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Division of Dockets Management  
Food and Drug Administration  
5630 Fishers Lane  
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Rockville, Maryland 20857

**Re: Response to Citizen Petitions by Ivax Pharmaceuticals, Inc. and  
Ranbaxy Laboratories Limited  
Docket Nos. 2005P-0008; 2005P-0046**

These comments are respectfully submitted in response to the above-referenced Citizen Petitions, filed by Ivax Pharmaceuticals, Inc. ("Ivax") on January 5, 2005, and Ranbaxy Laboratories Limited ("Ranbaxy") on February 1, 2005. In their Petitions, Ivax and Ranbaxy request that the Food and Drug Administration ("FDA") reverse its decision to de-list from the Orange Book two patents for which Ivax and Ranbaxy had previously filed Paragraph IV Certifications in their respective Abbreviated New Drug Applications ("ANDAs") for generic versions of Merck & Co.'s Zocor® (simvastatin) tablets. Petitioners also request that FDA delay approval of any other simvastatin tablet ANDAs until 180 days after the first commercial marketing of their respective simvastatin products under their ANDAs.

Ivax's and Ranbaxy's Petitions are without merit and should be denied, because the patents at issue were improperly listed in the first instance as they do not claim the listed drug. Errors that occur with respect to the listing of patents should always be subject to correction, and should not be the basis for a 180-day exclusivity period. Petitioners are merely seeking to gain a specific benefit to which they were never lawfully entitled – i.e., a 180-day exclusivity period based on patents that do not qualify for listing in the Orange Book, and to force upon FDA and the generic industry a rule that makes no sense and which would lead to absurd results.

## **I. BACKGROUND**

The FDCA requires that a sponsor of a New Drug Application ("NDA") must submit information to FDA with respect to "any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1). There does exist the possibility and, in fact, it sometimes occurs that improper patents (e.g., patents that do not claim the NDA drug, or an approved use of the drug) are submitted to FDA and listed in the Orange Book and it is appropriate that such errors be subject to correction.

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When a generic drug applicant files an ANDA, it is required by law to submit one of four types of patent certifications “with respect to each patent which claims the listed drug...or which claims a use for such listed drug for which the applicant is seeking approval and for which information is required to be filed [by the NDA holder for the listed drug].” In practice, FDA only requires patent certifications to be filed or maintained by an ANDA applicant with respect to patents that are listed in the Orange Book. Thus, if an improper patent is initially listed, but is subsequently withdrawn from the Orange Book, an ANDA applicant’s obligation to maintain any certification to that patent ceases. That is what happened with respect to simvastatin.

At the time Ivax submitted its ANDA in December 2000, there were three patents listed, at Merck’s request, for Zocor in the Orange Book. These were U.S. Patent No. 4,444,784 (the ‘784 patent), that claimed simvastatin and the use of simvastatin to treat high cholesterol; and two re-issued U.S. Patents: Nos. RE36,481 (the ‘481 patent) and RE26520 (the ‘520 patent). Ivax and Ranbaxy filed paragraph III certifications with respect to the ‘784 patent, and paragraph IV certifications with respect to the ‘481 and the ‘520 patents. Merck did not file a patent infringement lawsuit against any Paragraph IV ANDA applicant within the relevant statutorily mandated 45-day periods after receiving Ivax’s and other applicants’ Paragraph IV Notifications.

On or about November 3, 2003, FDA received a letter asserting that the ‘481 and ‘520 patents did not claim the reference listed drug Zocor, and requesting that FDA initiate its administrative procedure for determining whether those patents may remain listed in the Orange Book. Letter from Steven J. Lee, Esq. to FDA’s Drug Information Services Branch (Nov. 3, 2003) (Exhibit A hereto). FDA’s de-listing procedure involves FDA forwarding the listing challenge to the NDA holder (Merck) with a request to confirm whether the patent(s) should remain listed. *See* 21 C.F.R. § 314.53(f). Mr. Lee’s de-listing request letter noted that the ‘481 and ‘520 patents do not claim simvastatin, but rather different compounds that are not present in the approved finished drug product Zocor, and requested that FDA forward the letter to Merck.

After receiving Mr. Lee’s letter from FDA, Merck evidently realized its mistake in submitting these patents to FDA for listing in the Orange Book and thus requested that FDA de-list the patents. Following that request, FDA removed the two patents from the Orange Book in September 2004. As a result of these de-listings, all ANDA applicants are required to amend their paragraph IV certifications with respect to the two patents as required by FDA’s regulations. 21 C.F.R. § 314.94(a)(12)(viii)(B). Ivax and Ranbaxy refuse to do so, however, and have instead submitted the above-referenced Petitions. As demonstrated herein, the Petitions are without merit and should be denied.

## **II. INCORRECTLY LISTED PATENTS CANNOT SUPPORT EXCLUSIVITY**

The fundamental flaw of the Ivax/Ranbaxy Petitions is that they request FDA to expand the scope of the 180-day exclusivity period provisions of the FDCA in a way that is contrary to the plain language of the statute and FDA’s governing regulations. Petitioners’ position would require FDA to grant and enforce exclusivity based on Paragraph IV Certifications to patents that do not claim the listed drug. This would be legally improper and bad policy.

As FDA is well aware, in matters of implementing the FDCA (or any federal regulatory statute) the first, and often last, interpretive step is to determine whether the statute clearly addresses the issue. If the statute is clear, that is the end of the inquiry and the agency must effectuate the statutory mandate. [See, e.g., *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 81 L. Ed. 2d 694, 104 S. Ct. 2778 (1984).] Here, the clear statutory mandate precludes the interpretation proffered by the Petitioners by limiting 180-day exclusivity solely to ANDAs that contain the first Paragraph IV Certification to a patent that claims the reference listed drug. Specifically, the statutory exclusivity provision, 21 U.S.C. § 355(j)(5)(B)(iv), gives rise to exclusivity only where an ANDA contains a certification “described in” 21 U.S.C. § 355(j)(2)(A)(vii)(IV). That provision in turn only “describes” certifications to patents “which claim[] the listed drug...or...a use for such listed drug...and for which information is required to be filed under [21 U.S.C. § 355] subsection (b) or (c).” Subsections (b) and (c) likewise require the filing of information by an NDA sponsor, and the listing of such information in the Orange Book, only with respect to patents which claim the reference listed drug or a use of the drug. 21 U.S.C. §§ 355(b)(1), (c)(2). Where, as here, information on a patent is initially incorrectly submitted and listed, but the NDA sponsor, upon further investigation, determines that the patent does not cover the listed drug, the patent was never eligible for listing in the Orange Book, and no ANDA applicant was ever lawfully entitled to exclusivity as to that patent. In such an instance, it is appropriate that the NDA sponsor be permitted to de-list the patent(s).

### **III. FDA HAS NOT ACTED INCONSISTENTLY IN PRIOR DE-LISTING SITUATIONS**

FDA’s simvastatin decision is consistent with other de-listing decisions including one involving the drug nefazadone. In that case, the NDA holder requested, and FDA agreed to, the de-listing of a patent for which at least one ANDA applicant had filed a Paragraph IV Certification, but for which no patent litigation had been initiated against any applicant. As FDA explained,

The agency considered and rejected whether, alternatively, it is required to maintain the ’664 patent in the Orange Book because at least one ANDA was submitted containing a Paragraph IV Certification, in spite of the fact that no applicant was sued. Under FDA’s current interpretation of section 505(j)(5)(B)(iv), the first ANDA applicant to submit a Paragraph IV Certification to a patent need not be sued as a result of that certification to be eligible for 180 days of exclusivity. However, the agency does not believe that because an ANDA applicant may be eligible for exclusivity merely by submitting a Paragraph IV patent challenge, the FDA must maintain the patent listing when no litigation results from that certification and the NDA holder requests that the patent be removed from the list. Moreover, even if FDA were to believe that it would be reasonable to leave a patent in the Orange Book, as a matter of equity based on the broad eligibility for exclusivity under the current regulations, the statutory language giving control over patent listings to the NDA holder, and the very limited exception in the regulations, mitigate against doing so.

Letter from Gary Buehler to Nefazadone HCl Tablet ANDA Applicants (July 31, 2003) (Exhibit B hereto).

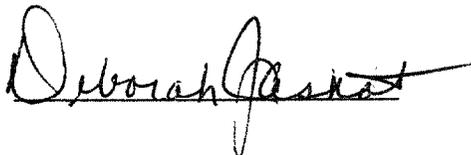
In the instance of nefazadone, it was TEVA who was the first applicant to file a Paragraph IV certification to the subsequently de-listed metabolite patent. Rather than petitioning FDA to maintain such an improper listing to preserve its exclusivity, TEVA acknowledged the Agency's decision as legally appropriate and well aligned with the intentions of the FDCA.<sup>1</sup>

In addition, metabolite patents have been removed for other products at the request of the NDA applicant as noted in Mr. Lee's letter to FDA.

#### IV. CONCLUSION

The Ivax and Ranbaxy Petitions are nothing more than an ill-conceived attempt to extract a benefit to which they are not entitled – namely, exclusivity under patents that are legally incapable of providing exclusivity. The approach advocated by these companies is not only without support in the law, it would wreak havoc on FDA's implementation of the statutory and regulatory patent listing and 180-day exclusivity period provisions, and would provide no added public benefit. Accordingly, the petitions should be denied.

Respectfully submitted,



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<sup>1</sup> We do not address the merits of FDA's "de-listing" regulation (21 C.F.R. §314.94(a)(12)(viii)(B)), because the instant issue is whether improper patent listings can be corrected rather than whether litigation status should affect de-listing.