DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

ANDA 76-089

JUN 9 2004

IVAX Pharmaceuticals, Inc.
Attention: Patricia Jaworski
140 Legrand Avenue
Northvale, NJ 07647

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated December 28, 2000, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Ciprofloxacin Tablets USP, 100 mg, 250 mg, 500 mg, and 750 mg.

Reference is also made to the Tentative Approval letter issued by this office on September 25, 2003, and to your amendments dated February 27, March 12, June 1, and June 2, 2004.

We have completed the review of this tentatively approved abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, because of an exclusivity issue explained below, your Ciprofloxacin Tablets USP, 100 mg, is not eligible to receive final approval at this time. Therefore, only your Ciprofloxacin Tablets USP, 250 mg, 500 mg, and 750 mg are approved. The 100 mg strength will remain tentatively approved and will not be eligible for final approval until the 180-day generic drug exclusivity issue noted below has been satisfactorily resolved.

The Division of Bioequivance has determined your Ciprofloxacin Tablets USP, 250 mg, 500 mg, and 750 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug, Cipro Tablets 250 mg, 500 mg, and 750 mg, respectively, of Bayer Pharmaceuticals Corporation (Bayer). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

The listed drug product (RLD) referenced in your application, Cipro Tablets of Bayer Pharmaceuticals Corp., is subject to a period of patent protection. As noted in the agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations, the "Orange Book", U.S. patent 5,286,754 (the '754 patent) is scheduled to expire on August 15, 2011. Your application contains a paragraph IV certification to the '754 patent under Section 505(j)(2)(A)(vii)(IV) of the Act stating that the '754 patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Ciprofloxacin Tablets, USP under this ANDA. Section 505(j)(5)(B)(iii) of the Act provides that approval of an abbreviated application shall be made effective immediately unless an action is brought against IVAX Pharmaceuticals, Inc. (IVAX) for infringement of the '754 patent prior to the expiration of 45 days from the date the notice you provided under Section 505(j)(2)(B) was received by the owner of the new drug application (NDA) for the reference listed drug product and the patent holder. You have notified the agency that IVAX has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for infringement of the '754 patent was brought against IVAX within the statutory 45 day period.[1]

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

Post-marketing reporting requirements for this abbreviated application 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 this drug.

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

1 Because information on the `754 patent was submitted before August 18, 2003, the references are to sections of the Act as in effect prior to December 8, 2003, when the Medicare Prescription Drug, Improvement and Modernization Act (MMA) (Public Law 108-173) was enacted. See MMA § 1101(c)(3).

recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising, and Communications, HFD-42
5600 Fishers Lane
Rockville, MD 20857

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications (HFD-42) with a completed Form FDA 2253 at the time of their initial use.

As noted previously, we are unable to grant final approval to your Ciprofloxacin Tablets USP, 100 mg, at this time because an ANDA providing for the 100 mg strength and containing a paragraph IV certification to the patents listed in the Orange Book was submitted to OGD prior to the submission of your application. Accordingly, your Ciprofloxacin Tablets USP, 100 mg, will be eligible for final approval beginning on the date that is 180 days after the date the agency receives notice of the first commercial marketing of the 100 mg strength under the previous application.[2]

In order to reactivate this application to provide for final approval of the 100 mg strength, you must submit a "Supplemental Application - Expedited Review Requested". This supplemental application should be submitted for prior approval approximately 90 days prior to the date you believe that your Ciprofloxacin Tablets USP, 100 mg, will be eligible for final approval. The supplement should include a brief statement of the regulatory basis upon which you are requesting final approval and the date upon which you believe final approval should be granted. It should also include updated information such as final-printed labeling, chemistry, manufacturing, and controls

2 Note that because in this case there is no possibility of a court decision (see section 505(j)(5)(B)(iv)(II) of the Act), first commercial marketing is the only action by which exclusivity can begin to run. Because your ANDA was filed before the date of enactment of the MMA on December 8, 2003, this reference is to a section of the Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1).

data as appropriate. This supplemental application should be submitted even if no changes have been made to the application since the date of this tentative approval. Significant changes, as well as an update of the status of the manufacturing and testing facilities' compliance with cGMPs, are subject to agency review before final approval of the supplemental application will be granted. We request that you categorize the changes 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 supplemental application requested above, the agency may request at any time prior to the date of final approval that you submit an additional document containing the requested information. Failure to submit either or, if requested, both documents, may result in the rescission of the tentative approval status of your application for Ciprofloxacin Tablets USP, 100 mg, or may result in a delay in the issuance of the final approval letter.

Please note that under Section 505 of the Act, your Ciprofloxacin Tablets USP, 100 mg, may not be marketed without final agency approval. The introduction or delivery for introduction into interstate commerce of your Ciprofloxacin Tablets USP, 100 mg, before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the agency issues the final approval letter, your Ciprofloxacin Tablets USP, 100 mg, will not be deemed approved for marketing under 21 U.S.C. 355, and will not be listed in the "Orange Book".

For further information on the status of this application, or prior to submitting an amendment providing for the final approval of your Ciprofloxacin Tablets USP, 100 mg, please contact Thuyanh (Ann) Vu, R.Ph., Project Manager, at (301) 827-5754.

Sincerely yours,

(b)(6)

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