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February 25, 2005

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

Re: Docket Number 2005P-0520 (Citizen Petition) – Submission of
Comments by IVAX Pharmaceuticals

Dear Sir or Madam:

These comments are submitted on behalf of IVAX Pharmaceuticals, Inc., (IVAX) in response to comments filed by Eon Labs¹ (Eon Comments) regarding the Citizen Petition filed by IVAX on November 19, 2005² (IVAX Petition). IVAX's petition requests confirmation that IVAX is entitled to 180-day exclusivity with regard to ANDA No. 76-724 if IVAX is the first applicant to submit a paragraph IV certification and satisfy the statutory notice requirement for that certification.

Eon contends in its comments that IVAX's petition should be denied because (1) IVAX's position is contrary an agency interpretation of the statute that Congress presumed reasonable, (2) the MMA³ provisions regarding forfeiture of 180-day exclusivity do not support IVAX's position, and (3) Eon's proposed interpretation of the statute would not be unfair to IVAX. Eon is wrong on each point.

1. FDA Must Determine Eligibility for 180-day Exclusivity Based on the New Notice Provisions of the MMA.

Eon concedes that the new notice provisions of the MMA apply to the ANDAs at issue in this matter, but argues that those provisions are irrelevant to determining 180-day exclusivity.⁴ According to Eon, FDA's interpretation of the "first applicant" eligibility requirement for exclusivity under the pre-MMA statutory provisions (1) precludes the relief sought by IVAX and (2) was implicitly ratified by Congress in its passage of the MMA and that that interpretation.

Eon's argument misses the mark because IVAX does not challenge FDA's interpretation of the pre-MMA 180-day exclusivity provisions. FDA interprets those provisions to require a determination of exclusivity based on the date that the first applicant satisfies the statutory notice requirement. Under this interpretation, where the

¹ Docket No. 2005P-0520: C1 (Dec. 17, 2004).

² Docket No. 2005P-0520: P1 (Nov. 19, 2004).

³ Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (Dec. 8, 2003).

⁴ Eon Comments at 5.

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statutory notice requirement is expressed as a command that notice be provided by a date certain, the applicant is deemed to have submitted a substantially complete application only when the notice requirement is satisfied.⁵ IVAX proposes that the agency follow the same interpretation in determining 180-day exclusivity in the case of DuoNeb.

Eon attempts to dismiss the new MMA notice provisions as irrelevant by ignoring the critical role that the notice provisions play under the pre-MMA exclusivity provisions. The pre-MMA notice provisions directed the applicant to give notice by a date certain only with regard to a paragraph IV certification submitted in an ANDA amendment.⁶ In the case of a paragraph IV certification filed with an original ANDA, the pre-MMA provisions did not require that notice be provided by a date certain and, in fact, did not even include an express mandate that notice be given.⁷ The statutory notice requirement was satisfied in the case of an original ANDA by the filing of a statement that the applicant would give notice upon FDA receipt of the ANDA.

Under the MMA notice provisions, Congress eliminated the distinction between original ANDAs and ANDA amendments and in each case directed that the applicant give notice by a date certain.⁸ The agency's pre-MMA interpretation of the 180-day exclusivity provisions, when applied in the context of notice under the MMA notice provisions, requires that the date of actual notice determine eligibility in both instances. Thus, while the agency's interpretation does not change, the outcome changes depending on the nature of the applicable notice requirement.⁹

⁵ As noted in Ivax's petition, the agency's interpretation of 180-day exclusivity eligibility based on notice was based on the failure of ANDA applicants to satisfy the statutory requirement of notice by a date certain. The courts agreed with FDA's approach because (1) the statute provided a mandate that the notice be provided by a date certain, (2) the statute provided no express enforcement mechanism for the notice requirement, and (3) FDA fashioned a reasonable enforcement mechanism by determining eligibility for exclusivity based on the date of compliance with the notice requirement. *Purepac v. Thompson*, 354 F.3d 877 (D.C. Cir. 2004), *aff'g TorPharm, Inc. v. Thompson*, 260 F. Supp. 2d 69, 79-81 (D.D.C. 2003).

⁶ FDCA § 505(j)(2)(B)(ii) as in effect prior December 8, 2003 (emphasis added).

⁷ *Id.* § 505(j)(2)(B)(i) as in effect prior December 8, 2003 (emphasis added). Based on this provision, FDA's implementing regulation similarly requires that the original ANDA provide a statement that the applicant will provide notice and does not expressly direct that the notice be given. See 21 C.F.R. 314.94(a)(12)(i)(A)(iv). Eon notes IVAX's statement in prior litigation that, under this regulation, the ultimate giving of notice for an original ANDA filer is irrelevant for purposes of whether the original ANDA was complete with filed. Eon Comments at 4. This regulation is, of course, superseded where the new MMA notice provision applies. The regulation is thus not applicable here.

⁸ *Id.* § 505(j)(2)(B)(ii) (emphasis added).

⁹ IVAX's position is correct even if deemed to be based on a new "interpretation" of the statute. To the extent that IVAX's position can be characterized as a new "interpretation," the new interpretation is based on a change in the statutory provision that forms the basis for the prior "interpretation." There can be no clearer indication of congressional intent to negate an agency's interpretation than elimination of the statutory language upon which the interpretation was based. Although Eon cites *Williams Natural Gas Co. v. FERC*, 943 F.2d 1320, 1335 (D.C. Cir. 1991), for the proposition that Congress must be presumed to have known FDA's "interpretation" and could have "expressly changed it had it so desired," Eon Comments at 5, that case is inapposite. In *Williams* the agency's interpretation had been placed squarely before Congress and Congress had clearly left the relevant statutory provisions unchanged during the time

2. IVAX Does Not Contend that the MMA Provisions Regarding Forfeiture of 180-Day Exclusivity Apply Here.

Eon oddly crafts an argument based on the notion that IVAX relies on the applicability of the MMA exclusivity forfeiture provisions to this matter.¹⁰ IVAX's petition states the opposite:

Although the notice provisions of the MMA apply to the ANDAs filed by Eon and IVAX, the 180-day exclusivity provisions, including the definition of first applicant, do not apply. FDA must thus apply the MMA notice provisions in determining 180-day exclusivity under the pre-MMA exclusivity provisions.¹¹

The MMA provisions on 180-day exclusivity are relevant only insofar as they reflect Congress' view at the time of the passage of the MMA that first applicant status should be determined based on the date of actual notice rather than on the date of submission of the ANDA.¹²

3. Eon's Proposed Interpretation Would Be Unfair to IVAX and to Other Applicants Who Must Certify to Patents Listed During the Review of Their ANDAs.

IVAX notes in its petition that one of the key purposes of the MMA was to eliminate delays from 30-month stays that might result from serial listings of patents following the submission of an ANDA. Eon proposes an interpretation of the statute that would reimpose 30-month stays on ANDAs submitted prior to patent listings by favoring ANDAs submitted subsequent to patent listings in determining eligibility for 180-day exclusivity. Under Eon's approach, the later filed ANDAs would have an advantage over ANDAs already under review with regard to exclusivity because first applicant status for

in question. *Id.* Here Congress modified the statutory provision that that is relevant to determining IVAX's eligibility for exclusivity based on date of notice.

¹⁰ Eon Comments at 6.

¹¹ IVAX Petition at 4 (citation omitted).

¹² The MMA provides an express enforcement mechanism for the notice requirements by defining 180-day exclusivity as a delay that would apply to an ANDA "submitted by an applicant other than a first applicant," and by defining a "first applicant" as an applicant that "submits a substantially complete application that contains *and lawfully maintains* a [paragraph IV] certification" on the first day that any applicant submits such a certification. FDCA § 505(j)(5)(B)(iv)(II)(aa), (bb). Although Eon notes that it satisfied the MMA notice requirement, Eon Comments at 6, the question in determining first applicant status is not *whether* an applicant satisfies the notice requirement but *when* the applicant satisfies the requirement.

the pioneer ANDA applicants would be determined based on the date of submission of the certification rather than on the date of satisfaction of the notice requirement.¹³

This would mean that, where the later filed ANDA is subjected to a 30-month stay, the pioneer ANDA would be delayed by the exclusivity period plus the period of the 30-month stay. In the matter at issue, Eon's proposed interpretation would not only award Eon 180-day exclusivity but would also block approval of IVAX's ANDA during the 30-month stay that applies to Eon. This outcome would be directly contrary to Congress' clear intent to protect pending ANDAs from delays in approval based on serial patent listings following submission of an ANDA. It would also impose an unwarranted delay on the introduction of generic competition, which would be contrary to the public interest.

Eon argues that this outcome, even if "unfair," is a direct consequence of the plain language of the statute and that there is no room for a different interpretation. Eon fails to identify the "plain language" of the statute to which it refers. Eligibility for 180-day exclusivity in this matter is not based on the plain language of the pre-MMA 180-day exclusivity provisions, which provide no mention of notice, but rather on the agency's interpretation of the statutory notice provisions and their relationship to the requirement that the applicant submit a substantially complete application.¹⁴ The plain language of the statute that is relevant here is the plain language of the MMA notice provisions.

Respectfully submitted,



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¹³ Moreover, the applicant submitting the new ANDA would be deemed a first applicant even if it later failed to comply with the statutory requirement that notice be provided within 20 days of FDA's acknowledgment of receipt of the ANDA.

¹⁴ Eon also suggests that IVAX had an opportunity to avoid an unfair result by submitting its paragraph IV certification and providing notice prior to the date that Eon submitted its ANDA. Eon obfuscates the critical issue. Eon's proposed outcome is unfair because Congress exempted IVAX from being subjected to a 30-month stay late in the review cycle of its product and clearly did not intend to reintroduce such a stay by placing IVAX in a horse race with new ANDA applicants to file paragraph IV certifications for serially listed patents. It is more reasonable to infer that Congress intended to protect ANDAs undergoing review from back-door 30-month stays brought about by awarding 180-day exclusivity to subsequently submitted ANDAs.

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Dear Sir or Madam:

Please accept the attached comments (in four copies) submitted on behalf of
IVAX Pharmaceuticals, Inc., pursuant to 21 C.F.R. § 10.35.

Sincerely,



David G. Adams