DEPARTMENT OF HEALTH & HUMAN SERVICES

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Food and Drug Administration
Rockville MD 20857

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Re: Docket Nos. 2005P-0008/CP1, 2005P-0046/CP1, 2006P-0241/CP1, and 2006P-0258/CP1

Dear Mr. Browder, Ms. Beardsley, Ms. Shepard, and Mr. Pollack:

This letter provides an update on the status of the Food and Drug Administration's (FDA's) October 24, 2005, response to the citizen petitions in Docket Nos. 2005P-0008 and 2005P-0046, in light of the April 30, 2006, decision and order of the U.S. District Court for the District of Columbia in *Ranbaxy Labs. v. Leavitt*, No. 05-1838 (D.D.C. April 30, 2006). This letter also addresses the issues raised by the related citizen petitions in Docket Nos. 2006P-0241 and 2006P-0258, submitted on behalf of Zydus Pharmaceuticals USA, Inc. (Zydus), and received by FDA on June 6 and June 20, 2006, respectively.

As you know, the issue before the court was whether it was permissible for FDA to remove U.S. Patent Nos. RE 36481 (the '481 patent) and RE 36520 (the '520 patent) from *Approved Drug Products with Therapeutic Equivalence Ratings* (the Orange Book), at the request of Merck, the holder of the NDA for the listed drug, Zocor, when Abbreviated New Drug Application (ANDA) applicants had already submitted certifications to those patents under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act (the Act), and thus had become eligible for 180-day exclusivity under section 505(j)(5)(B)(iv).[1] Ranbaxy and IVAX,

[1] Amendments made to section 505(j)(5)(B)(iv) of the Act by Title XI (Access to Affordable Pharmaceuticals) of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Public Law 108-173) (MMA) amended the provisions related to 180-day exclusivity. The relevant Title XI provisions concerning 180-day exclusivity apply only to drug products for which the first ANDA containing a paragraph IV certification to a listed patent was submitted after December 8, 2003. *See* MMA, Pub. L. No. 108-173, section 1102(b)(1), 117 Stat. 2066, 2460 (2003). This letter refers to the pre-MMA version of the statute.

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who would have been eligible for 180-day exclusivity had the patents remained listed, sued FDA in response to the Agency's delisting of the '481 and '520 patents and refusal to relist the patents as requested in the citizen petitions. The April 30, 2006, district court decision found that the Agency's denial of the citizen petitions was contrary to the intent of Congress and the court remanded the decision to the Agency. FDA has appealed the district court decision, and that appeal has been granted an expedited review by the D.C. Circuit. *See Ranbaxy Labs. v. Leavitt*, No. 06-5154 (D.C.Cir. June 1, 2006)(order granting expedited review and setting briefing schedule). Although the Agency is appealing the district court decision, it has not sought a stay of the decision.

Because the district court's decision has not been stayed pending appeal, unless and until the appellate court reverses, we must address the listing of the '481 and '520 patents and any resulting 180-day exclusivity in a manner consistent with the district court's decision. The court found that FDA's delisting of the '481 and '520 patents in this case was inconsistent with congressional intent regarding eligibility for exclusivity. The Agency believes that the order effectively requires that the patents be relisted, and that eligibility for 180-day exclusivity be determined based on the paragraph IV certifications made to the patents. To accomplish this, the Agency on June 16, 2006, relisted the '481 and '520 patents in the Orange Book, where they are accompanied by annotations explaining the circumstances of the relisting. We are also staying the October 24, 2005, response to the petitions in Dockets 2005P-0008 and 2005P-0046, which explained the Agency's reasons for permitting the delisting of the '481 and '520 patents.

Because the '481 and '520 patents for Zocor are relisted in the Orange Book, any new or pending ANDA referencing Zocor must, pursuant to section 505(j)(2)(A)(vii) of the Act, contain patent certifications to these patents. See Apotex, Inc. v. Thompson, 347 F.3d 1335, 1350-51 (Fed. Cir. 2003). Those applicants who may have withdrawn certifications to these patents after the patents were delisted may request that the Office of Generic Drugs reinstate the withdrawn certifications. While the patents remain listed in the Orange Book, any ANDA for simvastatin that does not contain certifications to the '481 and '520 patents will not be eligible for approval.

The timing of FDA's approval of simvastatin ANDAs will be governed by, among other factors, IVAX's and Ranbaxy's eligibility for 180-day exclusivity for different strengths of simvastatin. This exclusivity is likely to be triggered by the commercial marketing of these products, as described in section 505(j)(5)(B)(iv)(I) of the Act. The '481 and '520 patents will remain listed in the Orange Book until IVAX's and Ranbaxy's periods of exclusivity have been triggered and have run, unless the appeal is decided in the Agency's favor before the exclusivity periods have expired.

Finally, we turn to the Zydus petitions. In 2006P-0241, Zydus asserts that IVAX and Ranbaxy should not be eligible for 180-day exclusivity based on their certifications to the '481 and '520 patents. Rather, Zydus believes that the FDA's October 24, 2005 denial of the Ranbaxy and IVAX petitions was the correct resolution of the matters raised in those petitions. Zydus therefore requests that FDA appeal the district court's decision, and that we deny IVAX's and Ranbaxy's petitions. In its June 6 petition (2006P-0258), Zydus requests that FDA immediately

give tentative approval to ANDA No.77-837 and provide full approval of this ANDA upon expiration of a third patent listed by Zocor, U.S. Patent No. 4,444,784, which is set to expire on June 23, 2006.

Because we have already appealed the district court's decision as discussed above, Zydus's June 6 petition is granted in part. To the extent the June 6 petition addresses the merits of the Ranbaxy and IVAX petitions, we addressed those issues at length in our October 24 decision, and we decline to do so again here. With regard to the remaining relief requested in that petition which asks FDA, in effect, to reinstate the October 24 decision that was reversed by the court, the petition is denied. Because the district court's decision remains in effect pending the outcome of the appeal, unless and until the appellate court reverses, we are constrained from maintaining the delisting of the '481 and '520 patents. Similarly, with regard to the request in Zydus's June 20 petition (2006P-0258) that we grant tentative and then full approval to ANDA No. 77-837, regardless of whether Zydus's ANDA may otherwise be eligible for approval, as long as the district court's decision remains in effect and the 180-day exclusivity has not expired, FDA is unable to grant full approval to the ANDA. Accordingly, Zydus's June 20 petition is also denied.

If you have questions regarding the status of the listings of the '481 and '520 patents or related patent certifications, please contact Ms. Cecilia Parise, Regulatory Policy Advisor to the Director, Office of Generic Drugs, at 301-827-5845.

Sincerely,

Steven K. Galson, M.D., M.P.H.
Director
Center for Drug Evaluation and Research

cc: Applicants with pending ANDAs referencing Zocor