DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDA 76-052

Food and Drug Administration
Rockville MD 20857

JUN 23 2006

IVAX Pharmaceuticals, Inc.
Attention: Patricia Jaworski
Director, Regulatory Affairs
125 Wells Avenue
Congers, NY 10920

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated December 14, 2000, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, 40 mg, and 80 mg.

Reference is also made to the tentative approval letter issued by this office on May 25, 2006, and to your amendment dated June 1, 2006.

We have completed the review of this ANDA, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, because of the 180-day generic drug exclusivity issue explained below, at this time we are unable to grant final approval to your Simvastatin Tablets USP, 80 mg. Therefore, only your Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, and 40 mg are approved. Your Simvastatin Tablets USP, 80 mg, remain tentatively approved and will not be eligible for final approval until the 180-day generic drug exclusivity period associated with this strength has expired.

As discussed in our tentative approval letter, the reference listed drug (RLD) upon which you have based your ANDA, Zocor Tablets of Merck Research Laboratories, is subject to periods of patent protection. The following patents and expiration dates (with pediatric exclusivity added) are currently listed in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for this drug product:

U.S. Patent Number	Expiration Date
4,444,784 (the '784 patent)	June 23, 2006
RE36481 (the '481 patent)	January 10, 2007
RE36520 (the '520 patent)	November 26, 2009

Your ANDA contains a paragraph III certification under section 505(j)(2)(A)(vii)(III) of the Act to the '784 patent, which states that you will not market this drug product prior to the expiration of the patent. The '784 patent, with pediatric exclusivity added, expired on June 23, 2006.

Your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that the '481 and '520 patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of this drug product. Section 505(j)(5)(B)(iii) of the Act provides that approval shall be made effective immediately unless an action was brought against IVAX Pharmaceuticals, Inc. (IVAX) for infringement of one or more of these patents that were the subject of the certifications. You have notified the FDA that IVAX complied with the requirements of section 505(j)(2)(B) of the Act and that no action for infringement of either the '481 or '520 patents was brought against IVAX within the statutory 45-day period, which action would have resulted in a 30-month stay of approval under section 505(j)(5)(B)(iii).

I. Approval of Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, and 40 mg

The Division of Bioequivalence has determined your Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, and 40 mg, to be bioequivalent, and therefore, therapeutically equivalent to the listed drug, Zocor Tablets, 5 mg, 10 mg, 20 mg, and 40 mg, respectively, of Merck Research Laboratories. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA.

With respect to 180-day generic drug exclusivity for Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, and 40 mg, we note that IVAX was the first ANDA applicant to submit a substantially complete ANDA for Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, and 40 mg, with a paragraph IV certification to the '481 and '520 patents. Therefore, with this approval, IVAX is eligible for 180 days of generic drug exclusivity for Simvastatin Tablets USP, 5 mg,

10 mg, 20 mg, and 40 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act,[1] will begin to run from the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv). Please submit correspondence to your ANDA informing the Agency of the date exclusivity begins to run.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, and 40 mg.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

II. Tentative Approval of Simvastatin Tablets USP, 80 mg

We are unable at this time to grant final approval to your Simvastatin Tablets USP, 80 mg. At least one other ANDA providing for the 80 mg strength and containing paragraph IV certifications to the '481 and '520 patents was submitted to the

[1] Because your ANDA was filed before the date of enactment of the Medicare Prescription Drug, Improvement and Modernization Act (MMA)(Public Law 108-173) on December 8, 2003, this reference to the 180-day exclusivity provision is to the section of the Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1).

agency prior to your ANDA for this strength. Another ANDA, therefore, is eligible for 180-day generic drug exclusivity for Simvastatin Tablets USP, 80 mg. Accordingly, your Simvastatin Tablets USP, 80 mg, will be eligible for final approval on the date that is 180 days after the date, with respect to the other ANDA, of the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv) of the Act.

Our decision to continue the tentative approval status previously granted to your Simvastatin Tablets USP, 80 mg, is based upon information currently available to the agency, i.e., data in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product. This decision is subject to change on the basis of new information that may come to our attention.

To reactivate this ANDA to provide for final approval of your Simvastatin Tablets USP, 80 mg, please submit a "Supplemental Application - Expedited Review Requested" 90 days prior to the date you believe that this product will be eligible for final approval. Your supplement must provide a summary of the legal basis upon which you believe the ANDA should be approved, as well as:

1. updated information related to final-printed labeling or chemistry, manufacturing and controls data, or any other change in the conditions outlined in this ANDA, or
2. a statement that no such changes have been made to the ANDA since the date of tentative approval.

Any changes in the conditions outlined in this ANDA and the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (cGMPs) are subject to agency review before final approval of the 80 mg strength will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt.

In addition to the supplement requested above, the agency may request at any time prior to the final date of approval that you submit an additional supplement containing the requested information. Failure to submit either supplement may result in rescission of this tentative approval determination, or delay in issuance of the final approval letter.

Your Simvastatin Tablets USP, 80 mg, may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of a drug before the effective final approval date is prohibited under section 501 of the Act. Also, until the agency issues the final approval letter, the 80 mg strength will not be listed in the "Orange Book."

For further information on the status of this ANDA, or prior to submitting a supplement providing for the final approval of your Simvastatin Tablets USP, 80 mg, please contact Peter Chen, R.Ph., Project Manager, at (301) 827-5848.

Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research