> (V) AGREEMENT WITH ANOTHER APPLICANT, THE LISTED DRUG APPLICATION HOLDER, OR A PATENT OWNER- The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the Federal Trade Commission or the court with regard to the complaint from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 12 of Title 15, except that the term includes section 45 of Title 15 to the extent that that section applies to unfair methods of competition).

21 U.S.C. § 355(j)(5)(D)(i)(V) (sometimes is referred to as the "collusive agreement" forfeiture event).[3] Thus, Congress has expressly considered and spoken to the precise issue of what

[3] The MMA enumerates six forfeiture events. *See id.* § 355(j)(5)(D)(i) (providing that a forfeiture event "means" one of the six enumerated events). All of the other five enumerated forfeiture events apply solely to ANDAs for which the first paragraph IV certification was filed after December 8, 2003. *See* MMA § 1102(b)(1) (providing that all forfeiture events, except the collusive agreements forfeiture provision, "shall be effective only with respect to an application filed under [21 U.S.C. 355(j)] after the date of the enactment of this Act for a listed drug for which no certification under section 505(j)(2)(A)(vii)(IV) of that Act was made before the date of the enactment of this Act.").

happens to 180-day generic exclusivity when the first-applicant and brand company enter into an agreement.

III. Discussion

A. Congress Has Enacted Legislation Expressly Addressing When An Agreement Results In The Forfeiture Of Generic Exclusivity And Under That Statutory Provision, No Forfeiture Occurs In This Case.

The submission made by Hyman, Phelps & McNamara, P.C. ("the HPM Submission") argues that "[n]either the FDC Act or FDA's ANDA regulations address" what happens to generic exclusivity when the first-applicant and NDA holder reach an agreement terminating their patent litigation. (HPM Submission at 5). This is incorrect. Using clear and unambiguous language, Congress directly addressed this issue. As discussed above, Congress, in the MMA, expressly provided that the first-applicant forfeits its exclusivity if, and only if, there is a final, unappealable order finding that the terms of an agreement with the NDA holder violate the federal antitrust laws. *See* 21 U.S.C. § 355(j)(5)(D)(i)(V). Congress did not provide for such a forfeiture as the result of any other type of agreement. Extending the collusive agreement forfeiture provision to agreements that have not been found by a court to violate the antitrust laws would require the Agency to disregard the plain language and intent of Congress. But FDA cannot lawfully do so because where, as here, "the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 842-43 (1984); *see also Nat'l Treasury Employees Union v. FLRA*, 392 F.3d 498, 500-01 (D.C. Cir. 2004) (reversing agency's statutory interpretation under *Chevron* step one because it conflicted with congressional intent and purpose); *First Nat'l Bank & Trust Co. v. Nat'l Credit Union Admin.*, 90 F.3d 525, 530 (D.C. Cir. 1996) (same); *Bedroc Ltd., LLC v. U.S.*, 541 U.S. 176, 183 (2004) ("[O]ur inquiry begins with the statutory text, and ends there as well if the text is unambiguous." (citations omitted)); *Hughes Aircraft Co. v. Jacobson*, 525 U.S. 432, 438 (1999) ("As in any case of statutory construction, our analysis begins with the language of the statute. And where the statutory language provides a clear answer, it ends there as well." (quotations and citations omitted)).

In this case, no court has entered a final, unappealable order finding the Cobalt/ramipril agreement to violate the antitrust laws. Consequently, FDA has no legal basis or right to conclude that Cobalt has forfeit its statutory right to exclusivity as a result of its agreement. For FDA to so conclude, the Agency would have to invent statutory language found no where in the FFDCA, and the D.C. Circuit already has made clear that the Agency cannot lawfully do such a thing. *See Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1069 (D.C. Cir. 1998).

In *Mova*, the Agency sought to defend its so-called "successful-defense" requirement, under which the first-applicant would lose generic marketing exclusivity if it did not successfully defend a lawsuit brought as a result of that applicant's paragraph IV certification. *Mova*, 140 F.3d at 1065. The D.C. Circuit struck down this requirement under the first prong of *Chevron*:

> We conclude that the FDA's successful-defense requirement is inconsistent with the unambiguously expressed intent of Congress. The rule is gravely inconsistent

> with the text and structure of the statute. Nor can the FDA show that the successful-defense requirement is needed to avoid a result demonstrably at odds with the intentions of [section 355(j)(5)(B)(iv)'s] drafters.

Mova, 140 F.3d at 1069 (quotation marks and citations omitted) (alteration in original). In so doing, the court explained that "the literal language of the statute" prevents FDA from approving subsequent paragraph IV filers "'not earlier than one hundred and eighty days after' the commercial-marketing trigger or the court-decision trigger is satisfied." *Id.* (quoting § 355(j)(5)(B)(iv)). The Agency's successful-defense requirement, however, permitted "later applications to be approved even though neither trigger has been satisfied, simply because the first applicant's litigation has not yet come to a successful conclusion." *Id.* That requirement is unlawful under *Chevron* step one. *Id.* at 1069; *see also Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120, 125 (D.C. Cir. 2006) (noting that *Mova* "rejected at *Chevron* step one the FDA's attempt to add to the statutory requirements for exclusivity by making it contingent upon success in litigation").

Here, as in *Mova*, the start of Cobalt's exclusivity can be triggered only by commercial marketing or a "decision of a court." At present, neither of these events apparently has taken place. And Cobalt forfeits its exclusivity only if a court determines that the Cobalt/ramipril agreement violates federal antitrust laws. Without question, the Cobalt/ramipril agreement does not fall within the category of prohibited agreements. And because Congress has spoken in § 355(j)(5)(D)(i)(V) directly to the question of when an agreement results in the loss of exclusivity, FDA has no authority to create another forfeiture or exclusivity-triggering type provision. The issue presented here is, in fact, even more clear cut than the one addressed in *Mova*. Specifically, the MMA expressly states that "the term 'forfeiture event', with respect to an [ANDA] application under this subsection, *means* the occurrence of any of the" six enumerated forfeiture events. *See* 21 U.S.C. § 355(j)(5)(D)(i) (emphasis added). In *Schering Corp. v. Sullivan*, 782 F. Supp. 645, 649 (D.D.C. 1992), *vacated as moot*, 995 F.2d 1103 (D.C. Cir. 1993), the court found the term "means" to be a "limiting term" in another part of § 355:

> The absence of language indicating that Section 355(j)(7)(B) provides the exclusive means for determining bioequivalence becomes significant when the two subsections of Section 355(j)(7) are read together. Subsection (j)(7)(A) provides that bioavailability "*means* the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug or becomes available at the site of drug action" (emphasis added). Such language clearly indicates that "bioavailability" means what the statute says and no more. An inveterate rule of statutory construction is that if one section of a statute contains a limiting term and a related section does not, the omission can be presumed intentional.

782 F. Supp. at 649 (citation omitted); *see also id.* (noting that "comparable limiting language [*i.e.*, "means"] is found throughout Section 355").

In this case, Congress expressly stated that a forfeiture event "means" only one of the six events enumerated in the statute. Thus, the statute "means what the statute says and no more." FDA cannot lawfully expand this provision to include a forfeiture event that Congress has not enumerated. The Agency, therefore, cannot find that an agreement falling outside the plain language of § 355(j)(5)(D)(i)(V) constitutes a forfeiture event.

In sum, FDA cannot compel an ANDA applicant in Cobalt's position to withdraw or amend its current paragraph IV certification, and the Agency has no authority to deem that certification to have been withdrawn or amended or to do anything else that would result in the forfeiture of the statutory right to generic exclusivity. Any other result would constitute arbitrary and capricious and unlawful agency action. *See Ranbaxy*, 469 F.3d at 124-26 (striking down FDA's policy of delisting patents to which an ANDA applicant has submitted a paragraph IV certification unless the brand company has initiated patent litigation because it was inconsistent with the plain language of 21 U.S.C. § 355(j)(5)(B)(iv)); *Mova*, 140 F.3d at 1069.

B. FDA Cannot Lawfully Require Cobalt To Withdraw Or Amend Its Existing Paragraph IV Certification, Or Deem That Certification To Have Been Withdrawn Or Amended.

1. Under The Governing Statutory Provisions, Cobalt's Paragraph IV Certification Is Accurate And Proper.

The HPM Submission asserts that because Cobalt purportedly is no longer challenging the Orange Book patent, Cobalt's paragraph IV certification is inaccurate and improper. This is incorrect. Hatch-Waxman requires an ANDA applicant to address each properly-listed Orange Book patent. *See* 21 U.S.C. § 355(j)(2)(A)(vii). That statute unambiguously specifies the type of certification an ANDA applicant must make when it seeks FDA approval prior to the expiration of a patent that has been submitted under § 355(b) or (c); namely, such an application must contain a paragraph IV certification stating that the listed patent "will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted." *Id.* § 355(j)(2)(A)(IV). This clear statutory provision binds FDA and all generic applicants. *See Chevron*, 467 U.S. at 842-43.

In this case, the NDA holder has submitted patent information, making a paragraph I certification to these patents improper. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(I). The patent has not expired, making a paragraph II certification improper. *See id.* § 355(j)(2)(A)(vii)(II). Cobalt sought FDA approval prior to patent expiration, making a paragraph III certification improper. *See id.* § 355(j)(2)(A)(vii)(III). Because Cobalt sought FDA approval prior to patent expiration – and in fact received approval prior to patent expiration – a paragraph IV certification is the only proper patent certification to the listed patent. *See id.* § 355(j)(2)(A)(vii)(IV); *see also* 21 C.F.R. § 314.94(a)(12)(i)(A) (requiring a paragraph IV certification where the ANDA applicant seeks FDA approval prior to patent expiration).

Therefore, Cobalt's continued paragraph IV certification to the listed patent not only is accurate, but required by the controlling statute, as noted above. Consequently, any attempt to deem Cobalt's paragraph IV certification to have been withdrawn or amended would be arbitrary, capricious, and contrary to law.

2. FDA's Regulations Do Not Provide Any Basis For Withdrawal Or Amendment Of Cobalt's Existing Paragraph IV Certifications.

Section 314.94(a)(12)(viii) provides three circumstances under which a patent certification should be amended. Even if this regulation is presumed to be permissible and thus lawful, none of these circumstances exist here.

Subclause (A) addresses amendments when "a final judgment in the [infringement] action against the applicant is entered finding the patent to be infringed":

> After finding of infringement. An applicant who has submitted a certification under paragraph (a)(12)(i)(A)(4) of this section and is sued for patent infringement within 45 days of the receipt of notice sent under § 314.95 shall amend the certification ***if a final judgment in the action against the applicant is entered finding the patent to be infringed***.

21 C.F.R. § 314.94(a)(12)(viii)(A) (emphasis added). Again, even if permissible, this regulation is irrelevant here because no "final judgment" has been entered against Cobalt finding the patent valid and infringed. As an initial matter, it does not appear as though Cobalt conceded infringement of the '722 patent in the way the HPM Submission suggest. Rather, from the stipulation, it appears that Cobalt admitted infringement if the '722 patent is valid and enforceable. (HPM Submission at Ex. 1). The '722 patent, according to the Federal Circuit, is invalid and thus no one – including Cobalt – can infringe its claims. More importantly, however, the stipulation about which the HPM Submission makes so much is not a "final judgment," as required by the regulation. Indeed, no final judgment was ever entered in the Cobalt ramipril litigation. Instead, as the HPM Submission concedes, that litigation was dismissed *without prejudice*. (HPM Submission at Ex. 3). And, of course, FDA already has determined that a stipulation entered into by the parties, even if signed by a court, is not a "decision of a court." (*See* FDA 11/3/06 Letter regarding Ondansetron Exclusivity at 14). Such a stipulation most assuredly, therefore, cannot be a "final judgment." Thus, nothing in § 314.94(a)(12)(viii)(A) allows, let along requires, Cobalt to amend from a paragraph IV to a paragraph III certification.

Under subclause (B), "[i]f a patent is removed from the list, any applicant with a pending application . . . who has made a certification with respect to such patent shall amend its certification." 21 C.F.R. § 314.94(a)(12)(viii)(B). The '722 patent remains listed in the Orange Book, rendering this provision inapplicable.

Under subclause (C), "an applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted

certification is no longer accurate." 21 C.F.R. § 314.94(a)(12)(viii)(C)(1). Cobalt's paragraph IV certification was accurate when submitted and remains accurate today for the simple and uncontested reason that Cobalt sought (and obtained) FDA approval prior to patent expiration. Consequently, this regulation has no relevance here and certainly does not require Cobalt to withdraw or amend its paragraph IV certifications.

Thus, nothing in § 314.94(a)(12)(viii) requires Cobalt to withdraw and/or amend its existing paragraph IV certification.

3. There Is No Case Law Support For The Proposition That FDA Can Lawfully Deem Cobalt's Paragraph IV Certification To Have Been Amended Or Withdrawn.

The HPM Submission asks FDA to ignore the court's decision in *Mylan Pharms. v. Thompson*, 207 F. Supp. 2d 476 (N.D. W.Va. 2001), and find that Cobalt no longer is entitled to exclusivity. (HPM Submission at 7-10). FDA cannot lawfully do so.

In *Mylan*, the first-applicant, Mylan, resolved its patent litigation by a settlement under which Mylan immediately launched a product manufactured by the brand company, rather than a product made under its ANDA. *Id.* at 481. Mylan did not amend its paragraph IV certification to a paragraph III. *Id.* Teva, a subsequent paragraph IV filer, submitted a citizen petition asking FDA to rule, among other things, that Mylan had effectively amended its patent certification to a paragraph III and thus had no right to exclusivity. *Id.* at 482. FDA granted Teva's petition. *Id.* The Agency found a "gap" in the statute as to the effect of Mylan's settlement. In filling that perceived gap, FDA determined that Mylan's decision to settle and market a branded product, rather than an ANDA product, to be evidence that Mylan no longer sought to market an ANDA product prior to patent expiration. *Id.* The Agency also "presume[d]" that because Mylan had had final approval for over a year but had not marketed its ANDA product, Mylan must believe that its ANDA product infringed the relevant patent and thus Mylan no longer contested validity, enforceability, or infringement. *Id.* at 486-87. From all this, FDA concluded that Mylan had effectively changed its paragraph IV certification to a paragraph III. *Id.* Mylan challenged FDA's ruling.

Upon careful examination of the relevant statute, the district court found the Agency's ruling to be arbitrary and capricious under *Chevron* step one. *Mylan*, 207 F. Supp. 2d at 487-88. Specifically, the court found that "there is no explicit gap in the statute on the subject of the change of a 'IV certification' to a 'III certification,' particularly when one considers the somewhat severe results such a change by agency ruling can have." *Id.* at 487. The court stated:

> [The] Court finds after a careful analysis of the FDA ruling of February 6, 2001 and the relevant statute, that the FDA's interpretation is an unreasonable one. First, there is no statutory provision which grants to the FDA, either expressly or implicitly, the authority to change a "IV certification" to a "III certification." Second, there is no FDA regulation that provides any basis for such a change.

> Third, the FDA ruling is based upon a presumption that is inadequately reached in this particular case. Finally, the sole precedent that the FDA relies upon, *Mylan v. Henney*, 94 F. Supp. 2d 36 (D.D.C. 2000), is clearly distinguishable because in that case Barr Laboratories, an ANDA applicant with a "IV certification" by its own actions changed its "IV certification" to a "III certification" as part of its settlement with the NDA holder. In this case, Mylan has not effected a change to its certification and there is no evidence that its settlement agreement with Pfizer requires it to make such a certification change. The FDA ruling, at least on this subject, is therefore unreasonable, even if it possesses a right to make a ruling on this subject on a "case-by-case" basis.

Id. at 487-88. While, as the HPM Submission notes, this decision subsequently was vacated for reasons unrelated to its merits, the conclusion remains inescapable. Nothing in the FFDCA gives FDA the authority to deem Cobalt to have amended its paragraph IV to a paragraph III. Indeed, the FFDCA precludes such action. For FDA to conclude otherwise would be arbitrary, capricious and contrary to law.

Finally, the HPM Submission cites three other cases that it argues are relevant here and support its request to strip Cobalt of its exclusivity. (HPM Submission at 10). Those cases have no relevance:

In two of the cases cited in the HPM Submission, the courts upheld FDA's decision to amend, or require an applicant to amend, paragraph IV certifications to paragraph II certifications where the listed patents had expired prior to the final approval of the ANDAs at issue. *Ranbaxy Labs. Ltd. v. FDA*, 307 F. Supp. 2d 15, 21 (D.D.C.), *aff'd*, 96 Fed. Appx. 1 (D.C. Cir. 2004); *Dr. Reddy's Labs. v. Thompson*, 302 F. Supp. 2d 340, 351 (D.N.J. 2003). But the '722 patent has not expired. Consequently, these cases are wholly irrelevant to Cobalt's paragraph IV certification and the challenge that the HPM Submission raises.

The third case that the HPM Submission cites, *Mylan Labs. v. Thompson*, 389 F.3d 1272 (D.C. Cir. 2004), also is irrelevant. In that case, Mylan filed a paragraph IV certification, but the brand company failed to bring suit within 45 days and thus the belated infringement action did not trigger a 30-month statutory stay. *See* 389 F.3d at 1277. Mylan obtained final approval, but later lost its patent infringement case. *See id.* Consequently, "Mylan's ANDA was subject to two conflicting approval effective dates: the date of the FDA's approval decision (November 21, 2003) and, pursuant to the Vermont district court's order, a date 'no earlier than the date of expiration of the '580 patent family' (i.e., July 23, 2004)." *Id.* at 1280. At the administrative level, FDA determined that the "district court's order that 'the effective date of any approval of Mylan's ANDA product shall be no earlier than the date of expiration of the '580 patent family,' transformed Mylan's ANDA approval into 'an approval with a delayed effective date,' which 'is a tentative approval that cannot be made effective until FDA issues a letter granting final effective approval.'" *Id.* at 1277 (quoting FDA's letter ruling (internal citation omitted)). In light of the patent court's order, the Agency revoked Mylan's final approval and issued a tentative approval. As the D.C. Circuit's opinion makes clear, FDA did not require Mylan to

amend its certification from a paragraph IV to a paragraph III certification (or deem it to have been so amended), but rather simply changed the status of Mylan's approval from final to tentative:

> The FDA might well have concluded that in this situation too, as ALZA suggested in the administrative proceeding, *see* Letter 1 at 11, the paragraph IV certification should have changed to a paragraph III certification immediately upon the district court's finding of validity/infringement, consistent with the directive of 21 C.F.R. § 314.94(a)(12)(viii)(C)(1)(i) that "an applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate."

Id. at 1283 n.10. Citing *Ranbaxy Labs. Ltd. v. FDA*, 307 F. Supp. 2d 15 (D.D.C. 2004), FDA further determined that upon patent expiration, Mylan's paragraph IV certification would convert to a paragraph II. *Mylan Labs.*, 389 F.3d at 1278. As a result, Mylan's final approval would be delayed by the brand company's right to pediatric exclusivity. *Id.* Thus, *Mylan Labs.* in no way supports HPM's claim that somehow FDA can or should require Cobalt to amend its paragraph IV certification, or that the Agency can somehow deem Cobalt to have made such an amendment.[4]

Thus, there is no statutory, regulatory, or case law support for a request that the Agency extinguish Cobalt's right to generic exclusivity under § 355(j)(5)(B)(iv).

C. Maintaining Cobalt's Exclusivity Is Required By The Statutory Scheme, And Is Fully Consistent With Congressional Intent. Any Other Result Would, In Fact, Have A Chilling Effect On Future Patent Challenges, Thereby Harming Consumers.

Before 1984, a company seeking to market a generic version of a previously-approved drug had to repeat the same safety and efficacy studies that the brand company already had completed. *See SmithKline Beecham Corp. v. Apotex Corp.*, 247 F. Supp. 2d 1011, 1018 (N.D. Ill. 2003). And any company seeking to develop a generic product had to wait for patent protection on the branded product to expire before even starting the lengthy approval process because carrying out the required studies constituted patent infringement. *See Roche Prods. v. Bolar Pharm.*, 733 F.2d 858, 861-63 (Fed. Cir. 1984). This unintended period of extended market exclusivity for branded products has been referred to as a "*de facto* patent term extension." *See generally* Susan Kopp Keyack, *The Drug Price Competition and Patent Term Restoration Act of 1984: Is It a Healthy Long Term Solution?*, 21 RUTGERS L.J. 147, 153-54, 160-61, 165 (1989); Jonathan L. Mezrich, *The Patentability and Patent Term Extension of*

[4] The *Mylan Labs.* case also is irrelevant because no final judgment of infringement has been entered against Cobalt on an Orange Book-listed patent, and no order has been entered prohibiting FDA from approving Cobalt's ANDA until expiration of an Orange Book patent. Indeed, Cobalt has final ANDA approval.

Lifesaving Drugs: A Deadly Mistake, 6 J.L. & HEALTH 111, 115-16 (1991/1992). Because generic drugs are sold for a fraction of their branded counterparts and because revenues would be long delayed, few companies undertook the significant expenses of the duplicate studies needed for approval.

The high regulatory barriers to market approval and the *de facto* patent term extension combined to delay generic market entry until well after patent expiration. As a result, consumers and taxpayers paid unnecessarily high pharmaceutical prices years longer than could reasonably be justified.

Congress knew that increased competition would lower drug prices, and that competition would increase more quickly if companies sought to market generic products prior to the expiration of the patents protecting brand products from competition. Congress also recognized, however, that mounting the first patent challenge is a very expensive and risky proposition. Thus, a critical part of the carefully-crafted balance struck in the 1984 Hatch-Waxman Amendments is the 180-day generic exclusivity period, which Congress specifically created to encourage generic drug manufacturers to expend the significant resources necessary to initiate the first patent challenge. *See, e.g.*, 64 Fed. Reg. 42,873, 42,874 (Aug. 6, 1999); *Apotex v. Shalala*, 53 F. Supp. 2d 454, 461 (D.D.C. 1999) (recognizing that Congress enacted Hatch-Waxman in order to "make available more low cost generic drugs" to the public (quotation marks and citation omitted)); *In re Barr Labs.*, 930 F.2d 72, 76 (D.C. Cir. 1991) (noting that Congress enacted Hatch-Waxman with the goal of "get[ting] generic drugs into the hands of patients at reasonable prices–fast").

In this case, Cobalt accepted the *quid pro quo* that Congress created – *i.e.*, expend the resources to mount the first patent challenge in exchange for "the right to sell [the] drug without competition for 180 days." *Purepac Pharm. v. Thompson*, 354 F.3d 877, 878 (D.C. Cir. 2004). And recognizing Cobalt's right to generic exclusivity fully is consistent with Congressional intent. The 180-day generic exclusivity is "an incentive to the first generic maker to expose [itself] to the risk of costly patent litigation . . . ." *Mylan*, 94 F. Supp. 2d at 40. To obtain the benefit of generic exclusivity, Cobalt took the risks, and bore the burdens, of patent litigation long before others decided to follow Cobalt's lead.

Furthermore, declaring a forfeiture of Cobalt's statutory right to generic exclusivity on the basis of its agreement would, without question, have significant anti-consumer consequences. Specifically, a determination by FDA that all agreements that terminate litigation, no matter how pro-competitive, result in the automatic forfeiture of generic exclusivity would cause generic drug companies to invest in fewer patent challenges – the challenges that Congress sought to encourage with Hatch-Waxman.

A generic company's ability to bring a Hatch-Waxman challenge depends in significant measure upon its having the flexibility to decide whether, when, and on what terms, to resolve the ensuing patent litigation. If an agreement with the NDA holder necessarily results in the automatic and immediate loss of exclusivity, no matter how much competition is achieved,

generic companies will know that, in all likelihood, they will have to take a paragraph IV challenge all the way to final decision. The lack of a resolution option inevitably raises the risks and costs of initiating patent challenges, thereby reducing the number of patent challenges brought. Thus, the ability to resolve a patent challenge by an agreement that does not violate the antitrust laws necessarily has a pro-competitive effect because it increases the number of patent challenges by decreasing barriers to entry, *i.e.*, the risks and costs of bringing and maintaining a patent challenge. Similarly, taking away the ability to resolve litigation without forfeiting 180-day exclusivity would increase the barriers to bringing a patent challenge and fewer patent challenges means that consumers will wait longer, much longer, for access to less expensive generic products.

Finally, the position put forth in the HPM Submission also runs afoul of those legal authorities recognizing the "strong public interest in settlement of patent litigation . . . ." *Flex-Foot, Inc. v. CRP, Inc.*, 238 F.3d 1362, 1369 (Fed. Cir. 2001); *see also D.R. by M.R. v. East Brunswick Bd. of Educ.*, 109 F.3d 896, 901 (3d Cir. 1997) (discussing "the federal policy of encouraging settlement agreements," explaining that "[s]ettlement agreements are encouraged as a matter of public policy because they promote the amicable resolution of disputes and lighten the increasing load of litigation faced by courts" (citing *McDermott, Inc. v. AmClyde*, 511 U.S. 202, 213-15 (1994) ("Public policy wisely encourages settlements."))). Thus, it would be unsound (and unlawful) for the Agency to adopt a policy that discourages settlements of ANDA patent litigation. This is especially true given the clear and unambiguous statutory language under which the first-applicant forfeits its statutory right to 180-day exclusivity if, but only if, there is a final, unappealable order finding that the agreement violates the federal antitrust laws.

For these reasons, a policy of finding an agreement that does not violate the antitrust laws to result in a forfeiture of generic exclusivity not only violates the plain language of the statute and FDA's regulations, but runs afoul of Congressional intent and the public interest. There is no lawful way the Agency can take away Cobalt's statutory right to generic exclusivity.

IV. Conclusion

Barr appreciates the opportunity to provide these comments. If you have any questions concerning this submission, please contact me by phone at (201) 930-3650 or by fax at (201) 930-3318.

Sincerely,
BARR LABORATORIES, INC.

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